ORIGINAL RESEARCH

Investigation of the Tableting Properties of Modified *Dioscorea dumetorum* Starch in Direct Compressed Diclofenac Tablet Formulations

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ABSTRACT

Background: Modification of starch enhances their performance and improves properties such as compressibility, visco-stability, texture and dissolution.
Objectives: The aim of the study was to investigate the direct compression properties of modified starch of *Dioscorea dumetorum* in diclofenac tablet formulations.
Method: Isolated starch from *Dioscorea dumetorum* tubers was subject to two forms of modification and the modified products characterized with the native starch for their physicochemical and powder properties. The modified starches (5, 7.5 and 10%w/w) and microcrystalline cellulose (MCC) (10%w/w) were used in the formulation of batches of diclofenac potassium tablets via slugging and direct compression. Flowability of granules from their slugs and tablet parameters from their tablet were evaluated using standard procedures. Drug-excipient interaction studies was carried out using FTIR analysis.
Results: The extracted starch was white, while the modified forms were off-white in colour. All the starches were smooth in texture and insoluble in water with swelling capacities ≤ 2.85, hydration capacities ≥ 1.22 and moisture contents ≤ 14.5%. Granules gave Carr's indices, Hausner's ratios and angles of repose values ranging from 10.71-18.03%, 1.12-1.22 and 20.16-28.15°, respectively, indicating good flow. Tablet's friability ranged from 0.01-0.04% while their hardness values was between 4.20-5.50 kp and disintegration times < 7.0 min. Dissolution profiles of the tablets showed over 70% diclofenac release within 45 min. FTIR studies showed no interaction between diclofenac and formulation excipients.
Conclusion: Modified *Dioscorea dumetorum* starch possesses binding and disintegrating properties comparable with MCC, hence it can be used as an alternative to MCC in direct compression of tablets.

Keywords: *Dioscorea dumetorum*, diclofenac, direct compression, starch

INTRODUCTION

Pharmaceutical excipients are substances incorporated with the pharmacologically active compound to aid the formulation and transport of the subsequent dosage form to its site of action in the body[1,2]. With respect to its weight, excipients constitute the most vital part of medicines[3]. Direct compression excipient such as microcrystalline cellulose play multifunctional roles (diluent, binder or disintegrant) in tablet formulations and also

confer desirable physical characteristics such as colours and flavours to the finished tablet[4,5]. Over the years, pharmaceutical scientists have continually searched, extracted and modified starches for use as direct compression excipients in the formulation of dosage forms[6-9].

Native starches are intolerant to conditions such as high temperature, high shear rate, and varying pH due to their large molecular size, insolubility in water, instability in viscous solutions and susceptibility to microorganisms. These limitations make them unfit for use hence the need for modifications such as acid hydrolysis and dextrinization[10]. Modification of starch enhances their performance and improves properties such as compressibility, visco-stability, texture and dissolution[9,11,12]. Starches from various species of yam including cocoyam, white yam, yellow yam and bitter yam have been modified and used as excipient in tablet formulations[13].

African bitter yam also referred to as wild yellow yam, trifoliate yam and cluster yam is a root crop that grows in various parts of West Africa, and it is popular in the south eastern part of Nigeria[14]. *Dioscorea dumetorum* belongs to the Dioscoreacae family and contains proteinous phyto-nutrients[15]. Though these tropical tubers have been underutilized in the world, their high starch content have made them a potential source of pharmaceutical excipient and for use in food and non-food applications[16-18]. Also, several studies involving various forms of modified *D. dumetorum* native starch[19,20] and their use as tablet excipient have been investigated[5,21,22], but the potential of these modified products as direct compression excipients have received little attention. Acid or thermal hydrolysis of starch have been reported to improve the swelling and bonding properties of starch powders[23-25].

Diclofenac is a non-steroidal anti-inflammatory drug (NSAID). It can be formulated as tablets, dispersible tablets, gastro resistant tablets, prolonged-release tablets and capsules. Diclofenac potassium tablets formulated with direct compression excipients gives the advantage of preventing hydrolytic reaction that may occur with wet granulation. The aim of the study is to compare the direct compression properties of modified African bitter yam starch with microcrystalline cellulose in diclofenac tablet formulations.

MATERIALS AND METHODS

Materials

Diclofenac potassium powder (Edo Pharmaceuticals Limited, Benin City, Nigeria), lactose (Sigma Chemicals, St. Louis, USA), microcrystalline cellulose, concentrated hydrochloric acid (BDH Chemicals Ltd, Poole, England), sodium hydroxide (CDH Ltd, New Delhi, India), magnesium stearate (A.H.A. International Co. Ltd, China), talc (Chemic Laboratory Reagents & Fine Chemicals, France), sodium hypochlorite (Reckitt and Coleman Nig. Ltd). All sieves were BSS (Endecotts Ltd. London, England) and water was distilled. African bitter yams were purchased locally and processed in our laboratory.

