RESEARCH ARTICLE

Determining the Influence of Breadfruit Mucilage on the Disintegration and Dissolution of Losartan Fast-Dissolving Tablets

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ABSTRACT

This study investigated breadfruit starch as a potential excipient for immediate-release losartan tablets. The solubility, pH, organoleptic characteristics, hydration, swelling capacity, and pasting temperature of breadfruit starch were determined. It was found that breadfruit starch exhibited partial solubility in warm water, a pH of 5.8, and good hydration and swelling capacities. Furthermore, a compatibility test using differential scanning calorimetry confirmed the compatibility of losartan and breadfruit starch. It was determined that the formulated losartan tablets were satisfactory in terms of flow properties as well as consistent drug content both before and after compression. Dissolution studies *in-vitro* showed improved drug release profiles than those of losartan tablets marketed on the market. According to stability studies, the physical appearance and color of the drug did not change over 3 months, but there was a slight decrease in the amount of the drug and the rate of drug release during that period. Overall, breadfruit starch showed promise as an excipient for losartan tablets, offering potential benefits in terms of enhanced drug release characteristics. Further investigations are necessary to optimize the formulation and evaluate its clinical efficacy and safety.

Keywords: Breadfruit starch, Fast disintegration tablet, Direct compression, Super-disintegrants, Losartan.

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INTRODUCTION

They were designed to assist individuals who have trouble swallowing conventional tablets. Fast dissolving tablets (FDTs) dissolve rapidly in the mouth. By disintegrating and dissolving rapidly in the oral cavity, it can be administered easily, and patients can comply with it more easily.[1,2] Breadfruit is a tropical fruit that is rich in carbohydrates and fiber. Some research suggests that it may have a potential as a super-disintegrant in the pharmaceutical industry. Superdisintegrants are substances that are added to tablets and other solid dosage forms to improve their disintegration and dissolution in the body. This allows for faster and more efficient absorption of the active ingredients. Various studies investigated the use of breadfruit powder as a superdisintegrant in tablets. Research findings indicated that breadfruit powder was as effective as common superdisintegrants like croscarmellose sodium and sodium starch glycolate at improving tablet disintegration and dissolution. Comparing the disintegration rate of breadfruit powder with a control formulation, the researchers found that it significantly improved the disintegration rate. While these studies suggest that breadfruit powder may have potential as a superdisintegrant, further research is needed to fully understand its effectiveness and potential applications in the pharmaceutical industry. Breadfruit mucilage has also been studied as a potential superdisintegrant in pharmaceutical formulations. Mucilage is a viscous, gel-like substance found in many plants and has traditionally been used as a natural remedy for various ailments. Using mucilage instead of synthetic superdisintegrants has gained interest in recent years.[3-11]

In tablet development, selecting consistent super-disintegrants is crucial. They improve drug release in FDT. Superdisintegrants make up 1 to 10% of the formulation and aid tablet disintegration. Examples: croscarmellose, cross povidone, sodium starch glycolate. Disintegrants should break tablets into granules and powder particles. Breadfruit starch is a potential superdisintegrant. Losartan has poor absorption due to low solubility and high ionization in acidic pH.[12-15] Losartan FDTs are disintegrated and dissolved by breadfruit starch as a super disintegrant in this study. The study investigates the optimal concentration of breadfruit starch in losartan FDTs to enhance their disintegration and dissolution properties and improve their therapeutic efficacy. As a prototype drug,

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Losartan is also utilized as the study's disintegration test, which uses Breadfruit and corn starch to construct Losartan FDTs.

MATERIALS AND METHODS

Losartan was procured from Micro-Labs Pvt. Ltd. in India, while starch paste, lactose, magnesium stearate, and talc were sourced from LOBA Chemie Pvt. Ltd., located in Mumbai, India.

Extraction of Breadfruit Starch Powder

The extraction of breadfruit starch powder typically involves several steps, including washing, peeling, grinding, and sieving the breadfruit fruit to obtain a starch slurry. Wash the breadfruit fruit thoroughly to remove any dirt or debris. Peel the breadfruit fruit to remove the outer skin. Cut the breadfruit fruit into small pieces and grind them in a blender or food processor until a fine paste is obtained. To extract starch, pH 11.2, 45°C, and the speed of 2,900 rpm were selected as the optimal conditions. Transfer the paste to a large bowl and add water while stirring to create a slurry. Allow the slurry to settle for several hours to allow the starch to settle at the bottom. Carefully decant the water on top of the settled starch. Collect the starch sediment at the bottom of the bowl and transfer it to a fine sieve or cheesecloth. Rinse the starch sediment with water while stirring to remove any impurities. Allow the starch to dry completely by spreading it out in a thin layer on a flat surface or using a dehydrator. A mortar and pestle or a grinder should be used to grind down the starch once it has dried. Specific conditions and parameters for each step may vary depending on the equipment and materials used. It is important to ensure that the extracted starch powder is of high quality and free from any impurities.[3-6]

Powder Properties of Breadfruit Starch

Iodine check

This is the most commonly used test for the presence of starch. Iodine reacts with the helical amylose and amylopectin components of starch to produce a blue-black color. Upon adding a drop of iodine solution to the sample, the presence of starch will be indicated by the appearance of a blue-black color.

Solubility test

Starch is insoluble in cold water, but it swells and forms a gel when heated in water. A small amount of the sample is added to a test tube containing cold water, and the tube is shaken. If the sample contains starch, it will not dissolve in the water and may form a suspension. When the test tube is heated, the suspension will turn into a gel.

Reducing sugar test

Starch is a polymer of glucose units. When starch is heated in the presence of an acid, it is hydrolyzed to glucose. Glucose is a reducing sugar, which can be detected using a reducing sugar test, such as Benedict's test. A small amount of the sample is heated in the presence of Benedict's reagent, and if the sample contains starch, a red precipitate will be observed.

