Research Article

Properties of Cocoyam Starch as Binders in Ibuprofen Tablets

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ABSTRACT

The study was undertaken to evaluate the suitability of native cocoyam starches as binders in ibuprofen tablet formulations. The starches were used as binders for 400 mg ibuprofen tablets produced by wet granulation at various concentrations (2, 4, 6 and 8 % w/w) and compressed at different punch settings (23-27 Pa). The produced tablets were evaluated for weight uniformity, hardness, friability and disintegration against corn starch tablets. The best operating conditions for the produced tablets were the punch setting of 24 Pa and binder concentration of 2 % w/w. Mzuzu cocoyam starch was found to be the most appropriate binder. Malawi needs therefore to exploit cocoyam starch in tablet formulations.

Keywords: starch, ibuprofen, binder, tablet, cocoyam starch.

INTRODUCTION

Starch, a polysaccharide obtained from roots, stems, tubers, fruits and seeds is used as an excipient in the pharmaceutical industry.[1, 2] Corn starch is the most utilized Excipient in the pharmaceutical industry while corn is a staple crop for most people in sub-Saharan Africa including Malawi.[3, 4] Most industries in Malawi use corn starch for tablet formation. [5] Increased food demands in the sub-Saharan Africa have necessitated the search for alternatives and starchy root crop like cocoyam (*Colocasia esculenta*) is a potential raw material. All the starches that are used in the Malawian industries are imported from South Africa, Zimbabwe, Tanzania, United Arab Emirates, China, India, Kenya and United Kingdom constituting corn, potato and wheat. [6, 7] The importation of starch has lead to loss of foreign currency and increased unemployment. [6, 8] Increased costs, supply capacity, availability and late deliveries are some of the major challenges the industries face due to starch importation. [9] Furthermore, the importation of the starches depends on the availability of foreign currency, hence the need to explore locally grown starchy root crops as alternative raw materials. [7]

Cocoyam (commonly known as *koko* or *masimbi* in Malawi) produces edible starchy tubers and vegetables. The corms are used as an important source of food which can be eaten boiled, roasted or fried. Cocoyams are rich in vitamin B_6 and magnesium which help in glucose metabolization and preventing high blood pressure. [10] For many years, the cocoyam plant has been used in traditional medicine. Cocoyam leaves are used as anti-poisonous agents against scorpion and snake bites. In addition, the plant is used in preventing and treating cancer, anaemia, asthma, arthritis, muscle cramps and diarrhoea.[11] The corm produces juice which is used to treat baldness and body ache.[12] There is need therefore to evaluate the suitability of the Malawian cocoyam starch for pharmaceutical use. Utilization of these starches can economically empower local farmers, create employment opportunities and save foreign currency. The study was therefore undertaken to establish the effect of Malawian native cocoyam starch as a binder in ibuprofen tablets.

MATERIALS AND METHODS

Materials

The study used cocoyam purchased from Thekerani and Mzuzu, Malawi. Ibuprofen powder, Ac-Di-Sol, Magnesium stearate and lactose monohydrate were purchased from Sandoz South Africa (PTY) Limited, Crest Chemicals (PTY) Limited, Warren Chem Specialties (PTY) Limited and Amchem (PTY) Limited (South Africa), respectively. Only analytical and pharmaceutical grade reagents and chemicals were used.

Starch extraction

Fresh tubers were washed with tap water, peeled, washed again, chopped to about 1 cm^3 cubes. The 1 cm^3 cubes were mixed with water and pulverized in a high speed blender (Waring Commercial, model 8011ES) for 5 min. The pulp was suspended in 10x its volume of tap water, stirred for 5 min and filtered using a double muslin cloth. The filtrate was allowed to stand for 2 h to facilitate sedimentation and the top liquid decanted as a waste. The sediment was re-suspended in 10x its volume of tap water, stirred for 5 min and filtered using a double muslin cloth. The filtrate was allowed to stand for 2 h for the starch to sediment and the top liquid decanted. The sediment was washed and air dried at room temperature for 48 h, pulverized into fine powder and stored in polyethylene containers for further analysis.[13]