Methods

Starch extraction

Starch was extracted from the tubers of *Dioscorea dumetorum* using the method of Eraga *et al*[5]. Tubers weighing about 4.0 kg were washed and peeled. The peeled tubers were washed again and cut into pieces before wet milling into a slurry with an electric blender (Moulinex, France). The slurry was soaked overnight in 1 L of water containing 30 m1 of 3.5%w/v sodium hypochlorite. The mixture was filtered with a muslin cloth and the filtrate allowed to stand for 4 h. The supernatant was carefully decanted, and the starch sediment re-suspended in excess water. The suspension was allowed to stand for 3 h and the supernatant decanted again. This washing procedure was repeated several times until the supernatant tested neutral to litmus. The wet starch sediment was air-dried for 72 h

and further dried in a hot air oven at 60 °C for 1 h. The dried starch was milled into fine powder, sieved with a 250 µm size sieve and stored in an airtight container until use.

Starch modifications

Using the method of Nagahata *et al.*[26] with some modifications, about 150 g of the extracted starch was suspended in 650 ml ethanolic solution of 1.0 M HCl in a 1L conical flask. The hydrolysis reaction was allowed to proceed for 12 h at 50 °C in a water bath. The reaction was terminated by neutralizing with drops of 3.0 M NaOH solution. The sample was cooled under a running tap and allowed to stand for 4 h before decanting the supernatant. The sediment was repeatedly washed with 50% ethanol solution until neutral to litmus. The wet sediment was collected and dried in an oven at 40 °C for 4 h. The dried acid modified starch was pulverized into fine powder, sieved with a 250 µm size sieve and stored in an airtight container until use.

Also, a 150 g quantity of the extracted starch was weighed into pan and sprayed with 15 ml 0.5% hydrochloric acid solution. The acidified starch was mixed and spread over the pan before been heated in a hot air oven at 100 °C for 5 h and allowed to cool. The obtained starch dextrin was sieved with a 250 µm size sieve and stored in an airtight container until use.

Evaluation of native and modified starches

Organoleptic properties

The taste, odour, texture and colour of the starches were assessed by twelve individuals by touching, smelling and tasting the starch powder and a matching result given by at least ten of the individuals was recorded.

Solubility

Using a gravimetric method, 200 mg of the starch sample was placed in 5 ml of water in a test-tube at room temperature and shaken. The suspension was filtered with a pre-weighed Whatman filter paper No.1 and the filter paper with its residue was air dried. The dried filter paper was re-weighed and the difference in weight was used as a measure of solubility of the starch powder.

Iodine test

A 5.0 ml aliquot of each starch derivative suspension was prepared, and a few drops of 0.01 M iodine solution were added. The resulting colour change was recorded.

Bulk and tapped densities

About 30 g of the starch powder was poured gently into a 100 ml measuring cylinder and the volume occupied by the powder was recorded. The cylinder was tapped 100 times on a wooden platform to a constant volume. The ratio of the weight of the starch powder to the respective volumes was calculated as the bulk and tapped densities.

Carr's index and Hausner's ratio

The Carr's indices of the native and modified starch powders were calculated as the difference between their tapped and bulk densities, divided by their tapped densities and the ratio expressed as percentage while their tapped - bulk densities ratios was calculated as their Hausner's ratios.

Swelling capacity

About 10 g of the starch powder was tapped to a constant volume in a 100 ml measuring cylinder and dispersed with 85 ml of distilled water. Thereafter, the cylinder was made up to volume with more water. The dispersion was allowed to stand for 24 h and the volume of the sediment (Vb) noted. The difference in volume between the tapped starch sample and the sediment was computed as the swelling capacity.

Hydration capacity

A 10 ml dispersion of 500 mg weight of starch was introduced into a 15 ml pre-weighed centrifuge tube and shaken for about 2 min. The dispersion was allowed to stand for 10 min and centrifuged at 2000 rpm for 10 min using a bench centrifuge. The resulting supernatant was decanted, and the sediment weighed. The ratio of the weights of the sediment and the starch sample was calculated as the hydration capacity of the starch.

Moisture content

A 1.0 g quantity of the starch powder was dried in a hot air oven for 4 h at 105 ºC. The

initial weight of the powder and the weight after drying were recorded and their difference was calculated as the moisture content of the starch powder.

Preparation of granules and tablets

Using the formula shown in Table 1, a total of seven (7) batches of diclofenac potassium powder blends were prepared by dry mixing the quantities of the powdered ingredients required to prepare 100 tablets per batch in a mixer for 10 min. The powder blend was compressed into large tablets (slugs) using a heavy-duty tableting machine (Koln Niehi, Germany). The slugs were broken down into granules using a mortar and pestle and passed through an 850 µm sieve. The glidant (talc) and lubricant (magnesium stearate) were weighed and mixed in a mortar and then added to the granules in geometric proportion and mixed intimately. The granules were kept in an airtight container in readiness for analysis.

