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Studies on the *Artocarpus lakoocha* Seeds for Drug Delivery

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Abstract. This study aimed to evaluate the effect of modification on non-conventional native starch derived from the seed of *Artocarpus lakoocha* or monkey fruit (Native Starch). The current study determined the excipient characteristics of native and modified starches by examining their physicochemical properties, flow properties, and release characteristics. It showed better improvement in the physicochemical and functional properties and was helpful in the formulation of immediate-release formulations when tested with paracetamol as a model drug. The results from the Field Emission Scanning Electron Microscopy (FESEM) Micrograph revealed a disruption of the granular structure. FTIR analysis confirmed the carbohydrate nature of the starch. The X-ray diffraction pattern demonstrated the decrease in crystallinity following thermal modification. Here, we utilized waste seeds of *Artocarpus lakoocha* to isolate starch, its modifications, and their usage in effective drug delivery formulations, such as tablets and suppositories, compared to the marketed formulations. In summary, this study aims to assess the effects of starch modification and demonstrates the potential advantages of using starch derived from *Artocarpus lakoocha* seeds. It addresses the need for improved excipients in pharmaceutical formulations, promotes sustainability through waste utilization, and highlights the versatility of these starches in various applications, including drug delivery and functional foods.
Keywords: *Artocarpus lakoocha* starch; immediate drug delivery; physical modification; physicochemical properties; suppository; tablet.

Resumen. Este estudio tuvo como objetivo evaluar el efecto de la modificación sobre el almidón nativo no convencional derivado de la semilla de *Artocarpus lakoocha* o fruto de mono (Native Starch). El presente estudio determinó las características de los excipientes de los almidones nativos y modificados examinando sus propiedades fisicoquímicas y de flujo así como sus características de liberación. Mostró una mejor mejora en las propiedades fisicoquímicas y funcionales y fue útil en la formulación para su liberación inmediata cuando se probó con paracetamol como fármaco modelo. Los resultados de la micrografía de microscopía electrónica de barrido por emisión de campo (FESEM) revelaron una alteración de la estructura granular. El análisis FTIR confirmó la naturaleza glucosídica del almidón. El patrón de difracción de rayos X demostró la disminución de la cristalinidad después de la modificación térmica. También utilizamos semillas de desecho de *Artocarpus lakoocha* para aislar el almidón, sus modificaciones y su uso en formulaciones efectivas de administración de medicamentos, como tabletas y supositorios, en comparación con las formulaciones comercializadas. En resumen, este estudio tuvo como objetivo evaluar los efectos de la modificación del almidón y demuestra las ventajas potenciales del uso de almidón derivado de semillas de *Artocarpus lakoocha*. Aborda la necesidad de mejorar los excipientes en las formulaciones farmacéuticas, promueve la sostenibilidad mediante la utilización de residuos y destaca la versatilidad de estos almidones en diversas aplicaciones, incluida la administración de medicamentos y los alimentos funcionales.

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Palabras clave: almidón de *Artocarpus lakoocha*; entrega inmediata de medicamentos; modificación física; propiedades fisicoquímicas; supositorio; tableta.

Introduction

Artocarpus lakoocha Roxb. is a deciduous tree belonging to the family Moraceae. It is also known as Monkey fruit in English and Lakuch in Ayurveda. In India it is known as "lakuchi," "dahu," and "barhal," in Thailand as "lokhat," and in Malaysia is called as "tampang" [1-2]. Starches are natural polysaccharides, Because of their unique characteristics, and serve as a food type for humans and are one of the most essential raw materials for numerous industries. Their resource is cheap, readily available, renewable and biodegradable. However, native starch still has several restricted properties and fails to meet demands in several fields adequately. Almeida et al., evaluated and compared the effect of the utilization of five different non-conventional starches extracted from chickpea, common bean, Peruvian carrot, sweet potato and white bean and four different commercial starches obtained from cassava, corn, potato and rice in pound cake [3].

So far, scientists have discovered a way to modify the native starch's structure and properties to increase its economic efficiency and ease to use. Studies have been conducted on various starch modification processes, specifically physical modification [4]. *Artocarpus heterophyllus* Lam. seed starch has already been reported as a natural starch candidate as a potential pharmaceutical excipient in various pharmaceutical dosage forms, such as binding agents and disintegrants in pharmaceutical tablets [5]. Lakoocha trees have crimson male and orange-yellow female blooms. There are approx. 20 to 30 seeds in a fruit. Generally, *Artocarpus* species are recognized for their therapeutic and nutritional benefits and also have been used medicinally and nutritionally for years [50]. *Artocarpus lakoocha* has been studied for its bioactive properties, extracts, and bioactive compounds from various parts of the plant, including the bark, leaves, seeds, and pericarp, have been found to possess exceptional phytochemicals. [2] However, specific statical data on the availability and constraints for procuring *Artocarpus lakoocha* seeds are not readily available. Many pharmaceutical and food companies utilize starch as a binder and dissolver. Potato, rice, and maize are commercial starches. Unexplored starch sources like *Artocarpus lakoocha* starch offer several advantages over other starches, making it a valuable asset [6]. Significantly less work has been done on *Artocarpus lakoocha* Roxb. seed starches (ASS), includes its modification, formulation, and evaluation. The main aim of this study was to investigate the effect of native and modified starch with its change in functional and physicochemical parameters of starch isolated from *Artocarpus lakoocha* seed. So that in the future, ASS can be used in the pharmaceutical and food industries.

