Carboxymethylation of Starches Obtained from Three *Dioscorea* Species: Effect on Powder, Granule and Tablet Properties.

Jolly A. Nnamdi, * Matthew I. Arhewoh, Sylvester O. Eraga and Magnus A. Iwuagwu.
Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, University of Benin, Benin City, 300001, Nigeria.

ABSTRACT

Excipients used in tablet production can be modified to enhance tablet properties. The aim of this study was to prepare carboxymethyl starch (CMS) using starches obtained from three *Dioscorea* (yam) species viz *D. rotundata, D. dumetorum* and *D. alata,* and to investigate the effect of carboxymethylation on their powder, granules and tablet properties. Comparative evaluation studies were carried out on the native and modified starch powders. Fourier Transform Infrared Spectrophotometry (FTIR) and Differential Scanning Calorimetry (DSC) were carried out on the powders to ascertain carboxymethylation. The properties of paracetamol granules and tablets obtained from the powders were analyzed according to official methods. The modified and native starches were comparable in powder micromeritics, bulk and flow properties. The modified starches exhibited superior swelling capacity of 3.2-14.4 % above the native starches. Granule properties were influenced by the concentration of starch incorporated as disintegrant. The FTIR and DSC spectra confirmed changes in functional groups. Tablet hardness ranged from 5.62 to 16 N while disintegration was achieved in < 3 min. Excellent disintegrant was obtained at 5 %w/w CMS in paracetamol tablet formulation. The modified starch will find usefulness as enhanced disintegrant in compressed tablet dosage forms especially where shorter disintegration times are desired as a result of its superior swelling capacity.

Keyword: Carboxymethylation, Yam starch, Tablet properties.

INTRODUCTION

The performance of pharmaceutical excipients is influenced by the physicochemical properties and the quality of the excipients. These physical properties can be manipulated during the production of these excipients. An option to improve the physical properties of excipients is to alter their chemical nature or structure by carrying out reactions like substitution, condensation, hydrolysis etc. Examples include modified cellulose gum which is a cross-linked form of sodium carboxymethyl cellulose (CMC) and carboxymethyl starch (CMS) which is a substituted form of starch from various plant sources (Vaclavik and Christian 2007). All green plants produce starch as an energy store. Pure starch is a white tasteless and odourless powder that is insoluble in cold water and alcohol. Starches are modified by physically, enzymatically or chemically treating the native form of the starch (Gotlieb and Capelle, 2005). Yam is the common name for some plant species in the genus *dioscorea* (Dioscoreaceae) that form edible tubers. They are perennial herbaceous vines cultivated for consumption of their starchy tubers.

Modified excipients have been reported to improve tablet properties such as compressibility and dissolution characteristics in pharmaceutical preparations. Recently, they have also been widely employed in formulation of oral dispersible tablets (Chaudary, 2010). Oral dispersible tablets are fast disintegrating tablets that readily dissolve or disperse when placed in the oral cavity. Their characteristic advantages such as administration without water anywhere and at any time lead to their suitability in formulating products that are advantageous or useful to geriatric and pediatric patients. They are also suitable for the mentally ill, the bedridden and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability and good stability, make these tablets popular as a dosage form of choice in the present day market (Chang *et al,* 2000; Bi *et al,* 1996). CMS has been applied to improve the properties of starch in the production of paper. Cationic carboxymethyl starch had a strengthening effect on paper which distinguishes it from other retention aid. (Shumei *et al,* 2012) CMS has been used as a printing thickener. (Haang *et al,* 2013) and in the production of fast disintegration tablet (Nattawat *et al,* 2009).

This study seeks to evaluate the powder, granules and tablets properties of carboxymethylated yam starches. This is compared to native yam starches, Sodium carboxymethyl cellulose (Ac-di-sol®) and corn starch powder which were used as control in making fast disintegrating tablets.

Paracetamol powder was used as the model active pharmaceutical ingredient (API).

***Correspondence: Email**: korgban@yaahoo. com; **Tel:** +2348035402038

MATERIALS AND METHODS

Materials

Isopropyl alcohol and talc were products of BDH Chemicals, England, sodium hydroxide was purchased from Tiasin Chemical Co. Ltd, China, while monochloroacetic acid was obtained from Qualikems, Germany. Ethanol (96%, absolute) was purchased from Sigma-Aldrich, Germany. Maize starch BP is a product of Roquette Freres, France while lactose and magnesium stearate were obtained from Evans Medical, UK. Sodium carboxymethyl cellulose (Ac-di-sol®) was a product of FMC Corp. USA. All other chemicals used were of analytical grade. The yam tubers; *Dioscorea dumetorum* (bitter yam), *Dioscorea alata* (water yam) and *Dioscorea rotundata* (white yam) were purchased from local markets in Southern part of Nigeria. All sieves were British Standard Sieves (Endecotts Ltd. England).

