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Research Article

New Direct Compression Excipient from Tigernut Starch: Physicochemical and Functional Properties

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Abstract. Tigernut starch has been isolated and modified by forced retrogradation of the acidic gel by freezing and thawing processes. Relevant physicochemical and functional properties of the new excipient (tigernut starch modified by acid gelation and accelerated (forced) retrogradation (ST_{AM})) were evaluated as a direct compression excipient in relation to the native tigernut starch (ST_{NA}), intermediate product (tigernut starch modified by acid gelation (ST_A)), and microcrystalline cellulose (MCC). The particle morphology, swelling capacity, moisture sorption, differential scanning calorimeter (DSC) thermographs and X-ray powder diffraction (XRD) patterns, flow, dilution capacity, and tablet disintegration efficiency were evaluated. The particles of ST_{NA} were either round or oval in shape, ST_A were smooth with thick round edges and hollowed center while ST_{AM} were long, smooth, and irregularly shaped typically resembling MCC. The DSC thermographs of ST_{NA} and MCC showed two endothermic transitions as compared with ST_A and ST_{AM} which showed an endothermic and an exothermic. The moisture uptake, swelling, flow, and dilution capacity of ST_{AM} were higher than those of MCC, ST_A, and ST_{NA}. The XRD pattern and moisture sorption profile of ST_{AM} showed similarities and differences with ST_{NA}, ST_A, and MCC that relate the modification. Acetylsalicylic acid (ASA) tablets containing ST_{AM} disintegrated at 3±0.5 min as compared with the tablets containing ST_{NA}, ST_A, and MCC which disintegrated at 8.5±0.5, 10±0.5, and 58±0.8 min, respectively. The study shows the physicochemical properties of tigernut starch modified by forced retrogradation as well as its potential as an efficient direct compression excipient with enhanced flow and disintegration abilities for tablets production.

KEY WORDS: direct compression excipient; forced retrogradation; functional properties; physicochemical properties; tigernut starch.

INTRODUCTION

Starch and its derivatives have widely been used as pharmaceutical excipients in the manufacture of pharmaceutical dosage forms. Their functional versatility is essentially due to their biocompatibility, biodegradability, diverse intrinsic physicochemical properties, and relative ease of modification (1). Starches from different botanical sources have properties that translate to their functional characteristics and applications which when modified alter their physicochemical and functional properties (2,3). Starch modification may be tailored to suit specific applications and has been achieved by diverse physical techniques (such as gelation and moisture treatment), chemical methods (such as depolymerization, crosslinking, and substitution reactions), as well as enzyme treatment (4–6).

In conventional pharmaceutical manufacture, native starches are used primarily as binders and disintegrants in the preparation of tablets often by wet granulation method. Direct compression is however a popular choice because it provides the shortest, most effective, and least complex way to produce tablets, an attribute not characteristic of native starches. The essential attributes of direct compression excipients are good compaction and flow-abilities which are properties lacking in native starches, thus, are not favored as direct compression excipient (7,8). Considering the numerous sources of starch and its modification potential, the production of starch derivatives with enhanced flow and direct compression ability is yet to be fully exploited as only a few starch derivatives with direct compression application are available (9).

The primary sources of starch used for pharmaceutical production are corn, potato, wheat, cassava, and rice: these reflect diverse botanical species and properties (10–13). Apart from these, numerous unexplored sources with commercial potential and desirable properties which can be modified to suite certain functional applications abound (14,15). One of such is tigernut, obtained from *Cyperus esculentus* (Fam. Cyperaceae). Tigernut is an underutilized potential source of starch (16,17).

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ABBREVIATIONS: ST_{NA}, Native tigernut starch; ST_A, Tigernut starch modified by acid gelation; ST_{AM}, Tigernut starch modified by acid gelation and accelerated (forced) retrogradation; MCC, Microcrystalline cellulose; Apn, Acetaminophen; ASA, Acetyls alicylic acid; SEM, Scanning electron micrograph; RH, Relative humidity.

C. esculentus is a perennial herb that produces rhizomes and spherical nuts. It is a common weed in many parts of Nigeria, although some varieties are cultivated. Among these, only the yellow and brown varieties are available in the market. The yellow variety is preferred because of its inherent properties, such as large size, attractive color, and fleshier nature. It also yields more starch, with lower fat, higher protein, and less anti-nutritional factors (18,19). Tigernut can be eaten raw, roasted, dried, baked, or made into a refreshing nonalcoholic beverage (20).

Tigernut starch has previously been isolated and characterized. This starch has been shown to conform well to US Pharmacopeia standards established for widely used starches like maize and potato. The native tigernut starch (ST_{NA}) showed flow properties comparable to maize and potato starch as well as excellent binder activity when metronidazole tablets' hardness and friability were evaluated (15). The objective of this study was to modify tigernut starch by forced retrogradation of the acidic gel by freezing and thawing and evaluating the physicochemical and functional properties of the product as a potential direct compression excipient.

MATERIALS AND METHODS

Materials

Sun-dried tigernut was collected from a study farm in Abuja, Nigeria. Acetylsalicylic acid (ASA) was a kind donation from JUHEL Pharmaceutical Company Limited, Nigeria. Acetaminophen, acetone, *n*-hexane, ethanol, sodium metabisulphite, sodium chloride, and magnesium chloride were purchased from Sigma–Aldrich Chemie, Germany. Potassium dihydrogen phosphate was purchased from May & Baker, UK. Magnesium stearate, sodium chloride, potassium thiocyanate, potassium chloride, potassium iodide, and calcium chloride were purchased from BDH, UK. Microcrystalline cellulose (Avicel® PH-101) was purchased from Fluka Biochemica, Ireland.

