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Original Article

FORMULATION AND *IN VITRO* EVALUATION OF CURCUMIN LOADED JACKFRUIT SEED STARCH NANOPARTICLES

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ABSTRACT

Objectives: To meet the above aim the following objectives are undertaken: (1) Isolation of starch from jackfruit seeds and formulation of curcumin loaded jackfruit seed starch nanoparticles (2) *In vitro* evaluations of the drug loaded nanoparticles

Methods: Jackfruit seed starch nanoparticles were prepared by Nanoprecipitation technique. In this technique, jackfruit seed starch was mixed with curcumin and acetone solution using a magnetic stirrer at 600 rpm. To the above solution, water were added dropwise and stirred at room temperature until acetone was completely vaporized. Nanoparticles were separated by centrifugation at 4000 rpm after 40 min.

Results: Particle size of prepared nanoparticle formulations was found to be 371 to 411.72 nm with PDI of 0.148 to 0.356. The maximum % drug entrapment was found to be 57.34 % with formulation F5. *In vitro* release studies showed sustained release of drug till 12 h.

Conclusion: The prepared nanoparticles were evaluated for its particle size, drug entrapment efficiency, *in vitro* drug release study, and surface morphology studies by scanning electron microscopy. The results of Fourier transform infrared studies of 1:1 physical mixture of drug and excipients confirmed the absence of incompatibility. Thus, the study concludes that curcumin loaded jackfruit seed starch nanoparticles were developed successfully by nanoprecipitation, which is expected to enhance the oral bioavailability of curcumin.

Keywords: Curcumin, Nanoparticles, Starch, Nanoprecipitation, *In vitro* drug release

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INTRODUCTION

Nanoparticles are to be defined as a particulate dispersion or solid particles with a size range of 10-1000 nm. Nanoparticles can be divided into main two groups: nanospheres and nanocapsules. Nanospheres are considered as matrix particles whose entire mass are solid whereas nanocapsules are composed of a liquid or empty core surrounded by an organic solid shell. Nanospheres and nanocapsules are generally spherical but non-spherical shape can be encountered [1]. Polymeric nanoparticles plays a vital role in drug delivery as they generally increase the stability of any volatile pharmaceutical agents and that they are easily and cheaply fabricated in large quantities by a multitude of methods [2]. From among the polymers, biodegradable polymers like starch has received great attention in drug delivery applications as they are hydrophilic, biodegradable, versatile, inexpensive and biocompatible with tissue and cells. The major aim in designing nanoparticles as a delivery system are to achieve control particle size, surface properties and to release pharmacologically active agents to achieve the site-specific action of the drug at the therapeutically optimal rate and dose regimen [3].

Jackfruit is the name of the fruit from a jacktree (Artocarpus heterophyllus) that belongs to the Moraceae family. Jackfruit seeds contain considerably high amount of starch that qualify as a sustainable source of starch for food and pharmaceutical industries. Starch content in jackfruits seeds, as in other cultivars, depends of their structural composition, growing conditions, harvesting periods, and climates [4].

Curcumin is a phytopolylphenol pigment isolated from the plant Curcuma longa, commonly known as turmeric, with a variety of pharmacologic properties. Curcumin, has been the subject of several studies due to its known anti-cancer, antioxidant, anti-inflammatory, antimicrobial and antiviral activities [5-7]. Nevertheless, use of curcumin is hindered by its low water solubility, fast degradation, and low bioavailability [8]. Hence, there is a need for the development of new formulation for delivery, efficient loading, and sustained release of poorly water-soluble drug curcumin to increase its therapeutic efficacy and to decrease its side effects [9].

In this study, starch nanoparticles loaded with curcumin was prepared to improve the bioavailability of curcumin and was evaluated for its particle size and polydispersity index (PI), *in vitro* drug release, surface morphology by scanning electron microscopy (SEM) and drug-excipients compatibility studies by Fourier transform infrared (FT-IR).

MATERIALS AND METHODS

Material

Jackfruit seeds was bought from local market of Maligaon and starch was isolated, Curcumin from Ottokemi (Mumbai), Acetone from Merck Specialities Pvt. Ltd (Mumbai), Methanol Krishna Enterprise (Guwahati), Dialysis membrane from Sisco Research Laboratories Pvt. Ltd (Mumbai) and Sodium hydroxide from B S Trading (Kolkata). All other solvents and chemicals are of analytical grade.