Solubility of starches

Starch suspensions (2 %, w/w) were prepared in flasks in triplicate and heated to 50, 65, 75 and 85 °C, respectively, for 30 min with shaking every 5 min and then left to cool at room temperature for 15 min. The suspensions were centrifuged for 15 min at 3000 × g to separate gel and supernatant. The supernatant was dried in an oven for 2 h at 130 °C and the residue (A) obtained after drying represented the amount of starch solubilized in water. [14] The solubility was calculated using equation 1, where S is the sample weight.

$$\text{Solubility } (\%) = \frac{100 \times A}{S} \quad (1)$$

Moisture content of the starches

In order to determine moisture content in the starch samples, the hot oven method was used.[13, 15] Porcelain dishes with covers were washed and dried in an oven at 105 °C overnight, cooled to room temperature in a dessicator for 1 h, then weighed to the nearest 1 mg. Starch samples (3 g) in triplicates, were weighed in pre-heated, cooled and pre-weighed porcelain dishes to the nearest 1 mg. The dishes containing the samples were dried for 24 h at 105 °C, cooled in a dessicator for 1 h and immediately weighed after removal from dessicator to the nearest 1 mg. The moisture content was determined using equation 2:

$$\text{Moisture}(\%) = 100 - \left[100 \times \frac{(W_2 - W_0)}{(W_1 - W_0)}\right] \quad (2)$$

pH of starches

Starch samples (5 g) in triplicates, were weighed into a beaker and mixed with 20 mL of distilled water. The resulting suspension was stirred for 5 min with a magnetic stirrer and left to settle for 10 min. The pH of the water phase was measured using an 827 calibrated pH meter (Metrohn, Switzerland), which were calibrated using pH 4 and 7 buffers.[13]

Ash content of the starches

Ashing crucibles were carefully cleaned and heated for 3 h in a furnace at 575 °C. The crucibles were cooled to room temperature in a desiccator for 1 h and weighed to the nearest 0.1 mg. Approximately 1.0 g of the starch samples, to the nearest 0.03 mg was weighed in the pre-weighed crucibles. The crucibles with the samples were placed in a furnace at 300 °C overnight; removed from the furnace, cooled in a desiccator for 1 h at room temperature and immediately weighed after removal from desiccators. [13] The ash content was calculated using equation 3:

$$\text{Ash content}(\%) = 100 \times \frac{(W_2 - W_0)}{(W_1 - W_0)} \quad (3)$$

Formulation and compression of tablets

Batches (320 g) of basic formulations comprising ibuprofen, Ac-Di-Sol, magnesium stearate, starch and lactose were prepared. Accurately weighed amount of ibuprofen, lactose and Ac-Di-Sol were dry-mixed for 10 min in a mixer (Model T2C, willy A. Bachofen Maschinenfabrik, Switzerland). The mixture was moistened with appropriate amounts of starch mucilage to achieve various concentrations (2, 4, 6 and 8 % w/w) of the starch binders. The wet masses were granulated manually by passing them through a 10- mesh sieve, dried in a hot-air oven for 3 h at 50 ˚C, and re-sieved through a 20- mesh sieve. The obtained granules, magnesium stearate and Ac Di-Sol were measured and mixed for 10 min in a mixer. The resultant granules were stored in airtight containers for 2 days at room temperature. The granules were compressed into 400 mg tablets at compression pressure forces ranging from 23-27 Pa using a Cadmach single punch (Type SSF_3 Ahmedabad-India) tabletting machine and the produced tablets were stored in airtight bottles for 24 h at room temperature.[16,17]