Method

Extraction of yam starch

The yam tubers were washed to remove extraneous materials, peeled, chopped into pieces and soaked in water for 3 h to soften the tissues. The yam pieces were milled into pulp using a blender (Moulinex, France). The starch was extracted by straining the pulp through a muslin cloth. The fibrous materials were removed and the filtrate was allowed to stand for 6 h after which the supernatant was discarded and the precipitated starch recovered. This procedure was repeated twice. The starch extracted was initially air dried and then further dried in a hot air oven (Kottermans, Germany), at 50oC for 6 h, and stored in airtight containers (Iwuagwu et al, 1986).

Preparation of carboxymethyl starch (CMS) powder

The CMS was prepared according to the method of (Nattapulwat and Suwithayapanth, 2009). The extracted starch powder (50 g) was suspended in 150 mL of 2-propanol. An aqueous solution of 3 M sodium hydroxide (50 mL) was added. The mixture was stirred at a temperature of 30oC for 10 min. The monochloroacetic acid solution (25 mL) was added and stirring continued up to 6 h. The pH of the mixture was adjusted to 5.0 with the addition of 50% glacial acetic acid. The carboxymethyl starch formed was filtered, washed with 80% ethanol and dried at 50oC for 6 h. The dried starch was sieved through 150 mesh sieve and stored in an airtight container away from light.

Characterization of native and carboxymethyl yam starches

Organoleptic properties

Physical examination for color, taste, odour and texture were carried out by five different assessors. Each character attribute was assigned scores (from 5 to 0) to define extreme conditions of acceptability or not acceptable. The independent scores of the five assessors were compiled and the most dominant 3 responses of the 5 was taken as positive (Nnamdi et al, 2009).

Particle size analysis

The starch powder was thinly spread over a glass slide and viewed under a light microscope (Labo Microsystems GmbH, Germany) incorporating a calibrated eyepiece interfaced with a digital camera and a computer. The sizes and shapes of the particles were recorded at a magnification of 40 (MICAM 1.4, Scope Image 9.0). Particles that appear in four representative fields of view were counted and the values recorded. A minimum of four different fields of view was captured and their mean particle size was calculated (Stanforth and Taylor 2013).

Bulk and flow properties

The bulk and flow properties of the powders like bulk density, tapped density, Carr`s compressibility index, Hausner's ratio, angle of repose and swelling capacity were evaluated using established procedures (Staniforth and Aulton, 2007).

Swelling capacity

This was determined using the method of Bowen and Vadino (1984), as modified by Iwuagwu and Okoli (1992). This involved weighing 5 g of various starch powder into 100 mL measuring cylinder and the bulk volume (Vx) was noted. Exactly 85 mL of distilled water previously flushed with nitrogen at room temperature was added and the measuring cylinder agitated to disperse the starch. The volume of the suspension was made up to 100 mL with more distilled water. The dispersion was allowed to stand for 24 h after which the volume of the sediment (Vy) was read. The swelling capacity was computed using Equation 1. V_y/V_x x 100/1 …. (1)

Differential Scanning Calorimetry (DSC)

The DSC spectra were obtained using Netzsch DSC 204 F1 (Germany). Approximately 1 mg of starch sample was weighed into an aluminum pan. The pan was sealed and the seal pierced for aeration and placed in the combustion chamber. The equipment was operated at a heating rate of 10 ^oC/min from room temperature up to 400 ^oC under nitrogen gas at a flow rate of 70 ml/min. The results were analyzed using a themokinectic data analyzer (Van-Dooren and Mullar, 1984).

Fourier-Transform Infrared Spectroscopy (FTIR)

The FTIR spectra were obtained using a Perkin-Elmer FTIR Spectrophotometer (UK). Between 3 to 5 mg of starch was blended with dried potassium bromide and compressed to a 200 mg tablet using a Sigma FTIR tablet press. The compressed tablet was placed in the sample holder, while the equipment was set to read at wave number from 4000 to 750 cm-1.