Molisch's test

This test detects the presence of all carbohydrates, including starch. A small amount of the sample is added with a few drops of alpha-naphthol, then concentrated sulfuric acid. A violet ring will appear at the interface between the two liquids if the sample contains starch.[4-8]

Organoleptic Evaluation of Isolated Starch[3-11]

Organoleptic evaluation entails employing the human senses (sight, smell, taste, and touch) to assess the characteristics of a sample. In the case of isolated starch, the following organoleptic evaluations can be performed:

Appearance

The visual appearance of isolated starch can be evaluated based on its color, particle size, and uniformity. The starch should be white or cream-colored and have a uniform particle size without any visible impurities.

Odor

The odor of isolated starch should be mild and free from any unpleasant or off-odors.

Taste

Isolated starch is tasteless and should not impart any flavor to foods or beverages.

Mouthfeel

Mouthfeel refers to the tactile sensations experienced when starch is consumed. The mouthfeel of isolated starch can be evaluated based on its texture, viscosity, and ability to form a smooth paste.

These organoleptic evaluations can provide useful information about the quality and purity of isolated starch. However, they are subjective and can be influenced by individual preferences, previous experiences, and environmental conditions.

In addition to organoleptic evaluations, various physicochemical tests can also be performed to evaluate the properties of isolated starch, such as gelatinization temperature, water absorption capacity, solubility, and rheological properties. These tests can provide more objective and quantitative data about the functional properties of isolated starch.

Hydration Capacity

Hydration capacity quantifies the starch's water absorption and gel-forming ability. Determining the hydration capacity involves measuring the amount of water absorbed by a specific weight of extracted starch under standardized conditions. Here are the steps to measure the hydration capacity of extracted starch: Weigh a known amount of extracted starch (e.g., 1-gram) and place it in a clean, dry container. Add a known amount of water (e.g., 10 mL) to the container and stir the mixture thoroughly to ensure complete wetting of the starch. Cover the container and allow it to stand at room temperature for a specified period (e.g., 30 minutes). After the specified time, weigh the container and its contents and record the

weight. Divide the final container, starch, and absorbed water weight by the starch weight to determine the hydration capacity of the extracted starch. The hydration capacity of extracted starch can also be expressed as a percentage by multiplying the hydration capacity value by 100.

$$Hydration\ capacity\ = \frac{weight\ of\ dry\ sample\ (Ws)}{weight\ of\ sediment\ (Wd)} * 100$$

Swelling Capacity of Isolated Starch Powder

Its swelling capacity indicates how well starch absorbs water and increases in volume. When immersed in water, a known weight of starch powder can be measured to determine its swelling capacity. Here are the steps to measure the swelling capacity of isolated starch powder:

Weigh a known amount of isolated starch powder (e.g., 1-gram) and place it in a clean, dry container. Add a known amount of water (e.g., 10 mL) to the container and stir the mixture thoroughly to ensure complete wetting of the starch. Cover the container and allow it to stand at room temperature for a specified period (e.g., 30 minutes). After the specified time, measure the volume of the swollen starch and record the value. Multiplying the swelling capacity value by 100 gives the swelling capacity value of isolated starch powder in percentage form.

Swelling Capacity= Vw-Vd

S welling Index = Vw/Vd

Where: Material volume before hydration and material volume after hydration, respectively, are Vd and Vw.

pH Determination

To assess the pH of isolated starch, begin by preparing a 10% starch solution. This method dissolves 10 grams of isolated starch in 100 mL of dis. H_2O. The solution should be stirred continuously to avoid lumps. Next, a pH meter should be calibrated using standard pH buffers. Once calibrated, the pH electrode should be dipped into the starch solution, and the pH should be recorded. Ensuring complete immersion of the pH electrode in the solution is crucial, and it should not come into contact with the container's bottom or sides. Failure to observe this may compromise the accuracy of the pH reading. The pH of the isolated starch solution changes depending on various features, such as the type of starch, temperature, and the presence of other compounds. The pH of starch is typically slightly acidic, ranging from 5.0 to 7.0. It is significant to note that the pH of a starch solution can alter over time due to factors such as microbial growth or the breakdown of the starch by enzymes. Therefore, it is recommended to measure the pH of the solution as soon as possible after preparation.

Loss on Drying

The amount of starch lost when dried is determined by accurately weighing a small sample and placing it in a pre-weighed dish. The dish with the sample is then placed in a drying oven, typically set to a temperature between 105 and 110°C. The sample is dried for a specified period of time, typically 2 to 3 hours, until a constant weight is achieved. Afterward, a desiccator is used to cool the dish. This prevents moisture from absorbing from the air. Weighing the dish again after it has cooled is used to measure the weight loss caused by drying the isolated starch. Once the dish has cooled, it is weighed again, and the difference between the weight before and after drying is recorded. By dividing the weight of the sample by its initial weight and multiplying by 100, the percentage of moisture content in the sample can be calculated.

Stock Solution Preparation

Weighing losartan carefully and transferring it to a volumetric flask of 100 mL is the first step. We will add 50 mL of methanol at a time, followed by 15 minutes of sonication to ensure thorough mixing. The mixture will be diluted further with methanol until the flask is filled to the mark. Losartan will be prepared as a standard stock solution with a concentration of 100 µg/ml.

Working Standard Solution

To identify the λ-max concentration of Losartan in the 100 µg/mL stock solution, the drug working standard solutions were diluted and scanned out across the full ultraviolet range. Losartan was diluted to a concentration of 10 g/mL and subjected to spectrum mode scanning between 400 and 200 nm to determine the optimal analytical wavelength. The drug's spectra were then investigated at a maximum absorbance of 296 nm.