Methods

Starch Extraction

The modified method of Sathe *et al.* (21) was used for the starch extraction: 1 kg quantity of the tigernut was washed to remove any adhering dirt and dried in a hot air oven (Unitemp Drying Cabinet, Britain) set at 50°C for 3 h (21). The dry nuts were then pulverized into coarse particles of large multiparticulate sizes (>1 mm). The particles were boiled in ethanol for 1.5 h to denature proteins and inactivate enzymes before treating with several portions of *n*-hexane to remove lipids (22,23). The defatted granules were dried in the hot air oven (50°C) for 2 h and thereafter soaked in 2 l of 0.075% (*w*/*v*) sodium metabisulphite for 6 h.

The hydrated mass of coarse tigernut granules was milled into a homogenous fine pulp using a Braun homogenizer (Type-4142, Germany). The pulp was dispersed in 12 l of the sodium metabisulphite solution (0.075%, *w*/*v*) and filtered through a muslin cloth of 150 μm pore size. The suspension obtained was allowed to stand for 18 h for complete sedimentation of the starch granules before the supernatant was decanted. The starch layer was repeatedly washed with distilled water and recovered by centrifugation at 3,000 rpm for 10 min. The resulting starch cake was dried for 5 h at 50°C in the hot air oven. The dry starch was thereafter pulverized to a fine powder, passed through a 250-μm mesh and stored in a dry airtight container until used (24).

Starch Modification

One liter of 2% (*w*/*v*) of ST_{NA} gel was prepared in buffer solution of pH 4.0 by heating to and maintaining at 76°C for 5 min with continuous stirring with a magnetic stirring rod (200 rpm). The gelatinized starch was allowed to cool to room temperature (≈27±3°C). Two hundred milliliters of the cooled starch gel was transferred into a Kenwood mixer (Kenwood Ltd., USA) set to a mixing speed of 1,000 rpm. Five hundred milliliters of acetone was then gradually added with continuous mixing for 5 min. The material (tigernut starch modified by acid gelation (ST_A)) recovered by filtration were washed with more portions of acetone and dried in the hot air oven at 50°C for 1 h. Another 200 ml portion of the starch gel was dispensed into a plastic container and placed in a freezer maintained at −60±3°C. This was subjected to four cycles of freezing and thawing before precipitating with acetone (tigernut starch modified by acid gelation and accelerated (forced) retrogradation (ST_{AM})). Each freezing and thawing cycle implies 18 h of freezing at a temperature of −60°C and thawing at 27±3°C. The dried product was weighed and then stored in an airtight container.

Evaluation of Physicochemical Properties

Differential Scanning Calorimetry Analysis. The thermal properties of ST_{NA}, ST_A, ST_{AM}, and MCC were studied using a Differential scanning calorimeter (DSC 204F1, Phoenix NETZSCH, Germany) equipped with a thermal analysis system. The instrument was calibrated using indium (156.88°C) as internal standard and dry nitrogen was used as the purge gas (purge 20 ml/min). Seven milligram of the desiccated samples of ST_{NA}, ST_A, ST_{AM}, and MCC respectively were weighed into an aluminum pan and covered with a perforated lid. The probes were heated at a temperature of 25–500°C at a rate of 5°C/min. The glass transition (T_g), cold crystallization (T_{cr}), and melting (T_m) temperatures were then evaluated using a computer Proteus software (22).

X-ray Powder Diffraction. Structural characterization was carried out using a Siemens D5000 X-ray diffractometer (Siemens, Munich, Germany). ST_{NA}, ST_A, ST_{AM}, and MCC were each packed in rectangular aluminum cells, and illuminated using CuKα radiation (λ=1.54056 Å) at 45 kV and 40 mA. Samples were scanned between diffraction angles of 5° to 40° 2θ, which was sufficient to cover all significant diffraction peaks of starch crystallites. Scan steps of 0.1° were used, and the dwell time was 15.0 s. A nickel filter was used to reduce the K_β contribution to the X-ray signal. Measurements were made at ambient temperature (14). The "*d*" spacing was computed according to Bragg's law of diffraction, using Eq. 1.

$$n\lambda = 2d\sin\theta \tag{1}$$

Where λ is the wavelength of the X-ray beam, d is spacing between unit cell edge of the powder and θ is angle of diffraction and n is the order of interference.

Scanning Electron Microscopy. The granule morphology and distribution of ST_{NA}, ST_A, ST_{AM}, and MCC were determined using a FEI Quanta 400 scanning electron microscope (FEI QUANTA 400, FEI Company, USA). The powders were mounted on a double-backed, cellophane tape attached to a stub and then coated with gold-palladium. The images were taken at an accelerating voltage of 5.0 kV.

Functional Properties

Flow Properties. The flow properties of the powders were determined by the indirect methods: Carr's compressibility index and angle of repose (24).

