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Preparation and Evaluation of Carboxymethylated *Dioscorea bulbifera* Starch as Disintegrant in Ibuprofen Oral Tablet

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ABSTRACT

Background and Objective: *Dioscorea bulbifera* (climbing yam) is a species of yam not too common to many but is an edible meal in the Southeast and South-South Regions of Nigeria. This work was to modify this yam starch by carboxymethylation and use the starch as a disintegrant in a given tablet formulation. The effect of the reaction conditions of amount of sodium hydroxide and time of reaction on the degree of substitution and properties of the modified starch was investigated. **Materials and Methods:** *Dioscorea bulbifera* starch was obtained from its tubers purchased locally, modified by carboxymethylation (varying the concentration of sodium hydroxide and time of reaction) and evaluated for physicochemical properties, swelling power and photomicrography. The degree of substitution of the carboxymethylation reaction of the native starch was determined and the modified starch with desired properties was selected for use as a disintegrant in the formulation of ibuprofen oral tablet. Ibuprofen granules were prepared by wet granulation and then evaluated. Ibuprofen compacts were formed, the disintegration parameters determined and these compared with that of a commercial ibuprofen brand. **Results:** The degree of substitution on the starches by the carboxymethylation reaction was in the range of 0.01-0.35. Carboxymethylation significantly improved the flow properties, water interaction properties (swelling, hydration capacity) and particle size of starches (79-188 µm) but lowered the viscosity (2.86-3.48 mPas) when compared with the native. **Conclusion:** Carboxymethylation improved the swelling index of *Dioscorea bulbifera* starch and would be a good alternative to conventional starch as a disintegrant.

KEYWORDS

Carboxy methylation, disintegrant, *Dioscorea bulbifera*, degree of substitution, starch

INTRODUCTION

Discretionary use of functional excipients is a key step in the preparation of immediate-release tablets so as to meet the desired intentions of the formulator. For example, the choice of disintegrants is vital as it affects how efficient the process of break-up of such tablets in an aqueous environment will be to enable

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drug release[1]. The addition of disintegrants to formulations is reported to be more effective when usedintra and extra-granularly, although this is not a general rule for al disintegrant[1,2]. An ideal disintegrant should possess good hydration capacity and compressibility but poor solubility, gel formation and effective at the low quantity[3].

Polymers such as starch and its modified forms from several sources have been reported to be useful as disintegrants[4-6]. Some modified starches (e.g., sodium starch glycolate) have even been termed super disintegrants based on their efficiency in triggering a fast onset of disintegration even at low concentrations. Swelling, capillary action (wicking) and deformation are mechanisms disintegrants employ to exert their effects on solid compacts but for starch and its derivatives swelling is the main mode of action[7,8].

Swelling is reported as the main mechanism of disintegrant action of starch and its derivatives[8]. Native starches have poor compression properties and are effective as disintegrants in rather high concentrations (10-15% w/w). Physical and chemical modifications have been attempted to improve the properties of native starches[9]. Pre-gelatinization (a form of physical modification of starch) improves the flowability and compressibility of starch. Also, sodium starch glycolate is a product of chemical modification of starch and is effective at lower concentrations (2-8%) and shows improved moisture absorption[8].

Starches from cereals (corn and wheat) potatoes and cassava dominate the world markets in the food and pharmaceutical industries. In the recent past, however, more attention has been directed at sourcing starches from other botanical plants[10]. The starch content and wide distribution of *Dioscorea bulbifera* make it such a possible alternative source of starch[11]. *Dioscorea bulbifera* is a species of yam (Dioscoreaceae) family. It is commonly called air potato or aerial yam because it produces potato-like aerial bulbs in the leaf axils of the twining stem. It is native to West and East Africa, India, Southern China and North America[12]. Starch obtained from these bulbs contains about 29.37% amylose and most of the starch granules were of irregular shape, similar to pyramids with rounded vertices and a smaller number were elongated with smooth surfaces[12,13]. In a study by Kashyap *et al.*[14], the binding property of starch obtained from *D. bulbifera* in ketoprofen tablet formulation was evaluated. That study reported the starch to be a good binder when employed at concentrations (5, 10 and 15%)[14]. Ugoeze *et al.*[6] studied the effect of *D. bulbifera* starch at varying concentrations on the physical properties of paracetamol tablets and submitted that at concentrations greater than 5% the starch elicited a good disintegrant effect.

