Original Article

Studies on jackfruit seed starch as a novel natural superdisintegrant for the design and evaluation of irbesartan fast dissolving tablets

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ABSTRACT

Background: In the present investigation, an attempt was made to isolate starch from jackfruit seed powder and utilize it as a superdisintegrant to design fast dissolving tablets of irbesartan.

Methods: Starch was isolated from jackfruit seeds via aqueous and alkali extraction processes and evaluated for its physicochemical properties, for phytochemical tests, and for acute toxicity studies. Irbesartan fast dissolving formulations were prepared using the wet granulation technique.

Results: Acute toxicity studies for the extract indicated that all rats were healthy with no physiological changes in their behavior. The prepared irbesartan tablet formulations were found to be stable according to the Indian Pharmacopoeia-specified limits for postcompensation parameters. From in vitro dissolution studies, it was observed that formulations F5 and F8 containing 5% w/w of alkali extracted starch and 5% w/w of croscarmellose sodium showed faster disintegration and improved dissolution rate compared with the other formulations. Fourier transfer infrared spectroscopic and differential scanning colorimetric analysis performed on optimized formulations indicated that there were no major interactions between the drug and excipients. Accelerated stability studies carried out on optimized formulations showed all tablets to be stable.

Conclusion: The tablets prepared from jackfruit seed starch as superdisintegrant were found to be suitable for preparation of fast dissolving tablets.

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1. Introduction

The oral delivery of drugs is considered the most accepted route for the administration of drugs because of the convenience of self-administration and patient compliance. Oral administration remains to be the suitable route for administration of active pharmaceutical ingredients despite the numerous advancements in drug delivery. However, the oral administration of drugs also has several drawbacks especially while administering the dosage forms such as tablets and capsules, which can lead to difficulty in swallowing (dysphagia), and administration of unpalatable drugs, which leads to patient noncompliance especially among pediatric and geriatric patients. This is also observed in people who are ill in bed or who are busy or traveling, especially those who have no access to drinking water. Therefore, to improve patient compliance, especially among pediatric and geriatric patients, emphasis is given on the development of novel formulations. One such approach is development of fast dissolving tablets (FDTs). These FDTs are synonymous with orally dispersible tablets (ODTs), fast dissolve, rapidly disintegrating tablets, rapid dissolve, fast melts, quick disintegrating, melt in mouth tablets, porous tablets, and freeze-dried wafers. When these formulations are placed in the mouth, saliva quickly penetrates into the pores to cause rapid tablet disintegration without any chewing by the patients. The time for disintegration of ODTs is generally <1 minute, and the actual disintegration time that a patient can experience ranges from 5 seconds to 30 seconds.

FDTs are generally manufactured or prepared using several excipients such as bulking agents, emulsifying agents, superdisintegrants, organoleptic agents, lubricants, and glidants. Among these excipients, superdisintegrants play an important role in achieving faster disintegration of tablets.

In the past, several fast disintegrating agents such as cellulose derivatives, starch derivatives, and some synthetic agents have been investigated for their influence on the mechanism of tablet disintegration. Some of the superdisintegrants that are already in the market are synthetic superdisintegrants such as croscarmellose sodium (CCS), sodium starch glycolate, crospovidone, modified cellulose, and L-HPC. Examples of coprocessed superdisintegrants include Ludiflash, Pharmaburst, Modified mannitol, Polacrillin potassium, and Glucidex IT. The earlier reports indicated that there is a high potential in exploring superdisintegrants from natural sources. Some of the natural superdisintegrants available are Plantago ovata seed mucilage, Lepidium sativum mucilage, fenugreek seed mucilage, Ocimum mucilage, Mango peel pectin, and Hibiscus rosa-sinensis Linn. mucilage. They are economical, ecofriendly, widely available, and nontoxic in nature. Superdisintegrants facilitate rapid disintegration owing to the combined effect of swelling and water absorption by the dosage form. Because of the swelling of superdisintegrants, the wetted surface of the carrier increases; this promotes the wettability and dispersibility of the formulation, thus increasing the disintegration and dissolution. The selection of the optimum concentration for the superdisintegrant is done according to the critical concentration of the disintegrant. Below this concentration, the tablet disintegration time is inversely proportional to the concentration of the superdisintegrant. If the concentration of the superdisintegrant is above the critical concentration, the disintegration time remains constant or even increases.

They act by different mechanisms of actions: (1) swelling action, (2) capillary action (wicking), (3) combination action, (4) deformation recovery, (5) heat of wetting, (6) chemical reaction (acid–base reaction), (7) particle repulsive forces due to disintegrating particle, and (8) enzyme reaction.