Table 1: Formula used in the preparation of the diclofenac granules and tablets

Ingredients	Quantity (mg/tablet)						
	A	B	C	D	E	F	G
Diclofenac potassium	50	50	50	50	50	50	50
Microcrystalline cellulose (MCC)	10	-	-	-	-	-	-
Acid-hydrolyzed starch (AHS)	-	5	7.5	10			
Dextrin starch (DXS)		-	-	-	5	7.5	10
Lactose	34	39	36.5	34	39	36.5	34
Magnesium stearate	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3
Total	100	100	100	100	100	100	100

Pre-compression (granule flow) analysis

Micromeritic properties of prepared granules

The bulk and tapped densities of the prepared granules were evaluated using the same methods employed with the modified starch powders. Similarly, the results obtained were used in calculating the Carr's indices and Hausner's ratios of the granules.

Angle of repose

Using the funnel method, a transparent glass funnel was clamped at 2.7 cm above a flat horizontal surface. Granules were carefully poured through the funnel onto the horizontal surface until the apex of the cone made by the heap of granules touched the tip of the funnel. The height of the heap and the diameter of the cone base were measured. The angle of repose, θ, was calculated using

Equation 1.

$$\theta = \tan^{-1} (h/r) \ldots . (1)$$

Where h is the height of the heap of granules and r is the radius of the circular base.

Flow rate

Using the funnel method, a glass funnel was clamped to a retort stand at a certain distance from a horizontal surface. Fifty grams of granules was poured into the funnel with its orifice blocked with a glass sheet. The glass sheet was withdrawn, and the granules allowed to fall freely under the influence of gravity. The time taken for the entire granules to pass through the orifice was recorded. This was carried out in triplicate and the mean values recorded.

Compression of granules

The various batches of the granules were compressed into tablets using a single punch tableting machine (F-3 Manesty Machines, UK) at a compression pressure of 30 arbitrary units. Granules of uniform weights were fed into the machine die with an adjusted volume sufficient to hold 100 mg of granules and compressed into tablets. The tablets made were then kept in air tight containers and stored in a desiccator until evaluation.

Post compression (tablet) evaluations

The following tests were carried out on the compressed tablets employing standard procedures: weight uniformity, dimensions, crushing strength (hardness), friability, disintegration time and dissolution studies[27].

Weight uniformity

Twenty (20) tablets were selected at random from each batch and weighed individually using an electronic balance (College B154, Mettler Toledo, Switzerland). Mean weight and standard deviation were computed.

Dimensions

The thickness and diameter of each of ten tablets per batch were measured using a micrometre screw gauge and mean and standard deviation values recorded.

Crushing strength

Ten tablets randomly selected per sub-batch were used in the determination. The force required to break a tablet by diametric compression of the tablet placed in a motorized tablet hardness tester (Campbell Electronics, Model HT-30/50, India) was recorded. The mean value and standard deviation were calculated.

Friability

The weight of 10 tablets per batch was determined on the electronic balance. The tablets were placed in the drum of a Roche friabilator (Erweka, Germany) and subjected to cascading free falls for 4 min at a drum speed of 25 rpm. The tablets were brought out, de-dusted and reweighed. The weight was recorded, and friability calculated as percentage loss in weight.

Disintegration time

The disintegration times of six tablets per batch of the tablets were determined using an Erweka ZT 120 basket and rack assembly with 0.1 N hydrochloric acid solution maintained at 37 ± 0.5 °C as the disintegration medium. The time taken for each tablet to break into primary particles and pass through the mesh of the apparatus was recorded and used to calculate average disintegration time and standard deviation.

Dissolution studies

In vitro dissolution profiles of the various batches of the diclofenac potassium tablets were determined using the USP Type II (paddle) method. A dissolution apparatus (Caleva ST7, UK) containing 900 ml of 0.1 N HCl solution maintained at 37 ± 0.5 °C with a paddle speed of 50 rpm was used. The apparatus was operated for 60 min and at various time intervals, a 5 ml volume of the dissolution fluid was withdrawn and replaced with an equivalent volume maintained at same temperature (37 ± 0.5 °C). The withdrawn samples were filtered and diluted with an equal volume of 0.1 N HCl and their absorbances determined at λmax of 245 nm with a UV-VIS Spectrophotometer (Shimadzu, Japan). The concentration and the percentage of diclofenac potassium released at each time interval was determined using the equation from the standard calibration plot earlier obtained from the pure drug.

Drug-excipient interaction studies

Drug-excipients interaction studies were carried out on granules prepared with the modified starches and pure diclofenac potassium powder using FTIR analysis. The analysis was done using FTIR-4100 Spectrophotometer (Shimadzu Co. Japan). Five milligrams of the granule sample was blended with potassium bromide to give a 200 mg weight powder. The blended powder was compressed using a Sigma KBr press into a tablet, and then placed in the sample compartment of the spectrophotometer and scanned over a range of 4000 - 1000 cm^{-1}.