Materials and methods

Collection of seeds and isolation of starch from *Artocarpus lakoocha* seed

The seeds were collected from the botanical garden of Birla Institute of Technology, Mesra, Ranchi. Using the method described by Zhang et al. and Banyal *et al.* [6,9,16] with exhibiting minor modification, separated starch was from the seed. The seed was soaked with distilled water to make a paste, and the paste was filtered three times. After drying at 50 °C, the starch was powdered and sieved using a 100 particle sieve size and packed in a closed container and for further analysis. The ground paste was then, immersed in 0.05 % (w/v) sodium hydroxide and left overnight at room temperature. Finally, the resulting suspension was thoroughly washed with water to obtain a clear supernatant. The isolated wet starch was collected and dried overnight in a hot air oven at 50 °C. Fig S1[16]**.**

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Modification of starch

Ultrasonication of starch (UMS)

By using an ultrasonicator, ultrasonic modification of starch was done. 30 % (w/v) of the starch solution was prepared. The sample was ultrasonicated for 20 min at 25 ºC, the frequency was 20.5 kHz, and the power was 170 watts. The ultrasonicated modified starch was centrifuged at 3000 rpm for 30 min. Then starch was sieved and dried in a hot air oven at 50 ºC for 24 hrs [10,11].

Pregelatinized modification of starch (PMS)

For pregelatinized modification of native starch, 10 gm of the starch sample was dissolved in 100 mL of distilled water and incubated at 90 ºC for 20, 25, and 35 minutes with constant agitation at 500 rpm. After that, pregelatinized starch was dried for 24 hours at 50 ºC. The dried and flaky starch was then powdered using an analytical mill and passed through a sieve with a mesh size of 100 µm, and pregelatinized starch with intervals of 20, 25, and 30 minutes were designated as PM-1, PM-2, and PM-3 respectively [12,13].

Starch hydrolysis

For starch hydrolysate (SH-2) or (SH-4), starch was mixed with solutions of Citric acid, glacial acetic acid, and water and then, heated to 95 ºC for 2 and 4 hours respectively. The sediments were washed using ethanol several times after the solvent was removed by an evaporation method. When hydrolysates were dissolved in water, they produced pH values of 3.74 and 3.54 respectively, whereas with phosphate buffer solutions they achieved pH values of 7.11 and 7.07 respectively [14].

Physicochemical analysis of starch

Various techniques were used for the physicochemical analysis of non-conventional starch, which includes percentage yield, moisture, ash, amylose, pH, elemental analysis, water holding capacity, oil absorption capacity, dispersibility, micrometric properties, swelling and solubility (for methods, please refer to *supporting information file*) [9,22].

Field emission scanning electron microscope (FESEM)

Using FESEM (Carl Zeiss, Germany, Sigma 300 model), the morphological properties of starch were determined in which it was done with double-sided carbon adhesive tape for mounting 4-5 mg of starch samples on a sphere of aluminum, and then a thin coating of gold was added on top. Images were recorded at magnifications ranging from 100 to 5.00K at 5 kV accelerating voltage [12, 23].

Thermogravimetric analysis

For the determination of thermostability (Netzsch, Germany LFA-467) model was used. The Alumina crucible containing starch powder (5 mg) was heated from 30 to 600 ºC at a rate of 20 ºC/min and filled with nitrogen maintaining a flow rate of 20 mL/min [17].

Differential scanning calorimetry (DSC)

DSC (TA Instruments, USA, Q 10) model was used to determine starch thermal properties. 5 mg of starch samples were taken into aluminum pans and sealed for that analysis. At a heating rate of 10 ºC/min, samples were scanned from 60 to 300 ºC. All samples were equilibrated for 15 minutes. Thermal analysis was performed in a nitrogen atmosphere. The temperatures at the start (To), peak (Tp), end (Tc), and ΔH have been calculated automatically. (Tc-To) was used to calculate the gelatinization temperature range (R). The ratio H/(Tp-To) was used to calculate the PHI (φ) [24].

Fourier transform infrared spectroscopy (FTIR)

The Frontier (Perkin Elmer, USA) was used to determine FTIR spectroscopy. The dried KBr and starch samples were combined and pressed to form a pellet and were scanned between 400 and 4000 cm^{-1} frequency [12].

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X-ray diffraction (XRD)

The XRD (model: Bruker Kappa Apex II) was used to determine the crystal properties of dried starch specimens. The instrument was calibrated to 35 mA and 40 kV to a diffraction pattern (2Θ) varying from 10 to 80 ºC at 15 ºC/ minute [16].