In this investigation, an attempt was made to extract starch from jackfruit seed powder (JFSP) and use it as a superdisintegrant to explore the possibilities of designing FDTs. Jackfruit (Artocarpus heterophyllus) is a species of tree in the mulberry family (Moraceae), which grows abundantly in India, Bangladesh, and in many parts of Southeast Asia. The large seeds from this nonleguminous plant are also edible. A single seed is enclosed in a white aril encircling a thin brown sphermoderma, which covers the fleshy white cotyledon. Jackfruit cotyledons are fairly rich in starch and protein. Irbesartan (IRB), which is an angiotensin II type, receptor antagonist, is selected as a model drug. It belongs to Biopharmaceutics Classification System Class II drugs and has very poor solubility in Gastro Intestinal fluids. The elimination half-life (t1/2) of IRB is in the range of 11–15 hours. IRB shows a linear pharmacokinetics over the therapeutic dose range. Steady-state levels of IRB are achieved within 3 days, and a limited accumulation of IRB (<20%) is observed in plasma upon repeated once-daily dosing. Thus, there is a strong clinical need and market potential for a dosage form that delivers IRB immediately to a patient needing this therapy, resulting in better patient compliance. Based on the biopharmaceutical and pharmacokinetic parameters described above, IRB was selected as a drug candidate for designing FDTs.

The present work was aimed to extract starch from JFSP and explore the possibilities of designing FDTs. IRB fast dissolving formulations were prepared by using different concentrations of superdisintegrants such as JFSP extracts and a standard superdisintegrant such as CCS using the wet granulation method.

2. Methods

2.1. Materials

IRB was a gift sample from Aurobindo Laboratories Ltd. (Hyderabad, India). Hydrochloric acid, Avicel PH101, magnesium stearate, and t alc were procured from S.D. Fine Chem. Ltd. (Mumbai, India). Isopropyl alcohol (IPA) was obtained from High Pure Fine Chem. (Chennai, India); CCS was a gift from M/S NATCO Pharma Ltd. (Hyderabad, India), and jackfruit seeds were procured from the local market (Guntur, Andhra Pradesh, India).

2.2. Extraction of starch from jackfruit seeds

The extraction of starch from jackfruit seeds was done via aqueous and alkali extraction processes. About 5 g of JFSP was added into 100 mL distilled water (JFS1) and 0.1N sodium hydroxide (JFS2) separately and set aside for 6–8 hours at room
temperature with constant stirring. Then the slurry was filtered through sieve no. 212, and the remaining sediment was washed with distilled water for three times. The filtrates were collected and precipitated overnight at 4°C. Then the supernatant was discarded, and the crude starch was washed with distilled water. This step was repeated three times, and the starch cake obtained was dried at 40°C for 24 hours in a tray dryer. Then the starch was ground with a mortar and pestle. The starches thus obtained were packed in air-tight containers and kept at room temperature until further use.

2.3. Phytochemical tests for JFSP and extracted starches

The raw jackfruit powder and starch extracts were subjected to phytochemical tests for the identification of carbohydrates, proteins, alkaloids, glycosides, and steroids by various tests such as Molish’s test, biuret test, and Mayer’s test. The results are given in Table 1.

2.4. Evaluation of physicochemical properties of JFSP and extracted starches

2.4.1. Gelatinization temperature
For the determination of gelatination temperature, the starch powders were moistened with water and transferred into capillary tubes by means of intrusion. The temperature of gelling and the time from swelling to full gelatination were recorded with a melting point apparatus. The results are given in Table 2.

2.4.2. Determination of pH
The pH values of 1% starch suspensions were measured using a digital pH meter. The results are given in Table 2.

2.4.3. Viscosity
The viscosity of 1% starch suspensions was measured using a Brookfield viscometer (Lab Indainstruments Private Limited, Gurgaon, Haryana, India). The results are given in Table 2.