Statistical analysis

Descriptive statistics using Microsoft Excel (2007) was done for all data. Mean and standard deviations of replicate determinations were computed and reported. Differences between mean was determined using one-way ANOVA while $p < 0.05$ was considered significant.

RESULTS

Starch powder properties

Some physicochemical properties of the starch powders studied are shown in Table 2. The acid-hydrolyzed and dextrin starch

powders were off-white in colour while that of the native starch was white. All the starches were odourless, tasteless and smooth in texture. They were insoluble in water and gave a blue black colouration with iodine solution, confirming the presence of starch. The acid hydrolyzed and dextrin starch powders had bulk and tapped densities of 0.52, 0.70 g/cm^3 and 0.50, 0.69 g/cm^3, respectively as against 0.48, 0.68 g/cm^3 of the native starch. The Carr's index (41.66%) and Hausner's ratio (1.41) of the native starch was higher than those of the modified starches while the reverse was the case with their swelling and hydration capacities. The starch powders exhibited similar moisture content values ≤ 14.5 % with the dextrin starch as low as 12.5%.

Pre-compression parameters

The results from the evaluations of the batches of diclofenac granules produced with various amounts of microcrystalline cellulose, acid-hydrolyzed and dextrin starch powders are shown in Table 3. Their bulk density values ranged from 0.50 - 0.54 g/cm^3 while their tapped densities were in the range of 0.56 - 0.66 g/cm^3. Their Carr's indices (10.71 - 18.18%) and Hausner's ratio (1.13 - 1.22) decreased with increase in the amount of the modified starches incorporated in the granule formulation while on the other hand, their angles of repose (20.16 - 28.15°) and flow rates (4.30 - 5.88 g/sec) increased with the amounts of starch in the formulation.

Table 2: Some physicochemical properties of the native and modified starch powders

Properties		Starches		
		Native	**Acid-hydrolyzed**	**Dextrin**
Organoleptic	Appearance	White	Off-white	Off-white
	Taste	Tasteless	Tasteless	Tasteless
	Odour	Odourless	Odourless	Odourless
	Texture	Smooth	Smooth	Smooth
Chemical	Solubility	Insoluble	Insoluble	Insoluble
	Test for starch	Positive	Positive	Positive
Powder parameters	Bulk density (g/cm^3)	0.48	0.52	0.50
	Tapped density (g/cm^3)	0.68	0.70	0.69
	Carr's index (%)	41.66	34.61	38.00
	Hausner's ratio	1.41	1.34	1.38
	Swelling capacity	1.1	2.25	2.85
	Hydration capacity	1.22	1.55	1.58
	Moisture content (%)	14.5	14.0	12.5

Table 3: Micromeritic properties of the batches of diclofenac potassium granules (n=3)

Batch	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's index (%)	Hausner's ratio	Angle of repose (°)	Flow rate (g/sec)
A	0.50 (0.02)	0.61 (0.03)	18.03 (0.01)	1.22 (0.10)	26.27 (0.11)	5.41 (0.60)
B	0.52 (0.02)	0.60 (0.02)	13.33 (0.01)	1.15 (0.10)	24.20 (0.10)	4.30 (0.30)
C	0.51 (0.03)	0.58 (0.01)	12.06 (0.01)	1.13 (0.11)	22.10 (0.10)	4.50 (0.74)
D	0.50 (0.03)	0.56 (0.03)	10.71 (0.02)	1.12 (0.12)	20.16 (0.11)	5.20 (0.12)
E	0.54 (0.05)	0.66 (0.01)	18.18 (0.01)	1.22 (0.11)	28.15 (0.10)	4.50 (0.46)
F	0.51 (0.03)	0.62 (0.01)	17.74 (0.02)	1.21 (0.11)	26.24 (0.11)	5.30 (0.62)
G	0.50 (0.02)	0.60 (0.03)	16.66 (0.02)	1.20 (0.12)	24.50 (0.12)	5.88 (0.66)

Standard deviation in parenthesis

Drug-excipient compatibility

The FTIR spectra obtained from the drug-excipient interaction studies are shown in Figure 1. The spectrum of pure diclofenac powder (Figure 1 (a)) showed distinguishing peaks at 958.38, 1562.55, 1922.13 and 3424.00 cm^{-1}. The spectral data of granules formulated with the acid-hydrolyzed (Figure 1 (b)) and the dextrin (Figure 1 (c)) starches retained these distinctive peaks observed for diclofenac, hence ruling out the likelihood of chemical interaction or complex formation between diclofenac sodium and excipients during the mixing and slugging processes.