Carr's compressibility indices—the bulk and tapped densities of ST_{NA}, ST_A, ST_{AM}, and MCC particles were evaluated in a 50-ml graduated measuring cylinder as a measure of densification of a predetermined weight of the powders. The measuring cylinder with its content was tapped mechanically with a Stampfvolumeter (STAV 2003 JEF, Germany). The bulk volume corresponds to the volume before tapping while the tapped volume corresponds to the stable final volume with unchanging particle arrangement. The compressibility indices of the powders were determined using Eq. 2 (22).

$$\text{Compressibility}(\%) = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100 \quad (2)$$

The angles of repose of the powders were determined by measuring the internal angle between the surface of the heap of the powders obtained when 50 g of each of the powder was allowed to flow through a glass funnel (orifice diameter, 2 cm) and clamped 10 cm above a flat surface. The angle of repose was calculated using Eq. 3 (24,25).

$$\text{Angel of repose} = \text{Tan}\,\theta = \frac{\text{Height of cone}}{\text{Radius of cone(r)}} \quad (3)$$

Powder Water Uptake. One gram quantity of ST_{NA}, ST_A, ST_{AM}, and MCC respectively were placed in a 15-ml graduated plastic tube before 10 ml of distilled water was added and mixed on a Vortex–Gennie vortex mixer for 2 min. The mixture was allowed to stand for 10 min and immediately centrifuged at 1,000 rpm for 10 min. The supernatant was carefully decanted and the weight of the sediment determined. The water uptake capacity corresponding to the ratio of the weight of the sediment to the dry sample weight expressed as a percentage (26,27).

Equilibrium Moisture Sorption. Quantities of ST_{NA}, ST_A, ST_{AM}, and MCC were placed in Petri dishes and stored in an activated desiccating chamber at 25°C for 48 h to remove residual moisture. The moisture sorption isotherms were determined using the gravimetric method (28). One gram quantity of each sample from the desiccator was placed in an aluminum foil and put in a relative humidity chamber with a gauze holding tray containing either distilled water or saturated solution of different salts to provide the required RH (water (100%), potassium chloride (84%), sodium chloride (75%), potassium thiocynate (47%), and calcium chloride (31%)). The samples were weighed at 12-h intervals until equilibrium was attained. The equilibrium moisture sorption (EMS) was determined using Eq. 4.

$$\text{EMS}(\%) = \frac{M_e}{M_d} \times 100 \quad (4)$$

Where M_e is the amount of moisture absorbed at equilibrium and M_d is the dry weight of the material (29). The moisture sorption profile was then presented as a plot of percentage weight gain *versus* relative humidity.

Dilution Capacity. The dilution capacity of the new excipient was determined by evaluating the effect of acetomenophen loading on the tensile strength of compacts of ST_{NA}, MCC, ST_A, and ST_{AM}.

The loss of compactibility observed in coprocessed excipients also reflected in result of the tablet friability. Expectedly, all the coprocessed excipients failed the friability test. The friability values for batches II–V were in the range of 4.2–7.0 kgf. Therefore, tablets produced with coprocessed excipients using the fully pregelatinization method were unsatisfactory in terms of strength and friability of compact. However, all the tablets produced with FPMSAC disintegrated within 15 min, and the disintegration time was directly proportional to the amount of acacia gum present in the coprocessed excipients. However, the unexpected decrease in crushing strength and increase in friability that was observed for the FPMSAC may be due to electrostatic forces preventing adhesion of particles to one another. The particles of the FPMSAC may have acquired surface charges as a result of longer milling time required to obtain particles of desired sizes of the coprocessed excipients. The coprocessed excipients produced using the fully pregelatinization method on drying formed very hard compact which required longer milling time of 30 min. Friability test A number of tablets (20 numbers) are weighed and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall 6 in. in each turn within the apparatus. After 4 min of this treatment or 100 revolutions, the tablets are weighed and the weight compared with initial weight. The loss due to abrasion is a measure of tablet friability. The value is expressed in percentage.

The friability of the compacts evaluated for acetomenophen loading were determined—the friability of ten tablets was determined using Roche Friabilator (TA3R Erweka, Germany) at a rotation speed of 25 rpm for 4 min. The tablets were removed, dusted, and weighed. Percentage of weight loss was determined.

Friability Test. Compacts containing different ratios of binary mixtures of acetaminophen and ST_{NA}, ST_A, ST_{AM}, and MCC, respectively, were prepared. The binary mixtures such that each of the 400 mg tablets contained acetaminophen (Apn) and the excipients in complimentary ratios, Apn/excipients respectively of 200:0, 160:40, 120:80, 100:100, 80:120, 40:180, and 0:200. The tablets were prepared by compressing the powder mixtures at a pressure of 22.5 kN using a single press compression machine (Shanghai Tiaxiang & Chenta, Pharmaceutical Machinery Co. Ltd, China) fitted

with an 11.5 mm flat faced punch and die. The punch and die were lubricated with a 10% (*w*/*v*) dispersion of magnesium stearate in ethanol before any compression. The compacts were stored in airtight containers for 24 h to allow for equilibration before evaluating for tensile strength and friability.

Tensile strength—the diameter and thickness of the compacts were determined with a vernier caliper (Mitutoyo, Japan) as well as their hardness (Erweka ZT2, Germany). Their radial tensile strengths were evaluated using Eq. 5 (30).

$$T = 2F/\pi dt \quad (5)$$

Where T is the radial tensile strength, F is the load needed to break the compact, and d and t are the diameter and thickness, respectively.

Friability—the friability of ten compacts (of predetermined weight) of each ratio mix was determined using a Roche Friabilator (Erweka TA220, Germany) at a rotation speed of 25 rpm for 4 min. The compacts were removed, dusted, and reweighed. The percentage of weight loss was determined.

