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Physicochemical properties of tablet dosage form based on pre-gelatinized- and phosphorylated- modified starches from white-water yam (*Dioscorea alata* L.)

Original Paper

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Abstract **Background:** White-water yam (*Dioscorea alata L.*) is one of the potential sources of starch; however, it is not yet available for commercial purposes. Besides, native white-water yam starch (WS) presents limited functionality due to poor flowability, mechanical properties and instability at high temperature and acidic conditions. Therefore, this study aims to modify the starch to improve its characteristics and make it useful as an excipient for the preparation of the tablets.
Materials and methods: The modification of WS was achieved by physical and chemical treatments, specifically pre-gelatinization and phosphorylation, respectively. Pre-gelatinization WS involves heating, meanwhile phosphorylation WS is obtained by treating WS with sodium tripolyphosphate.
Results: The results showed that the powder of the modified WS has good characteristics which improved the flowability of the powder mixture as a granule based on density, porosity, compressibility index and swelling power determination. The WS granules were found to display the oval or irregular (polygonal) shape with the amylose content 11.92±0.61% for unmodified WS, 10.41±0.90% for pre-gelatinized WS and 12.61±1.75% for phosphorylated WS. Furthermore, the granule was formulated as an excipient in tablet preparations, and the formulas were compressed after wet granulation. The mechanical properties of the tablets were assessed using uniformity of mass and size, hardness, friability and disintegration time. WS modification affects the hardness of tablets when used as a binder. Phosphorylated WS is recommended to be used as a binder in wet granulation formulations because it produces tablets with a longer disintegration time, which means better binding ability. However, the utilization of modified WS with both pre-gelatinization and phosphorylation leads to tablets with low brittleness compared to others with unmodified binder with the disintegration time still met the requirement of fast disintegrating tablet (<15 minutes).
Conclusion: All the physical properties studied indicated that the modified WS is a promising pharmaceutical excipient in tablets.

Keywords *modified-starch – white-water yam – pre-gelatinization – phosphorylation – tablet excipient*

INTRODUCTION

White-water yam (*Dioscorea alata* L.) is one of the climbing plants of the Dioscoreaceae family with a height of up to 12 m. They grow up to 800 m above sea level on a flat land and are still planted with the elevation of up to 2,700 m above sea level. Furthermore, it is a potential source of starch used as an excipient in tablet formulation; however, it is not yet available for commercial purposes (Jiang et al., 2023; Oliveira et al., 2021).

Starch is one of the most commonly used excipients in tablets where they are used as diluents, binders and disintegrants. Native starches consist of 20% water soluble (amylose) and 80% water insoluble (amylopectin) (Rowe et al., 2012). The amount of amylose is directly associated with the water-absorbing properties and exhibited a good swelling power leading to the disintegration of solid bridges. In contrast, the amylopectin is more sticky and tends to form a highly viscous gel when suspended with water. Amylopectin has the ability to form aggregates through the binding process between particles which shows more binding properties (O. Kunle, 2020).

In tablet formulation, the utilization of white-water yam starch (WS) in its unmodified form is limited due to its unfavourable characteristics such as poor flowability, low mechanical properties and instability at high temperatures and acidic condition (Alcázar-Alay and Meireles, 2015). Therefore, unmodified WS is not widely used, and its modification is needed to enhance some physicochemical properties such as morphology, flowability and compressibility for industrial application. Compared to native starch, physically treated starch by pre-gelatinization exhibits more organized chains, greater paste stability and stronger gels, with greater resistance to shear and heat even after of extreme situations, such as acid or heating conditions (Lawal et al., 2014). Meanwhile,

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chemically treated starch by phosphorylation improves the flowability of starch when used in tablets (Onwuatuegwu et al., 2019). Furthermore, the modified WS undergoes a physical or chemical treatment that changes the granular structure and modifies its functional properties, which makes WS suitable for certain purposes (Ashogbon and Akintayo, 2014). One of its advantages is that the disintegration time does not depend on the compressive force (B. M. Rahman et al., 2008). Chowdary et al. (2011) reported that the modified starch has a good compressibility index and flow properties. Changes in morphology and density contribute to the enhancement of these properties, allowing the use of the modified starch as a tablet excipient by either granulation or direct compression method.