Application of starches in the drug delivery

Preparation of tablets

We used the wet granulation method for the preparation of tablet formulation. All the ingredients were taken in mortar and pastle along with paracetamol drug, and then the distilled water was added for the preparation of dough illustrated in Table S1[16,20]**.**

Granules were prepared by passing the resulting wet mass through ASTM # 10 mesh. Then the granules were dried at 45 °C in a hot air oven for 30 minutes. After that, lubricants were added. Finally, the tablets were punched on a 16-station tablet punching machine (Cadmach, Ahmadabad, India).

Evaluation of tablets

20 tablets from each formulation were taken and weighed to determine the average weight. Erweka Hardness Tester was used for the determination of tablet hardness. Tablet friability was measured using Roche Friabilator. USP disintegration device Erweka ZT3 (Heusenstamm, Germany) was used for the disintegration test [27].

Assay of paracetamol tablet

Assay of paracetamol was determined by using earlier method described by Venkataswamy 2018 [28].

In vitro release study

For the determination of in vitro release, USP type-II dissolving test apparatus (LAB INDIA DS 8000, India) was used while taking, an intestinal medium with a pH of 6.8 buffers and 50 rpm at 37±0.5 °C was used for the in-vitro release profile. 1 mL sample was taken from an intestinal medium of pH 6.8 buffers using a syringe with a membrane filter (0.45µm) and was replaced with 1 mL of fresh buffer at a predefined interval. The proportion of drug release was estimated using UV-VIS spectroscopy (Shimadzu UV-2450) and absorbance at 243nm [12,20,28].

Formulation of suppository

Rectal suppositories were made using the fusion method at 36°C on a lipophilic base - cocoa butter. Each one contained 125 mg of paracetamol drug. The molten bases were combined with SH2 and SH4 and then poured into a polyethylene mold. After solidification, the suppositories were stored at 4 ºC until use, as illustrated in Table S2 [14]**.**

Evaluation of suppositories

Twenty suppositories were taken for the weight variation test. Softening time of lipophilic suppositories was determined. Suppositories were disintegrated using the Erweka ZT3 disintegration device (Heusenstamm, Germany) [29].

Assay of acetaminophen-based suppository

The Assay of the paracetamol suppository was done by the previously described method Khatri *et al.* 2017 [29]**.**

Dissolution test for suppositories (*In vitro* release of suppositories)

Dissolution apparatus used to evaluate paracetamol suppositories (NS, UMS, PM-1, PM-2, and PM-3). In a stirred beaker, the Suppository was placed on the bottom. While the stirrer spun at 100rpm, maintained the system at 37 ± 1° C. 1 mL sample was taken and replaced with 1 mL of fresh medium at 0, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55 and 60 minutes. Samples were filtered using a membrane filter (0.45µm) connected

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to a syringe and diluted. UV-VIS spectroscopy (Shimadzu UV 2450) was used to measure the absorbance at 243 nm and calculate the % drug release of suppositories [14,29].

Results and discussion

Physicochemical analysis of starch

The physicochemical properties of starch are illustrated in Table 1, Micromeritic properties and elemental analysis illustrated in Table S3, swelling and solubility shown in Table 2 and 3.

Table 1. Physicochemical properties of NS and modified starch (UMS, PM-1, PM-2, and PM-3)

Starch	WHC (%)	Amylose content (%)	Moisture content (%)	Ash content	pH	Dispersibility	OAC
NS	179.5 ± 0.01	10.954 ± 0.01	11.36 ± 0.11	0.009 ± 0.01	7.1 ± 0.03	73.00 ± 0.02	15.00 ± 0.25
UMS	185.6 ± 0.03	24.418 ± 0.03	10.1 ± 0.01	0.010 ± 0.03	7.2 ± 0.01	72.00 ± 0.01	12.07 ± 0.15
PM-1	294.5 ± 0.01	25.704 ± 0.02	9.54 ± 0.04	0.014 ± 0.02	7.4 ± 0.04	71.00 ± 0.02	12.01 ± 0.17
PM-2	302.1 ± 0.02	33.048 ± 0.04	9.23 ± 0.02	0.015 ± 0.03	7.5 ± 0.01	70.00 ± 0.03	11.03 ± 0.23
PM-3	323.1 ± 0.04	42.846 ± 0.03	9.11 ± 0.01	0.015 ± 0.05	7.5 ± 0.03	69.00 ± 0.02	10.05 ± 0.11

Table 3. Swelling properties of Native (NS) and modified starch (UMS, PM-1, PM-2, and PM-3).

Starch	Swelling power (%)				
	30 ºC	**45ºC**	**60 ºC**	**75 ºC**	**90 ºC**
NS	2.13 ± 0.34	3.78 ± 0.21	5.11 ± 0.35	7.01 ± 0.21	9.58 ± 0.36
UMS	4.11 ± 0.11	6.65 ± 0.11	10.51 ± 0.24	12.34 ± 0.34	14.37 ± 0.11
PM-1	6.31 ± 0.13	10.11 ± 0.41	11.41 ± 0.11	15.11 ± 0.23	17.41 ± 0.23
PM-2	8.55 ± 0.01	11.31 ± 0.35	12.42 ± 0.01	16.01 ± 0.39	19.21 ± 0.16
PM-3	9.13 ± 0.12	12.52 ± 0.12	14.31 ± 0.43	18.03 ± 0.32	22.64 ± 0.22

Table 4. Solubility powers of Native (NS) and modified starch (UMS, PM-1, PM-2, and PM-3).