Bulk and tapped densities of the granules

Granules (20 g), in duplicate, were weighed into a 50 mL measuring cylinder. The volume occupied by the granules was recorded as bulk volume. The cylinder was then tapped on the wooden platform height of 2.5 cm three times at 2 seconds intervals until the volume occupied by the granules remained constant. The data generated was used in computing the Hausner ratio (equation 4) and compressibility index (equation 5).

$$\text{Hausner ratio} = \frac{\rho_t}{\rho_b} \quad (4)$$

$$\text{Compressibility Index} = \left[\rho_t - \frac{\rho_b}{\rho_t}\right] \times 100 \quad (5)$$

where ρ_b is the bulk density (g/cm^3) and ρ_t is the tapped density (g/cm^3)

Weight and thickness of tablets

Twenty tablets from each batch were randomly selected and weighed individually using an electronic balance. Ten tablets from each batch were also selected at random and the thickness of the tablets was measured accurately to 0.01 mm using a digital caliper (Mitutoyo, England).[16, 18]

Friability of tablets

Twenty tablets were selected at random, put in a 10-mesh sieve, dedusted and weighed together using the electronic balance in duplicate and placed in the friabulator (Pharmatest, USA) for 4 min at 120 rev/min. The tablets were dedusted again and reweighed.[16, 18] The percentage losses were calculated for each batch of the tablets using equation 6:

$$\text{Friability}(\%) = 100 \times \frac{W_o - W_f}{W_o} \quad (6)$$

Disintegration of the tablets

The disintegration times of the tablets were determined in distilled water at 37 °C ± 0.5 °C using the disintegration testing apparatus (Erweka ZT500). Six tablets were selected at random from each batch placed in a cylindrical tube basket and supported on the wire mesh just above the surface of the water and the apparatus was started. The tablets were kept in contact with distilled water in the tube and the time taken for all the tablets to disintegrate and go through the wire mesh was recorded.[17, 19] The disintegration efficiency (DER, a measure of tablet quality) and disintegration parameter (DER_c) were also determined.[20]

$$DER = \frac{(C_s/F_t)}{D_t} \quad (7)$$

$$DER_c = \frac{DER_{test}}{DER_{ref}} \quad (8)$$

Where C_s = crushing strength, F_t = friability and D_t = disintegration time

Hardness of the tablets

Ten tablets were selected at random from each batch in duplicate and a hardness tester (Pharma test PTB 301) was used. The tablet was placed between spindle and anvil of the tester and the calibrated length adjusted to zero. The knob was screwed to apply a diametric compression force on the tablet and the position on the calibrated length at which the tablet broke was recorded.[16]

Statistical analysis of data

Analysis of variance (ANOVA) was performed using the Genstat Discovery 13th edition to establish the effect of cocoyam starches as binders in ibuprofen tablets. The statistically significant differences among means were tested at 95 % confidence interval.

RESULTS AND DISCUSSION

The moisture and ash contents, pH and solubility results of the starches are presented in Table 1. The moisture content for the starches ranged from 9.36-14.00 %; and these values fall within the recommended range of less than 15 %.[19] The ash content for the starches varied from 0.29 - 0.36 % and these values are within the required maximum of 0.6 %.[19] The obtained results are higher than those reported by Mweta; 0.14 % was obtained for cocoyam.[15] The pH values of the starches ranged from 4.35-5.85. The present results are lower than those reported by Mweta in which a high pH value of 6.4 was obtained from cocoyam.[15] Solubility of all the starches in water increased as the temperature was raised from 50 °C to 85 °C and differed at all temperatures ($p \leq 0.05$).