As at the time of study, there were yet to be any reports on using modified starch of *D. bulbifera* as disintegrant in tablet formulations. This study thus sought to chemically modify (by carboxymethylation) starch isolated from *D. bulbifera* and evaluate its disintegrant potentials using ibubrofen tablet formulation. Ibuprofen is a non-steroidal anti-inflammatory agent commonly indicated for management of moderate pain. As a class II drug in the biopharmaceutical classification system, it possesses poor dissolution and tableting behavior because of its hydrophobic nature hence the need for disintegrant to improve its dissolution[15]. This is an important study in evaluating an alternative starch source to find importance in the pharmaceutical industry.

MATERIALS AND METHODS

Study area: This study was carried out in the pharmaceutics laboratory, pharmaceutical technology laboratory, tabletting unit and dosage form evaluation unit, all in the Department of Pharmaceutics and Pharmaceutical Technology Department, while some evaluations were done at the Pharmacognosy and Natural Medicine Laboratory, all of the faculty of Pharmacy, University of Uyo, Nigeria, between November, 2019 and March, 2020.

Materials: The following materials were used: Ibuprofen anhydrous obtained (Bass and Boney Pharmaceuticals Inc., North Carolina, United States of America), magnesium stearate and talc (Shermen Chemical Ltd., Sunderland and Sandy, England). Other excipients (such as monochloroacatic acid) used in this work were of analar grade.

Methods

Preparation of *Dioscorea bulbifera* starch: Peeled and chopped tubers of 560 g weight of *Dioscorea bulbifera* (yam) soaked into 2% sodium metabisulphate, for 30 min were wet-milled and left to stand in the antioxidant solution for 1 hr and afterwards, filtered using muslin cloth. The filtrate was allowed to stand for 24 hrs, after which it was decanted but the sediment was washed and dried in a hot air oven (Laboratory Oven TT-9053 Techmel and Techmel, United States of America) at 60°C. The dried yam was pulverized and sieved using 500 micron sieve. The product was stored in an airtight container for further processing.

Modification of starch: The method employed by Odeniyi *et al.*[16] was adopted, with slight modification, for the preparation of *Dioscorea bulbifera* starch. To ethanol (80%) equal volume of an aqueous solution of sodium hydroxide (10, 15 and 20% w/v, respectively) was mixed. Exactly 20 g of the native starch of *D. bulbifera* starch was dispersed and the temperature was maintained at 50°C. After stirring, 5 g of monochloroacetic acid (MCA) was added and subsequently, the reaction time varied at 2 and 3 hrs using a water bath with intermittent shaking. After reaction completion at the designated times, the pH of slurry was adjusted to 7 using glacial acetic acid. The liquid supernatant was decanted and the gummy sediment was washed with a methanol 80% v/v solution several times and separated using filter paper. Slurry of the residue prepared by suspending it in 90% ethanol and washed was recovered using a sufficient quantity of acetone, stirred then sediments dried at room temperature. Dried samples were sized-reduced and sieved through a 0.25 mm sieve.

Evaluation

Photomicrography: The particle size and morphology of the starch and modified form were determined using a digital armscope attached to a light microscope (Olympus CX21).

Densities and micromeritics: The densities and micromeritics (flow rate, angle of repose, Hausner's ratio and Carr's index) of the starches and the ibuprofen granules were determined as reported in Uwah *et al.*[17].

Viscosity, swelling power and hydration capacity: The viscosity of 0.5% w/v aqueous slurry of the starch was determined using spindle size 2 in viscometer (Brookfield viscometer NDJ-5S digital model). The same procedure was done to the modified and reference starches.

For the hydration capacity, about 10% w/w slurry of the native starch in dry test tubes was allowed to stand for 5 min. The starch slurries were then centrifuged on a laboratory top centrifuge (Model 80-2) at 1000 rpm for 5 min and the supernatant was discarded. The sediment was weighed to determine the gain in weight of the dry sample as the amount of water adsorbed by the starches.