Starch	Solubility power (%)				
	30 ºC	**45ºC**	**60 ºC**	**75 ºC**	**90 ºC**
NS	8.60 ± 0.22	8.23 ± 0.09	10.06 ± 0.35	12.11 ± 0.41	14.32 ± 0.24
UMS	13.12 ± 0.11	14.65 ± 0.12	16.21 ± 0.16	18.23 ± 0.45	19.57 ± 0.13
PM-1	14.31 ± 0.14	16.12 ± 0.31	19.47 ± 0.81	22.14 ± 0.23	22.36 ± 0.04
PM-2	15.55 ± 0.12	18.51 ± 0.26	22.34 ± 0.56	24.21 ± 0.43	15.11 ± 0.08
PM-3	17.11 ± 0.15	19.80 ± 0.14	24.56 ± 0.43	30.23 ± 0.12	33.14 ± 0.23

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Starch yield and moisture content

The starch yield was found to be 50 % (db) [31]**.** Moisture content serves as a gauge for the starch's stability when kept in storage. The moisture content of NS, UMS, PM-1, PM-2, and PM-3 was from 9.11 to 11.36 % [32]**.**

Amylose, ash, and pH content

The range of amylose contents of NS, UMS, PM-1, PM-2, and PM-3 were 10.954 %, 24.418 %, 25.704 %, 33.048 %, and 42.846 %, respectively. The amylose content in starch was significantly affected by the pregelatinized treatment. Starch hydrolysis depolymerized and amylose resulting in smaller chain sizes [33]**.** Ash concentration was reported to range from 0.012 to 0.15 %. The pH of starch was between 7.1-7.5. The pH typically affects the stability of pharmaceutical formulations.

Water holding capacity (WHC)

The WHC of NS samples was found to be 179 ± 0.01 %, whereas UMS, PM-1, PM-2, and PM-3 were reported to be 185 ± 0.03 %, 294.5 ± 0.01 %, 302.1 ± 0.02 and 323.1 ± 0.04 respectively [12]**.** The findings revealed that the modification of starch increased its water absorption capacity [33,34]. The WHC increases as the pre-gelatinization time increases because starch undergoes hydrothermal treatment, which causes the granules to rupture and release their soluble components.

Oil absorption capacity (OAC)

The oil absorption capacity of the NS sample was found to be 15 ± 0.25 %, whereas for the UMS, PM-1, PM-2, and PM-3 decreased with modification, with values of 13 ± 0.15 %, 12 ± 0.17 %, 11 ± 0.23 %, and 10 ± 0.13 % respectively. Earlier reported OAC was slightly higher values (17.00 ± 1.37 %) [34].

Dispersibility

NS dispersibility decreased with modification. When particles collide, their kinetic energy increases, and they do not sink to the bottom which further results in dispersion stability depicted in Table 1[9]**.**

Micromeritic properties

Bulk density

The bulk densities (BD) were between 0.41–0.82 g/cc. NS contains the lowest BD (0.41 g/cc). However, after modification, bulk densities of starch were increased, and PM-3 was the highest (0.82 ± 0.21 g/cc) [36].

Tapped density

Tapped densities were 0.52 ± 0.01, 0.62 ± 0.04, 0.89 ± 0.13, 0.91 ± 0.71, and 0.93 ± 0.04 g/cc of NS, UMS, PM-1, PM-2 and PM-3.

Carr's index and hausner's ratio

The PM-3 shows a lower Carr's index (11.82 ± 0.34) and Hausner's ratio (1.13 ± 0.06) indicating good flow.

Angle of repose

The Angle of repose of NS and UMS was 33.35 ± 1.06, and 32.16 ± 0.60 indicates good flow properties and the value of PM-1, PM-2, and PM-3 ranged between 28.11 ± 0.71, 27.7 5± 0.22, and 26.35 ± 1.06, with excellent flow properties after modification [37] illustrated in Table 2. Micromeritic found PM-3 valuable for pharmaceutical industries. The Carr's index of pregelatinized starches exhibited a reduction as the pregealatinization time increased, signifying improved compressibility compared to NS. Additionally, a decrease in the angle of repose for all modified starches indicated enhanced powder flow properties. This improvement is likely attributed to the transformation of spherical starch granules into irregular shapes and the filling of void spaces with irregular particles in the pregelatinized and ultrasonicated starch [16].

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Table 2. Powder characteristics of NS and modified starch (UMS, PM-1, PM-2, and PM-3).