Disintegration Efficiency. Tablets containing 300 mg of ASA and 10% (*w*/*w*) of either ST_{NA}, ST_A, ST_{AM}, and MCC (added as disintegrant) were produced by mixing the aspirin crystals and the excipients in a tumble mixer (JEL, KARL KOLB, Germany) and compressing with a load of 20 kN using a single press compression machine fitted with the 11.5 mm flat faced punches (31). The ASA tablets were stored in airtight containers for 24 h before evaluation of the disintegration time. Tablets disintegration time were determined in distilled water at 37±0.5°C in a BP disintegration test unit (Erweka ZT4, Germany) (32). Tablets were considered to have disintegrated when all particles had passed through the wire mesh.

Data and Statistical Analysis

All experiments were performed in triplicates for validity of statistical values. Results were expressed as mean±scanning electron microscopy (SEM). Differences were considered significant for p values<0.05.

RESULTS

Physicochemical Properties of Modified Tigernut Starch

Isolation and Modification

Approximately 32% of ST_{NA} was obtained from tigernut after extraction. The modified products obtained after processing of ST_{NA} were approximate of 95% and 92% for ST_A and ST_{AM}, respectively.

Particle Morphology

The SEM images of ST_{NA}, ST_A, ST_{AM}, and MCC are presented in Fig. 1. The appearance, size and shapes of ST_{NA} and its modification products were distinct and characteristic. The particles of ST_A and ST_{AM} were larger than the granules of ST_{NA}. The granules of ST_{NA} were either round or oval in shape as compared with those of ST_A, which have smooth surfaces with thick round edges and, thin or hollow centre while ST_{AM} were smooth, disc-like, irregularly shaped aggregates resembling MCC as shown in Fig. 1.

Moisture Uptake

The isothermal moisture sorption of the ST_{NA}, ST_A, ST_{AM}, and MCC are presented in Fig. 2. The equilibrium moisture uptake of MCC, ST_{NA}, ST_A and ST_{AM} increased with increase in RH. Between 27% and 75% RH, moisture uptake was low. There was however increased uptake at 81% and 100% RH as shown in Fig. 2.

Differential Scanning Calorimetry

The thermal characteristics of ST_{NA}, ST_A, ST_{AM}, and MCC based on DSC thermal analysis are presented in Fig. 3 and Table I. The thermographs of ST_{NA} and MCC are characterized by two endothermic transitions with the initial corresponding to the polymers' glass transition and the latter the melting of the crystalline domain respectively as compared with those of ST_A and ST_{AM} which have an initial endothermic transition corresponding to their glass transition and an exothermic transition curve corresponding to the cold crystallization.

X-ray Diffraction Pattern

The X-ray diffraction patterns of ST_{NA}, MCC, ST_A, and ST_{AM} showed different patterns as presented in Fig. 4. Consequently, the reflection angle, 2θ, along with the interplanar spacing d, and the relative intensity of the peaks differed. The native starch showed strong peaks at approximately 2θ=15°, 17°, 18°, and 23°. ST_A showed a single strong peak at 2θ=20°, while ST_{AM} showed three strong peaks at 2θ=15°, 17°, and 23° similar to MCC with its peaks at 16°, 20°, and 34°.

Flow Properties

The compressibility index and angle of repose of ST_{NA}, MCC, ST_A, and ST_{AM} are presented in Table II. ST_{AM} showed enhanced flow in relation to MCC, ST_A, and ST_{NA}.

Powder Swelling Capacity

The swelling studies showed that ST_{AM} had the highest relative swelling capacity, which could be ranked thus, in order of decreasing swelling capacity: ST_{AM}>ST_A>ST_{NA}>MCC.

Dilution Capacity

The dilution capacity of ST_{AM} comparative to ST_{NA}, ST_A, and MCC were determined by evaluating the tensile strength and

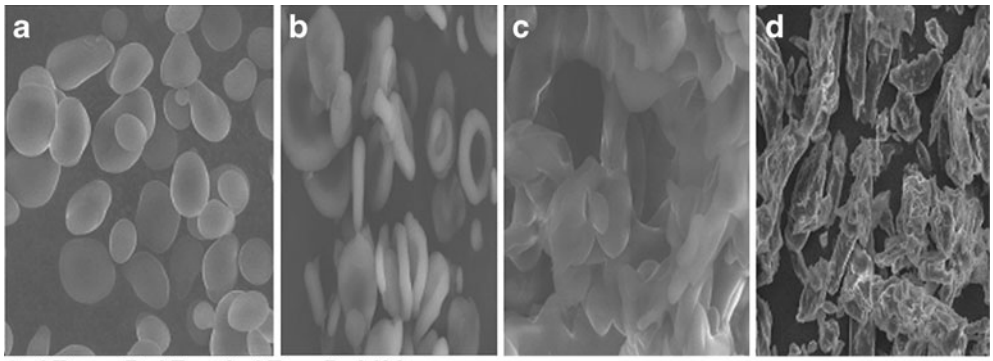

Fig. 1. SEM of **a** ST_{NA}, **b** ST_A, **c** ST_{AM}, and **d** MCC (magnification, ×2,000)

friability of the compacts prepared with varying ratio mixtures of the excipients and Apn. The tensile strength and friability of the compacts are presented in Fig. 5 and Table III, respectively. The tensile strength of the respective compacts containing ST_{NA}, ST_A, ST_{AM}, or MCC showed significant increases as the proportion of the excipient in a compact increased. Compacts produced with ST_{AM} showed the highest increase in tensile strength as compared with compacts containing ST_{NA}, MCC, and ST_A (Fig. 5). The friability characteristics of the compacts were similar to the tensile strength profile (Table III; Fig. 5). The compacts containing only Apn without additional excipients and those containing 120 mg of Apn and 80 mg ST_{NA} crumbled completely into powder at the end of the abrasive and shock test, thus, friability was not determined. The compacts containing the different ratio mixtures of ST_{NA} and Apn as well as compacts containing only ST_{NA}, all showed friability greater than 10%. However, compacts containing ST_A, MCC, and ST_{AM} each showed an optimal ratio mix that has friability less than one percent (Table III).