Preparation of granules

The wet granulation method (BP. 2003) of massing and screening was used in preparing all the batches of paracetamol granules using the formula shown in Table 2. Three batches of granules that will be used for tablet production were prepared using 2.5, 5.0 and 7.5% w/w of disintegrants in the formulations. The required amounts of paracetamol and corn starch not lactose powders were mixed for 15 min in a mixer. Half of the weighed amount of disintegrant was incorporated intragranularly to the powder mix in geometric proportions during the mixing.

Sufficient quantities of the binder solution (10 %w/v) required to form a wet mass was gradually added to the powder mix. The wet mass produced was passed through a 2-mm mesh screen and the resulting granules dried at 60 ºC for 30 min in a hot air oven (Gallenkamp, UK). The granules were rescreened through a 710 µm diameter sieve and further dried for another 30 min. The glidant, lubricant and the other half of the disintegrant previously weighed and mixed in a mortar were added to the dry granules in geometric proportion and mixed in readiness for compression. The granules were subjected to various analyses.

Granule analysis

The bulk and flow properties of the granules; bulk density, tapped density, true density, Carr`s compressibility index, Hausner ratio, angle of repose and flow rate were evaluated using established procedures (British Pharmacopeia, 2003).

Preparation of tablet

Three batches of granules for the tablet were prepared using 2.5, 5 and 7.5% w/w of disintegrants in the formulations, respectively. Maize starch (10 %w/v) as binder, talc as glidant, magnesium stearate as lubricant. The yam starches native and modified, corn starch and sodium carboxymethyl cellulose (Ac-di-sol) were used as disintegrant for the different batches. The tablets were prepared using a single punch tablet forming machine (F3-Manesty, Manesty machine Ltd, England). The compression pressure was set at 38 N (BP, 2003; USP, 2003).

Evaluation of the tablets

Some physicochemical properties of the paracetamol tablets like weight uniformity, crushing strength, disintegration time and friability were compared to those of tablet prepared with Corn starch BP and Modified cellulose gum N.F (Ac-di-sol®).

Uniformity of weight and dimension

Twenty tablets were randomly selected from each batch and weighed using an electronic balance (Scout-Pro, China). The mean weight as well as standard deviations were calculated. The thickness of the tablets was determined using a Micrometer screw gauge (Sterling Manufacturing Company, England). The mean thickness and standard deviation were computed (BP 2003, USP 2003).

Tablet hardness and friability testing

A motorized digital hardness tester (Campbell Eletronic Hardness Tester. Model HT 3050 India) was used to determine the hardness of ten randomly selected tablets from each batch. The load required to cause diametric fracture in a tablet was determined. The mean values were computed. For friability testing, ten randomly selected tablets were dedusted and weighed. The tablets were placed in the drum of an Erweka Friabilator (Erweka, Germany) and subjected to cascading and free fall stress at 25 rpm for 4 min. The tablets were removed from the Friabilator, dusted and reweighed to determine the percentage weight lost (BP 2003; USP 2003)

Disintegration time

The test was carried out using six tablets from each batch in distilled water at 37 ± 1 ºC in a BP Disintegration Apparatus at 30 cycles per min (MK IV Manesty Machine Ltd, England). The test was carried out for 15 min (BP 2003, USP 2003).

Dissolution test

In vitro drug release studies were carried out using a dissolution apparatus (Model DT-D6, Erweka, Germany). The dissolution medium was 900 mL of 0.1 N HCl maintained at 37± 1 °C for 60 min to simulate the gastric medium. In all experiments, 5 mL of sample was withdrawn at 10, 15, 20, 30 and 60 min intervals and replaced with fresh medium at same temperature to maintain sink condition. Samples were filtered through a filter paper and suitably diluted. The samples were then assayed at 249 nm using a UV/Visible spectrophotometer (T70, PG Instruments Ltd, USA) using 0.1 N HCl as blank. Percentage drug released was computed (BP 2003, USP 2003).

Statistical analysis

Descriptive statistics was carried out on the data obtained using Microsoft Excel (2007) package. Results were computed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) was done using Instat Graph Pad and $p < 0.05$ was considered significant.

RESULTS

Organoleptic properties of the yam starches

The results of organoleptic tests of the starch powders showed no difference in color, taste, odour and texture among the various native starches but upon carboxymethylation, changes were observed only in their color from white to off-white.

Microscopy

Results of the microscopic examination of the various starches and their modified CM formsare shown in Figure 1. There was no significant difference in the particle size distribution of the various starches whether modified or unmodified ($p < 0.05$). The starches and their modified forms had a particle size range of 10 - 30 µm. The shapes of the starches were mainly oval.