Post-compression parameters

Results from the tablet evaluations of the various batches of the diclofenac tablets produced are shown in Table 4. The tablet weight uniformity tests showed that the mean weight of the tablets varied between 105 - 108 mg. The friability test results of the tablets showed a variation from 0.1 - 0.4% and decreased with the increase in the concentrations of the starches. The hardness test of the tablets revealed crushing strength values ranging from 4.2 - 5.5 kp with the hardness increasing with increase in the concentrations of the acid modified and dextrin starches. Most of the tablets disintegrated within 7.0 min with the batches of tablets formulated with the acid-hydrolyzed starch, having the shortest disintegration times. The dissolution profiles of the various batches of the tablets shown in Figure 2, showed variable diclofenac release profiles with an initial burst release (over 40.0%) in the first 5 min of dissolution testing. However, all the batches of tablets release over 70.0% of their drug content within 45 min of dissolution profiling.

Table 4: Post-compression parameters of the formulated diclofenac potassium tablets (n=3)

Batch	Weight uniformity (mg)	Dimensions (mm)		Friability (%)	Crushing strength (kp)	Disintegration time (min)
		Diameter	Thickness			
A	107.00 (2.58)	6.50 (0.01)	2.16 (0.02)	0.01 (0.02)	4.30 (0.43)	5.20 (0.21)
B	105.25 (3.33)	6.32 (0.02)	2.12 (0.03)	0.04 (0.01)	4.60 (0.50)	5.16 (0.20)
C	105.50 (2.33)	6.36 (0.02)	2.14 (0.01)	0.03 (0.02)	4.30 (0.50)	5.08 (0.18)
D	108.20 (2.32)	6.45 (0.01)	2.17 (0.03)	0.02 (0.02)	4.20 (0.70)	5.00 (0.17)
E	105.00 (2.75)	6.36 (0.03)	2.21 (0.02)	0.01 (0.01)	5.10 (0.50)	6.58 (0.37)
F	106.20 (2.60)	6.40 (0.01)	2.22 (0.01)	0.01 (0.01)	5.40 (0.50)	6.45 (0.39)
G	108.50 (2.30)	6.50 (0.01)	2.24 (0.03)	0.01 (0.01)	5.50 (0.43)	6.25 (0.37)

Standard deviation in parenthesis

DISCUSSION

Dry granulation of powders and their direct compression into tablets is the most cost-effective process of tablet manufacturing, because it only involves powder blending and compression[28]. Though native starches are not directly compressible, studies have shown that their modified derivatives can possesses direct compression ability to a more or less degree depending on the type of modification[5,8,13]. The effect of acid-hydrolysis and dextrinization of the African bitter yam native starch on its direct compression property in diclofenac potassium tablet formulation was investigated in this study.

Results from the powder evaluations of the African bitter yam native and modified starches revealed that the acid-hydrolyzed and dextrin starch powders had higher powder densities, though comparable with the native starch. The Carr's indices and Hausner's ratios of the modified starches suggests a better flowing powder in comparison with the native starch. These values of the modified starches may be attributed to the starch particle shapes,

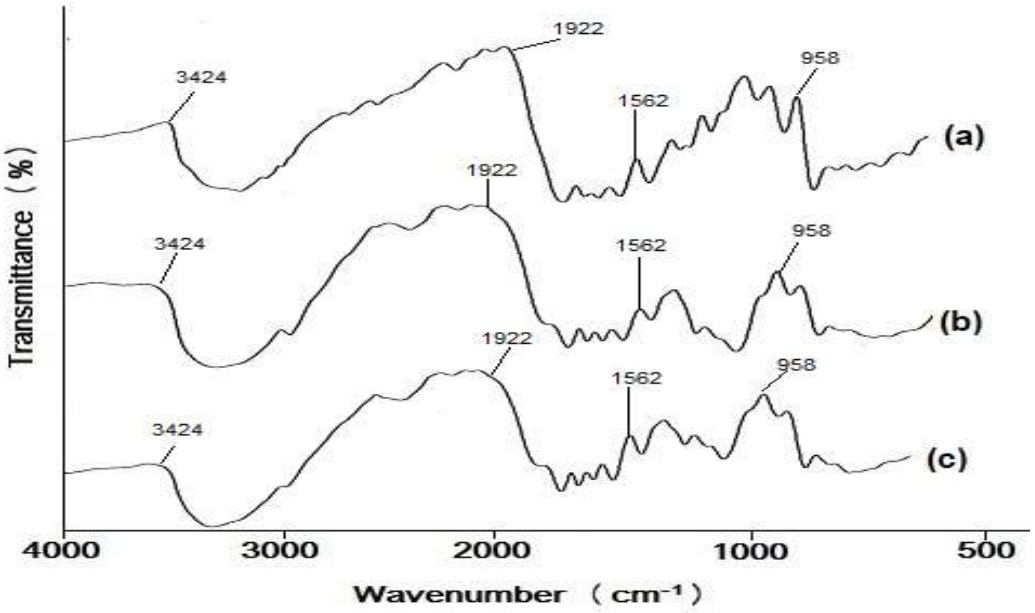

Figure 1: FTIR spectra of pure diclofenac potassium powder (a) and the granules prepared with acid hydrolyzed (b) and dextrin (c) starches