The swelling power was determined as follows, a slurry of starch was prepared by adding 0.5 g of the starch powder to 10 mL of distilled water. The initial volume was recorded as V. The slurry was kept at room temperature for 24 hrs. The swelling volume was observed and recorded as V. The same process was carried out on the modified starches. The swelling index of the powder was calculated as[17]:

$$\text{Swelling power} = \frac{\text{Total volume of swollen starch}}{\text{Volume of original dry starch}} \times 100$$

Hydrogen ion concentration: The pH of a 0.5% w/v aqueous solution of native and modified starches was determined using a pH meter (pH meter 3305, Jenway).

All determinations were done in triplicates with the values of mean and standard deviation presented $_{COOH}$.

Determination of degree of substitution:
In this determination, the works of Stojanovic *et al.*[18] was modified. Accordingly, exactly about 0.25 g of modified starch was added to 10 mL of a 0.2 m NaOH and 25 mL of distilled water was added afterwards. The solution was transferred into a 50 mL capacity volume flask, then made up of the 50 mL mark with distilled water. As 12.5 mL of the solution was transferred to a flask and diluted with 25 mL of the distilled water. The excess NaOH was back titrated with standard 0.05M HCl with phenolphthalein as the indicator. The titration was repeated three times and the average volume of the HCl used was determined and used to calculate the DS from the equation given below. A blank was also titrated and the degree of substitution (DS) given as:

$$DS = 1/4\,\frac{162\times n_{COOH}}{m_{ds} - 58\times n_{COOH}}$$

Where, 162 g/mol is the molar mass of an anhydroglucose unit (AGU); n_{COOH} (in mol) is the amount of $_{COOH}$ calculated from the obtained value of the equivalent volume, Ve, of known molarity NaOH (1 M); 58 g/mol is the net increase in the mass of an AGU for each carboxy methyl group substituted and m_{ds} in (g) is the mass of dry starch[18].

Preparation of granules: The granules were prepared using the wet granulation method. The 10 batches of granules were prepared using different concentrations of corn starch, modified starches and native starch as disintegrant as presented in Table 1. The batches 1 and 2 consisted of 5 and 7.5% corn starch, batches 3 and 4 consisted of 5 and 7.5% modified starch (M), batches 5 and 6 consisted of 5 and 7.5% modified starch 5 (M), batches 7 and 8 consisted of 5 and 7.5% modified starch 3 (M), batch 9 and 10 consisted of 5 and 7.5% native starch (N), respectively. The Ibuprofen granules (400 mg) composed of Ibuprofen (50%) as the active pharmaceutical ingredient, lactose (to 100%) as diluent, polyvinyl pyrrolidone, PVP (2.5%) as binder. The required amount of Ibuprofen was dry mixed with lactose and starch and moistened with PVP solution. The damp mass was screened through a 2 mm sieve and the dried in a hot air oven (Techmel and Techmel, United States of America) at 50°C for 2 hrs. The granules were screened using a 1 mm sieve. The granules were evaluated before passing it through a 0.5 mm sieve to obtain finer granules.

Evaluation of ibuprofen granules: The micromeritics of the formed granules were carried out as described for the starch powders above.

Table 1: Composition of the Ibuprofen tablets

Batches/tablet ingredients	1	2	3	4	5	6	7	8	9	10
Ibuprofen (%)	50	50	50	50	50	50	50	50	50	50
PVP (%)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Dioscorea bulbifera starch N (%)	-	-	-	-	-	-	-	-	5	7.5
M_3 (%)	-	-	-	-	-	-	5	7.5	-	-
M_5 (%)	-	-	-	-	5	7.5	-	-	-	-
M_6 (%)	-	-	5	7.5	-	-	-	-	-	-
Corn starch (%)	5	7.5	-	-	-	-	-	-	-	-
Magnesium stearate (%)	1	1	1	1	1	1	1	1	1	1
Talc (%)	1	1	1	1	1	1	1	1	1	1
Lactose to (%)	100	100	100	100	100	100	100	100	100	100

PVP: Polyvinyl pyrrolidone

Preparation of tablet: Carefully weighed Magnesium stearate (1%) and talc (1%) were mixed in each batch of granules in a sample bottle. The tablets were compressed with a single punch electrical tabletting machine (SSF-3, Cadmach Machinery Co., Pvt Ltd., India), at the punch pressure of 15 KN.