In the present study, paracetamol tablet, which is one of the widely used analgesic–antipyretic drugs, is being formulated. In order to achieve a good flow and compressibility properties, WS was first modified physically and chemically and then characterized to evaluate the mechanical properties of granules and tablets. Finally, the modified WS was used as a binder in tablet formulation by the wet granulation method. The aim is to investigate the effect of the chemically or physically modified WS (in pre-gelatinized or phosphorylated form) used as a binder in paracetamol tablets on the main characteristics, such as flowability of granules affecting the compressibility of the material and final properties of the tablets.

EXPERIMENTAL

Materials

Tubers of white-water yam (*Dioscorea alata* L.) were obtained from the Banggai Islands in Central Sulawesi. Acetic acid, ethanol, hydrochloric acid, iodine solution, sodium tripolyphosphate and sodium hydroxide were purchased from Merck (Germany) and Sigma (UK). Excipients such as magnesium stearate, talc, lactose and Avicel pH 102 were purchased from Bratachem (Brataco PT, Indonesia). All reagents used were of an analytical grade.

Starch isolation

Preparation of isolated starch was carried out according to the method of Lim and Seib (Lim and Seib., 1993) with modifications. Six months old tubers of white-water yam (*Dioscorea alata* L.) were peeled, washed and cut into small pieces. These pieces were then soaked in salt water to remove toxic compounds found in the white-water yam mucus and crushed into a fine pulp. Subsequently, the slurry was collected in a container, suspended with distilled water and filtered repeatedly through a flannel cloth until the filtrate becomes clear. The precipitated starch from the suspension was kept in a jar for 24 hours to settle, and the supernatant with starch was dried at a temperature of 60 °C for 1x24 hours and passed through an 80-µm mesh sieve.

Starch modification

Physical modification: Preparation of pre-gelatinized starch

A total of 10% (w/v) starch powder was suspended in distilled water and heated at 70 °C while stirring at 100 rpm for 30 minutes. The suspension was allowed to cool to room temperature and then decanted. The water layer was removed, and the bottom was oven-dried at 40°C for 48 hours. The dry starch powders were grinded for 5 minutes. For further processing, the fraction which passed the 80-µm mesh sieve was used (Odeku et al., 2008).

Chemical modification: Preparation of phosphorylated starch

Phosphorylated starch was prepared using the Khondkar method with modification (Woo and Seib, 2002). A 50% (w/v) starch mixture was stirred at 200 rpm and 40 °C for 30 minutes, and then sodium tripolyphosphate was added. The pH level was checked before adjusted to 9 using sodium hydroxide 1N. The mixture was then stirred again at 200 rpm and 40 °C for 2 hours. To stop the reaction, hydrochloric acid 1N was added until a neutral pH was reached. The starch was filtered using a cloth, and the residue was washed using cold water. It was then dried in an oven and then passed through a sieve with a diameter of 80 µm.

Characterization of WS

Organoleptic and morphological properties

All organoleptic tests (colour, odour and taste) were performed by human sense organs to study the visual appearance of native and modified WS. Each 1 g of samples was visually analysed by a human panel, consisting of three trained undergraduate students from the Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Tadulako University. The shape and surface morphology of the powders were determined using a scanning electron microscope (FEI S50®).

Loss on drying and moisture content

The porcelain crucible with the lid was pre-heated at 105 °C for 30 minutes, and the weight was recorded (Wo). While compacted, 1 gram of WS was placed in the porcelain crucible until they were evenly distributed. The sample was heated in an oven at 105 °C with the lid removed until a constant weight was obtained (W'). The porcelain crucible was left to cool to room temperature in a desiccator. Furthermore, loss on drying and moisture content were determined by the following equations (European Pharmacopoeia, 2019) :

$$Loss\ on\ drying = \frac{Wo - W'}{Wo} x\ 100\% \quad (1)$$

$$Moisture\ content = \frac{Wo - W'}{W'} x\ 100\% \quad (2)$$

Bulk and tapped densities

The bulk and tapped densities were determined according to European Pharmacopoeia methods under modification. A total of 10 grams of WS was placed into a 50 mL measuring cylinder, and the initial volume was recorded (V_o). The measuring cylinder was tapped for 500 times until the WS volume reached the minimum, and the final volume was noted (V'). The tests were performed in triplicate according to the European Pharmacopeia. Bulk and tapped densities were calculated using the following formulas (European Pharmacopoeia, 2019) :

Bulk density = mass of powder (g)/bulk volume (V_o) (3)

Tapped density= mass of powder (g)/tapped volume (V') (4)

Apparent particle density

A pre-weighed pycnometer with a 25 mL volume was filled with liquid paraffin and sealed, and excess fluid was washed off. The filled pycnometer was weighed. Then, 1 g of the WS powder was added and then refilled with liquid paraffin, sealed, wiped clear of any excess fluid and reweighed. Three sets of determinations were made (Nwachukwu and Ofoefule, 2020).