The bulk and tapped densities, Hausner ratio and Carr's compressibility of the starch based ibuprofen granules are presented in Table 2. The results indicated that the bulk and tapped densities were low indicating that the granules were not porous and are poor flowing. The low densities are due to void spaces created by larger powder particles. The flow ability of the granules decreased with increasing binder concentration for all the binders except Mzuzu cocoyam (6 % w/w). This means there was increased bonding and cohesiveness between particles leading to reduction in the flow of granules.[21] Granules prepared using Mzuzu cocoyam (6 and 8 % w/w) and Thekerani cocoyam (6 % w/w) exhibited fair and passable flow properties; the Carr's compressibility and Hausner ratio were below 25 % and 1.34 respectively. All the formed ibuprofen tablets gave acceptable uniformity of weight; no tablet afforded greater than 5 % deviation in weight. The weights of the tablets varied from 388 to 418 mg. The differences in weight variation were probably due to segregation of larger granules from the fines or non-uniform flow rate.[22]

The friability of the cocoyam based ibuprofen tablets are provided in Table 3. The results revealed that friability decreased with increasing pressure for Mzuzu cocoyam (at 6 and 8 %w/w) and Thekerani cocoyam (at 4, 6 and 8 %w/w). Friability value of less than 1 % is the required specification.[19, 23] The compression pressures of 26 and 27 Pa produced tablets which gave friability values of more than 1 % for all the starch varieties at all the concentrations except Mzuzu cocoyam (2, 6 and 8 %w/w) and Thekerani cocoyam (6 and 8 % w/w). The compression pressure of 24 Pa gave less than 1 % values for all the starch formulations and thus, the tablets had good mechanical strength to withstand pressure or stress during handling, packaging and transportation. As a result, the best compression pressure was 24 Pa because it produced tablets which were less friable.

Table 1: Functional properties of the native starches

Botanical source	Genotype	Functional property						
		Moisture content (%)	Ash content (%)	pH	Solubility (%)			
					50 °C	65 °C	75 °C	85 °C
Cocoyam	Thekerani	11.88 ± 0.67	0.36 ± 0.01	4.67	0.15 ± 0.04	1.58 ± 0.08	8.73 ± 2.62	15.69 ± 0.41
	Mzuzu	14.00 ± 0.02	0.31 ± 0.02	5.40	0.36 ± 0.05	1.63 ± 0.07	5.69 ± 0.05	10.85 ± 0.28
Corn	Corn	9.36 ± 0.30	0.29 ± 0.03	4.35	0.23 ± 0.04	1.69 ± 0.37	4.85 ± 0.81	8.84 ± 2.14

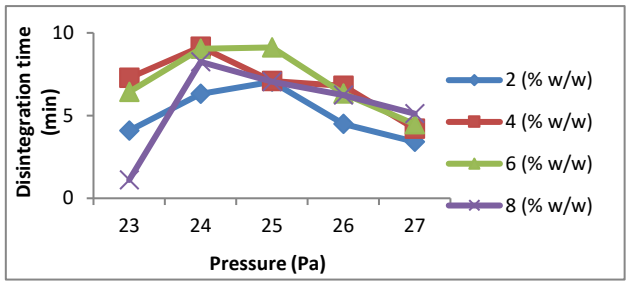
Table 2: Granule properties of starch based ibuprofen

Binder conc. (% w/w)	2				4				6				8			
Genotype	Bulked density	Tapped density	Hausner ratio	Carr's index	Bulked density	Tapped density	Hausner ratio	Carr's index	Bulked density	Tapped density	Hausner ratio	Carr's index	Bulked density	Tapped density	Hausner ratio	Carr's index
Thekerani	0.49	0.62	1.25	19.76	0.49	0.65	1.32	24.39	0.50	0.62	1.23	18.75	0.47	0.62	1.32	24.42
Mzuzu	0.48	0.66	1.37	27.12	0.48	0.66	1.38	27.38	0.49	0.62	1.26	20.73	0.48	0.60	1.25	20.24