Flow and bulk properties of the starch powders

The results of flow and bulk properties of native and carboxymethylated starches are as shown in Table 1. The carboxymethylated starches of *Dioscorea dumetorum* (bitter yam), *Dioscorea alata* (water yam) and *Dioscorea rotundata* (white yam) showed more swelling capacity than their native forms. This could be harnessed in the production of products such as super absorbent hydrogel. The Carr's indices and Hausner`s ratio of the various yam starches indicate that the powders have reasonably good flow and bulk properties. It can be seen from the data that the various yam starches gave Carr's indices and Hausner's ratios of less than 25 % and 1.25, respectively. Values less than these, show good powder flow. It can be observed from the result that the flow properties of the powders were enhanced by carboxymethylation because it made the powders coarse.

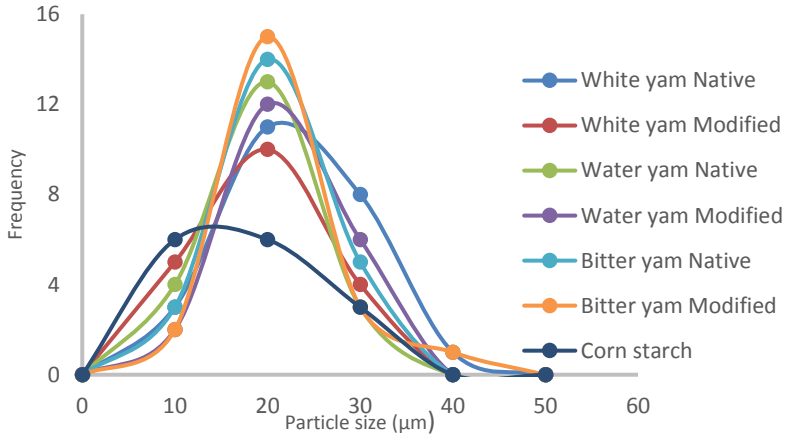

Figure 1: Particle size distribution of the various starch powders tested

Table 1: Some powder properties of native and modified starches from *Dioscorea spp*

Properties	*D. dumetorum* (Bitter yam)		*D. alata* (Water yam)		*D. rotundata* (White yam)		Corn starch
	Native	Modified	Native	Modified	Native	Modified	
Swelling capacity	1.66	1.75	1.25	1.43	1.25	1.29	0.50
True density (g/cm^3)	0.48	0.31	0.60	0.38	0.53	0.32	0.53
Bulk density (g/cm^3)	0.44	0.45	0.40	0.39	0.39	0.38	0.39
Tapped density (g/cm^3)	0.49	0.49	0.53	0.48	0.49	0.47	0.49
Carr's index (%)	11.04	8.04	23.61	17.63	19.89	18.92	20.69
Hausner's ratio	1.124	1.09	1.31	1.21	1.25	1.23	1.26

FTIR and DSC characterization studies

Fourier transform infrared (FTIR) spectra of the yam starches (native and carboxymethyl modified forms) are shown in Figure 2. In the three native yam starches (a), (c) and (e), the band stretch around 3365 cm^{-1} is attributed to hydrogen bonded hydroxyl groups on the yam starch molecules. The band at v = 2930.54 cm^{-1} is assigned to CH_2 symmetrical stretching vibrations, the band v = 1642.33 cm^{-1} is assigned to scissoring of two O-H bonds of absorbed water molecules. The bands at v = 928.49 and 848.70 cm^{-1} are due to skeletal stretching vibrations of starches. However, in the carboxymethyl bitter yam starch (f), the intense band at v = 1602.55 cm^{-1} is assigned to carbonyl functional group and the new band v = 1401.55 cm^{-1} is attributed to -CH_2 scissoring. These bands confirm that carboxymethylation took place. This is similar to the change obtained in the white (b) and water (d) yam starches. The band change of v = 1365.44 cm^{-1} of the native yam starch to 1408.58 cm^{-1} of the carboxymethylated starch, is attributed to –CH_2 scissoring. This new band confirms that carboxymethylation took place on the white and water yam starch molecules. The results from differential scanning calorimetry (DSC) showed a disappearance of a peak in all the native starches after 300oC as a result of carboxymethylation. The initial broad trough that occurred before 100oC in all the spectra was as a result of loss of water of hydration due to evaporation (Figure 3).