Disintegration Characteristics

The disintegration efficiency of STNA, ST_A, ST_{AM}, and MCC are presented in Fig. 6. The disintegration time of the nondisintegrating ASA tablets was enhanced when the excipients were incorporated as disintegrant. While the ASA compacts containing ST_A and ST_{AM} disintegrated before 3 min, compacts prepared with ST_{NA} and MCC disintegrated at 8.5±0.5 and 58±11 min, respectively. Though the various materials reduced the disintegration time of ASA, compacts containing ST_{AM} however, showed the least disintegration time. The disintegration efficiency of MCC, ST_{NA}, ST_A, and ST_{AM} which is equivalent to the disintegration time can generally be ranked as follows: ASA>MCC-ASA>ST_A-ASA>ST_{NA}-ASA>ST_A-ASA>ST_{AM}-ASA.

DISCUSSIONS

Tigernut contain protein, lipids, sugars and starch as the major component (33,34). The pretreatment with petroleum ether was aimed at removing lipids which interfere with the extraction of the starch thereby reducing yield. Further repeated washing with water was to remove soluble components such as sugars (33). A total starch content of 42% has been reported for the tigernuts (34), a yield of 32.3±0.8% (*w*/*w*) was however obtained in our study. The yield can be regarded as satisfactory, when related to the fresh tubers with a moisture content of over 60% (18). Factors such as geographical origin, variety and age of plant are known to affect the amount of extractable starch from tigernut (2). The yields of 95% and 92% obtained for ST_A and ST_{AM} respectively is also considered to be satisfactory as this indicates minimal lose of the

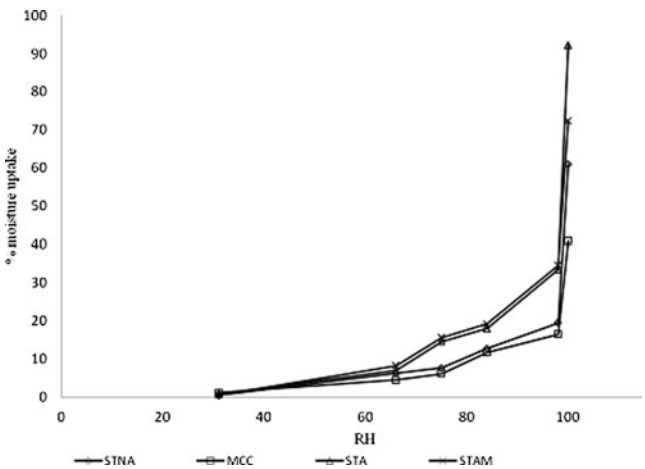

Fig. 2. Moisture sorption profile of *diamonds* ST_{NA}, *triangles* ST_A, and *error marks* ST_{AM}, *squares* MCC

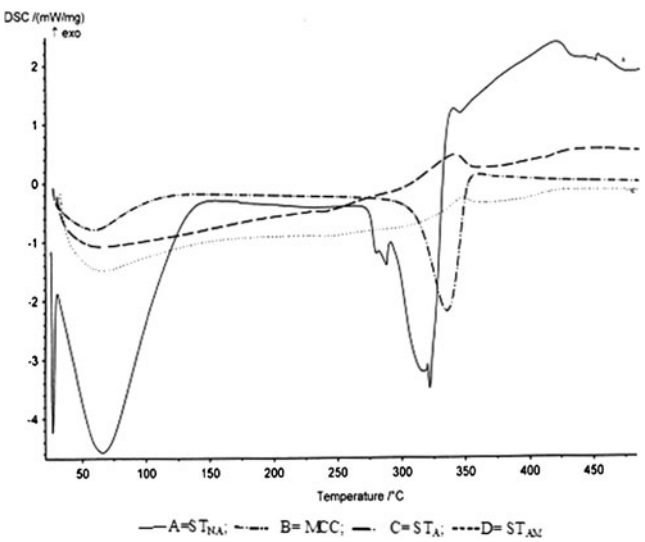

Fig. 3. DSC thermographs of *solid line* ST_{NA}, *dashed–dotted line* ST_A, *dotted line* ST_{AM}, and *dashed line* MCC

Table I. Thermal Properties of ST_{NA}, MCC, ST_A, and ST_{AM}

Parameters	ST_{NA}	MCC	ST_A	ST_{AM}
T_g (°C)	89.4	92.9	90.1	59.4
ΔH (J g^{-1} K^{-1})	16.068	4.073	0.794	2.673
T_m (°C)	322.0	346.2	–	–
T_{cr} (°C)	–	–	348.7	341.7

ST_{NA} native tigernut starch, *ST_A* tigernut starch modified by acid gelation, *ST_{AM}* tigernut starch modified by acid gelation and forced retrogradation, *MCC* microcrystalline cellulose, *T_g* Glass transition temperature, *T_m* peak melting temperature, *T_{cr}* peak crystallization temperature

start material. The high yield thus, indicates the high throughput and efficiency of this technique.