Sample	Bulk density (g/cc)	Tapped density (g/cc)	Carr's index (%)	Hausner's ratio	Angle of repose (^{0})
NS	0.41 ± 0.03	0.52 ± 0.01	21.15 ± 0.21	1.26 ± 0.03	33.35 ± 1.06
UMS	0.53 ± 0.01	0.62 ± 0.04	14.5 ± 0.61	1.16 ± 0.02	32.16 ± 0.60
PM-1	0.77 ± 0.49	0.89 ± 0.13	13.48 ± 0.02	1.15 ± 0.03	28.11 ± 0.71
PM-2	0.79 ± 0.71	0.91 ± 0.71	13.18 ± 0.51	1.15 ± 0.07	27.75 ± 0.22
PM-3	0.82 ± 0.21	0.93 ± 0.04	11.82 ± 0.34	1.13 ± 0.06	26.35 ± 1.06

Swelling and solubility power

The ability of starch to form hydrogen bonds with water molecules influences swelling volume. Because of intermolecular hydrogen bonding in amorphous regions, starch granules swell rapidly at temperatures below 70 °C [38,39]. The reported values for swelling power for the NS, UMS, PM-1, PM-2, and PM-3 were 9.58 ± 0.36, 14.37 ± 0.11, 17.41 ± 0.23, 19.21 ± 0.16 and 22.64 ± 0.22 % respectively illustrated in Table 3 [40]. For NS, UMS, PM-1, PM-2, and PM-3, the solubility percent values were recorded as14.32 ± 0.24 %, 19.57 ± 0.13 %, 22.36 ± 0.04, and 33.14 ± 0.24 % respectively illustrated in Table 4. [40]. The study showed that modified starches had a higher solubility index than native starches [41]. Thermal modification altered the granular structure of native starch, enhancing water absorption and improving drug release characteristics. Typically, the swelling power of starch is influenced by the level of amylose content and its water-holding capacity [16].

Field emission scanning electron microscope (FESEM)

The NS, UMS, PM-1, PM-2, and PM-3 micrographs are shown in Fig. 1. The NS and UMS starch were round to oblong in shape with a smooth surface and texture [42]. Pregelatinized starches were discovered to have an irregular shape, a rough surface and deep groves. The hydrothermal treatment restructured the modified starch granules causing an irregular shape and uneven texture. The groves and crevices on the surface of starch aid in trapping of the drug and facilitating immediate release drug delivery [43].

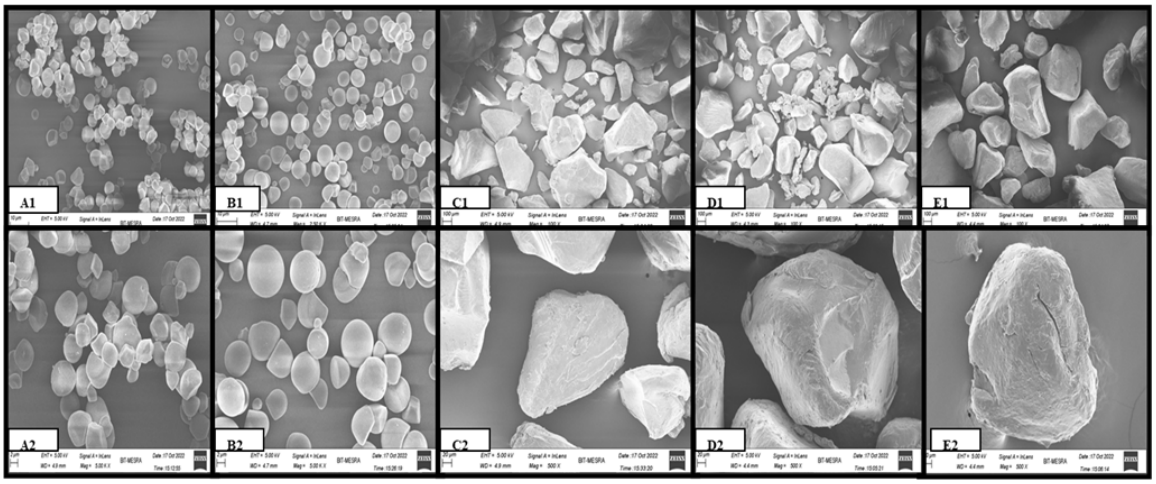

Fig. 1. FE-SEM (5.00kx),(1.00kx) of NS (A1 and A2), UMS (B1 and B2), PM-1 (C1 and C2), PM-2 (D1 and D2), PM-3 (E1 and E2)

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Thermogravimetric analysis (TGA)

Fig. 2, Fig. S2 illustrates the TGA curve of NS, UMS, PM-1, PM-2, and PM-3 revealing three distinct degradation patterns. The first mass loss occurred at 20 to 240 ºC possibly related to bound water evaporation. The de-polymerization of the starch structure causes the second and most significant mass loss in the temperature range of 240-456 °C. The oxidation of organic matter is responsible for the third mass loss between 456 and 600 °C [44]. The thermogram showed starches were chemically stable at 20 to 270 °C.