Evaluation of tablets

Weight uniformity test and tablet dimensions: The 10 tablets were randomly selected from each batch and individually weighed using an electronic balance (OHAUS, Galaxy). The mean and standard deviation were calculated. For the thickness and diameter, each of the 10 tablets from each batch was measured using the micrometer screw gauge (KFW Scientific Industries Ambala Cantt, India) and the mean value was calculated.

Crushing strength, friability and tensile strength: The crushing strength of the tablets was determined using the Monsanto hardness tester (Rolex, Chandigarh). The 5 tablets from each batch were selected for this test and the mean was determined. The friability of 5 tablets from each batch was taken and determined using the Roche friabilator (UNID Campbell Electronic, Mumbai, India). The tablets were pre-dusted and initially weighed. The tablets were then placed in the apparatus and operated at a speed of 25 rpm for 4 min after which their new weight was noted and the weight difference determined so that the friability could be calculated as below[17]:

$$\text{Friability} = \frac{\text{Weight difference of tablets}}{\text{Original tablet weight}} \times 100$$

$$\text{Tensile strength} = \frac{2C_s}{\pi_{rt}}$$

Where, C_s is srushing strength, r is radius of the tablet and t is tablet thickness.

Disintegration test: Disintegration test was carried out in distilled water using the (Digital tablet disintegration apparatus). Two tablets from each batch were placed in the cylindrical glass and the time taken for the tablets to disintegrate was recorded. The average time was calculated and recorded as the disintegration time.

Crushing strength friability ratio: The crushing strength to friability ratio (CSFR) of tablets in each batch was calculated using the equation below[1,19]:

$$\text{CSFR} = \frac{\text{Crushing strength}}{\text{Friability}}$$

Determination of disintegration efficiency ratio and its constant.

The disintegration efficiency ratio (DER) was determined using the relationship:

$$\text{DER} = \frac{\text{CSFR}}{\text{Dt}}$$

Where, CSFR is crushing strength friability ratio and Dt is disintegration time.

And the constant is formed when the DER of each batch of tablet is compared to that of the reference tablet batch:

$$DERc = \frac{DER}{DERr}$$

RESULTS AND DISCUSSION

Micromeritics properties of *Dioscorea bulbifera* starch: All six batches of *Dioscorea bulbifera* starches that were modified had yields ranging from 53.4% to 88.6% with the ranking of $M_6>M_3>M_5>M_2>M_4>M_1$. The colour range was from off-white through slight orange to brown colour. Table 2 presents the micromeritic properties of the native and modified starches studied. The bulk density had a range of 0.60-0.74 g/mL and followed the ranking $M_1>M_2>M_4>M_3$, $M_5>M_6>N$ whereas the tapped density had a range of 0.80 to 0.87 g/mL (Table 2). The bulk density of a powder describes the consolidation and flow of a powder mass. It also gives information on the compressibility of the starch powders. Smaller particle sizes resist free flow because of adhesion between the powders[19]. Although, the density of the powders (batches of native and modified) increased on tapping due to particle rearrangement to fill interparticle spaces, there was no significant difference between the native starch and modified starches as ($p>0.05$) in both the bulk and tapped densities. It could be deduced from the results that the starches studied exhibited satisfactory bulking properties for pharmaceutical use[20]. The seeming differences observed in the bulk values of the native and modified starches were likely due to the different particle sizes and shapes which influence the packing arrangement of the powder particles. Smaller sizes or shape (sphericity) of powder particles increases the bulk density of the powders[17].

Hausner's ratio and Carr's index assess the powder flow properties indirectly. The Hausner's ratio gives information as to the extent of powder densification due to rearrangement or vibration during process of tableting. A higher value of Hausner's quotient shows significant powder densification but a lower value indicates better flow property[16]. The results (Table 2) show that M_1 to M_3 recorded good flow properties while M_4 to M_6 and N had poor flow properties. Carr's index also gives an indication of the compressibility of a powder (USP, 2017)[20]. According to values on Hausner's ratio and Carr's index, M_6 has an excellent flow property, M_1, M_2, M_3 and M_4 all have a good flow property, M_5 has a passable flow and N has a poor flow. With modification, there was a significant difference in the Hausner's ratio and Carr's index as ($p<0.05$). Carboxymethylation of the *D. bulbifera* starch improved the flow properties.

