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Integrative Medicine Research

journal homepage: www.imr-journal.com

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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ARTICLE INFO

Article history:
Received 27 December 2016
Accepted 4 April 2017
Available online 26 May 2017

Keywords:
fast dissolving tablets
irbesartan
jackfruit seeds
superdisintegrants

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 postcompression 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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http://dx.doi.org/10.1016/j.imr.2017.04.001

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.[1] 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 (dysphasia), 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.[2] 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.[3] 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, crosspovidone, modified cellulose, and L-HPC.[4–6] Examples of coprocessed superdisintegrants include Ludiflash, Pharmaburst, Modified mannitol, Polacrilin potassium, and Glucidex IT.[7] 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*,[8] 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.[9]

They act by different mechanisms of actions: (1) swelling action, (2) capillary action (wicking), (3) combination action, (4) deformation recovery,[10] (5) heat of wetting, (6) chemical reaction (acid–base reaction), (7) particle repulsive forces/due to disintegrating particle,[11] 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 spermoderm, 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 ($t_{1/2}$) 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.[12] 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 talc 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.[13] 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