For drug delivery applications, starch from different botanical sources have been modified using different techniques to impact new properties to enhance performance of known applications or impart new applications. Although starch has traditionally been modified by acid and alcohol treatment (18,35), the technique currently been studied is based on gelatinization of acidic dispersion of tigernut starch accompanied by freezing and thawing. This technique was used to generate a material with enhanced direct compression, flow and disintegrant properties when compared with MCC and ST_{NA}. The modification technique is generally based on the combination of controlled pH gelatinization, gelation, forced retrogradation, and recovery with acetone to generate a highly compressible, free-flowing powder with enhanced disintegration ability. The forced retrogradation impacted by freezing at a temperature of −60°C results in formation of crystallites by accelerated re-association of the disrupted polymer network. The re-association is initiated predominantly by the amylose component of the starch and slowly by the amylopectin portion. The functional efficiency of the modified tigernut starch as a potential direct compression excipient can be attributed to the amount and nature of the amylose and amylopectin content of the starch which re-associates after the disruption of the crystalline component of the native starch due to gelatinization and gelation processes to form the semicrystaline domain as shown by the DSC thermal analysis.

Particle morphology is an important property in the characterization and identification of especially powdered pharmaceutical excipients. It can also be used to predict certain functional properties that relate especially to the powder compaction and flow (36). The round and oval shapes of ST_{NA} granules, the smooth surface with thick round edges and thin or hollow center of ST_A, and the smooth, disc-like, irregularly shaped aggregates of ST_{AM} are characteristic and establish the physical identity of the products at different stages of the modification process (37). Figure 1, thus, shows the basic differences and similarities in the appearance, shapes, and sizes of the native starch, the modified motifs, and MCC.

An understanding of the moisture sorption characteristics of pharmaceutical excipients is imperative since most of physicochemical and functional properties of these materials either depend or are affected by it. Moisture may also induce unpredicted phase transitions in excipients which may also be imparted to the APIs when used for formulation. Generally, when starch is exposed to a moisture rich environment, the water molecules interact strongly with the polar groups of the

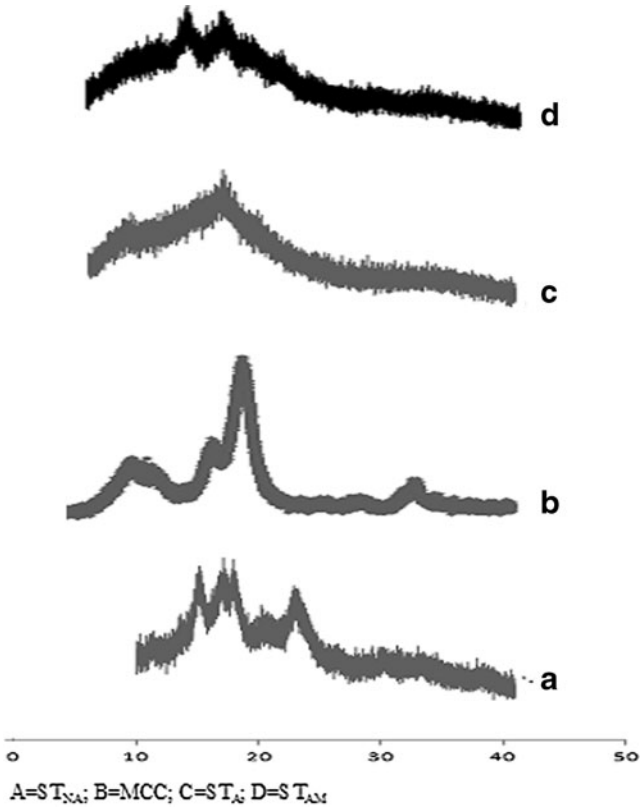

Fig. 4. X-ray diffraction spectra of *A* ST_{NA}, *B* MCC, *C* ST_A, and *D* ST_{AM}

amylose and amylopectin units, forming a monomolecular layer (38–40). ST_{NA} and MCC showed similar moisture sorption profile corresponding to type III as compared with type II shown by ST_A and ST_{AM} when evaluated according to the International Union of Pure and Applied Chemistry (IUAPAC) classification (41,42). The moisture sorption isotherm shown by MCC and ST_{NA} is characteristic of multilayer moisture absorption throughout the range of RH assessed. This mode of moisture sorption is typical of polymers with high crystalline domain (41). The moisture sorption profiles of MCC and ST_{NA}, though similar, showed remarkable difference when the equilibrium moisture uptake at 100% RH is considered (Fig. 2). The type II moisture sorption isotherm shown by ST_A and ST_{AM} is typically characteristic of combination of monolayer and multilayer uptake (43). Generally, evaluation of the mechanism of the moisture sorption of the four powders shows that it was controlled by the combinations of colligative and capillary effects, and surface-water interactions (44). The higher moisture uptake of ST_{AM} can be related to the disruption of the polymer chain network of the native starch resulting in the exposure of numerous polar functional groups, which interact with the water molecules.