Losartan Calibration Curve

The volume of the stock solution has been adjusted to 100 µg/mL after 10 mg of Losartan has been weighed and dissolved in methanol. In the subsequent step, Losartan concentrations of 3, 6, 9, 12, 15, and 18 µg/mL were determined by diluting the solution with pH 7.5 buffer. A pH 7.5 buffer was used as a blank in a UV-visible spectrophotometer measurement of absorbance at 296 nm. It was meticulously replicated three times, and the linearity of the standard curve was evaluated across the entire concentration range using a graph plotting the absorbance against concentrations.[12]

Granules Preparation

Formulations 1 to 10 were prepared using a wet granulation process. A 5-minute mixing period was conducted between the active component and disintegrant. Then, a binder mucilage was gradually added (at 5% concentration), and the mixture was massed for another 5 minutes. The resulting bulk was sieved at 1.7 mm and dried. Following the mixing process, the granules were passed through a 1.66 mm sieve, and subsequently, after they were dried once more, they were stored in a desiccator for future use per the specified formulations. The compressibility of partially pregelatinized starch formulation 11 has been assessed based on the direct compression method using a laboratory device.[12-14]

Granule's Evaluation

Angle of repose

In order to determine the angle of repose, we will use the funnel method. Graules that have been weighed with precision will be collected using a funnel, which will be used to collect the

granules. To ensure the funnel tip barely touches the granule heap, its height will be adjusted. A funnel will then be used to pour the granules down onto the surface. Using the following equation, we will calculate the angle of repose by measuring the diameter of the powder cone that results.[13-17]

Tan ɵ= h⁄r

Where *h* = height of the powder cone;

r = radius of the powder cone.

Bulk density and tapped density

After gently shaking a 10 mL measuring cylinder to disperse any agglomerates, 8 g of powder was placed in a 10mL measuring cylinder to determine the loose bulk density (LBD) and tapped bulk density (TBD) of each formulation. In order to determine the initial volume of powder, the cylinder was tapped 30 times from a height of 2 cm on a hard surface under its own weight. The tapping was carried out until the volume did not change further.[13-17]

LBD = Weight of the powder/Volume of the packing

TBD = weight of the powder/Tapped volume of packing

Compressibility index and hausner's ratio

Their simplicity, speed, and ease of use make them popular for predicting powder flow behavior. Several factors affect these parameters, including bulk density, particle size and shape, surface area, moisture content, and cohesion. The compressibility index can indirectly determine powder flow and cohesiveness properties. The granules' bulk volume and tapped volume are essential measurements for determining the compressibility index and Hausner's ratio. Powder or granular materials can be characterized by these parameters in terms of their flow and compressibility.[13-17]

Carr's index (%) = [(TBD – LBD) × 100]/TBD

Hausners Ratio= Tapped Density/Bulk Density

Preparation of tablets

The formulations listed in Table 1 will be used to prepare tablets containing 40 mg of Losartan. An 8.00 mm concave punch and a six metric ton compression die will be used in a rotary tablet punching machine to compress the granules. To prevent corrosion of the die and punch, magnesium stearate will be applied to their surfaces before compression. Granules will also be enriched with 1.5% talc. A total of 24 hours period of time on silica gel is then recommended to facilitate elastic recovery and hardening, ensuring the tablets' strength and stability.[18-21]

Post Compression Evaluation

Tablet thickness

A vernier caliper determined tablet thickness, and the mean and standard deviations were reported.[18-31] The consistency and uniformity of tablet sizes are ensured by this measurement.

Weight variation

According to the USP XXIV monograph, all tablets manufactured were evaluated for weight variation. We calculated the mean and standard deviation of twenty tablets from each batch. To ensure that each tablet contains the prescribed dosage of medication, this process is essential. Weights of 80 to 250 mg tablets were measured and compared to the average weight, keeping an IP limit of 7.5% in mind. We then calculated deviations and standard deviations.[18-31]

Friability

Tablet friability was measured using the Roche friabilator, a laboratory instrument. During 100 revolutions, ten tablets dropped six inches each time they were rotated at 25 rpm in a plastic chamber. We reweighed the tablets after rotating them to determine the percentage weight loss, which should be less than 1% as directed by IP. The formula provided was used to calculate tablet friability. As well as determining the average hardness, the standard deviation was calculated.[18-31] When handling and transporting tablets, this evaluation helps determine whether they will chip or break.

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

Hardness

Using the EL = 500N, Electrolab Digital Force Gauge, all batches were hardness tested according to the USP XXIV monograph. Triplicate tests were conducted on each batch of three tablets. The Monsanto hardness tester was used, consisting of two plungers and a barrel with a spring-loaded compression mechanism. Initially, a zero reading was taken by pressing the plunger against the tablet. In a subsequent step, the upper plunger was forced against the tablet until

Table 1: FDT tablet lots using breadfruit disintegrating agent

Formulation	*Losartan*	*Derived starch*	*Breadfruit starch*	*Starch paste*	*Lactose*	*Magnesium stearate*	*Talc*
B1	40	40	-	10	105	2	3
B2	40	30	-	10	110	2	3
B3	40	20	-	10	115	2	3
B4	40	10	-	10	120	2	3
B5	40	-	10	10	140	2	3
B6	40	-	20	10	135	2	3
B7	40	-	30	10	130	2	3
B8	40	-	40	10	125	2	3
B9	40	145	-	10	-	2	3
B10	40	-	-	10	145	2	3
B11	40	155	-	10	-	2	3

it fractured by rotating a threaded bolt. In response to the compression of the spring, the pointer on the gauge recorded the force of fracture.[18-31] The results of this evaluation indicate the mechanical strength of the tablet as well as its resistance to breaking.

Disintegration time

A tube of the disintegration apparatus was filled with water, which served as the immersion fluid, and the tablets were placed in that tube. When there were no residues of the tablet, except for particles of insoluble coating, on the apparatus's screen after 30 minutes, the disintegration time was recorded.[18-31] The test aimed is to determine whether the tablet is able to break down into smaller particles in the body, thus easing drug absorption.

Drug content

Triplicate UV measurements were conducted to determine the losartan content in the tablets. For drug content testing, six tablets were randomly selected from each batch. A thorough mixing of the contents of the crushed tablets was performed. To study the effect of losartan on a 40 mg tablet, a certain amount of crushed tablet powder was transferred into a 100 mL volumetric flask. A mixture of water and methanol (50 mL) was sonicated for 15 to 20 minutes before adding methanol. Using Whatman filter paper, the solution was filtered, and the volume was adjusted using methanol. A concentration of 10 g/mL was achieved by appropriately diluting the filtrate. The standard curve of each tablet was derived by comparing the absorbance (at 234 nm) of the sample with a blank solution.[18-31]

Dissolution profile study

Dissolution of Losartan tablets was studied using the USP type II dissolution testing apparatus. In 900 mL of phosphate buffer at 7.5 pH was used for rotating the paddle at 75 rpm for 60 minutes. At 5, 10, 15, 30, 45, and 60 minutes, 5 mL samples were collected and replaced with 5 mL of phosphate buffer, replenishing the 7.5 pH solution. Losartan was measured at 234 nm using a UV spectrophotometer based on the percentage amount released in the samples.[18-31] The study provides valuable information regarding tablet dissolution behavior and drug release patterns.