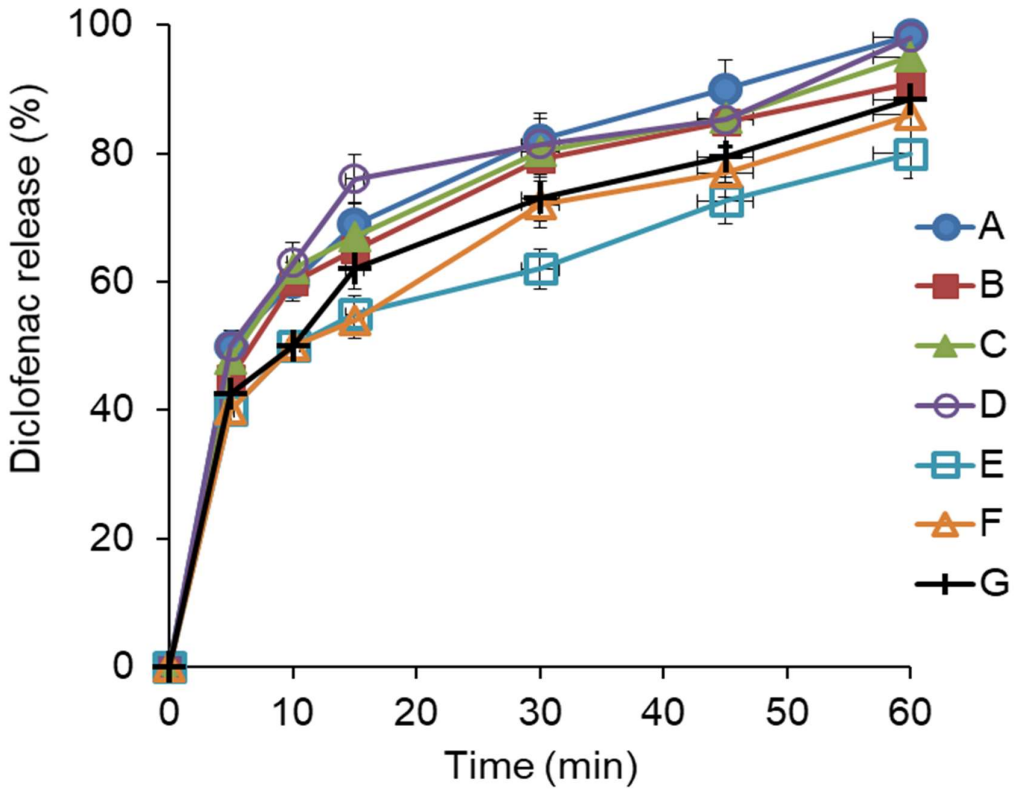

Figure 2: Dissolution profiles of the various batches (A-G) of diclofenac potassium tablets (n=3)

promoting an uneven packing resulting in increased void spaces[29]. Also the swelling and hydration capacities of the modified starch powders were higher than those of the native starch with their swelling capacities almost twice that of the native starch. The superior swelling ability of the modified starches would suggest good candidates as disintegrants.

However, the flow properties of granules formulated with the modified starches at different concentrations and in comparison, with granules of microcrystalline cellulose were found to increase with increasing amounts of the starch used in the formulation. This improvement in flow that is also evident in their angles of repose and flow rates, maybe a direct correlation of the particle shapes of the modified starch powders[30,31].

Furthermore, the tablets formulated with MCC and the modified starches compared favourably in their weight variation. The British Pharmacopoeia requirement stipulates that not more than two of the individual weights should deviate from the average weight by more than ± 5% and none should deviate by more than ± 10%[27]. Since weight variation is an indirect measurement of content variation, it might be implied that there may be no significant drug content variation in the formulated tablets.

Similarly, the values of the percentage friability of all the tablet's batches showed good friability indices (< 1%) thus indicating good mechanical properties as this test is a good measure of the mechanical stress tablets are expected to undergo during packaging, transportation and use[32]. The tablets prepared with dextrin starch were the least friable while those prepared with acid-hydrolyzed starch were the most friable. This could be attributed to the dextrinization process, which decreased the molecular size and increases the degree of branching and glucosidic linkages, turning the product into a more rigid form[33].

Also, tablets formulated with dextrin starch had better hardness values compared with their acid-hydrolyzed starch counterparts. However, while the crushing strength values of dextrin starch tablets increased with increasing starch concentration in the tablet formulation, the reverse was the case with acid-hydrolyzed starch tablets. Again, the increased degree of branching and glucosidic linkages in dextrin starch molecule may be responsible for the increasing tablet hardness, possibly due to the consolidation of the branchings and linkages of the starch particles from tablet compaction.