The angle describes interparticulate friction or resistance to free flow between powder particles. Thus the angle of repose indicates flowability of powders and values that are generally below 30° are considered desired low for solid dosage formulations[17]. The United States Pharmacopoeia rates materials with angle of repose values between 25 and 30° as having excellent flow property, values between 31 and 35°C as having good flowability, powders having 41-45° show passable flow properties while those with values >46° have very poor flow. All the modified starches had an angle of repose <30° indicating an excellent flow property while the native starch had an angle of repose of 38.28° indicating a fair flowability (Table 2). The modification resulted in a significant difference ($p<0.05$) in the angle of repose.

The flow rate ranged from 2.29 to 10.13 g/sec, N had a flow rate of 2.29 g/sec while the flow rate for M_5 was 10.13 g/sec (Table 2). There was a significant difference ($p<0.05$) in the flow rate due to modification of the starch.

Table 2: Micromeritics properties of native and modified starches of *Dioscorea bulbifera*

Batch	Bulk density (g/mL)	Tapped density (g/mL)	Hausner's ratio	Carr's index (%)	Angle of repose°	Flow rate (g/sec)
N	0.60	0.83	1.40	28.37±0.53	38.28±1.54	2.29±0.05
M_1	0.74±0.01	0.86±0.02	1.16±0.05	13.53±3.47	19.78±1.44	8.00±0.00
M_2	0.74±0.01	0.87±0.02	1.16±0.05	15.23±2.04	17.84±3.59	6.99±0.89
M_3	0.66±0.03	0.80±0.03	1.12±0.09	16.88±6.42	16.52±0.66	6.17±0.44
M_4	0.69±0.05	0.87±0.02	1.28±0.12	20.78±8.08	16.87±0.65	7.06±0.76
M_5	0.66±0.01	0.82±0.02	1.32±0.06	24.35±3.22	17.90±1.49	10.13±1.52
M_6	0.64±0.02	0.81±0.02	1.28±0.02	8.00±2.26	17.72±1.70	8.00±2.26