Porosity

Porosity of a powder was defined as the proportion of a powder bed or of a compact occupied by pores. It defines a measure of the packing efficiency. Its total porosity consists of the gaps and pores between and within the particles, respectively (European Pharmacopoeia, 2019).

$$Porosity = 1 - \left(\frac{bulk\ density}{apparent\ particle\ density}\right) \quad (5)$$

Flowability

Flowability and degree of densification during tableting were evaluated using parameters such as Hausner ratio and Compressibility index, respectively (European Pharmacopoeia, 2019).

$$Hausner's\ ratio = \frac{Tapped\ density}{Bulk\ density} \quad (6)$$

$$Compressibility\ index = \frac{Tapped\ density - bulk\ density}{Tapped\ density} x100\% \quad (7)$$

The flow rate was determined by pouring 5 grams of WS slowly into a steel funnel over the edge of the funnel. Its lid was opened slowly, and the time was recorded using a stopwatch until all the granules flow out as g/sec (Odeku et al., 2008).

Swelling power

A total of 10 mL of a 1% (w/v) WS suspension in water was prepared in a test tube and then heated in a water bath at a constant temperature of 70°C for 30 minutes while stirring continuously to avoid the formation of sediments. The tube was then centrifuged at 5000 rpm for 15 minutes, and the supernatant was separated by decantation. Subsequently, the sediment was taken and weighed, and the swelling power was expressed as the weight of sediment to the mass of dry WS.

Determination of the amylose and amylopectin contents

Determination of the amylose content was carried out using the colorimetric method. A total of 100 mg of WS powder was weighed and defatted by adding 1 mL 95% p.a ethanol and 9 mL of NaOH 1 N. It was then heated in a water bath for 10 minutes to gelatinize. The gel was transferred into a 100 mL volumetric flask and diluted to the mark with distilled water out of which 5 mL was carefully pipetted, transferred to a volumetric flask (size 100 mL), and added with 1 mL of 1 N acetic acid and 2 mL of iodine solution (0.2% iodine in 2% potassium iodide), and then, it was diluted with distilled water and left for 20 minutes. The absorbance was measured using a UV–visible spectrophotometer (Spectroquant®) at a wavelength of 625 nm. The amylose content in WS was determined using a comparative calibration curve for amylose at concentrations of 2, 4, 6, 8 and 10% (w/w). The amylose content in starch was calculated according to the following equation (Farhat et al., 1999):

$$Amylose\ content = \frac{Amylose\ in\ standard\ curve}{sample} \times the\ dilution\ factor x100\% \quad (8)$$

Amylopectin contents were determined by subtracting the amylose contents from the total of 100 mg starch analysed (Reddappa et al., 2022; Sowbhagya and Bhattacharya, 1971). The reagents used include acetic acid, which functions in the breaking of starch granules, and iodine that gives colour to the solution. The iodine solution was bounded by amylose in water, and therefore, its content was measured.
Furthermore, this high amylose content is difficult to gelatinize because the molecules tend to be in parallel positions. Consequently, the hydroxyl groups are able to bind freely forming strong aggregate crystals. However, starch with high amylopectin levels shows fewer binding properties because the chains are branched, while those with low amylopectin levels are prone to gelatinize (Fredriksson et al., 2000).

Preparation of tablets

Tablets were prepared using the wet granulation method with a weight of 650 mg/tablet. Unmodified WS and modified WS were used as a binder. Three different types of WS were applied onto the tablet formulation (Table 1). A 6% w/v binder solution was prepared by mixing the WS with water. The binder solution was *sprayed* onto a dry mixture of paracetamol, Avicel pH 102, and made up with lactose until a dough mass was formed. The blended mass was sieved with a 16-mesh sieve. Furthermore, the wet granules were dried in a hot air oven at 50 ^{0}C for 30 minutes. The dry granules were passed through a 20-mesh sieve, then blended with magnesium stearate and talc until homogeneous, and compressed using a single punch tablet press machine.