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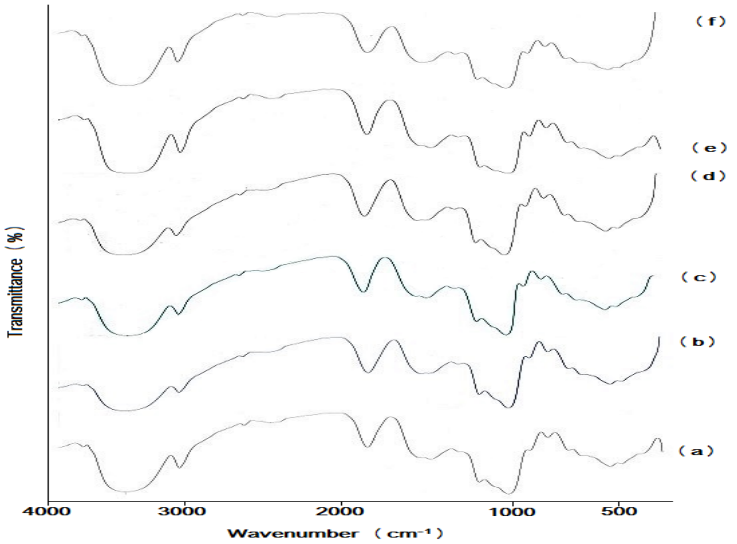

Figure 2: FTIR spectra of native and modified starches from *Dioscorea spp*
Key: a = Native water yam starch; b = carboxymethyl water yam starch; c = Native white yam starch; d = carboxymethyl white yam starch; e = Native bitter yam starch; f = carboxymethyl bitter yam starch.

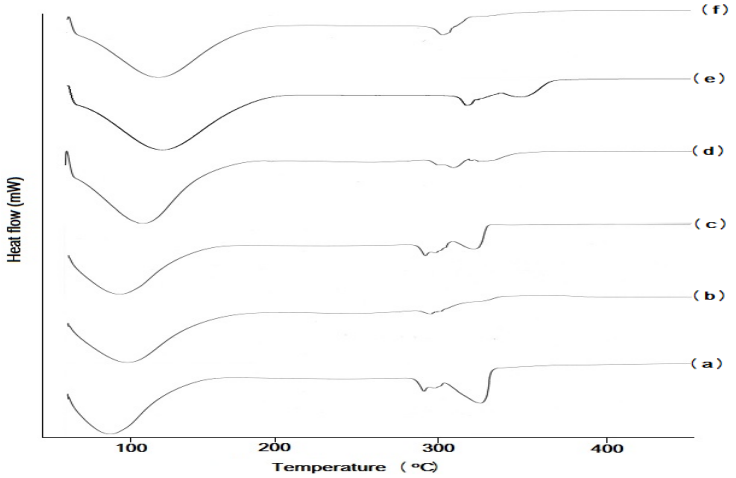

Figure 3: DSC thermograms of native and modified starches from *Dioscorea spp*
Key: a = Native water yam starch; b = carboxymethyl water yam starch; c = Native white yam starch; d = carboxymethyl white yam starch; e = Native bitter yam starch; f = carboxymethyl bitter yam starch.

Bulk and flow properties of granules

Apart from water yam starch, the result showed that the CM starch granules flowed better than granules prepared with the native yam starches (Table 2). As a general guide, powders with angles of repose greater than 50° have unsatisfactory flow properties, whereas powders with minimum angles close to 25°correspond to good flow, and granulation helps to improve flow (Staniforth and Aulton, 2007). Physicochemical properties of formulated paracetamol tablet

The result of some physicochemical testing of formulated paracetamol tablets at different concentrations of disintegrant is shown in Table 3. Weight uniformity showed no significant difference among the various starches and the tablet batches produced. These were in conformity with B. P standards (BP, 2003). The result of the hardness test showed that all the tablets produced passed the test. Hardness values ranged from 6 to 17 ± 1 kgf.

Friability test showed that, apart from tablets produced using 2. 5% concentrations of disintegrant of bitter yam and white yam starches, all other tablets passed the test. Their percentage friability was less than 1% as stipulated in the official books (BP, 2003).