Stability studies

The tablets underwent a three-month stability test at 45°C ± 2°C and 75% relative humidity (RH). Testing for stability assesses whether the formulation can maintain its physical characteristics, chemical properties, microbiological characteristics, therapeutic properties, and toxicological properties over an extended time. Stability testing under stressful conditions can provide satisfactory results in a shorter period, allowing a more accurate estimate of tablet shelf life and storage conditions to be provided.[32-35]

RESULTS AND DISCUSSION

According to Figure 1(A), a UV-visible spectrophotometer measured losartan's lambda max to be 234 nm. As can be seen from Figure 1(B), Losartan concentration and absorbance in

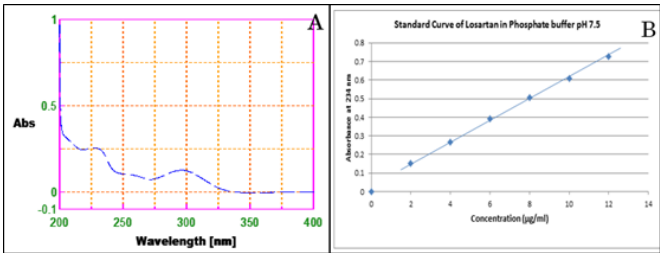

Figure 1: Losartan (A) shows its λmax absorbed energy at 234nm, while Losartan (B) shows its linearity at 234nm.

nm are linearly related (r^2=0.999) in phosphate buffer at pH 7.3. According to these results, losartan concentration adheres to Beer-Lambert's law in phosphate buffer at pH 7.4, proving that UV spectrophotometric analysis is valid and reliable for determining losartan concentration under these conditions.

Graph (A) illustrates the λ_{max} (maximum absorbance wavelength) of losartan at 234 nm, indicating the specific wavelength at which losartan exhibits its highest absorbance when subjected to UV-visible spectrophotometry. Graph (B) represents the linearity graph of Losartan at 234 nm, showing the correlation between the concentration of losartan and the corresponding absorbance values at this specific wavelength. The graph demonstrates the linear relationship between losartan concentration and absorbance, with a high coefficient of determination (r^2 = 0.999), indicating strong linearity and accuracy in the UV-visible spectrophotometric measurements. This linearity graph serves as the standard curve that allows for determining Losartan concentration in samples based on their absorbance values at λ_{max} of 234 nm, utilizing Beer-lambert's law.

The powder characteristics of breadfruit starch are presented in Table 2. Using cold and warm water, as well as 95% ethanol, the solubility of breadfruit starch was shown to be insoluble, partially soluble in warm water, and insoluble in cold water. The pH of the breadfruit starch solution was found to be 5.8. The organoleptic characteristics of breadfruit starch powder were determined to be yellowish-white and odorless powder. The hydration capacity of breadfruit starch was found to be 1.78 g, the swelling capacity was 20.4 mL, the swelling index was 2.54, and the pasting temperature was found to be 41.48ºC. The moisture content was determined to be 5.12%, and the percentage yield was 8.46%. The data indicates that the hydration capacity was 1.86 g, the swelling capacity 19.3 mL, and swelling index was 2.54, and the swelling capacity was 1.86 g. Due to the good hydration capacity of breadfruit starch, it can enhance the tablet's disintegration efficiency.

DSC Analysis

Breadfruit starch was utilized to create an FDT tablet containing immediately released losartan. The compatibility test was evaluated using a differential scanning calorimeter (DSC). The thermogram depicted in Figure 2 shows an endothermic peak. According to the DSC curves, losartan and breadfruit starch were found to be compatible. Figure 2(A) shows a peak

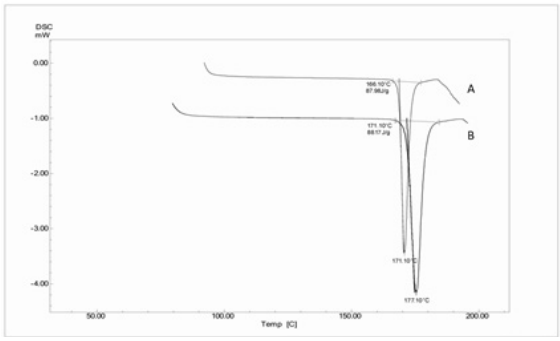

Figure 2: Thermograms of losartan (A) and losartan with breadfruit starch (B)

in endothermic response to losartan at 166.10°C in individual DSC studies. Figure 2(B) displays the DSC of the combination of losartan and Breadfruit starch, revealing an endothermic peak observed at 171.10°C. Based on this data, it was inferred that a reproducible drug peak was observed in the physical mixture compared to the pure losartan thermogram. The drug properties did not change polymorphically, and further analysis confirmed that the disintegrating agent did not interact with the drug. Graph (A) illustrates the DSC thermogram of losartan, showcasing its thermal behavior under specific conditions. Graph (B) represents the DSC thermogram of the mixture of losartan with breadfruit starch, providing insights into the thermal interactions and behavior of the combination.

FDT with Breadfruit Starch

The results of the assessment of powder characteristics of breadfruit starch, as presented in Table 2, provide important insights into its solubility, pH, organoleptic properties, iodine test, hydration capacity, swelling capacity, swelling index, pasting temperature, moisture content, and percentage yield. Let's discuss the implications and draw conclusions based on these results:

Solubility test

The solubility tests reveal that breadfruit starch is insoluble in cold water and 95% ethanol, indicating its limited ability to dissolve in these solvents. However, the starch shows partial solubility in warm water, suggesting that higher temperatures can enhance its dispersibility and solubility to some extent.

pH test

The pH value of 6.8 indicates that breadfruit starch is slightly acidic in nature. This information is important as the pH of a substance can influence its compatibility with other ingredients in various formulations or applications.