2.4.4. Swelling index
Starch samples (200 mg) were added to 10 mL of water, and light liquid paraffin was taken in two different test tubes and mixed thoroughly. The dispersions were allowed to stand for 12 hours. The volumes of the sediment in the tubes were recorded. The swelling index of the material was calculated as follows (and shown in Table 2):

\[ \text{Volume of sediment in water} \]
\[ \text{S.I}(\%) = \frac{\text{Volume of sediment in light liquid paraffin}}{\text{Volume of sediment in light liquid paraffin}} \]  
\[ (1) \]

2.4.5. Water absorption index
For the determination of the water absorption index, the starch sample was suspended in 10 mL distilled water at 30°C in a centrifuge tube, stirred for 30 minutes, and then centrifuged at 3000 rpm for another 10 minutes. The supernatant was decanted, and the weight of the gel formed was recorded. The water absorption index was then calculated as gel weight per gram of dry sample. The results are shown in Table 2.

\[ \text{Water absorption index}(\%) = \frac{\text{Bound water}(g)}{\text{Weight sample}(g) \times 100} \]  
\[ (2) \]

2.5. Acute toxicity studies of jackfruit seed starch in Wistar rats
Thirty male adult Wistar rats (250–300 g) were obtained from Mahaveer Enterprises (Hyderabad, India). They were housed

| Table 1 – Phytochemical tests for jackfruit seed powder extracted starches. |
|------------------|-------------|----------|----------|
| Chemical tests   | JFSP        | JFS1     | JFS2     |
| Tests for        | Molisch test| +ve      | +ve      | +ve      |
| carbohydrates    | Benedict’s test| +ve    | +ve      | +ve      |
| Test for         | Biuret test | +ve      | –ve      | –ve      |
| polysaccharides  | Mayer’s test| +ve      | –ve      | –ve      |
| Test for         | Iodine test | +ve      | –ve      | +ve      |
| proteins         | Salkiewsk test| +ve    | –ve      | –ve      |
| Test for         | Liebermann-Burchard test| +ve  | –ve      | –ve      |
| alkaloids        | Ferric chloride test| –ve | –ve      | –ve      |
| Test for         | Lead acetate test| –ve | –ve      | –ve      |
| glycosides       | Foam test   | –ve      | –ve      | –ve      |

JFS1, jackfruit seed starch extracted by using water; JFS2, jackfruit seed starch extracted using 0.1N NaOH; JFSP, jackfruit seed powder.

| Table 2 – Evaluation of physicochemical properties of jackfruit seed powder and extracted starches. |
|-----------------|-----------|----------|----------|
| Sample no.      | Parameter | JFSP     | JFS1     | JFS2     |
| 1               | Gelation temperature | 65–70 °C | 65–70 °C | 68–72 °C |
| 2               | pH        | 6.51     | 6.78     | 6.90     |
| 3               | Viscosity | 1.074 cps| 2.039 cps| 2.178 cps|
| 4               | Swelling index (%) | 78       | 156      | 180      |
| 5               | Water absorption index | Less  | More    | More    |

JFS1, jackfruit seed starch extracted by using water; JFS2, jackfruit seed starch extracted using 0.1N NaOH; JFSP, jackfruit seed powder.
five per cage for 7 days prior to experimentation under an ideal laboratory environment as per Organisation for Economic Co-operation and Development guidelines. Each experiment group consists of five animals.

### 2.5.1. Toxicological/safety evaluation studies in rats

Six groups containing a total of 30 Wister rats (250–300 g) were used in the study. All animals were fed orally once, and different doses of starch [100 mg/kg, 500 mg/kg, 1000 mg/kg, 2000 mg/kg, and 200 mg/kg (std) body weight] were administered to different groups of animals. After the experimental protocol is completed, the animals were kept under ambient conditions with normal feed for the next 10 days. After the washout period of 10 days, the same animals were further utilized in the acute toxicological studies for another type of starch. The experimental protocols are given in Table 3. Animals were weighed prior to dose administration. All animals were kept under continuous observation after the administration of the dose for any change in behavior or physical activities. The results are given in Table 4.

### 2.6. Preparation of IRB FDTs

IRB FDTs were formulated by the wet granulation technique using various concentrations of jackfruit seed starch 1, jackfruit seed starch 2, and CCS. IPA was used as granulating fluid. Accurately weighed raw materials were passed through sieve no. 80 and blended for 15 minutes in a double cone blender. The powder mixture was then converted into damp mass using IPA. The damp mass was passed through sieve no. 20 to obtain granules, which were kept in a tray dryer for drying at 60 °C for 1 hour. The dried granules were dry screened through sieve no. 16, and uniform granules thus obtained were further subjected to compression. The collected granules were then lubricated with 1% talc and magnesium stearate and compressed as tablets by using 10 station clt minipress with 6-mm flat round punches. The formulations along with compositions are given in Table 5.

### 2.6.1. Evaluation of precompression parameters on prepared granules

The precompression parameters such as angle of repose, Carr’s index, and Hausner’s ratio were performed on prepared granules as per the standards. The results are given in Table 6.