Table 1. Formulation of Paracetamol Tablets.

Ingredients	Concentration (%w/w)		
	F1	F2	F3
Paracetamol	77	77	77
Avicel pH 102	5	5	5
Unmodified WS	6	-	-
Pre-gelatinized WS	-	6	-
Phosphorylated WS	-	-	6
Talc	2	2	2
Magnesium stearate	1	1	1
Lactose	9	9	9

Evaluation of the physical properties of the tablet

Uniformity of mass

Mass uniformity test was conducted by following guidelines of European Pharmacopoeia. A total of 20 tablets of each formulation were taken at random and individually weighed using a digital analytical balance. The average mass and percent deviation of each tablet were calculated (European Pharmacopoeia, 2019).

Tablet thickness and diameter

The study of the tablet thickness was conducted by following the European Pharmacopoeia guidelines. A total of 20 tablets of each formulation were taken at random, and the diameter and thickness of each tablet were measured using a calibrated Vernier calliper. Unless stated otherwise, the diameter of the tablet is not more than 3 and not less than $1^{1}/_{3}$ times the thickness of the tablet (European Pharmacopoeia, 2019).

Hardness test

Tablet hardness was determined by following the guidelines of the European Pharmacopoeia using a tablet hardness tester (Electrolab EL-500). A total of 6 tablets were placed in the hardness tester, and when the tablet was compressed to break, the hardness was recorded in units of Newton (N). The requirements for a conventional tablet hardness value are 40–80 N (Dulla et al., 2018).

Friability test

The tablet friability test was examined using a friabilator European Pharmacopoeia test apparatus (Electrolab EF-2W). The 20 de-dusted tablets were weighed and placed into the friabilator tester. The machine was rotated at 25 rpm for 4 minutes after which the tablet was de-dusted and re-weighed. The acceptable friability of the tablets is less than 1%. The friability was expressed as a percentage according to the following formula (European Pharmacopoeia, 2019):

$$\% \text{ Friability} = \frac{Wo - W1}{W0} \text{ x } 100\% \quad (9)$$

where Wo is the initial weight and W1 is the final weight.

In-vitro disintegration time

The in-vitro disintegration time of the tablet was applied according to the European Pharmacopoeia requirements for uncoated tablets using a disintegration tester (Electrolab 2 station tester model ED-2L). Each of the tubes in the basket was inserted with 1 tablet and a disk was added. Phosphate buffer of pH 5.8, which was kept at 37 ± 2 ºC, was used as the immersion liquid. No fewer than 16 of the 18 tablets tested were completely disintegrated for a maximum of 15 minutes. The time it took for the tablets to completely disintegrate was then noted (European Pharmacopoeia, 2019).

Statistical analysis

The analyses were carried out using one-way analysis of variance in SPSS v. 26.0.0 (IBM, SPSS Statistics, Chicago, IL, USA). Significant differences between the results were calculated using analysis of variance (ANOVA). Differences at $p < 0.05$ were considered significant

RESULTS AND DISCUSSION

Starch isolation

White-water yam (*Dioscorea alata* L.) was obtained from Banggai Islands in Central Sulawesi. This research was conducted at the Laboratory, Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Tadulako University. During preliminary research, it was reported that 2 kg of white-water yam produced 1 kg of starch, which is a 50% yield.