When polymers are exposed to heat at different temperatures, they show thermographs that are characteristic and related to their crystallinity. The DSC technique is essentially useful in characterizing polymers based on their exothermic and endothermic transitions (45). The thermal response of the ST_{NA} and its modification motifs were typical and are characteristic of their thermodynamic transitions as presented in Fig. 3 and Table I. The melting peak of ST_{NA} is characteristic of the crystalline domain of the ST_{NA} (46,47). The absence of melting peaks and the presence of a glass transition and cold crystallization transitions, show a predominantly amorphous

Table II. Particle Properties of ST_{NA}, MCC, ST_A, and ST_{AM}

Parameter	MCC	STNA	STA	STAM
Bulk density	0.31±0.02	0.56±0.04	0.56±0.05	0.26±0.04
Tapped density	0.42±0.03	0.83±0.03	>0.83±0.01	0.53±0.01
Carr's index (%)	26.20±0.03	32.53±0.05	32.53±0.03	21.20±0.07
Angle of repose (deg)	23.80±0.61	34.80 ±0.50	34.20±0.50	9.30±0.50
Swelling capacity (%)	102.00±5.00	317.00±5.50	368.18±4.60	716.30±5.50

and pseudo-amorphous domain in ST_A and ST_{AM}. The dominance of these domains in this modification motifs are due to the deformation of the structural integrity of the ST_{NA} polymer chain network due to the gelatinization and retrogradation-based modifications. The deformation and reorientation of the polymer structure are responsible for the conversion of the crystalline domain to amorphous and semi-crystalline forms. The initial secondary transition is characteristic of the amorphous region typical of the glass transition. Further heating resulted in the re-association and the crystallization before decomposition of the material, hence the absence of a distinct melting peak.

The X-ray diffraction patterns of granular starches are dependent upon the arrangement of the double helical amylopectin chains and can be classified into A, B, and C starch types (14). The diffractogram and relevant peaks of ST_{NA} are typical of A-type starch (48). The A pattern shown by the ST_{NA} can be related to the close packing of water molecule and the amylopectin helices. The diffractogram of ST_{NA} (Fig. 4) is similar to those reported for potato and cassava starches (49–51). However, the modified tigernut starch showed X-ray patterns that are different and typical. The differences reflect the basic differences in the crystallinity of the different materials which relate to the modification processing.

The bulk and tapped densities is applied as an indirect method for predicting the flow and compactibility properties of the powders (24). Using this method, ST_{AM} showed better flow in relation to MCC, ST_{NA}, and ST_A. The lower values derived for the bulk and tapped densities for ST_{AM} and MCC (Table II), are due to the higher bulk volume per unit weight, a property imparted on ST_{AM} by the freezing and thawing process. The flow index of the powders as estimated by the Carr's compressibility index is based on the bulk and tapped densities. Generally, when assessing powder flow with the Carr's compressibility index, values below 15% represent good flow and 15% to 25% represent fair, while values above 25% are indicative of poor flow (24). Corresponding results were obtained for the powders' flow estimated by assessing their angle of repose. The flow qualities of the powders as determined by the angle of repose correlated well with the results obtained with the Carr's compressibility index. The flow of powders as assessed by the angle of repose is based on the inter-particulate cohesion: values less than 25° is indicative of "very-good flow," whereas values equal and greater than 25° but less than 50° indicate "good flow" while values greater than 50° indicate "poor flow" (24). Thus, ST_{AM} is classed as having "very good flow" while ST_A, ST_{NA}, and MCC qualified as having "good flow" (Table II).

Swelling is one of the mechanisms of disintegration and is a critical property for material with potential as disintegrant and intended for formulating quick release tablets and capsules especially where rapid disintegration is required. The swelling capacity of ST_{NA} and its modified motifs in relation to MCC can be ranked thus: $ST_{AM}>ST_A>ST_{NA}>MCC$. The higher swelling capacity of ST_{AM} may be related to the enhanced capillary water ingress into the powder (32,52).

An important property of direct compression excipients is their characteristic high dilution capacity (also known as loading capacity or carrying capacity) (53). The powder dilution capacity relates to the amount of the active pharmaceutical ingredient (API) that can be added to the excipients while

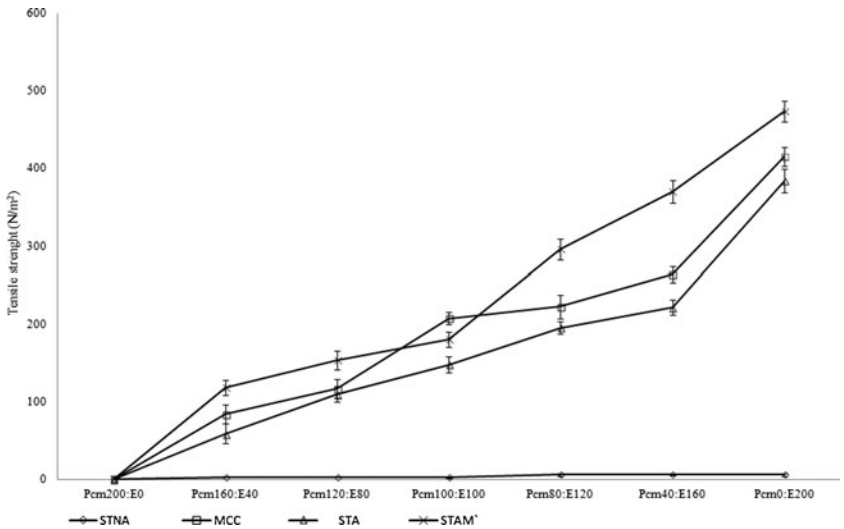

Fig. 5. Effect of acetomenophen loading on the tensile strength of *diamonds* ST_{NA}, *squares* MCC, *triangles* ST_A, and *error marks* ST_{AM} compacts

Table III. Friability of Compacts Prepared with Different Ratio Mix of Acetaminophen and MCC, ST_{NA}, ST_A, and ST_{AM}, Respectively

Acetaminophen: excipient	Percentage weight loss (mean±SEM)			
Ratio mix	MCC (%)	ST_{NA} (%)	ST_A (%)	ST_{AM} (%)
Apn 200:E0	≠	≠	≠	≠
Apn 120:E80	8.5±1.1	≠	13.1±1.0	10.6±1.3
Apn 100:E100	3.7±0.7	13.5±1.1	3.9±0.5	1.6±0.5
Apn 80:E120	0	13.1±0.8	1.3±0.5	0.4±0.3
Apn 40:E160	0	10.6±1.0	0.8±0.3	0
Apn 0:E200	0	10.2±0.9	0	0