### 2.6.2. Evaluation of postcompression parameters of FDTs

The postcompression parameters such as weight uniformity, hardness, friability, and drug content were performed for the prepared tablets. The results are given in Table 7.

| Table 3 – Oral administration of jackfruit seed starch dispersion to different groups of Wistar rats. |
| --- |
| **Group** | **Type of starch administered** | **Dose (mg/kg body weight)** |
| | Protocol I | Protocol II |
| Control | JFS1 | JFS2 | – |
| I | JFS1 | JFS2 | 100 |
| II | JFS1 | JFS2 | 500 |
| III | JFS1 | JFS2 | 1000 |
| IV | JFS1 | JFS2 | 2000 |
| V | Standard | Standard | 200 |
| JFS1, jackfruit seed starch extracted by using water; JFS2, jackfruit seed starch extracted using 0.1N NaOH; Std. |

| Table 4 – Acute toxicity studies in male Wistar rats. |
| --- |
| **Group** | **Dose (mg/kg body weight)** | **Mortality (x/N)** | **Symptoms** |
| | | Protocol I | Protocol II |
| Control | – | 0/5 | 0/5 | Normal |
| I | 100 | 0/5 | 0/5 | Normal |
| II | 500 | 0/5 | 0/5 | Normal |
| III | 1000 | 0/5 | 0/5 | Normal |
| IV | 2000 | 0/5 | 0/5 | Normal |
| V | 200 | 0/5 | 0/5 | Normal |

| Table 5 – Composition of irbesartan fast dissolving tablets with JFS1, JFS2, and CCS. |
| --- |
| **Ingredients (mg/tablet)** | **Formulations** |
| | F | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| Irbesartan | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 |
| JFS1 | – | 8.5 | 17.5 | 35 | – | – | – | – | – |
| JFS2 | – | – | – | – | – | 8.5 | 17.5 | 35 | – | – |
| CCS | – | – | – | – | – | – | – | 8.5 | 17.5 | 35 |
| Avicel PH101 | 189.5 | 181 | 172 | 154.5 | 181 | 172 | 154.5 | 181 | 172 | 154.5 |
| Saccarin | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 |
| Talc | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 |
| Magnesium stearate | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 |
| Total weight | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 |

CCS, croscarmellose sodium; JFS1, jackfruit seed starch extracted by using water; JFS2, jackfruit seed starch extracted using 0.1N NaOH; JFSP, jackfruit seed powder.
2.6.3. Wetting time
Five circular tissue papers (diameter 10 cm) were placed in the Petri dish. To this, 10 mL of amaranth solution was added. One tablet is then placed carefully on the surface of the tissue paper, and the time required for the amaranth solution to reach the upper surface of the tablet was noted. The results are given in Table 7.

2.6.4. Dispersion test
The test is performed by placing two tablets in 100 mL water and stirring it gently for 3 minutes and pass through a 22 mesh. The formulation is considered to form a smooth dispersion if the complete dispersion passes through a screen with a nominal mesh aperture of 710 μm (sieve no. 22) without leaving any residue on the mesh.17 The results are given in Table 7.

2.6.5. Drug content uniformity
FDTs of IRB from a batch were taken at random and were crushed to a fine powder and transferred into a 100-mL volumetric flask. To this, a few millimeters of methanol was added, and the mixture was shaken for about 30 minutes. Then, the final volume was made up to 100 mL by adding methanol. The resulting solution was set aside for a few minutes, and the supernatant solution was collected and filtered using Whatman filter paper. Next, the filtrate was subsequently diluted with 0.1N hydrochloric acid (HCl), and the absorbance was measured at 244 nm. The amount of IRB estimated from different batches is depicted in Table 7.

2.6.6. In vitro dissolution studies
The dissolution studies were performed in United States Pharmacopeia (USP) Apparatus Type II (paddle) using 900 mL of 0.1N HCl as dissolution medium at 37 ± 0.5°C and 50 rpm, respectively. Samples (5 mL) were taken at 5 minutes, 10 minutes, 15 minutes, 20 minutes, 30 minutes, 45 minutes, and 60 minutes. A fresh volume of the medium was replaced with same volume to maintain the sink conditions. The samples withdrawn were suitably diluted with the same dissolution medium, and the amount of drug dissolved was estimated using an UV spectrophotometer (UV 3000+) at 244 nm. The dissolution studies were carried out six times on all formulations. The dissolution profiles of various IRB tablets are shown in Figs. 1 and 2.