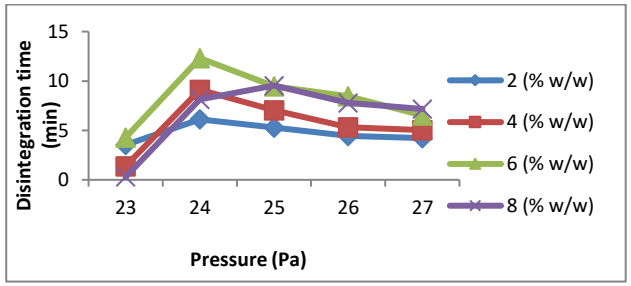
Table 3: Friability of ibuprofen tablets

Conc. (w/w)	2					4					6					8				
Setting	23	24	25	26	27	23	24	25	26	27	23	24	25	26	27	23	24	25	26	27
Mzuzu	0.31 ± 0.04	0.40 ± 0.04	0.39 ± 0.02	0.39 ± 0.02	2.19 ± 0.03	0.31 ± 0.01	0.47 ± 0.06	1.19 ± 0.09	4.81 ± 0.04	4.95 ± 0.09	0.34 ± 0.02	0.23 ± 0.02	0.40 ± 0.01	0.49 ± 0.02	3.81 ± 0.06	0.72 ± 0.03	0.35 ± 0.01	0.41 ± 0.03	0.45 ± 0.06	4.99 ± 0.01
Thekerani	0.28 ± 0.02	0.46 ± 0.06	0.42 ± 0.01	3.74 ± 0.11	4.92 ± 0.01	0.48 ± 0.01	0.42 ± 0.02	0.44 ± 0.06	3.61 ± 0.22	4.14 ± 0.06	0.39 ± 0.01	0.38 ± 0.02	0.43 ± 0.09	0.52 ± 0.02	4.97 ± 0.01	10.51 ± 0.67	0.36 ± 0.01	0.39 ± 0.04	0.42 ± 0.01	3.92 ± 0.06

The disintegration results of cocoyam starch based ibuprofen tablets are provided in Figure 1. The results show that all the tablets disintegrated within 15 min, the recommended maximum for the British pharmacopoeia for uncoated tablets.[19] Mzuzu cocoyam based ibuprofen tablets disintegrated in less than 10 min. The disintegration time increased with increasing pressure (23-25 Pa) and then decreased at higher pressure (26-27 Pa). Increasing compaction pressure either increases or decreases disintegration time.[24] At a pressure of 23 Pa, Thekerani cocoyam starch produced soft tablets which disintegrated in less than 1 min at 8 % w/w binder concentrations. The swelling mechanism induced disintegration easily probably due to ineffective binding between the particles. The 2 % w/w ibuprofen tablets disintegrated within 7 min at all the compression pressures and starch varieties. The results are understandable because a good disintegrant must be effective at low concentrations.[25] Eraga and co-researchers reported that the cocoyam tablets which they produced disintegrated within 7 min. [26]



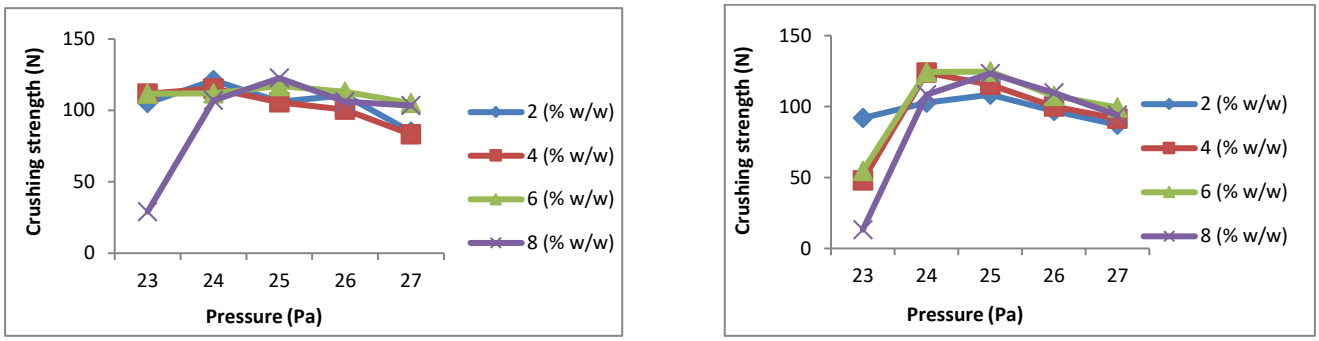
(a) Mzuzu cocoyam



(b) Thekerani cocoyam

Figure 1: Effect of pressure and concentration on the disintegration time of cocoyam starch based ibuprofen tablets