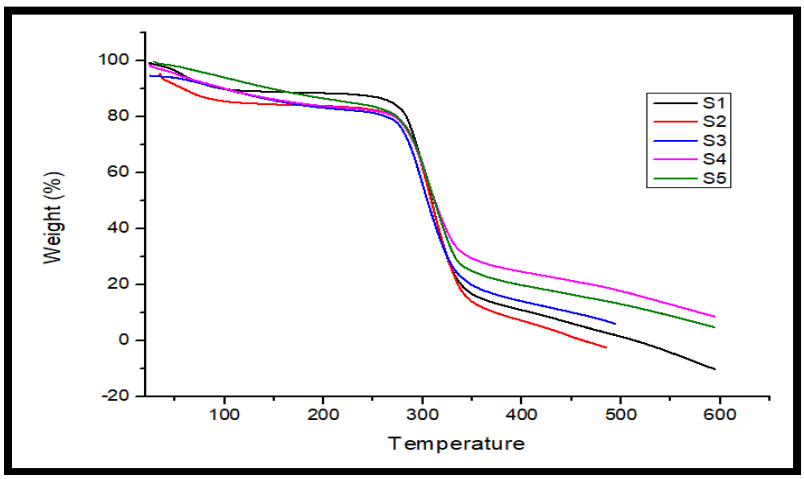

Fig. 2. Thermogravimetric Analysis of native and modified starch S1 (NS), S2 (UMS), S3 (PM-1), S4 (PM-2), S5 (PM-3).

Differential scanning calorimeter (DSC)

Fig. 3 illustrates the DSC curve. NS, UMS, PM-1, PM-2, and PM-3 starches exhibit wide variations in their PHI (φ), ΔH, transition temperatures (onset, peak and conclusion), transition temperature range (Tc -To). Three different peaks have resulted in NS, UMS, PM-1, PM-2, and PM-3 starches. NS has a low degree of crystallinity; it's enthalpy of gelatinization was significantly higher than PM-3. H gel indicates the loss of molecular order within the granules. *Artocarpus lakoocha* Roxb. seed starches (ASS) transition temperatures were higher than those previously reported starch [45].

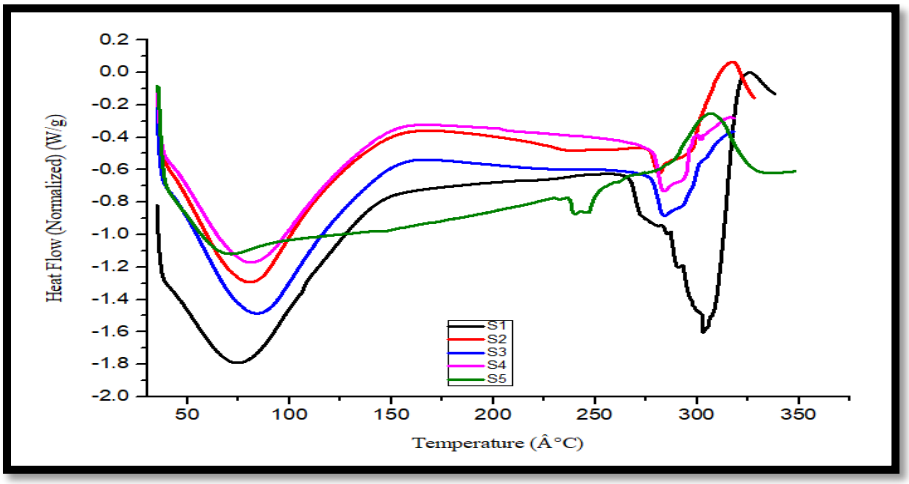

Fig. 3. DSC prepared from S1 (NS), S2 (UMS), S3 (PM-1), S4 (PM-2), S5 (PM-3).

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Fourier transform infrared spectroscopy (FTIR)

Fig. 4 shows the FTIR spectra of native and modified starches. The peaks in the 1000 cm^{-1} region indicated the glucopyranoside ring's presence. Pregelatinized starches resulted in a peak at 1055 cm^{-1}, which was caused by the starch recrystallizing during the modification process and the presence of OH stretching was characterized by broadband ranging from 3100 and 3300 cm^{-1}. The α- and β-type glycoside linkages were caused by absorption bands near 840 and 890 cm^{-1} [46]. A distinctive peak showed C-H stretching at 2931 cm^{-1} [47]. Asymmetric stretching of the C-O molecule has caused a small but sharp peak at 1650 cm^{-1}[48]. A peak caused C-O-C asymmetry stretching at 1092 cm^{-1} [49].

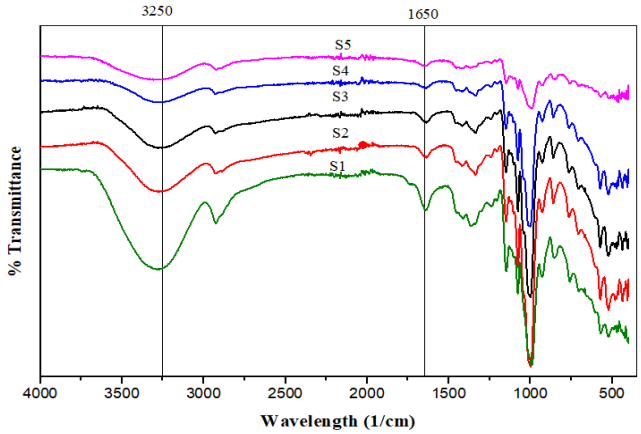

Fig. 4. FT-IR of NS and modified starch S1 (NS), S2 (UMS), S3 (PM-1), S4 (PM-2), S5 (PM-3).