Based on dissolution data, various dissolution parameters such as T50, T75, and DE20% first-order constant and Hixon–Crowell constant were determined for various tablet formulations using Microsoft Excel software. The results are given in Table 8.

2.6.7. Comparison of dissolution profiles by a model-independent method
The dissolution profiles comparison was done using difference factor f1 and similarity factor f2 to compare the dissolution profile of prepared IRB FDT formulations with formulation F8 containing 5% CCS with all time points included in the in vitro dissolution studies. The equation used for calculating difference factor and similarity factor is

\[
f_1 = \left[ \frac{\sum_{i=1}^{n} |R_i - T_i|}{\sum_{i=1}^{n} R_i} \right] \times 10
\]

where

\[
f_2 = \frac{100}{1 + \sum_{i=1}^{n} \frac{(R_i - T_i)^2}{R_i}}
\]
Fig. 1 – Dissolution profiles of irbesartan fast dissolving tablet formulations containing JFS1 starch in comparison with tablets containing CCS. CCS, croscarmellose sodium; JFS1, jackfruit seed starch extracted using water.

Fig. 2 – Dissolution profiles of irbesartan tablet formulation (F5) prior to and after storage under different conditions. RH, relative humidity.

\[ f_2 = 50 \times \log \left\{ \left[ 1 + (1/n) \sum_{J=1}^{N} (R_T - T_J)^2 \right]^{-0.5} \times 100 \right\}, \]  

where \( n \) is the number of dissolution time, and \( R_T \) and \( T_J \) are the reference (theoretical) and test dissolution values at time

| Formulation | % drug released at 60 min | \( T_{50} \) (min) | \( T_{75} \) (min) | DE\(_{20\%}\) | First-order constant | Hixon–Crowell constant |
|-------------|--------------------------|-------------------|-------------------|-------------|---------------------|------------------------|
|             |                          |                   |                   |             | \( K \) (min\(^{-1}\)) | \( R^2 \) | \( K \) (mg\(^{1/3}\)) | \( R^2 \) |
| FP          | 43.38                    | >60               | >60               | 12.5        | 0.008               | 0.9761                | 0.015                  | 0.9684                |
| EM          | 83                       | 21                | >60               | 22.5        | 0.031               | 0.9738                | 0.063                  | 0.9540                |
| F           | 50.3                     | 60                | >60               | 15          | 0.014               | 0.9652                | 0.023                  | 0.9570                |
| F1          | 84.3                     | 5                 | 20                | 55          | 0.045               | 0.9635                | 0.056                  | 0.823                 |
| F2          | 90.02                    | 3                 | 10.5              | 63.75       | 0.014               | 0.9461                | 0.009                  | 0.6972                |
| F3          | 89.9                     | 2.5               | 15                | 60          | 0.010               | 0.9518                | 0.011                  | 0.8109                |
| F4          | 92.31                    | 1.5               | 15                | 57.5        | 0.068               | 0.9898                | 0.047                  | 0.8416                |
| F5          | 97.45                    | 2                 | 12                | 79.5        | 0.026               | 0.9930                | 0.076                  | 0.8505                |
| F6          | 97.80                    | 1                 | 7                 | 77.5        | 0.035               | 0.9708                | 0.047                  | 0.9694                |
| F7          | 93.45                    | 6                 | 16.5              | 55          | 0.069               | 0.9744                | 0.075                  | 0.7329                |
| F8          | 97.87                    | 2.5               | 12.5              | 80          | 0.026               | 0.9901                | 0.016                  | 0.8467                |
| F9          | 98.78                    | 3.5               | 6.5               | 73.75       | 0.056               | 0.9472                | 0.042                  | 0.9849                |
t. The dissolution profile was considered satisfactory if $f_1$ is below 15 (nearing zero) and $f_2$ exceeds 50. Two dissolution profiles are considered similar when the $f_2$ value is 50 to 100. The similarity factor values are given in Table 9.

2.7. Statistical analysis

The dissolution test was carried out six times on all formulations. Formulations F5 and F8 were found to be optimised based on the similarity and dissimilarity factors. For each time, seven samples were withdrawn at different time intervals, and then we tested the significant difference between formulation F5 containing 5% w/w JFS2 and formulation F8 containing 5% w/w of standard CCS. Student t test was applied for comparison of the above two samples having different variance levels.

2.8. Characterization of FDTs

Based on the dissolution studies, the optimized formulations were selected, and Fourier transfer infrared (FTIR) and differential scanning calorimetry (DSC) studies were performed on formulations F5 and F8 to observe the drug–polymer interactions.