The disintegration times of the tablets were all within 7 min with no significant differences within the batches of acid-hydrolyzed and those of dextrin starch tablets. Though the tablets complied with BP disintegration time specification of 15 min[27], it was observed that the hardness of the tablets did not affect their disintegration but increasing the starches in the tablets favoured their disintegration times positively. Nevertheless, none of the tablets were fast disintegrating (≤ 3.0 min) but their modification revealed a level of disintegrant action comparable to MCC, especially the acid-hydrolyzed starch at the concentrations studied.

The dissolution profiles of the tablet batches showed a dissolution rate that was in direct correlation to the disintegration times of the tablets. Some researchers have maintained that disintegration times and dissolution rates are directly correlated, as shorter disintegration times will invariably lead to faster and increased rate of dissolution[32,24]. All the tablets achieved almost a 100% diclofenac release within 60 min, though batch E tablets containing 5.0%w/w of dextrin starch gave the least drug release of 80% within the 60 min. Nonetheless, all the tablets passed the BP specification of 70% drug release within 45 min of dissolution testing[35].

CONCLUSION

The study has shown that tablets prepared with the modified forms of the *Dioscorea dumetorum* starch have binding and

disintegrating properties and compared favorably in their tablet properties with those prepared with microcrystalline cellulose. Hence, acid-hydrolyzed and dextrin starches from the African bitter yam may serve as an alternative to MCC in its role as a direct compression agent.

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REFERENCES

1. Cooper JW, Gunn C and Carter SJ. Cooper and Gunn's Tutorial Pharmacy, Cater SJ ed. 6th ed. New Delhi: CBS Publishers; 2005:257-288.
2. Rowe RC, Sheskey PJ and Quinn ME. Handbook of pharmaceutical excipients. 6th ed. London: Pharmaceutical Press; 2009.
3. Pifferi G and Restani P. The safety of pharmaceutical ingredients. Farmaco, 2003; 58(8):541-550.
4. Chaerunisaa AY, Sriwidodo S and Abdassah M. Microcrystalline cellulose as pharmaceutical excipient. In: Ahmad U and Akhtar J, eds. Pharmaceutical Formulation Design - Recent Practices [Internet]. London: IntechOpen; 2019. https://www.intechopen.com/chapters/68199 [Accessed: 2022 Feb 19].
5. Eraga SO, Ndukwe JO and Iwuagwu MA. An investigation of the direct compression properties of pre-gelatinised African bitter yam and cassava starches in acetylsalicylic acid tablet formulation. Journal of Applied Science and Environmental Management, 2017;21(5):855-862.
6. Singh AV and Nath LK. Evaluation of acetylated moth bean starch as a carrier for controlled drug delivery. International Journal of Biological Macromolecules, 2012;50(2):362-368.
7. Builders PF, Ogwuche P, Isime Y and Kunle OO. Gum from the bark of *Anogeissius leiocarpus* as a potential pharmaceutical raw material granule property. African Journal of Pharmacy and Pharmacology, 2011;5(13):1603-1611.
8. Abdallah DB, Charoo NA and Elgorashi AS. Assessment of pre-gelatinized sorghum and maize starches as superior multi-functional excipients. Journal of Pharmaceutical Innovation, 2016;11:143-155.
9. Akin-Ajani OD, Itiola OA and Odeku OA. Evaluation of the disintegrant properties of native and modified forms of fonio and sweet potato starches. Starch/Stärke, 2016;68(1-2):169-174.
10. Ochekpe NA, Kemas UC and Nep EI. Chemical modification and their effects on binding/disintegrating properties of *Plectranthus esculentus*. American Journal of PharmTech Research, 2013;3(3):868-869.
11. Suzanne H. Starch in food. In: Starch: Physical and Mental Performance, and Potential Health Problems. Structure, Function and Applications. 2nd ed. Woodhead Publishing Series in Food Science, Technology and Nutrition, 2018:855-871.
12. Lawal MV, Odeniyi MA and Itiola OA. Effect of thermal and chemical modifications on the mechanical and release properties of paracetamol tablet formulations containing corn, cassava and sweet potato starches as filler-binders. Asian Pacific Journal of Tropical Biomedicine, 2015;5(7):585-590.
13. Eraga SO, Mudiaga-Ojemu BO, Okooboh T and Iwuagwu MA. Evaluation of directly compressed paracetamol tablets formulated with some locally sourced pre-gelatinized