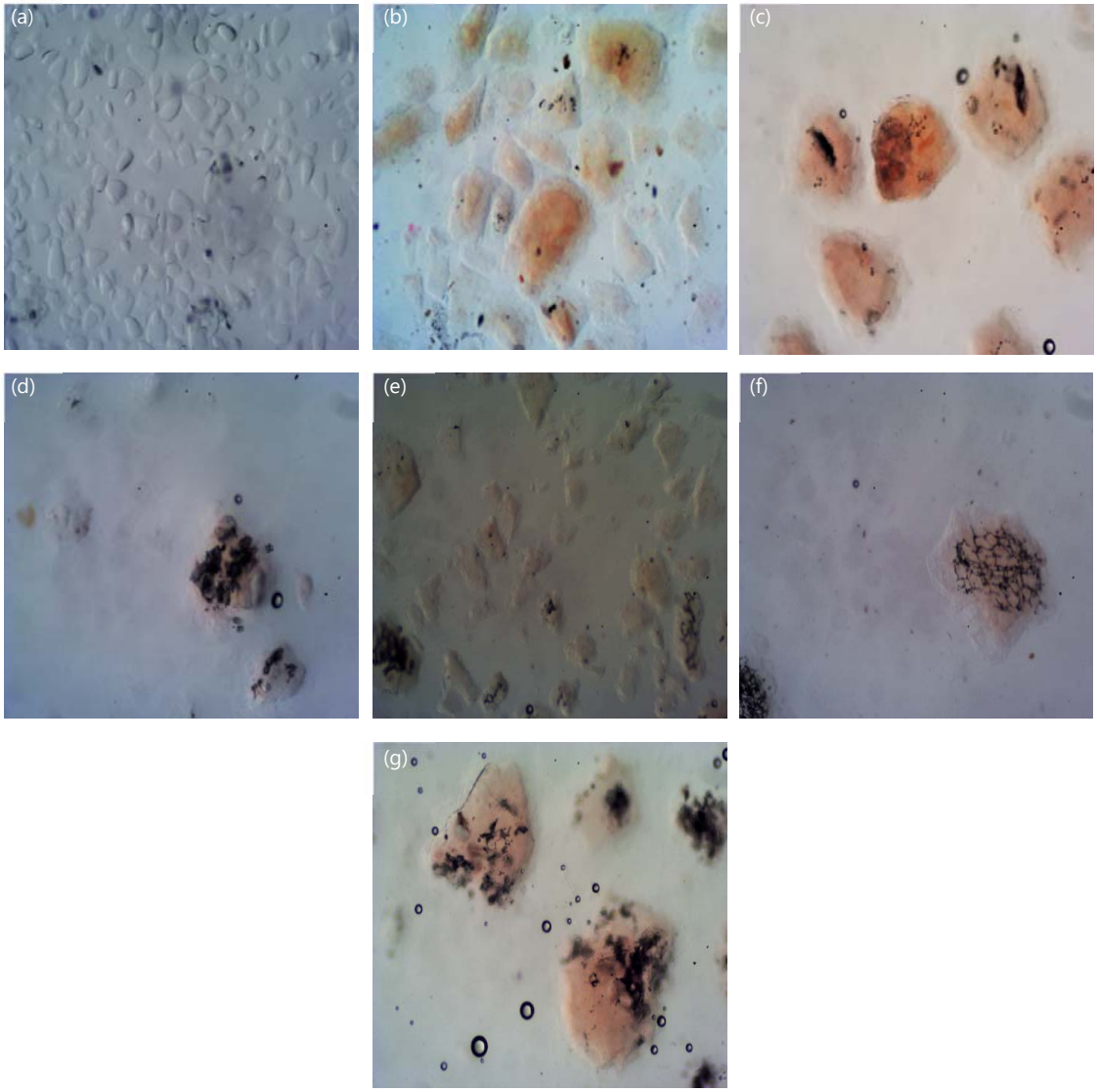

Fig. 1(a-g): Other physicochemical properties of *Dioscorea bulbifera* starch, (a) Native starch (×10), (b) Modified starch M_1 (×10), (c) Modified starch M_2 (×10), (d) Modified starch M_3 (×10), (e) Modified starch M_4 (×10), (f) Modified starch M_5 (×10) and (g) Modified starch M_6 (×10)

Particle size and shape of excipients affect various formulation characteristic such as flowability, water binding capacity and drug release. The photomicrograph of the powder of the native starch, in Fig. 1a, shows that the particles are polygonal in shape, with some having triangular and oval shapes. It also appeared to have dark patches at the edge of some shapes. The photomicrographs of the modified starches are represented in Fig. 1b-g. The modified starch shows irregular polygonal shapes forms. It also showed the similarities in the different batches of modified starch. Dark patches were observed on the particles and this became denser from M_6 to M_1. This is likely due to a by-product of the reaction between the starch and the monocloroacetic acid in the alkaline environment. There was a significant difference ($p<0.05$) in the particle sizes of the starches.

The swelling power of the starches increases in the order of $M_6>M_5>M_3>M_2>M_4>M_1$ as shown in Table 3. The swelling power measures the ability of each starch particle to absorb and hold water through hydrogen bonding and is a factor considered in the choice of use of gum for pharmaceutical drug delivery[21]. The swelling power of starches can predict the swelling of tablets during disintegration test in