Table 2: Bulk and flow properties of granules prepared using native and modified starches as disintegrant at different concentration

Parameters	Batches (%)	*D. dumentorium* (Bitter yam)		*D. alata* (Water yam)		*D. rotundata* (White yam)		Corn starch
		Native	Modified	Native	Modified	Native	Modified	
Flow rate (g/sec)	2.50	2.77	2.50	1.92	3.13	2.63	1.7	2.00
	5.00	5.28	5.43	5.87	6.50	5.58	6.90	6.07
	7.50	2.27	2.00	2.08	2.17	2.08	2.08	
Angle of repose (°)	2.50	26.21	30.14	30.90	30.14	28.09	30.96	30.60
	5.00	32.33	29.54	24.77	21.88	30.99	26.77	44.02
	7.50	27.29	28.35	26.90	26.21	26.90	28.35	
Bulk density (g/cm^3)	2.50	0.15	0.16	0.16	0.15	0.16	0.14	0.12
	5.00	0.44	0.45	0.40	0.40	0.39	0.38	0.39
	7.50	0.13	0.14	0.13	0.14	0.12	0.12	
Tapped density (g/cm^3)	2.50	0.22	0.24	0.23	0.23	0.23	0.23	0.12
	5.00	0.49	0.49	0.53	0.48	0.49	0.47	0.49
	7.50	0.17	0.19	0.16	0.16	0.16	0.16	
Carr's index (%)	2.50	31.81	32.33	46.56	34.78	40.36	39.18	25.00
	5.00	11.04	18.04	23.61	17.63	19.89	18.92	20.64
	7.50	23.52	26.31	18.75	18.75	21.87	25.00	
Hausner's ratio	2.50	0.68	0.66	0.69	0.65	0.69	0.60	0.75
	5.00	1.12	1.08	1.31	1.21	1.25	1.23	1.26
	7.50	0.76	0.73	0.81	0.81	0.78	0.75	

Key: HR < 1. 25 gives good flow; CI < 25% represents good flow

DISCUSSION

It has been reported that the morphological characteristics of starch granules vary considerably from one species to the other and it is also influenced by the place of cultivation (Farhat et al, 1999). Shapes reported with the scanning electron microscopy of the test starches from yams grown in Nigeria revealed that D. rotundata had oval shape while D. alata was rounded ovoid in shape and D. dumetorum had polygonal granules (Lawal et al, 2008b). SEM was not carried out in this study. However, previous studies already show that the granular shape of yam starches is distorted by carboxymethylation (Lawal et al, 2008a). This observation would suggest that carboxymethylation affects the structural arrangement of the starches. It is also reasonable to suggest that the strong alkaline condition used for the reaction process caused granular distortion. Strong NaOH solution (an alkaline solution) was used in the presence of monochloroacetic acid, to prepare CMS. The burning effects of these chemical agents caused the distortion in shape of the CMS yam starch when viewed in electron microscope (Lawal et al, 2008a).

Disintegration time and dissolution profile

Results of the study revealed that all yam starch tablets disintegrated within 3 min, which met the BP requirement of 15 min (BP,2003). The tablets produced from maize starch B. P disintegrated within 4 min. When the extracted starches were allowed to stand long enough to sediment, it was observed that the bitter yam starch took longer time to fully sediment when compared to the other starches. It was also more easily redispersible in water compared to white and water yam starches. This property can be taken advantage of in the formulation of pharmaceutical suspensions or dry powders to be reconstituted with water for use as syrups or injection purposes since the preparation will remain suspended long enough till the required dose is withdrawn. The higher yield of starch from the white yam makes it a more economical source of starch production and it is more easily available compared to water yam and bitter yam. The African bitter yam is easier to cultivate and not often used as food. It can be ready source of starch as raw material.

Table 3: Properties of Tablets at different concentrations of disintegrants

Parameters	Disintegrant concentration (%)	*D. dumetorium* (Bitter yam)		*D. alata* (Water yam)		*D. rotundata* (White yam)		Corn starch	Mod. Cell gum
		Native	Modified	Native	Modified	Native	Modified		
Weight (mg)	2.50	600±6	599±5	598±4	597±5	603±5	598±7		
	5.00	596±5	598±9	600±0	597±5	596±5	596±5	600±0	593±5
	7.50	600±9	598±8	602±9	594±5	596±5	600±0		
Hardness (kgf)	2.50	10±1	6±0	7±1	9±1	9±1	8±0		
	5.00	13±1	13±1	11.8±1.3	13.7±1	11±1	12.6±1	17±1	14±0
	7.50	15±1	15±0	13.6±0.6	13.7±1	13.5±0	8.9±1		
Friability (%)	2.50	1.1	1.7	0.3	0.8	1.7	1.9		
	5.00	0.5	0.9	0.3	0.3	0.5	0.5	0.8	0.5
	7.50	0.5	0.8	0.5	0.8	0.3	0.5		
Disintegration time (min)	2.50	1.9±0	1.4±0	2.8±1	1.9±1	2.7±1	2.3±2		
	5.00	1.7±0	1.5±0	1.9±0	1.9±1	1.4±0	1.1±0	3.3±0	5.4±1
	7.50	0.8±1	0.6±0	1.1±0	0.6±0	0.7±0	0.4±0		