X-ray diffraction (XRD)

The XRD patterns of NS, UMS, PM-1, PM-2, and PM-3 were shown in Fig. 5 and Fig. S3. The native starches NS and UMS were crystalline when compared to PM-1, PM-2, and PM-3 starches. The crystalline nature of the NS starches was demonstrated by their strong scattering peaks at 15.126°, 17.135°, 17.948°, 20.058°, 23.023°, 26.606°, 30.538°and 38.379° respectively and UMS at 15.151°, 17.161°, 17.916°, 20.058°, 23.073°, 26.538°, 28.981°, 30.453°and 38.173º. The diffraction pattern of pregelatinized starches revealed the lack of large peaks with very few sharp peaks at 17.177°, 22.289° and 34.106 º, showing a reduction in crystallinity due to heat treatment [16-17]. Pregelatinized starches decreased crystalline peak intensity which further suggests that a broken double helix and fewer crystalline amylopectin regions are present.

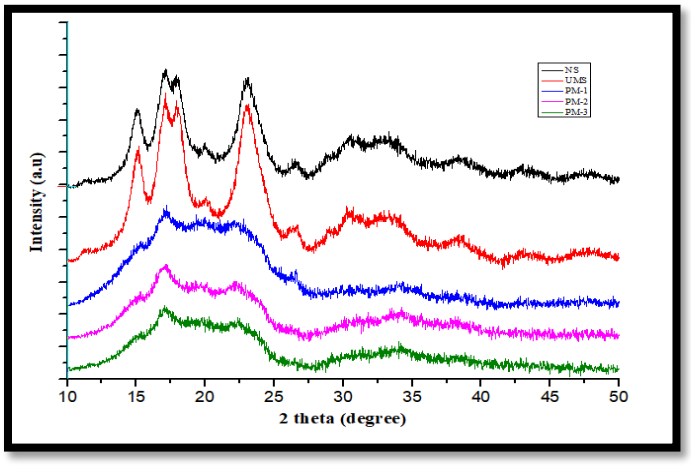

Fig. 5. X-ray diffraction of native and modified starch NS, UMS, PM-1, PM-2, PM-3.

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Evaluation of tablets

The physical parameters of the paracetamol tablets were shown in Table 5. All of the tablets, hardness, and friability were found to be within the acceptable range United States Pharmacopeia (USP). The Assay ranges from 99.82 to 104.29 %, and the average weight of all the tablets was found to be between 649.00 and 651.66 mg within the USP range. The disintegration time of tablets made with modified starch was shorter than those made with native starch. The amount of paracetamol was calculated from the line of the regression equation, y = 0.056x + 0.018, R^2=0.995 (Fig. S4) [12,15,20,24].

Table 5. Results of paracetamol tablets evaluation.

Sample	Thickness (mm)	Diameter (mm)	Hardness (Kg/cm^2)	Friability (%)	Weight variation (mg)	DT (min)
NS	4.22 ± 0.04	12.90 ± 0.04	6.50 ± 0.51	0.26	650.11 ± 0.42	3.15
UMS	4.32 ± 0.12	12.86 ± 0.02	6.60 ± 0.42	0.28	649.85 ± 0.45	2.45
PM-1	4.72 ± 0.07	12.91 ± 0.07	6.87 ± 0.01	0.27	650.56 ± 0.34	2.19
PM-2	4.27 ± 0.02	12.98 ± 0.01	7.66 ± 0.64	0.30	649.11 ± 0.75	2.15
PM-3	4.36 ± 0.03	12.88 ± 0.03	7.87 ± 0.22	0.31	651±23 ± 0.11	2.09

In vitro dissolution study

Fig. 6 illustrates an in-vitro dissolution study of tablets prepared with non-conventional native starch and modified starches along with commercial paracetamol tablets. All of the tablets demonstrated faster drug-release properties. However, when compared to the commercial and other modified starches, PM-3 demonstrated faster drug release. This could be because starch formed a loose granular structure, resulting in less binding capacity. The drug release was found to increase with increasing pre-gelatinization time. Finally, PM-3 can be a promising excipient for immediate-release formulations [12,16,20].