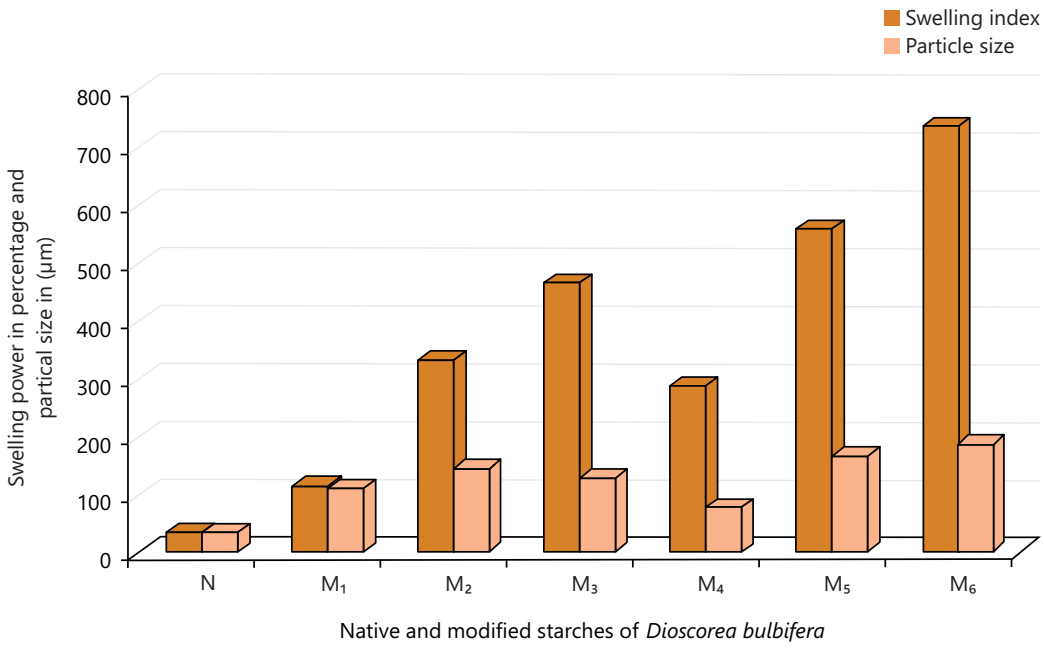

Fig. 2: Particle size and swelling index of modified *Dioscorea bulbifera* starches

Table 3: Physicochemical properties of native and modified starch of *Dioscorea bulbifera*

Batch	pH	Hydration capacity (%)	Swelling index (%)	Viscosity (mPas)	Degree of substitution	Particle size (µm)
N	7.60±0.00	27.43±7.47	36.17±5.90	4.03±0.28	_	35.54±5.66
M_1	6.93±0.04	14.07±0.96	116.67±23.57	2.86±0.17	0.13	113.08±20.77
M_2	7.58±0.01	34.03±5.44	333.33±146.36	3.01±0.14	0.08	146.58±40.23
M_3	7.91±0.01	44.87±2.89	466.67±160.28	3.28±0.23	0.03	130.65±44.84
M_4	6.67±0.02	17.3±0.570	288.87±78.58	2.86±0.16	0.35	79.07±6.79
M_5	7.40±0.01	44.27±7.30	560.00±69.76	3.19±0.14	0.03	170.00±49.23
M_6	7.89±0.01	43.17±3.75	738.33±149.24	3.48±0.21	0.01	188.28±32.64

N: Native starch, M_1: Starch hydrolysed with 10% NaOH for 2 hrs, M_2: Starch hydrolysed with 15% NaOH for 2 hrs, M_3: Starch hydrolysed with 20% NaOH for 2 hrs, M_4: Starch hydrolysed with 10% NaOH for 3 hrs, M_5: Starch+hydrolysed with 15% NaOH for 3 hrs and M_6: Starch hydrolysed with 20% NaOH for 3 hrs

order to release the drug for dissolution Adjei *et al.*[19]. Materials with high swelling power have good disintegrating properties indicating that M_6 swelled more than the rest. There was a significant difference ($p<0.05$) in the swelling power of the modified starches (Table 3). Also, the swelling power seemed to correlate with the particle size of the modified starches as represented in Fig. 2.

The pH of the starches increased with an increase in the concentration of the NaOH used in the modification. The pH values for the modified starch were found to be lower than that of the native starch except for M_3 and M_6. The drop in pH value of the modified starch may have been due to the acidic disposition of the carbonyl (-CH_2COO-) groups in solution which likely further aided their dispersibility in aqueous medium. The decrease in pH of the modified *Dioscorea bulbifera* is consistent with an earlier published work[16]. There seems to be a correlation between the pH and the degree of substitution. Batches with higher values of the degree of substitution (M_1 and M_4 on Table 3) had lower pH whereas those with small degrees of substitution (M_2 and M_6) had a pH higher than the native starch.