NB: Values are mean ± standard deviation

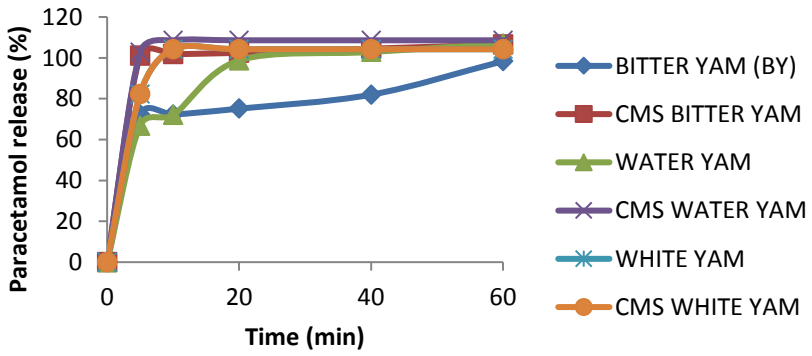

Figure 4: Representative Dissolution profile of paracetamol tablets prepared with different starch disintegrants at 5 % concentration.

There are reports that amorphous regions increased after carboxymethylation. (Lawal *et al*, 2008b). This makes carboxymethyl starches to enjoy wide application in fields where water absorption is important. The more amorphous the powdered substance, the more the water absorbed. This has been reported for other polysaccharides such as hemicelluloses (Ren *et al*, 2008). Since hydroxyl group was removed from the starch in the carboxymethylation process, the thermal energy needed for starch to breakdown through removal of water is higher, hence more stability. The main decomposition mechanism of starches is dehydration reaction between starch hydroxyls; this suggests that the smaller the amount of groups left on the starch, the more stable it is. This is also the reason for higher thermal stability of methylcellulose compared with the unmodified cellulose (Filho *et al*, 2007).

From the results, it can be seen that all the yam granules had good flow with the native bitter yam granules having the lowest angle of repose of 26.21° while CM white yam starch had an angle of 30.96°. There was no significant difference ($p > 0.05$) in bulk and tapped densities of the starches. The Hausner's ratios gave data less than 1 for all the starches. Thus, indicating a reasonably good flow and moderate cohesion. It would further suggest good consolidation of the granules in the die of a tableting machine.

Generally, tablets made from the CM starches of the yams exhibited faster disintegration time than their native starches irrespective of the concentration of disintegrant used. It is as a result of more amorphous nature of CMS and consequent better swelling capacity than the native yam starch and maize starch BP. This may translate to better release of the active pharmaceutical ingredient (API) from tablet when the CM starches are used as disintegrants (Ren *et al*, 2008; Lawal *et al*, 2008b).

The drug release profile revealed that, all the tablets prepared using CM starches as disintegrants,

released up to 100 % of their paracetamol (drug) content within 10 min. Tablets of the native bitter yam and water yam starches released less than 80 % of their drug content within 10 min (Fig. 4). It can therefore be inferred that, carboxymethylation of native bitter yam and water yam starches resulted in faster drug release from paracetamol tablets. The native white yam starch used as disintegrant gave similar drug release profile as the carboxymethylated white yam starch, with the later having a slightly superior drug release.

CONCLUSION

The results obtained from this investigation demonstrate that carboxymethylation improved the disintegrant ability of starches obtained from some *Diocorea species.* Paracetamol tablets prepared using CM modified starches exhibited faster disintegration time than tablets containing native yam starches as disintegrant.

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CONFLICT OF INTEREST

We declare no conflict of interest with regards to this work.