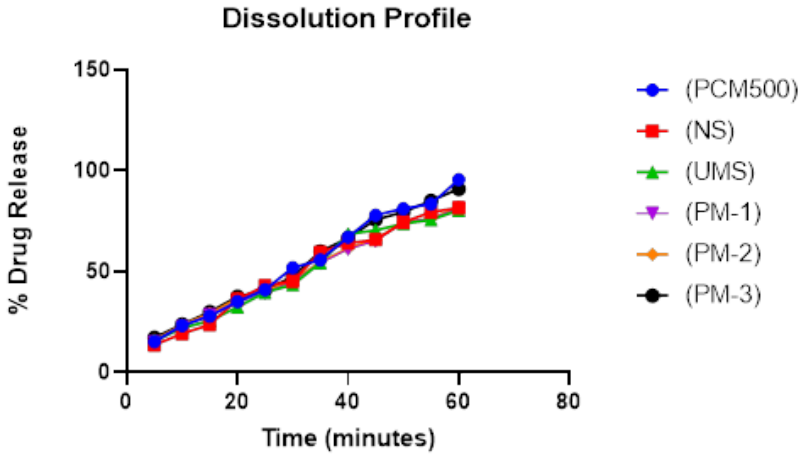

Fig. 6. *In vitro* release profile of paracetamol tablets using NS and modified starch (UMS, PM-1, PM-2, and PM-3).

Evaluation of suppositories

The absorption of suppositories at 243 nm standard value was 0.987. The amount of Acetaminophen was calculated from the line of regression equation y = 0.051x + 0.030, R^2 = 0.987 from Fig. S5.

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Table 6 summarizes the average results of the physicochemical test, and Fig. 7 shows the results of dissolution. The uniformity of mass of single-dose preparation test of all series of suppositories was found to be within 5 %, meeting USP requirements. The softening time of all suppositories was found to be within the USP range. All suppositories were dissolved within 60 minutes. The percentage of drug release of paracetamol suppositories was determined at a body temperature of 37°C. The percentage was 99.05 %. The use of modified starch as a physicochemical active suppository excipient appears to be promising [14].

Table 6. Results of paracetamol suppositories evaluation.

Sample	Average weight (g)	Softening time(min)	Disintegration time(min)	Drug content (%)
NS	1.319 ± 0.01	24.31 ± 0.03	14.32 ± 0.02	83 ± 0.06
UMS	1.326 ± 0.06	28.2 ± 0.01	17.43 ± 0.04	85 ± 0.02
PM-1	1.349 ± 0.02	20.32 ± 0.05	20.87 ± 0.03	89 ± 0.01
PM-2	1.352 ± 0.01	18.78 ± 0.02	15.21 ± 0.01	90 ± 0.03
PM-3	1.354 ± 0.03	15.31 ± 0.01	10.26 ± 0.02	95 ± 0.02

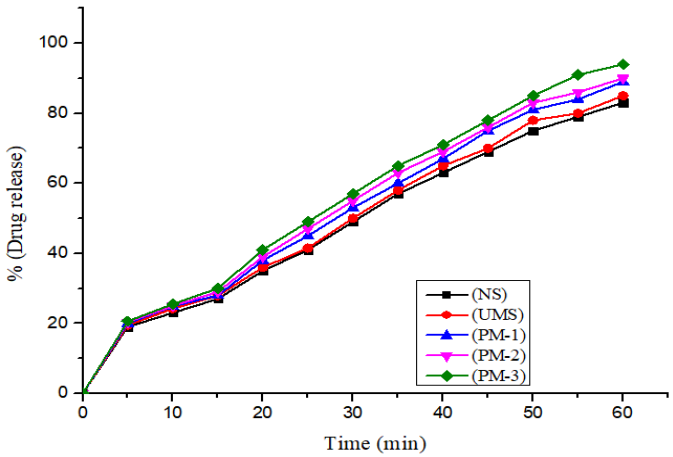

Fig. 7. *In vitro* release profile of Acetaminophen suppositories using NS and modified starch (NS, UMS, PM-1, PM-2, and PM-3).

Conclusions

In this study, we thoroughly examined the physicochemical and functional properties of non-conventional native and modified starches derived from *Artocarpus lakoocha* seeds. We found that these seeds yielded a starch content of 50 % (w/w). Through our investigations, we observed significant improvements in the physical characteristics of the starch after modifying the amylose content. Specifically, properties such as swelling power, solubility, WHC, and OAC exhibited enhancement. Our analysis using techniques like FTIR confirmed the presence of carbohydrates in native and pregelatinized starches. Furthermore, the hydrothermal treatment led to a notable reduction in crystallinity, which was substantiated by XRD and FESEM micrographs of both native and modified starches. Thermal stability, as revealed by TGA, demonstrated the suitability of these starches for various applications. Tablets formulated with both native and modified starches exhibited

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favorable in-vitro drug release profiles, underscoring their potential as excipient for immediate-release dosage forms. Additionally, the improved flow properties of the modified starches proved advantageous during tablet formulation processes, including mixing and compression. Our study also delved into the impact of starch hydrolysates on various physicochemical properties of suppositories. Notably, we found that starch hydrolysates could serve as cost-effective pharmaceutical aids, enhancing the physicochemical characteristics of suppositories. In summary, our investigation highlights *Artocarpus lakoocha*-derived non-conventional native and modified starches as promising excipients for immediate-release dosage forms. These findings offer potential avenues for the development of efficient pharmaceutical formulations.

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