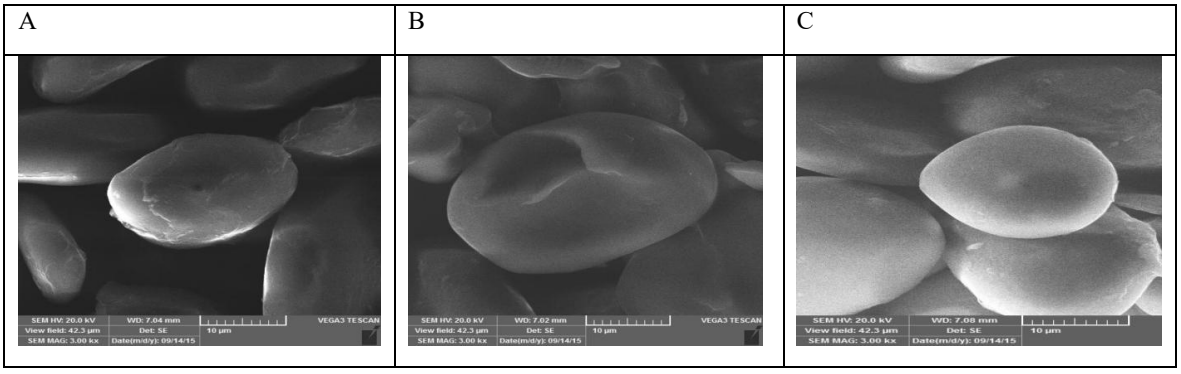


Figure 1. SEM results at 3000x magnification: A. unmodified WS, B. pregelatinized WS, C. phosphorylation WS.

Starch modification

The WS was modified using pre-gelatinization and phosphorylation methods. Heating the starch solution at optimum gelatinization conditions disintegrated the granule structure; therefore, some were dissolved in the amorphous state and then allowed to retrogradate to form aggregates or crystals (Reddy et al., 2013). Meanwhile, in the phosphorylation method, there was a substitution reaction of the phosphate group on the amylopectin hydroxy group causing starch to become more hydrophilic and also increasing the water-binding capacity, therefore raising the starch swelling power (Lewicka et al., 2015). As a phosphorylation reagent, sodium tripolyphosphate (STPP) has the benefits of safety, low cost and ease of use. It has also been given FDA approval as a food additive. From the perspective of toxicology, it is safe and feasible to modify WS with STPP (Miedzianka and Pęksa, 2013; Wang et al., 2019). Each of these methods yielded product with specific characteristics, and consequently, they are expected to produce starch as an excipient for both wet granulation and direct compression.

Characterization of the WS

The characterization was carried out to determine whether the powder met the established criteria and standards as well as to determine whether it could be used as an excipient, especially during tablet compression.

Organoleptic and morphological properties

Organoleptic testing was carried out by observing the colour, odour and taste of WS. It aims to determine whether the material is WS, which is detectible with the physical characteristics. The results indicated a white, odourless and tasteless powder. Furthermore, the unmodified and modified WS results showed relatively the same characteristics and agree with pharmacopoeia requirements (European Pharmacopoeia, 2019).

Micrographs of WS obtained observing starch arrangement as well as the shape of hilar and lamellae under a microscope with a magnification of 3000x. The results of the observations are presented in Figure 1.

These results indicate that WS granule shape tends to be oval or irregular (polygonal) because when the suspension is heated, its molecules become hydrated and expand. These oval-shaped granules have a smooth surface without pores. Furthermore, larger particles with this shape flow completely; therefore, they are more homogeneous when mixed. These findings are consistent with previous observations that starches from kernel of Trapa species are oval in shape with a smooth surface and a central hilum (Gao et al., 2014). In the meantime, rice and corn starch granules had a polyhedral shape with sharp edges and a generally smooth surface (Ali et al., 2016). There are differences in the shape and size of the starch granule particles due to variations in the amylose and amylopectin contents and their structure. Also, the size and shape depend on biological factors. The shapes of granules are influenced by individual modifications; therefore, in this study, their morphology for each modification was different both physically and chemically (Jiang et al., 2012).

Moisture content

The moisture content test showed that the WS that fulfils standard requirements was the modified type (4.12±0.19 and 3.13±0.10 for pre-gelatinized and phosphorylated WS, respectively) with a good moisture content of 1–5% (w/w). Meanwhile, the unmodified WS had the greatest moisture content (6.89±0.80). The moisture is to be kept within a limit as high values make the material adhere to the punch and die during tablet compression. Also, insufficient humidity usually makes the tablet become brittle (Probst et al., 2013). The results showed that WS modification affects the moisture content, with phosphorylation modification showing a lower moisture content compared to that of pre-gelatinization modification. The moisture content also affects the flow properties. Furthermore, high humidity interferes with the