Scanning electron microscopy (SEM) analysis was performed on JFSP, jackfruit seed starch, IRB, and blend of IRB and jackfruit seed starch (JFS2) to know the surface characteristics.

2.9. Stability studies

Accelerated stability studies were carried out on optimized formulations (F5 and F8) as per International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) guidelines. After the stability studies, the formulations were evaluated for physical parameters, drug content, and drug release studies. The results are shown in Figs. 3 and 4.

3. Results

Jackfruit seeds were procured from local vendors in the region of Guntur. The seed powder thus obtained was subjected to extraction of starch by aqueous and alkali extraction processes. The starches thus obtained (via different extraction processes) were dried under ambient conditions for 24 hours. Furthermore, these starches were evaluated for phytochemical studies as per the procedures described in the Methods section.

The raw jackfruit powder and starches extracted from it were evaluated for the presence of carbohydrates, polysaccharides, proteins, alkaloids, glycosides, steroids, flavonoids, and saponins. These phytochemical tests revealed that the raw JFSP contained carbohydrates, polysaccharides, proteins, alkaloids, glycosides, and steroids. The extracted starches confirmed the presence of only carbohydrates and polysaccharides. The phytochemical tests used are given in Table 1.

The physicochemical parameters revealed that the gelation temperature obtained was in the range of 65–72 °C. The pH of the 1% solution was in the range of 6.51–6.90. Viscosity was slightly higher than water and was in the range of 1.074–2.178 cps. Swelling index was in the range of 78–180%. Water absorption index is very high. The results are given in Table 2.

Acute toxicity studies on Wistar rats were conducted for extracted starches at different dose levels. It was observed that all groups of rats were healthy with no physiological changes in their behavior up to the 1000 mg/kg dose. The rats were found to exhibit corner sitting and salivation in their physiological behavior at 2000 mg/kg body weight dose; however, no incidence of death occurred in any group of rats even at the higher dose levels. The results are given in Table 4.

IRB FDT formulations that contained various concentrations of jackfruit starch 1, jackfruit starch 2, and CCS were prepared by the wet granulation technique using IPA as gran-
rotating fluid. Formulations F–F3 was prepared by using 0–10% of aqueous extracted starch (JFS1). Formulations F4–F6 were prepared by using 2.5–10% of alkali extracted starch (JFS2). Formulations F7–F9 were prepared by using 2.5–10% of CCS. The compositions are given in Table 5.

The precompression parameters such as angle of repose, Carr’s index, and Hausner’s ratio were performed for various prepared granules. The angle of repose, Carr’s index, and Hausner’s ratio values were in the range of 24–30°, 12–16%, and 1.14–1.19, respectively, which indicated that the granules exhibited good flow properties. The results are given in Table 6.

After the compression of granules along with lubricants into matrix tablets, the physical parameters such as weight uniformity, hardness, friability, wetting time, dispersion test, and drug content were evaluated. The weight uniformity, hardness, friability, wetting time, dispersion test, and drug content values were in the range of 348 ± 3–351 ± 1 mg, 3.0 ± 0.5–3.5 ± 0.4 kg/cm², 0.2–0.4% w/w, 4–600 seconds, all the formulations passed the dispersion test except for formulation F, and 148.96 ± 0.6–150, respectively, which indicated that the formulations were found to be stable and within the Indian Pharmacopoeia-specified limits. The results are given in Table 7.

In vitro dissolution studies were performed on all prepared matrix tablets using USP apparatus II with 900 mL of 0.1N HCl, with the temperature maintained at 37 °C and with the paddle rotating at 50 rpm. All dissolution studies were performed in triplicate, and the average values were taken for further investigations. The pure drug IRB was found to release and dissolve only 43.38% of the drug in its pure form, whereas the marketed formulation (Irovel 150) was found to exhibit 83% of drug release in 60 minutes. Formulations F, F1, F2, and F3 containing JFS1 as superdisintegrant released the drug IRB at 50.3%, 84.3%, 90.02%, and 89.9%, respectively. It was found that these formulations improved the rate of dissolution from 1.16-fold to 2.07-fold when compared to pure drug IRB. Formulations F4, F5, and F6 containing JFS2 as superdisintegrant released the drug IRB at 92.3%, 97.45%, and 97.8%, respectively. It was found that these formulations improved the rate of dissolution from 2.12-fold to 2.25-fold when compared to pure drug IRB. Formulations F7, F8, and F9 containing CCS as superdisintegrant released the drug IRB at 93.4%, 97.87%, and 98.78%, respectively. It was found that these formulations improved the rate of dissolution from 2.15-fold to 2.28-fold when compared to pure drug IRB. Formulations F5 and F8 containing 5% w/w of JFS2 and 5% w/w CCS as superdisintegrant released the drug IRB at 97.5% and 97.9%, respectively. It was found that these formulations improved the rate of dissolution from 2.25-fold to 2.26-fold when compared to pure drug IRB. It was also observed that the dissolution rate of F5 and F8 were improved up to 1.17 and 1.18 times, respectively, when compared to the marketed formulation.