Organoleptic evaluation

Breadfruit starch is described as a white, fine powder with a smooth texture. These organoleptic properties are desirable for their use in different food and pharmaceutical applications where a visually appealing and smooth texture is preferred.

Iodine test

The appearance of a dark blue color during the iodine test confirms the presence of starch in the breadfruit starch sample. This is an important confirmation as starch is the desired component in breadfruit starch and provides its characteristic properties.

Hydration capacity and swelling capacity

Breadfruit starch exhibits a hydration capacity of 10.12 g, indicating its ability to absorb and retain water. The swelling capacity of 8.6 mL suggests that the starch can absorb a significant amount of water, leading to a surge in volume. These properties are valuable in applications where water absorption and swelling behavior are desired, such as in the formulation of tablets or as a thickening agent in food products.

Swelling index

The swelling index of 20.68 further emphasizes the swelling behavior of breadfruit starch upon hydration. An increased swelling index indicates that the starch is more capable of absorbing water and expanding in size.

Pasting temperature

The pasting temperature of 41.48ºC indicates the temperature at which breadfruit starch starts to exhibit viscosity and undergo gelatinization. This information is relevant for applications that involve heating and cooking processes, as the pasting temperature influences the textural and functional properties of starch-based products.

Moisture content

The moisture content of 10.5% reveals the presence of a certain amount of water in the breadfruit starch sample. This information is critical for storage and stability considerations, as excess moisture can lead to microbial growth or affect the quality of the starch.

Percentage yield

A total of 9.6% is the percentage yield of breadfruit starch derived from a raw material of breadfruit.

This yield provides insight into the efficiency of the extraction process and the quantity of starch that can be obtained from a given quantity of raw material.

Table 2: Starch from *Breadfruit* evaluated for powder characteristics

Parameters	*Specification*
Organoleptic evaluation	White, fine powder, smooth texture
pH test	6.8
Hydration capacity	10.12 g
Iodine test	Dark blue color is seen. The presence of starch is confirmed.
Pasting temperature	41.48ºC
% Yield	9.6%
Solubility test	Cold water: not soluble Warm water: partially soluble 95% ethanol: not soluble
Swelling capacity	8.6 mL
Moisture content	10.5%
Swelling index	20.68

Inference

The evaluation of breadfruit starch powder characteristics demonstrates its insolubility in cold water and ethanol, partial solubility in warm water, slightly acidic pH, desirable organoleptic properties, confirmation of starch presence through the iodine test, good hydration and swelling capacities, moderate swelling index, a pasting temperature suitable for various applications, and a moisture content within acceptable limits. These findings collectively indicate that Breadfruit starch has promising properties for utilization in various food, pharmaceutical, and industrial applications where it's water-absorbing, thickening, and gelling properties can be beneficial.

Studies of Precompression Parameters

The results of the calculated parameters for the losartan FDT granules (formulations B1 to B11).

Precompression evaluation parameters of Losartan granules are shown in Tables 3 and 4 and are discussed as follows;

Angle of repose (Ɵ)

The angle of repose standards for the formulations range from 24.62 ± 1.28 to 29.62 ± 1.10 degrees. Formulation B2 has the lowest angle of repose (24.62 ± 1.28), indicating better flow ability compared to the other formulations. On the other hand, formulation B6 has the highest angle of repose (29.62 ± 1.10), suggesting relatively poorer flow properties. The other formulations fall within this range, indicating adequate flow properties.

Bulk density

The bulk density values range from 0.328 ± 0.010 to 0.378 ± 0.012 gm/mL. Formulation B7 has the lowest bulk density (0.328 ± 0.010 gm/mL), while formulation B3 has the highest bulk density (0.378 ± 0.012 gm/mL). Higher bulk density is desirable as it indicates strong packaging quality and efficient filling of the granules.

Tapped density

The tapped density values range from 0.454 ± 0.002 to 0.474 ± 0.012 gm/mL. Formulation B4 has the lowest tapped density (0.454 ± 0.002 gm/mL), while formulation B6 has the highest tapped density (0.474 ± 0.012 gm/mL). These values indicate the compactness of the granules and their ability to pack efficiently.

Carr's index

It values range from 5.10 ± 0.10 to 5.46 ± 0.12. Formulation B3 has the lowest Carr's index (5.10 ± 0.10), indicating better flow ability compared to the other formulations. Formulation B8 has the highest Carr's index (5.46 ± 0.12), suggesting a relatively lower flow ability. All the values fall within the permissible limits (5–15), indicating adequate flow properties.

Hausner's ratio

It values range from 1.012 ± 0.010 to 1.042 ± 0.014. Formulation B1 has the lowest Hausner's ratio (1.012 ± 0.018), indicating better flow ability compared to the other formulations. Formulation B11 has the highest Hausner's ratio (1.042 ± 0.014), suggesting relatively poorer flow properties. All the values fall within the permissible limits (1.2–1.3), indicating adequate flow properties.

Inference

Based on the comparison of the precompression evaluation parameters, formulations B2 and B3 exhibit better flow

Table 3: Losartan granules' precompression parameters *(mean ± SD; n=3)*

Formulation code	*Angle of repose*	*Bulk density (gm/mL)*	*Tapped density (gm/mL)*	*Carr's index*	*Hausner's ratio*
B1	25.62 ± 1.22	0.354 ± 0.008	0.468 ± 0.012	5.20 ± 0.10	1.012 ± 0.018
B2	24.62 ± 1.28	0.364 ± 0.006	0.456 ± 0.014	5.12 ± 0.12	1.024 ± 0.012
B3	26.64 ± 1.22	0.378 ± 0.012	0.466 ± 0.010	5.10 ± 0.10	1.012 ± 0.010
B4	25.60 ± 1.18	0.366 ± 0.010	0.454 ± 0.002	5.22 ± 0.12	1.022 ± 0.012
B5	28.64 ± 1.16	0.360 ± 0.012	0.468 ± 0.012	5.26 ± 0.10	1.024 ± 0.014
B6	29.62 ± 1.10	0.350 ± 0.010	0.474 ± 0.012	5.28 ± 0.12	1.024 ± 0.010
B7	26.34 ± 1.24	0.330 ± 0.012	0.468 ± 0.010	5.44 ± 0.10	1.028 ± 0.012
B8	28.68 ± 1.22	0.328 ± 0.010	0.468 ± 0.010	5.46 ± 0.12	1.032 ± 0.010
B9	26.24 ± 1.50	0.330 ± 0.010	0.466 ± 0.010	5.38 ± 0.14	1.030 ± 0.012
B10	27.88 ± 1.10	0.330 ± 0.012	0.468 ± 0.010	5.36 ± 0.12	1.040 ± 0.012
B11	26.68 ± 1.12	0.332 ± 0.012	0.458 ± 0.010	5.44 ± 0.16	1.042 ± 0.014