Table 2. Characteristics of Modified and Unmodified Water yam Starch (WS) Powder

No	Powder Characteristics	Unmodified WS	Pre-gelatinized WS	Phosphorylation WS
1	Loss on drying (%)	6.45±0.69	4.04±0.18	3.04±0.09
2	Moisture content (%)	6.89±0.80	4.12±0.19	3.13±0.10
3	Tapped density (g / ml)	0.60±0.02	0.54±0.02	0.60±0.02
4	Apparent density (g / ml)	2.50±0.47	1.00±0.12	1.28±0.03
5	Bulk density (g / ml)	0.43±0.01	0.48±0.01	0.54±0.02
6	Porosity (%)	82.53±2.80	50.95±7.73	58.24±0.63
7	Hausner ratio	1.40±0.04	1.11±0.00	1.12±0.00
8	Flow rate (g / s)	Does not flow	5.53±0.01	4.05±0.05
9	Compressibility index (%)	28.56±2.24	9.68±0.27	10.72±0.34
10	Swelling power	3.65±1.15	3.81±3.06	5.09±4.16

flow of granules into the mould hole due to the increasing thickness of the water-adsorbing layer, which elevates the liquid bridge formed between the powder particles.

Density

Density test on modified and unmodified WS aims to determine their effect on the properties of powder flow. This parameter indirectly affects material compressibility. Particles with high density are generally free flowing (Probst et al., 2013). Furthermore, the specific gravity is generally divided into three types: bulk, tapped and apparent particle density. The different values for the modified WS were due to the modification process leading to changes in the density and particle sizes. Meanwhile, this value was used to determine porosity, Hausner ratio and compressibility index of modified and unmodified WS. The porosity or hollow state is used in describing the level of powder consolidation. In addition, the oval-shaped particle had a fixed porosity value requirement of 36–40%. These results presented in Table 2 show that the porosity value of modified WS (50.95±7.73 and 58.24±0.63 for pre-gelatinized and phosphorylated WS, respectively) is better than without modification (82.53±2.80). Furthermore, an increase in porosity and density values generally results in a decrease in the amount of drug content per tablet.

Flowability

Table 2 shows that WS without modification flows less and has a poor compressibility index as indicated by the Hausner ratio and compressibility index. Meanwhile, the loss on drying test for both groups showed that the modified type agrees with the requirements for loss on drying of starch according to the Pharmacopoeia which is below 15% (European Pharmacopoeia, 2019).

The compressibility index (*Carr's index)* is also a parameter to evaluate the flow properties of a powder (Sarraguça et al., 2010). Table 2 shows that modified WS (9.68±0.27 and 10.72±0.34 for pre-gelatinized and phosphorylated WS, respectively) fulfilled the requirements (very good/excellent category), while the unmodified WS is categorized as having poor granular compressibility index. In addition, this parameter is related to the ease of compression, hardness and brittleness of the tablet. For elastic particles, when the pressure is withdrawn, it returns to the original shape; hence, when pressed, they produce a soft tablet; however, this is in contrast with plastic particles.

The basic properties which affect flow properties include size, shape, particle surface area and density. Spherical (oval/spherical) particles generally flow better than irregular ones, while powders have less flow properties compared to large particles. Furthermore, granules with smooth surfaces have better flow properties than those with rough surfaces (Fu et al., 2012). Starch modification using heat produces aggregates with large-sized particles.

The flow property is also influenced by the Hausner ratio. A powder with good flow properties usually have a Hausner ratio ranging between 1.00 and 1.18. The results showed that both modified WS met the category of free flow granules based on the Hausner ratio (1.11±0.00 and 1.12±0.00 for pre-gelatinized WS and phosphorylated WS, respectively) values except unmodified WS (1.40±0.04). The lower the Hausner ratio and Carr's index of a material, the better flowability it has, but the poorer the compressibility (Odeku et al., 2008) (Shah et al., 2008). Thus, the modified WS offers a utilization of being used as an excipient for the wet granulation method.