starches: Effect of compression pressure and starch concentration. Nigerian Pharmaceutical and Biomedical Research, 2018;3(3):300-316.
14. Egbuonu AC, Nzewi DC and Egbuonu ON. Functional properties of bitter yam (*Dioscorea dumetorum*) as influence by soaking prior to oven-drying. American Journal of Food Technology, 2014;9:97-103.
15. Daramola A and Amira P. A comparative evaluation of the proximate analysis, mineral contents and phytochemical screening of *Dioscorea dumetorum*. European Journal of Biology and Biotechnology, 2020;1(3).
16. Owuamanam CI, Iwuoha CI, Onuegbu NC, Ogueke CC and Nwosu JN. Quality characteristics of processed flours from trifoliate yam (*Dioscorea dumetorum*) as influenced by steeping and boiling in varying concentration of trona solution over time. American Journal of Food Technology, 2013;8:162-172.
17. Oyeyinka SA, Oyeyinka AT, Kayode RM, Olagunju OF, Karim OR and Joseph JK. A review on the functionality and potential applications of bitter yam starch. Annuls. Food Science and Technology, 2017;18(3):364-375.
18. Oluwasina OO, Wahab OJ, Umunna QC and Nwosa OC. *Dioscorea dumetorum* Pax as an alternative starch source for industrial applications. IOSR Journal of Applied Chemistry, 2017;10(5):5-13.
19. Okunlola A, Adebayo AS and Adeyeye MC. Solid state characterization of two tropical starches modified by pre-gelatinization and acetylation: Potential as excipients in pharmaceutical formulations. Journal of Pharmaceutical Research International, 2014;5(1):58-71.
20. Falade KO and Ayetigbo OE. Effects of tempering (annealing), acid hydrolysis, low-citric acid substitution on chemical and physicochemical properties of starches of four yam (Dioscorea spp.) cultivars. Journal of Food Science and Technology, 2017;54(6):1455-1466.
21. Okunlola A. Design of bilayer tablets using modified Dioscorea starches as novel excipients for immediate and sustained release of aceclofenac sodium. Frontiers in Pharmacology, 2015;5:294.
22. Okunlola A, Adebayo AS and Adeyeye MC. Development of repaglinide microspheres using novel acetylated starches of bitter and Chinese yams as polymers. International Journal of Biological Macromolecules, 2017;94(Pt A):544-553.
23. Egharevba HO. Chemical properties of starch and its application in the food industry. In: Emeje M. ed. Chemical Properties of Starch [Internet]. London: IntechOpen; 2019. https://www.intechopen.com/chapters/68437 [Accessed: 2022 Feb 19].
24. Amaraweera SM, Gunathilake C, Gunawardene OHP, Fernando NML, Wanninayaka DB, Dassanayake RS, *et al*. Development of starch-based materials using current modification techniques and their applications: A review. Molecules, 2021;26(22):6880.
25. Mohamed IO. Effects of processing and additives on starch physicochemical and digestibility properties. Carbohydrate Polymer Technologies and Applications, 2021;2:100039.
26. Nagahata Y, Kobayashi I, Goto M, Nakaura Y and Inouchi N. The formation of resistant starch during acid hydrolysis of high-amylose corn starch. Journal of Applied Glycoscience, 2013;60:123-130.
27. British Pharmacopoeia. Vol. III. London: The Pharmaceutical Press, Her Majesty's Stationer Office, 2009:6578-6585.
28. Hongbo C, Akham A and Changquan CS. Direct compression tablet containing 99% active ingredient - A tale of spherical crystallization. Journal

of Pharmaceutical Sciences, 2019;108(4):1396-1400.
29. Fu X, Huck D, Makein L, Armstrong B, Willen U and Freeman T. Effect of particle shape and size on flow properties of lactose powders. Particuology, 2012;10(2):203-208.
30. Janssen PHM, Depaifve S, Neveu A, Francqui F and Dickhoff BHJ. Impact of powder properties on the rheological behaviour of excipients. Pharmaceutics, 2021;13:1198.
31. Enferad S, Petit J, Gaiani C, Falk V, Burgain J, De Richter SK *et al*. Effect of particle size and formulation on powder rheology. Particulate Science and Technology, 2021;39(3):362-370.
32. Rahman M, Jahan FI, Fahim NF, Paul N, Jahan N, Rashid H *et al*. *In-vitro* comparative quality evaluation of leading brands of metronidazole tablets available in Bangladesh. Pharmacology Online, 2020;2:63-72.
33. Sabalingam S, Siriwardhene MA, Dharmawansha UA and Pathirana W. Dextrinized maize starch-maize starch combination as exclusive fillers in tablet manufacture. Indian Journal of Pharmaceutical Sciences, 2019;81(5):960-966.
34. Noor S, Abdus Salam FB, Hima HN, Bhuiyan SI and Chowdhury S. Comparative *in-vitro* quality evaluation of some brands metronidazole tablets available in Bangladesh. International Journal of Applied Research, 2017;3(7):753-758.
35. British Pharmacopoeia. Vol. I and II. London: The Pharmaceutical Press, Her Majesty's Stationery Office, 2003:249-252.