≠ =Not determined due to friable compacts

maintaining an intact compact (54). This is determined by evaluating the physical strength of the compacts after graded concentrations of the API and the potential direct compression excipient are compressed (30). Apn is a prototype API for evaluating the dilution capacity of direct compression excipients: it is used because of its poor compaction characteristic due to its potential to undergo elastic recovery after withdrawal of the compaction pressure (30,53). Tensile strength and friability were used to evaluate the dilution capacity of this potential direct compression excipient because these are properties that relate directly to the physical strength of compressed tablets. The compacts prepared with ST_{NA}, ST_A, ST_{AM}, and MCC showed increase in tensile strength profile as their ratio in the mix increased as compared with the noncompacting Apn (Fig. 6). The MCC (avicel^R) was used as the standard excipient for assessing the carrying capacity of the modified tigernut starch because it is a prototype direct compression excopient reputed for having a high carrying capacity (30). However, Apn compacts prepared with ST_{AM} showed higher tensile strength at the various ratios of mix with Apn when compared with MCC. Generally, the dilution capacity of the different materials as assessed by the tensile strength of Apn compacts can be ranked thus: ST_{AM}>MCC>ST_A>ST_{NA}. The absence of friability data for the compacts of Apn and ratio mixture of 120 mg Apn and 80 mg ST_{NA} is due to the inability of these to form a stable compact due to the influence of the poor compactibilty of Apn. Compacts of Apn with MCC and ST_{AM} showed similar friability profile over the same ratio mixture as they produced stable and acceptable compacts at similar dilution range as compared with the high friability of ST_{NA} (Table III). The low tensile strength and high friability of ST_{NA} may be related to the poor intrinsic compactibility that is characteristic of native starches. The enhanced dilution capacity of ST_{AM} as shown by the high tensile strength and low friability of its compacts may be related to its lower bulk density, optimal moisture content, and the higher density of interparticulate hydrogen bonding due to extensive deformation of the particles when compressed (8). In comparison to ST_{NA} and ST_A, the superior dilution capacity of ST_{AM} can be related to such properties as crystallinity, particle shape, as well as its low bulk density which contribute to the effective micro-squashing when load is applied to the powder mass thus, resulting in a more efficient plastic deformation (9).

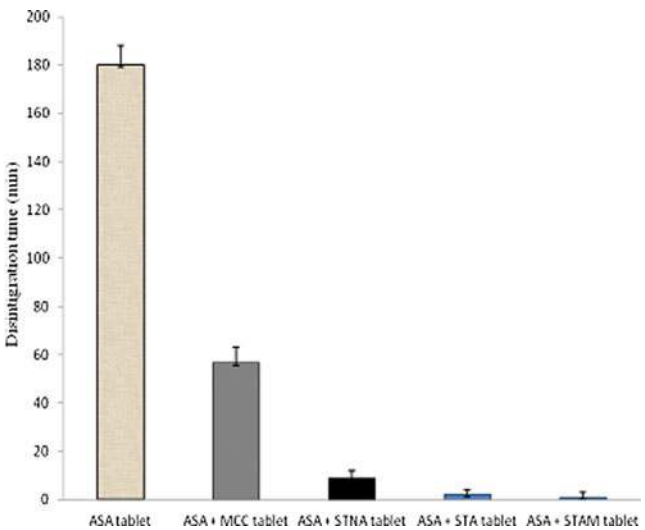

Fig. 6. Disintegration time for tablets made of ASA crystal, ASA+MCC, ASA+ST_{NA}, ASA+ST_A, and ASA+ST_{AM}

Rapid disintegration is an essential attribute of conventional tablets and capsules especially those intended for rapid release of the active ingredient. The needs for materials with enhanced disintegration ability as well as imparting high mechanical strength are among the reasons for the search for excipients with multifunctional properties (8). ASA was used to evaluate the disintegration efficiency of the novel excipient because of its high compactibility, poor solubility and nondisintegration in aqueous media (31). ST_{NA}, ST_A, ST_{AM}, and MCC showed varying degrees of disintegration efficiency when incorporated into the nondisintegrating ASA. ASA tablets prepared with the native starch and the modification products disintegrated before 15 min which is the acceptable compendia requirement for immediate release tablets when water is used as the disintegration media (32). The rapid disintegration of ASA tablets formulated with ST_{AM} and ST_A may be related to their high swelling capacity and possibly by the rapid penetration of water into the tablets matrix by capillary wicking (55). Though, rapid disintegration and hardness are divergent tablet properties, these are nevertheless complimentary and essential for a robust rapid release tablets. The motif, ST_{AM} potentially combined these attributes in the tablets and show superiority to MCC, ST_{NA}, and ST_A.

CONCLUSIONS

A new pharmaceutical excipient with very good flow, enhanced disintegration ability, and dilution capacity has been generated from the acidic gel of tigernut starch by the process of forced retrogradation. The novel excipient also showed physicochemical properties that were partly typical or similar to the ST_{NA} and MCC. Because this material portends a cheap and efficient direct compression excipient, further study on this potential direct compression pharmaceutical excipient has

been proposed to determine such properties as the effect of moisture content, aging (storage time), lubricant sensitivity, reworking on tablets quality, as well as its interactions with common API and other excipients.

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