Swelling power

Table 2 shows that phosphorylated WS has the highest swelling power (5.09±4.16). Meanwhile, this characteristic was associated with the higher amylose levels (12.61±1.75) as this polymer is more soluble in water. The factors that influence starch swelling include amylose–amylopectin ratio, molecular weight distribution, chain length and degree of branching and conformation (Cornejo-Ramírez et al., 2018). The swelling process generally occurs in the amorphous region. When exposed to heat, weak hydrogen bonds between molecules

Table 3. Determination of Amylose and Amylopectin content of WS

Water yam starch (WS)	Amylose (%) ($\bar{x}\mu\pm$ SD)	Amylopectin (%) ($\bar{x}\pm$ SD)
Unmodified WS	11.92±0.61	88.08±0.61
Pre-gelatinized WS	10.41±0.90	89.59±0.90
Phosphorylation WS	12.61±1.75	87.39±1.75

Table 4. Physical properties of paracetamol tablet

Testing	Formula		
	F1	F2	F3
Weight (mg)	603.15±1.95	606.05±1.32	610.75±1.58
Diameter (mm)	12.12±0.04	12.10±0.02	12.10±0.01
Thickness (mm)	4.58±0.09	4.54±0.11	4.62±0.10
Hardness (Kgf)	5.20±0.11	6.42±0.09	7.81±0.08
Friability (%)	0.79±0.06	0.38±0.02	0.24±0.03
Disintegration time (minute)	1.88±0.73	8.04±0.97	12.45±0.80

in the amorphous region are broken, facilitating the water to permeate into the inner space of starch granules. The higher the temperature, the more molecules proceed from the starch granules (Alcázar-Alay and Meireles, 2015) (Yuniar et al., 2019). However, the swelling power of pre-gelatinized WS (3.81±3.06) slightly increased from that of unmodified WS (3.65±1.15). It is due to the amount of amylose between these two types of WS is not descriptively significant ($p>0.05$).

Determination of amylose and amylopectin contents

Table 3 shows that higher amylose levels are found in phosphorylation-modified WS (12.61±1.75%) compared to those of pre-gelatinization-modified WS (10.41±0.90%) and unmodified WS (11.92±0.61). Pre-gelatinization slightly reduced the amylose content of the unmodified starch as heating the starch suspension at the gelatinization temperature causes the intermolecular hydrogen bonds between the amylose chains and the amylopectin branch chains to weaken. These weak bonds allow water to enter the granules and expand rapidly. The expanded granules have a softer structure and are irreversible (Tako et al., 2014). Furthermore, phosphorylation considerably increases swelling due to the phosphate group in the amylopectin branch chain. In this reaction, at a slight temperature of 40°C, the outermost chain branches begin to open and bind the phosphate groups. In addition, the water (H_2O) molecule binds easily to the phosphate group, making it easier for it to penetrate the starch structure. Moreover, the high amylose content of phosphorylated WS makes it more water soluble; therefore, this polymer can be used as a potential tablet disintegrant. Meanwhile, amylopectin is the component which forms the crystalline lattice. In addition, its branched structure enables starch with high amylopectin levels to have better potential as a tablet binder.

Evaluation of the physical properties of the tablet

Paracetamol was utilized as the active ingredient due to its common use as analgesic–antipyretic drugs, especially in government health care facilities (11). Paracetamol has poor compressibility. Consequently, the quantity in one tablet is quite large (500 mg). Therefore, to produce tablets with satisfactory physical quality, the wet granulation method was used.

Uniformity of mass

This test aims to determine the uniformity of tablet mass. Those with uniform tablet mass usually contain a uniform amount of drug content per tablet, which is necessary to ensure the precise pharmaceutical dose. The measurement based on the number of deviations in the mean mass that are acceptable depending on the specified requirements. The mass of the tablets F1, F2 and F3 was 603.15 ± 1.95 mg, 606.05 ± 1.32 mg and 610.75 ± 1.58 mg, respectively, while the relative standard deviation was 0.32%, 0.22% and 0.26%, respectively. Based on these results, all formulas agree with the requirements of the European Pharmacopoeia (PhEur), which states that for tablets weighing above 250 mg, no more than 2 of the individual masses deviate from above 5% and none deviates by more than 10% (European Pharmacopoeia, 2019).

Thickness and diameter of the tablet

Tablet sizes need to be controlled as those with the same drug but with the different size not only confuse the patient but also cause packaging problems. When the volume of prepared materials is inconsistent, using dosing units becomes difficult. Based on the results, the diameter and thickness of the tablets are indicated as follows: F1 12.12 ± 0.04 mm and 4.58 ± 0.09 mm, F2 12.10 ± 0.02 mm and 4.54 ± 0.11 mm, and F3 12.10 ± 0.01 mm and 4.62 ± 0.10 mm. Therefore, with respect to the European Pharmacopoeia, these results indicated that all formulas fulfil the requirements for size uniformity, which state that the tablet diameter is not more than three times, while the thickness is not less than $1^1/_3$ (European Pharmacopoeia, 2019).