REFERENCES

Bi Y, Sunada H, Yonezawa Y, Dayo K, Otsuka A, Iida K. (1996) Preparation and evaluation of a compressed tablet rapidly disintegrating in oral cavity. *Chemical and Pharmaceutical Bulletin* (Tokyo) 44: 2121–7. [PubMed: 8945778]

Bowen FE, Vadino WA. (1984) A simple method for differentiating starch sources. *Drug Development and Industrial Pharmacy, 10, 505-511.*

British Pharmacopeia (2003). Her Majesty Stationery Office. Crown Copyright UK. Vol 111, pp 2049-2051.

Lawal SO, Lechner MD, Kulicke WM (2008b). The synthesis conditions, characterization and thermal degradation studies of an etherified starch from an unconventional source. *Polymer Degradation and Stability*. 93; 1520 – 1542.

Van-Dooren A, Muller B (1984). Purity determinations of drugs with differential scanning calorimetry (DSC); critical review. *International Journal of Pharmaceutics* 20 (3): 217-233

Chang R, Guo X, Burnside B, Couch R. (2000) A review of fast dissolving tablets. *Pharm Tech* (North America) 2000; 24:52–8.

Chaudary SA (2010). Excipient update for orally disintegrating dosage form. International *Journal of Research in Pharmaceutical Science*. 1(2): 103-7.

Farhat IA, Oguntona T, Neaale R. (1999) Characterization of starches from West African yams. *Journal of Food Science Agriculture* 79; 2105-2115.

Filho GR, De Assuncao RM, Vieira JG, Meireles CD, Cerqueira DA, Barud HD, Rireiro SJ, Messaddeq Y (2007). Characterization of methylcellulose produced from sugar cane baggasse cellulose. Crystallinity and thermal properties. *Polymer Degradation and Stability*. 92 (2); 205-210.

Gotlieb KF, Capelle A. (2005). Starch derivatization; fascinating and unique industrial opportunities. *Wageningen Academic Publishers* ISBN 978-90-76998-60-2 pp 12 -30

Haang XH, Li L, Wang JY, Zhang GZ, Tao XC. (2013) Preparation and application of carboxy methyl starch. *Applied Mechanics and Materials*. Vol. 268-270, pp 594-600.

Iwuagwu MA, Okoli PC, (1992). The disintegrant properties of pregelatinized cassava and white yam starches. *Pharmacy World Journal*; 9(2): 49-53.

Iwuagwu MA, Nwaoshai CA, Isaghohi FE. (1986) Investigations into the binding and disintegrants properties of starches from selected dioscoreaceae plants. *Nigerian Journal of Pharmaceutical Sciences*. 2, 10-22.

Lawal SO, Kulicke WM, Lechner MD. (2008a). Single and Multi-step carboxymethylation of water yam starch; Synthesis Characterization. International Journal of Biological *Macromolecule*.5 (42) 429-438

Nnamdi JA, Arhewoh IM, Okhamafe AO, Enato EFO. (2009) Evaluation of the Pharmaceutical Quality of Some Quinine Preparations Sold In Nigeria. *Medical Principles and Practice*. 18: 193 - 197 DOI: 10.1159/000204349

Nattapulwat N, Suwithayapanth O. (2009) Preparation and application of carboxymethyl yam (Dioscorea esculenta) starch. *AAPS PharmSciTech*. 10,198-198.

Nattawat N, Narumol P, Ornamphai S (2009); Preparation and Application of Carboxymethyl yam (Dioscorea esculenta) Starch. AAPS Pharmaceutical Sciences Technology, 10 (1); pp 193 -199.Ren JL,Sun RC, Peng F, (2008). Carboxymethylation of hemicellulosesisolated from sugarcane bagasses. Polymer Degradation and Stability. 93 (3) 786-793.

Shumei W, Xuan S, Feng Y, Hongqi D, Shangtao M, Jingjing W. (2012). Application of carboxymehyl starch as a retention and drainage aid wet end system. *BioResources*. 7(3)

Staniforth JN, Aulton ME (2007). Powder flow: In Pharmaceutics the Design and Manufacture of Medicines. Edited by Aulton ME Third edition. Pp175 – 17

Stanforth JN, Taylor KG (2013). Particle size analysis: In Pharmaceutics the design and manufacture of medicine. Edited by Aulton ME and Taylor KMG. Fourth Edition Pp145 to 147.

United State Pharmacopoeia/National Formulary (USP25/NF20) (2003). Rockville M. D. United State Pharmacopoia Convention Inc. pp 2302-2305, 2577-2590, 2620-2623.

Vaclavik VA, Christian EW (2007). Essential of Food Sciences 3rd edition. Published by Springer, p61 ISBN 978-0-387-699-39-4.