Methods of starch isolation

Sample preparation

The seeds (5 kg) were clean and the white aril (seed coats) were peeled off. Seeds were then divided into two parts. One part was lye-peeled with 5% NaOH for 2 min to remove the thin brown spermoderm covers the fleshly white cotyledons were come out. The seeds were then slice into thin chips ans was tray dried at 50℃ -60˚C until their moisture content is less than 13%. The chips were ground in a pin mill and then passed through 70 no mesh flour was packed in plastic pouches and stored in a refrigerator (<5˚) until use [10].

Starch isolation

Starch isolation from flour was carried out by following the basic procedure washing steps. The flour was then mixed with 3 parts of distilled water and made into slurry. The slurry was filtered through a 70 no sieve to eliminate seed fibers. The starch suspension was allowed to settle and the liquid was decanted at<10 °C. This step was repeated several times until the supernatant was clean and clear. The starch was then dried in a convection oven at 40 °C to 60 °C

until the moisture content will be less than 13%, then grind with the help of mortar and pastel and pass through a 70 no sieve. Sample will store in air tight container at room temperature until use [10].

Preparation of jackfruit seed starch nanoparticles loaded with curcumin

Preparation of jackfruit seed starch nanoparticles (JSSN) loaded with curcumin was performed as follows by Nanoprecipitation method with some modifications: 10-50 mg Jackfruit seed starch at different concentration was mixed with a curcumin/acetone solution (10 mg curcumin/20 ml acetone) during 15 min by using a magnetic stirrer at 600 rpm. The 20 ml of water were added drop by drop with constant stirring. The resulting suspension was stirred at room temperature until acetone was completely vaporized. All experiments were carried out at 25 °C. Nanoparticles were separated by centrifugation at 4000 rpm during 40 min; samples were washed several times with ethanol to remove any excess of curcumin. Finally, the curcumin-loaded nanoparticles were dried in hot air oven at 30 °C during 48 h [11].

Drug-excipient compatibility study by FT-IR

This study was carried out to find out the compatibility between curcumin and different excipients to be used in formulations [7]. Physical mixture in ratio 1:1 of drug-excipients was prepared and scanned from 4000 cm−1 to 400 cm−1 in Bruker Alpha FT-IR spectrophotometer after placing the sample onto the sample holder. The spectra obtained were compared and interpreted for the functional group [11].

Characterization of prepared jackfruit seed starch nanoparticles

Particle size and polydispersity Index

To analyze particle size, each formulation of drug loaded lyophilized nanoparticles was dispersed in deionized water, centrifuged for 5 min at 5000 rpm and filtered using 0.2 µm membrane filter. Particle size and PI were determined by using Malvern Zetasizer Nano S90 at a temperature of 25 °C at a measuring angle of 90 ° to the incident beam [11].

Entrapment efficiency

Entrappment of Curcumin in starch nanoparticles were determined by extracting 5 mg nanoparticles with 1 ml acetone for 6 h. From this solution 0.2 ml was diluted with phosphate buffer pH 6.8 and analyzed by UV spectrophotometer (Shimadzu UV-1800, Japan) at 421 nm against appropriate blank [11].

The entrapment efficiency was calculated using the following equation:

$$\% \text{ Entrapment efficiency} = \frac{\text{Weight of drug in nanoparticles}}{\text{Weight of drug in the formulation}} \times 100$$

SEM of nanoparticles

The shape and surface characteristics of the nanoparticles were observed by SEM. The nanoparticle sample was thinly sprinkled onto a metal stub and vacuum coated with a thin layer of gold in an argon atmosphere. The SEM photomicrographs of the coated particles were obtained at 15 KV using a ZEISS, Germany, SEM [11].

***In vitro* drug release**

In vitro drug release was determined by Franz diffusion cell using Dialysis membrane where 20 mg of jackfruit seed starch nanoparticles was diluted with 6.8 buffer solution and added to donor compartment. The content of the receptor media contained 250 ml of buffer solution. At pre determine points (upto 12 h), 5 ml of the medium solution was withdrawn from the receptor compartment and replaced with the same amount of buffer solution, which was stirred continuously at 600 rpm and maintained at 370 °C [12].