Table 4: Precompression evaluation parameters of losartan granules

Parameter	*Range*	*Formulations P1 to P11*
Angle of repose (ɵ)	24.62 ± 1.28–29.62 ± 1.10	Adequate flow properties
Bulk density	0.328 ± 0.010–0.378 ± 0.012	High bulk density
Tapped density	0.454 ± 0.002–0.474 ± 0.012	Less porosity
Carr's index	5.10 ± 0.10–5.46 ± 0.12	Adequate flow properties
Hausner's ratio	1.012 ± 0.010–1.042 ± 0.014	Adequate flow properties

Table 5: Losartan granules post-compression evaluation parameters *(mean ± SD; n=3)*

Formulation Code	*Weight Variation (mg)*	*Hardness kg/cm²*	*Friability %*	*Thickness (mm)*	*Diameter (mm)*	*Drug Content (%)*	*Disintegration Time (min)*
B1	0.246 ± 0.012	4.4 ± 0.04	0.34 ± 0.02	2.16 ± 0.02	3.12 ± 0.02	84.54 ± 2.34	10.04 ± 1.12
B2	0.244 ± 0.010	4.6 ± 0.02	0.36 ± 0.02	2.18 ± 0.02	3.08 ± 0.02	82.46 ± 2.24	12.06 ± 1.14
B3	0.248 ± 0.014	4.8 ± 0.04	0.40 ± 0.02	2.18 ± 0.02	3.08 ± 0.02	80.42 ± 2.28	12.24 ± 1.12
B4	0.246 ± 0.016	4.6 ± 0.02	0.42 ± 0.02	2.18 ± 0.02	3.08 ± 0.02	82.48 ± 2.32	10.22 ± 1.08
B5	0.246 ± 0.018	4.8 ± 0.04	0.42 ± 0.02	2.16 ± 0.02	3.10 ± 0.02	84.68 ± 2.34	6.20 ± 0.62
B6	0.248 ± 0.018	4.6 ± 0.02	0.36 ± 0.02	2.16 ± 0.02	3.10 ± 0.02	83.80 ± 2.32	5.22 ± 1.12
B7	0.240 ± 0.020	4.6 ± 0.02	0.34 ± 0.02	2.18 ± 0.02	3.10 ± 0.02	84.66 ± 2.34	6.16 ± 1.02
B8	0.242 ± 0.020	4.6 ± 0.04	0.34 ± 0.02	2.16 ± 0.02	3.10 ± 0.02	86.88 ± 2.36	5.42 ± 1.02
B9	0.246 ± 0.022	4.8 ± 0.04	0.36 ± 0.02	2.18 ± 0.02	3.10 ± 0.02	84.56 ± 2.38	8.20 ± 0.12
B10	0.246 ± 0.022	4.4 ± 0.04	0.46 ± 0.02	2.18 ± 0.02	3.08 ± 0.02	84.58 ± 2.32	9.12 ± 0.22
B11	0.248 ± 0.024	4.6 ± 0.02	0.48 ± 0.02	2.20 ± 0.02	3.10 ± 0.02	84.68 ± 2.34	8.02 ± 0.16

properties with lower angle of repose, while formulations B6, B8, B9, B10, and B11 show relatively poorer flow properties. The bulk density and tapped density values indicate strong packaging quality and efficient filling for all the formulations. The Carr's index and Hausner's ratio values for all the formulations fall within the acceptable range, indicating satisfactory flow properties.

Studies of Post-compression Parameters

Post-compression evaluation parameters of losartan granules are shown in Table 5 and are discussed as follows;

Weight Variation

The weight variation values range from 0.240 ± 0.020 to 0.248 ± 0.024 mg. Formulation B7 has the lowest weight variation (0.240 ± 0.020 mg), while formulation B3 has the highest weight variation (0.248 ± 0.014 mg). These values indicate the consistency of weight among the granules within each formulation.

Hardness

The hardness values range from 4.4 ± 0.04 to 4.8 ± 0.04 kg/cm². Formulations B1, B4, and B9 have the lowest hardness (4.4 ± 0.04 kg/cm²), while formulations B3, B5, and B9 have the highest hardness (4.8 ± 0.04 kg/cm²). Hardness is an important parameter as it represents the tablet's ability to withstand mechanical stress without breaking.

Friability

The friability values range from 0.34 ± 0.02% to 0.48 ± 0.02%. Formulation B1 has the lowest friability (0.34 ± 0.02%), while formulation B11 has the highest friability (0.48 ± 0.02%). Friability measures the tablet's tendency to chip or break during handling and transportation.

Thickness

The thickness values range from 2.16 ± 0.02 mm to 2.20 ± 0.02 mm. Formulation B1 has the lowest thickness (2.16 ± 0.02 mm), while formulation B11 has the highest thickness (2.20 ± 0.02 mm). It indicates the tablet's physical dimension and is an important parameter for tablet uniformity.

Diameter

The diameter values range from 3.08 ± 0.02 mm to 3.12 ± 0.02 mm. Formulations B2, B4, and B5 have the lowest diameter (3.08 ± 0.02 mm), while formulations B1 and B3 have the highest diameter (3.12 ± 0.02 mm). Diameter is another critical dimension for tablet uniformity.

Drug content

The drug content values range from *80.42 ± 2.28%* to 86.88 ± 2.36%. Formulation B3 has the lowest drug content (80.42 ± 2.28%), while formulation B8 has the highest drug content (86.88 ± 2.36%). Drug content represents the amount of the active pharmaceutical ingredient present in each tablet.