It was observed that as the type of starch as superdisintegrant and the proportion of superdisintegrant have greatly influenced the dissolution parameters of various formulations. The superdisintegrant JFS2 has exhibited comparative dissolution profile with that of standard superdisintegrant CCS. Formulation F5 containing 5% w/w JFS2 as superdisintegrant exhibited similar dissolution profile with that of formulation F8 prepared by 5% w/w CSS. These were further confirmed by similarity factor (f2) and difference factor (f1) studies. In vitro dissolution parameters such as first-order rate constant and Hixon–Crowell constant were calculated for all formulations. Majority of the formulations including pure drug IRB and the marketed formulation were found to release the drug by first-order kinetics, which were indicated by R² values in the range of 0.946–0.909.

The similarity factor (f2) and difference factor (f1) were calculated for all formulations including pure drug and marketed formulation in comparison to formulation F8 containing 5% w/w of CSS as superdisintegrant. The f2 and f1 factors indicated that formulations F5 and F6 exhibited similar dissolution profiles with more than 50 as f2 value in comparison to the F8 formulation. Among all these formulations, F5 was found to exhibit the highest f2 value (84), indicating that the dissolution profiles are highly comparable with the standard F8 formulation. The results are given in Table 9.

Based on the statistical analysis using Student t test, the t value obtained was 1.3262. The tabulated t value obtained at 5% level of significance with 10 degrees of freedom is 2.228. Hence, tcal < tab and thus indicated that there was no significant difference between formulation F5 (test) and formulation.

Fig. 4 - Dissolution profiles of irbesartan fast dissolving tablet formulations containing JFS1 starch in comparison with tablets containing CCS. CCS, croscarmellose sodium; JFS1, jackfruit seed starch extracted using water.
F8 (standard). The dissolution studies indicated that jackfruit seed starches were found to be promising as naturally occurring superdisintegrants for the formulation of FDTs of poorly soluble drug IRB. The wetting time and swelling index values obtained for various starches indicated that they were highly hydrophilic, absorb water, and tend to swell moderately.

The FTIR spectral investigations were conducted on pure drug, JFS2, CCS blend of IRB and JFS2, and IRB and CCS. The pure drug IRB exhibited sharp peaks at 3444.91 cm\(^{-1}\), 2959.87 cm\(^{-1}\), 1732.96 cm\(^{-1}\), 1616.52 cm\(^{-1}\), and 1408.50 cm\(^{-1}\), indicating the presence of NH stretching, CH stretching, CO stretching, aromatic CC stretching, and NH bending. For JFS2, a broad peak observed at 3374.92 cm\(^{-1}\) and sharp peaks at 2930.94 cm\(^{-1}\), 1650.74 cm\(^{-1}\), and 1416.17 cm\(^{-1}\) indicated the presence of OH stretching, CH stretching, aromatic CC stretching, and NH bending. For CCS, a broad peak at 3469.80 cm\(^{-1}\) and sharp peaks at 2919.41 cm\(^{-1}\), 1603.96 cm\(^{-1}\), and 1417.57 cm\(^{-1}\) indicated OH stretching, CH stretching, aromatic CC stretching, and NH bending. For the IRB and JFS2 blend, a broad peak 3384.26 cm\(^{-1}\) and sharp peaks at 2932.30 cm\(^{-1}\), 1732.98 cm\(^{-1}\), 1617.36 cm\(^{-1}\), and 1408.98 cm\(^{-1}\) indicated the presence of OH stretching, CH stretching, CO stretching, aromatic CC stretching, and NH bending. For the IRB and CCS blend, a broad peak at 3443.11 cm\(^{-1}\) and sharp peaks at 2959.53 cm\(^{-1}\), 1732.79 cm\(^{-1}\), 1615.89 cm\(^{-1}\), and 1417.52 cm\(^{-1}\) indicated the presence of OH stretching, CH stretching, CO stretching, Aromatic CC stretching, and NH bending. The spectra of blends that exhibited overlapped peaks at 3400 cm\(^{-1}\).
indicated that N–H stretching of the drug IRB was covered by —OH stretching of superdisintegrants. The remaining peaks were unaltered, indicating that there were no drug-excipient interactions. The detailed spectral elucidations are shown in Fig. 5.