RESULTS AND DISCUSSION

Drug-excipients compatibility study by FTIR

The physical mixture of drug (curcumin) with polymer (Starch) clearly shows the retention of this characteristic peaks of Curcumin, thus revealing that there is no interaction between the selected drug and polymer.

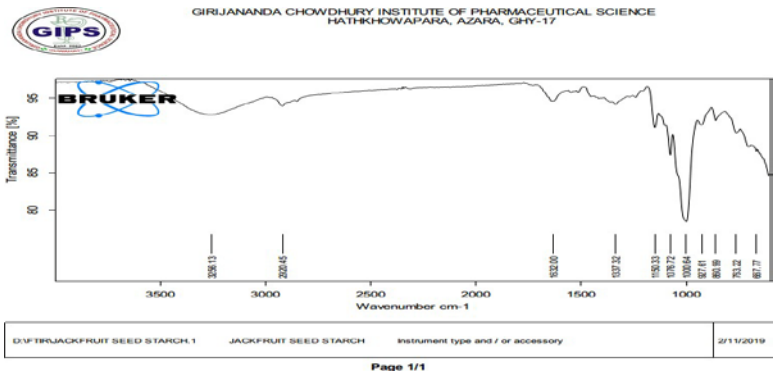

Fig. a: FTIR spectra of jackfruit seed starch

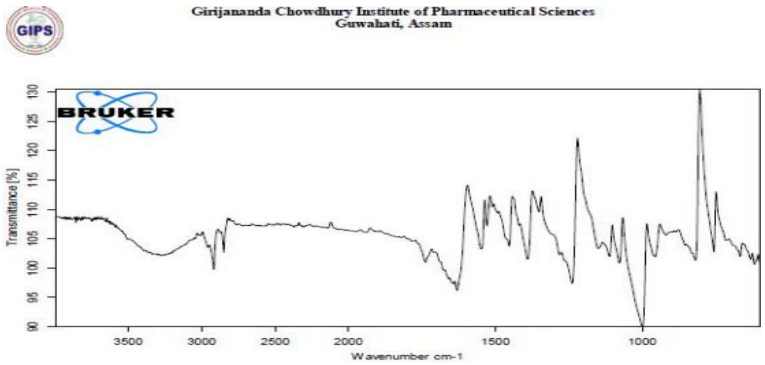

Fig. b: FTIR spectra of curcumin

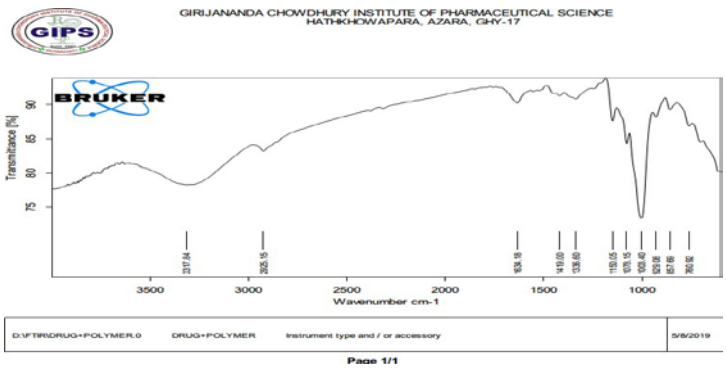

Fig. c: FTIR spectra of curcumin and starch

Physicochemical characteristics

The physicochemical characteristics of curcumin loaded jackfruit seed starch nanoparticles were briefly narrated in table 1. The results showed that the particle size of the prepared nanoparticles varied from 371 to 411.72 nm with a low PI in the range of 0.148 to 0.356 as shown in table 1. The PI was found to be<0.5, which is a considered as proof of a homogeneous nanoparticle formulation.