Disintegration time

The disintegration time values range from 5.22 ± 1.12 to 12.24 ± 1.12 minutes. Formulation B6 has the lowest disintegration time (5.22 ± 1.12 minutes), while formulation B3 has the highest disintegration time (12.24 ± 1.12 minutes). When a tablet is in contact with a dissolution medium, the disintegration time indicates how long it will take for the tablet to break down into smaller particles.

Inference

Based on the comparison of the additional evaluation parameters, the formulations exhibit variations in weight variation, hardness, friability, thickness, diameter, drug

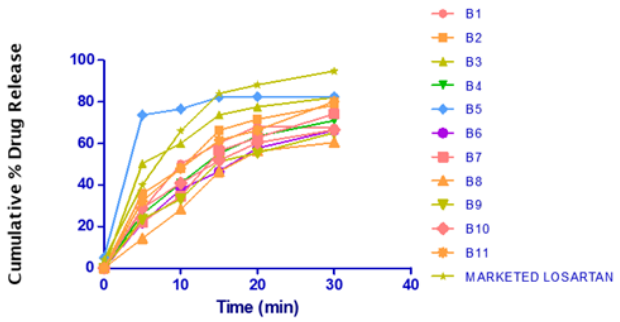

Figure 3: Breadfruit starch FDT tablet and market-placed losartan tablets relative *in-vitro* drug dissolution

Table 6: Stability study data of B8 FDT

Parameter	*Physical appearance*	*Color*	*Texture*	*Drug content (%)*	*% amount of drug release at 30 min.*
Initial	+++	white	Smooth and no defects	90.42 ± 2.44	82.24 ± 3.58
After 1 month	+++	white	Smooth and no defects	89.64 ± 2.68	82.12 ± 3.26
After 2 months	+++	white	Smooth and no defects	87.46 ± 2.88	81.26 ± 3.06
After 3 months	+++	white	Smooth and no defects	84.94 ± 2.78	78.90 ± 3.6

Note: ***+++** same as on zero day; *values are measured in mean ± SD; n=3, Physical appearance like weight variation, hardness, thickness and disintegration time.*

content, and disintegration time. Each formulation has specific characteristics within these parameters. The interpretation of these results would depend on the desired specifications and requirements for the losartan granules, such as regulatory standards, patient acceptability, and manufacturing constraints.

In-vitro drug dissolution studies

Comparing the data of the different formulations (from B1 to B11) with the marketed Losartan tablet was shown in Figure 3.

The dissolution at time 0 minute, *shows t*he marketed Losartan tablet shows a drug dissolution of 4.12 ± 2.00%. Among the evaluated formulations, B8 has no drug dissolution at time 0. The dissolution at time 5 minutes shows the marketed Losartan tablet exhibits a drug dissolution of 40.00 ± 3.89% at 5 minutes. Formulation B8, on the other hand, lags behind with a dissolution of 50.40 ± 3.12%. The dissolution at time 10 min, shows that the marketed Losartan tablet reaches a dissolution of 66.00 ± 2.48%. B8 exhibits a dissolution of 60.02 ± 3.22% respectively. The dissolution at time 15 minutes, shows that the marketed Losartan tablet achieves a dissolution of 84.00 ± 2.02% at 15 minutes, B8 shows a dissolution of 73.72 ± 3.14%, respectively. The dissolution at time 20 and 30 minutes shows similar trends persist at 20 and 30 minutes. The marketed losartan tablet exhibits dissolution rates of 88.22 ± 3.00% and 94.88 ± 2.45%, respectively. Formulations B8 consistently demonstrate higher dissolution rates during these time intervals. In summary, the evaluated formulations (B8) generally display higher drug dissolution rates compared to the marketed losartan tablet. This suggests that these formulations may have enhanced dissolution characteristics and potentially faster drug release profiles. However, further analysis is required to determine these formulations' overall performance and suitability in terms of meeting the desired therapeutic goals and regulatory requirements. These formulations (B8) consistently show higher drug dissolution rates across all time intervals than the marketed losartan tablet. This suggests that B8 may have a slower drug release profile, potentially resulting in delayed therapeutic effects. The evaluated formulations (B8) exhibit higher drug dissolution rates compared to the marketed losartan tablet, indicating a potential improvement in the formulation design. Enhanced dissolution rates can lead to better bioavailability and increased medication effectiveness. The marketed losartan tablet consistently demonstrated drug dissolution percentages higher than those of the breadfruit starch FDT tablet formulations at each time interval, suggesting a potentially more effective drug release profile. Although the dissolution data is promising, it is important to note that other factors, such as stability, bioavailability, and pharmacokinetics, need to be considered to assess the overall performance of the formulations. Additionally, *in-vivo* studies and clinical trials are necessary to determine these formulations' therapeutic benefits and safety. It's important to note that further analysis and interpretation are required to fully evaluate the performance of the Breadfruit starch FDT tablet formulations compared to the marketed losartan tablet. Factors such as the desired drug release profile, pharmacokinetics, and specific formulation objectives should be considered for a comprehensive assessment.

Stability Studies

Based on the data provided in Table 6, let's compare and discuss the parameters over the duration of evaluation:

Physical appearance

The physical appearance of the formulation was rated as "+++" throughout the evaluation period, indicating a consistently good appearance. There were no visible changes or defects observed in the formulation's physical characteristics, such as shape, size, or surface texture. This suggests that the formulation maintained its integrity and visual appeal over the course of the evaluation.

Color

The color of the formulation remained consistent throughout the evaluation period, with a white color observed initially and maintained after 1, 2, and 3 months. The color stability indicates that there were no significant changes or degradation in the formulation's color properties.

Texture

The formulation exhibited a smooth texture with no defects at the beginning of the evaluation, and this characteristic remained unchanged after 1, 2, and 3 months. The consistent texture suggests that the formulation maintained its structural integrity and did not undergo any noticeable changes or deterioration.