The hardness of cocoyam starch based ibuprofen tablets are presented in Figure 2. The hardness increased with an increase in binder concentration and compression pressure (23-25 Pa) for all formulations. The increase in hardness was due to strong bridges and tablet binding mechanism leading to greater association. High binder concentrations cause an increase in plastic deformation of the formulation, and formulation of more solid bonds which in return result in an increase in tablet strength.[17, 27] The minimum requirement for hardness is 4 kg or ≥ 60 N.[19, 28] Using a compression pressure of 23 Pa, Thekerani cocoyam (4, 6 and 8 % w/w) and Mzuzu cocoyam (8 % w/w) failed to comply with the specifications.



(a) Mzuzu cocoyam **(b) Thekerani cocoyam**

Figure 2: Effect of pressure and concentration on the hardness of cocoyam starch based ibuprofen table

Table 4: Hardness-disintegration ratio and disintegration efficiency ratio of ibuprofen tablets

Cultivar	Binder conc. (% w/w)	Hardness (N)	Friability (%)	Disintegration time (min)	HDR	DER	DER_c
Thekerani	2	102.70	0.46	6.12	16.78	36.48	0.47
	4	123.90	0.42	9.11	13.60	32.38	0.42
	6	124.50	0.38	9.44	13.19	34.71	0.45
	8	107.00	0.36	8.15	13.13	36.47	0.47
Mzuzu	2	121.10	0.40	6.31	19.19	47.98	0.62
	4	115.40	0.47	9.17	12.58	26.78	0.35
	6	111.90	0.23	9.05	12.36	53.76	0.70
	8	107.00	0.35	8.25	12.97	47.06	0.61
Corn		104.50	0.18	7.55	13.90	76.89	

Table 4 shows a comparison of the produced tablets at the punch setting of 24 with corn starch based ibuprofen tablets. The hardness of the tablet batches were within the acceptable range of ≥ 60 N and it was observed that the hardness increased with increasing binder concentration for most starches except Mzuzu cocoyam starch which decreased with increasing binder concentration. Thekerani (2 and 8 % w/w) and Mzuzu cocoyam (6 and 8 % w/w) starches produced tablets which were comparable in hardness to the corn starch ($p \geq 0.05$). It was found that increasing the binder concentration caused either a corresponding increase or decrease in friability of the tablets. The obtained friability values were less than 0.5 % for all the formulations.

The hardness-friability ratio (HFR) provides a parameter for measuring tablet strength.[29] The higher the HFR value, the stronger the tablet is.[17] However, the disintegration efficiency ratio (DER) can also measure the hardness and disintegration properties of tablets.[30] Tablets with good balance between disintegration and binding properties have higher DER values.[31] Corn based tablets have high DER value than cocoyam tablets. This means that the tablets which contained cocoyam starches had low balance between disintegration and mechanical properties. However, the disintegration times of the produced tablets at 2 % w/w were less than the reference tablets. This confirms that the best binder concentration is 2 % w/w.

CONCLUSION

The study has shown the potential of cocoyam as a binder in tablet formation. Cocoyam starches can be used as binders in ibuprofen tablets; compression pressure of 24 Pa and binder concentration of 2 % w/w. Under such conditions, less friable tablets are produced and reduced amounts of materials are used. Mzuzu cocoyam starch is the most appropriate binders for ibuprofen tablets.

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