Table 1: Particle size and polydispersity index

Formulation code	Drug: polymer	Mean diameter (nm)	PDI
F1	1:1	387.11	0.262
F2	1:2	410.67	0.266
F3	1:3	411.72	0.356
F4	1:4	406.44	0.148
F5	1:5	371	0.176

Entrapment efficiency

The prepared nanoparticles showed entrapment efficiency in the range of 19% to 57% depending on the drug polymer ratio shown in table 2. The entrapment efficiency of nanoparticles increased with increase in polymer concentration. The low drug entrapment efficiency values indicate relatively low affinity of the drug with the polymer matrix

Table 2: Entrapment efficiency data for different formulations

Formulations	Drug: polymer (in wt)	%Entrapment efficiency
F1	1:1	19.32
F2	1:2	31.14
F3	1:3	44.72
F4	1:4	51.22
F5	1:5	57.34

***In vitro* drug release studies**

The *in vitro* drug release studies of nanoparticles were carried out at 370±20 °C in Phosphate buffer pH 6.8 for a period of 12 h using dialysis bag technique. The drug release data of different formulations in Phosphate buffer pH 6.8 are given in table 3.

Table 3: *In vitro* drug release profiles of nanoparticles in phosphate buffer pH 6.8

Time(h)	% Cumulative drug release				
	F1	F2	F3	F4	F5
1	2.12	2.56	3.62	3.77	4.99
2	5.02	5.23	6.02	7.59	8.54
3	9.77	9.99	9.59	9.99	11.69
4	13.33	12.98	12.54	12.97	14.39
5	16.65	15.97	16.66	17.03	18.78
6	19.11	19.75	19.37	20.59	23.35
7	21.04	22.23	22.66	23.54	25.41
8	25.23	24.92	26.92	27.76	29.67
9	27.61	27.88	28.22	30.54	32.39
10	28.12	29.45	31.01	32.21	36.43
11	30.43	31.21	32.34	34.54	38.89
12	31.12	31.96	34.32	36.89	39.47

Here sustained release of drug was observed from the formulation in phosphate buffer pH 6.8 for duration of 12h. Here we found that with increased in concentration of polymer in formulation drug release was sustained for long period, which may be due to the hydration capability

of starch which on coming in contact with dissolution medium results to the formation of gelatinous mass that act as a retardant material for the drug to get diffused out. The cumulative % drug release from formulation F1, F2, F3, F4 and F5 are 31.12%, 31.96%, 34.32%, 36.89% and 39.47% respectively. Amongst all the formulations, F5 formulation showed better sustained release profile of the drug for a period of 12 h in phosphate buffer pH 6.8

SEM

The shape and surface characteristics of nanoparticles of optimised formulation (F5) was visualized using SEM, Zeiss, Germany. The SEM results are shown in fig. e.

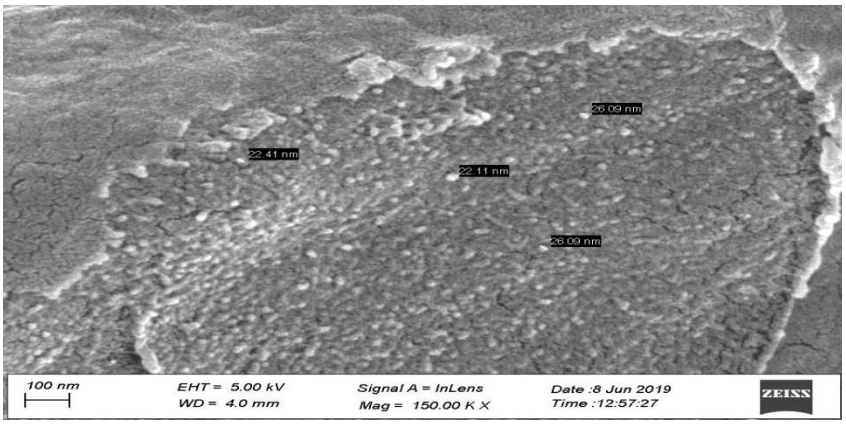

Fig. e: SEM of the formulation F5

CONCLUSION

In this study, Curcumin loaded jackfruit seed starch nanoparticles with particle size range between 371 to 411.72 nm were prepared successfully by nanoprecipitation technique. Nanoparticle size depends primarily on the excess of polymer added into the system and *in vitro* release study revealed the sustained release of drug for 12 h. The FT-IR study results confirm the compatibility of Curcumin with the excipients used in formulations. Thus, the developed nanoparticles are expected to the improvement of the oral bioavailability of the drug.

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Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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