DSC thermographic studies were carried out on pure drug IRB, JFS2, CCS, IRB and JFS2 blend, and IRB and CCS blend. These studies exhibited a sharp endothermic peak at 188.25 °C for the pure drug IRB, a broad endothermic peak at 312 °C for JFS2, and a sharp exothermic peak at 307.98 °C for CCS. In the IRB and JFS2 blend, a sharp endothermic peak at 188.04 °C and a broad endothermic at 311.52 °C were obtained, indicating that there is a slight shift in the temperature for drug and JFS2. Similarly, a sharp endothermic peak at 188.18 °C for IRB and a broad exothermic peak at 308.2 °C for CCS in the respective blend were observed. In this case also, a slight shift in peaks with a minute change in temperature was observed. These studies revealed that there were no drug-excipient interactions, which was confirmed by obtaining similar thermographic peaks at respective temperatures. The DSC thermogram interpretations are shown in Fig. 6.

SEM images were taken for JFSP, JFS2, IRB, and IRB and JFS2 blend. It was observed that the starch grains in JFSP were covered with some kind of resinous/mucilaginous mass, which was very clearly shown in the images. The JFS2 starch exhibited spherical free flowing with low dense form of starch grains.
without having any intact resinous/mucilaginous mass. IRB free drug exhibited a needle-like crystalline form of material. The SEM image of blend of IRB and JFS2 clearly exhibited the uniform dispersion of drug with the spherical globular starch grains. The SEM images are shown in Fig. 7.

The optimized formulations, F5 and F8, were subjected to accelerated stability studies as per ICH guidelines after storage under different conditions. Physical parameters and drug release studies were carried out on these formulations. The results are shown in Figs. 3 and 4.

4. Discussion

The starches obtained from jackfruit were crisp, slightly granular, free flowing, and stable in nature. Thus, the starches extracted from jackfruit seeds were selected as superdisintegrant for the formulation of FDT. Acute toxicity studies on Wistar rats indicated the safety of the superdisintegrant. IR8 FDT formulations that contained various concentrations of jackfruit starch extracts and CCS were prepared by wet granulation technique using IPA as granulating fluid. The evaluated precompression parameters indicated that the granules exhibited good flow properties. In vitro dissolution studies were performed on all prepared matrix tablets using the USP apparatus II with 900 mL of 0.1N HCl. From the results of dissolution studies, it was observed that the type of starch as superdisintegrant and the proportion of superdisintegrant have considerably influenced the dissolution parameters of various formulations. Starches derived from the jackfruit have potential application as tablet disintegrants. In recent studies, researchers have found that the starch extracted from jackfruit had the swelling ability and water uptake profile similar to CCS and sodium starch glycolate. The superdisintegrant JFS2 containing 5% w/w superdisintegrant exhibited a similar dissolution profile with that of the formulation prepared by 5% w/w CSS. The probable mechanism for the superdisintegrant action of these starches was ascribed to the rapid uptake of water, followed by swelling, which led to hydrostatic pressure in the tablet crust resulting in faster disintegration of the tablets. It was observed that as the proportion of superdisintegrant is increased in the tablet, the dissolution rate and drug release from the tablets were found to be rapid. Thus, IR8 FDTs prepared with CCS were found to exhibit high dissolution rates. This was because of the increased wettability,
rapid dispersion, and faster drug release. The optimized formulations were subjected to FTIR and DSC analysis to study the drug-excipient interactions. These studies revealed that there were no drug-excipient interactions.

The optimized formulations, F5 and F8, were subjected to accelerated stability studies. From the results, it was observed that there were no significant changes in physical parameters and drug release even after stability studies at various storage conditions, and thus indicated that these formulations were stable.

The present work provided an approach to formulate FDTs by using naturally extracted starch from JFSP, which was designed to release the drug at a faster rate. Among various tablet formulations, F5 and F8 were optimized and based on their in vitro dissolution.

Based on the above studies, it may be concluded that IRB FDTs prepared by using specific concentrations of alkali-extracted starch showed fast disintegration of tablets.

Conflicts of interest

The authors have no conflicts of interest to declare.

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