Hardness test

Tablet hardness reflects its overall strength. When it is too hard, it usually fails to crumble within the required timeframe or meet dissolution specifications. In contrast, when too soft, it lasts only temporarily during subsequent processes such as coating, packaging and distribution (Remington, 2016).

According to Dulla et al. (2018), the requirement for a good conventional tablet hardness value is 40–80 N. The results obtained in all formulas met the requirements as follows: F1 52.0 ± 1.1 N, F2 64.2 ± 0.9 N and F3 78.1 ± 0.8 N. From these results, it is evident that WS modification affects the hardness of tablets when used as a binder. Therefore, tablets made from the modified WS are harder compared to that from the unmodified WS, and this is due to the increased binding ability of the modified WS compared to that of unmodified WS.

Friability test

This test aims to evaluate the ability of tablets to withstand abrasion in the packaging, handling and distribution processes (Remington, 2016). The friability test is related to weight loss due to abrasion that occurs on the tablet surface. The greater the friability percentage, the greater the mass of tablets lost. The test results were as follows: F1 0.79 ± 0.06%, F2 0.38 ± 0.02% and F3 0.24 ± 0.03%. These results indicated that all formulas agree with the requirements for tablet friability which is less than 1% (European Pharmacopoeia, 2019). Furthermore, the use of different binders affects friability in each formula, while the use of modified WS with both pre-gelatinization and phosphorylation leads to tablets with low brittleness compared to others with unmodified binder. The best tablet formulas based on order of friability are F3, F2 and then F1. Meanwhile, the friability is influenced by the level of hardness. Therefore, tablets with high values are able to withstand weight loss due to the good adhesion and compactness between the granules and hence friability reduces.

In-vitro disintegration time

Disintegration time is the time taken for the tablet to disintegrate under specified conditions. For absorption, the active substances need to be in the form of a solution; hence, this test is a measure of the time it takes for tablets to completely disintegrate into particles (Markl and Zeitler, 2017). One of the factors that affects tablet disintegration time is hardness. Therefore, increasing this property inhibits water penetration into tablet pores, thereby extending the disintegration time. The tablet disintegration time (in minutes) obtained is as follows: F1 1.88 ± 0.73, F2 8.04 ± 0.97 and F3 12.45 ± 0.80, which shows all the formulas disintegrated rapidly. We compared the disintegration time of paracetamol tablets using modified WS with the brands of marketed tablet from previous research. The disintegration time of marketed tablets was faster than that of paracetamol tablets using modified WS, which was 3.95±0.93 minutes (M. Rahman et al., 2021). Furthermore, the differences in the disintegration time occur due to the distinct hardness in each formula, and hence, the greater the hardness of the tablets, the longer the disintegration time. The high hardness of modified WS usually makes it difficult for water penetration and the resultant breaking of the bonds between granules. Therefore, disintegration into constituent particles takes long time (Thapa et al., 2017). Although the disintegration time of paracetamol tablets using modified WS was longer (8.04 ± 0.97 and 12.45 ± 0.80 for pre-gelatinized WS and phosphorylated WS, respectively), the results still met the European Pharmacopoeia standards, which was less than 15 minutes for the uncoated tablet. Then, when the tablet disintegration time of the modified WS is compared to that of rice and maize starches, the modified WS disintegrates tablets faster because it has more amylose in its structure. The tablet's ability to disintegrate is affected by its high amylose concentration (Ali et al., 2016).

CONCLUSIONS

The modified starch of pre-gelatinized and phosphorylated white-water yam (WS) has a better flow rate and swelling properties compared to that of the unmodified starch. Other physicochemical parameters that we evaluated such as loss on drying (LOD), moisture content (MC), density and porosity also supported the flow characteristic of each granules tested. Phosphorylated WS is recommended to be used as a binder in wet granulation formulations because it produces tablets with a longer disintegration time, which means better binding ability. However, the utilization of modified WS with both pre-gelatinized and phosphorylation leads to tablets with low brittleness compared to others with an unmodified binder.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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