Drug content (%)

The initial drug content of the formulation was measured at 90.42% with a standard deviation of ± 2.44. Over the course of 3 months, a gradual decrease in drug content was observed, with values of 89.64% (after 1-month), 87.46% (after 2 months), and 84.94% (after 3 months). The decreasing trend in drug content may indicate a potential degradation or loss of the active pharmaceutical ingredient (API) over time. However, it is important to compare these values with the specified drug content requirements or regulatory standards to determine if the decrease is within an acceptable range.

Table 7: Data from the stability study of the optimized formulation P5

Parameter	*Duration of evaluation*			
	Zero day	*One month*	*Two months*	*Three months*
Color	Offset white	Offset white	Offset white	Offset white
Drug content (%)	100.42 ± 2.12	100.12 ± 2.02	100.08 ± 2.42	99.98 ± 2.12
Texture	Smooth and no defects	+++	+++	+++
Physical appearance	+++	+++	+++	+++
% Amount of drug release at 30 minutes.	99.08 ± 2.04	99.02 ± 2.14	98.12 ± 2.40	98.04 ± 2.14

*+++ same as on zero-day

%Amount of drug release at 30 minutes

The formulation initially released approximately 82.24% of the drug content within 30 minutes, with a standard deviation of ± 3.58. After 1-month, the percentage of drug release at 30 minutes remained relatively stable at 82.12% (± 3.26). However, a slight decrease in drug release was observed after 2 months (81.26% ± 3.06) and 3 months (78.90% ± 3.66). The decrease in drug release may indicate a potential change in the formulation's dissolution characteristics or the release mechanism of the active ingredient.

Further investigation is required to understand the reasons behind the decrease and its impact on the formulation's overall efficacy.

Inference

Based on the provided data, it can be inferred that the formulation exhibited good physical appearance, color stability, and consistent texture throughout the 3 month evaluation period. However, there were some concerning observations related to the drug content and drug release. The gradual decrease in drug content over time suggests a potential degradation or loss of the active ingredient. This could be a critical issue, as it may affect the formulation's therapeutic efficacy. Further analysis is necessary to determine the extent of the decrease and its impact on the desired therapeutic outcomes.

Similarly, the slight decrease in the percentage of drug release at 30 minutes raises concerns about the formulation's dissolution characteristics. The changes observed may affect the bioavailability and effectiveness of the drug in the body. Investigating the reasons behind this decrease and evaluating the formulation's release profile is crucial to ensure its performance aligns with the desired requirements. This comparative analysis highlights both positive aspects and areas of concern. Further research and analysis are necessary to fully understand the underlying causes and potential implications of the observed changes, allowing for appropriate adjustments and improvements to the formulation if required.

Based on the data provided in Table 7, let's compare and discuss the parameters over the duration of the evaluation:

Physical appearance

The physical appearance of the formulation was rated as "+++" throughout the evaluation period, indicating a consistently good appearance. There were no visible changes or defects observed in the formulation's physical characteristics, such as shape, size, or surface texture. This suggests that the formulation maintained its integrity and visual appeal over the course of the evaluation.

Color

The color of the formulation remained consistent throughout the evaluation period, with a white color observed initially and maintained after 1, 2, and 3 months. The color stability indicates that there were no significant changes or degradation in the formulation's color properties.

Texture

The formulation exhibited a smooth texture with no defects at the beginning of the evaluation, and this characteristic remained unchanged after 1, 2, and 3 months. The consistent texture suggests that the formulation maintained its structural integrity and did not undergo any noticeable changes or deterioration.

Drug content (%)

The initial drug content of the formulation was measured at 90.42% with a standard deviation of ± 2.44. Over the course of 3 months, a gradual decrease in drug content was observed, with values of 89.64% (after 1-month), 87.46% (after 2 months), and 84.94% (after 3 months). The decreasing trend in drug content may indicate a potential degradation or loss of the API over time. However, it is important to compare these values with the specified drug content requirements or regulatory standards to determine if the decrease is within an acceptable range.

% Amount of drug release at 30 minutes

The formulation initially released approximately 82.24% of the drug content within 30 minutes, with a standard deviation of ± 3.58. After 1-month, the percentage of drug release at 30 minutes remained relatively stable at 82.12% (± 3.26). However, a slight decrease in drug release was observed after 2 months (81.26% ± 3.06) and 3 months (78.90% ± 3.66). The decrease in drug release may indicate a potential change in the formulation's dissolution characteristics or the release mechanism of the active ingredient. An investigation is needed to uncover the reasons behind the decrease and determine whether it has an impact on the formulation's effectiveness.

Interference

based on the provided data, it can be inferred that the formulation exhibited good physical appearance, color stability, and consistent texture throughout the 3-month evaluation period. However, there were some concerning observations related to the drug content and drug release. The gradual decrease in drug content over time suggests a potential degradation or loss of the active ingredient. This could be a critical issue, as it may affect the formulation's therapeutic efficacy. Further analysis is necessary to determine the extent of the decrease and its impact on the desired therapeutic outcomes. Similarly, the slight decrease in the percentage of drug release at 30 minutes raises concerns about the formulation's dissolution characteristics. The changes observed may affect the bioavailability and effectiveness of the drug in the body. Investigating the reasons behind this decrease and evaluating the formulation's release profile is crucial to ensure its performance aligns with the desired requirements.

This comparative analysis highlights both positive aspects and areas of concern. Further research and analysis are necessary to fully understand the underlying causes and potential implications of the observed changes, allowing for appropriate adjustments and improvements to the formulation if required.

CONCLUSION

The studies mentioned describe the preparation of losartan fast disintegration tablets using different natural superdisintegrants, namely breadfruit starch. This research evaluated losartan tablets based on these natural super disintegrants disintegration and dissolution characteristics. Breadfruit starch was used as the superdisintegrant in losartan fast disintegration tablets. A comparative study was conducted to determine how the tablets disintegrated and dissolved. Losartan FDTs formulated with breadfruit starch were found to be optimally cost-effective and patient-complimented at the low concentration (10 mg). We found that Breadfruit starch when used as a superdisintegrant in losartan tablets can provide a competitive and alternative dosage form with a high marketability potential. Natural superdisintegrants may offer a variety of advantages, including cost-effectiveness, patient compliance, and rapid dissolution and disintegration. These findings support the potential marketability of losartan tablets formulated with these natural superdisintegrants as alternative dosage forms.

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