The hydration capacities for the native and modified starches are presented in Table 3 with values ranging from 14.07 to 44.87%. This means that the order of the hydration capacity follows: $M_3>M_5>M_6>M_2>M_4>M_1$.

Micromeritics and flow properties of ibuprofen granules: The results of the micromeritic and flow properties of granules are presented in Table 4 above. It was observed that there was an increase in

Table 4: Micromeritics of the granules formed using the native and modified *Dioscorea bulbifera* starches

Batch	Bulk density (g/mL)	Tapped density (g/mL)	Carr's index (%)	Hausner's ratio	Angle of repose (°)	Flow rate (g/sec)
B_1	0.48±0.02	0.55±0.01	13.26±4.54	1.15±0.06	21.62±1.16	2.35±0.14
B_2	0.42±0.0	0.54±0.01	21.57±1.16	1.27±0.02	29.5±2.07	1.58±0.03
B_3	0.37±0.01	0.46±0.01	19.49±3.02	1.24±0.05	27.69±2.17	2.33±0.04
B_4	0.39±0.01	0.44±0.01	12.77±1.99	1.15±0.02	20.76±0.98	3.21±0.04
B_5	0.33±0.02	0.42±0.0	20.95±5.87	1.28±0.09	26.51±1.83	1.28±0.17
B_6	0.35±0.01	0.43±0.01	18.44±1.58	1.23±0.03	25.47±3.38	2.13±0.02
B_7	0.33±0.02	0.45±0.02	26.26±7.26	1.37±0.13	21.93±1.0	4.06±0.15
B_8	0.36±0.0	0.45±0.02	19.69±3.81	1.25±0.06	25.13±3.01	1.75±0.3
B_9	0.33±0.02	0.43±0.0	21.93±5.07	1.28±0.09	28.63±2.23	1.59±0.02
B_{10}	0.33±0.02	0.42±0.0	22.85±4.12	1.3±0.07	29.48±2.13	2.29±0.03

B_1: Granules with 5% corn starch, B_2: Granules with 7.5% corn starch, B_3: Granules with 5% M, B_4: Granules with 7.5% M, B_5: Granules with 5% M, B_6: Granules with 7.5% M, B_7: Granules with 5% M, B_8: Granules with 7.5% M, B_9: Granules with 5% N and B_{10}: Granules with 7.5% N

density from bulk density to tapped density. This increase is a result of the densification of the granules leading to a reduction in the volume occupied by the granules in the container[16,22]. It was also observed that the bulk densities increased with an increase in concentration of the starches (B_3 to B_{10}) except in the bulk densities of the corn starch which showed a decrease in density with an increase in concentration. The reverse was seen in the case of the tapped densities of B_3 to B_{10} but same consistency was seen for B_1 and B_2.

Both Carr's index and Hausner's ratio describe the compressibility of the granules while the angle of repose characterizes the flow properties of powders and is dependent on the interparticulate resistance to movement between particles[17]. From the result obtained, Carr's index ranged from 12.77 to 26.26%, Hausner's ratio had a range from 1.15 to 1.37 while the angle of repose ranged from 20.76 to 29.5°. These values indicate that the granules had good flow properties[20]. The flow rate range of 1.28 to 4.06 g/sec indicates the batches of granules produced are good.

Physical properties of ibuprofen tablet: Weight uniformity test is a pharmacopeia or official test which ensures consistency of dosage units during compression. The tablet passed the United States Pharmacopoeia uniformity of weight test (<2 tablets ±5% mean weight, none should deviate by more than ±10%) as there was no significant difference ($p>0.05$) in the weights of the tablets from B_1 to B_9[20]. The tablets generally exhibited satisfactory thickness and diameter. There was no significant difference ($p>0.05$) in the thickness and diameter of the tablets among the batches.

The friability of all the formulations was in the range of 0.5 to 2.29%. How tablets withstand abrasion and impacts during packaging, handling and shipping is reflected in the value of friability. There was a statistical relationship between concentration of starches and the friability of the tablets as an increase in the concentration of the starches did not give any specific effect on friability of the tablet at ($p>0.05$). The strength of a tablet is determined by a measure of its crushing strength and is affected by the type and concentration of binder used in the granulation as well as the force of compaction during tableting[19]. On the Monsanto tester, soft and just handleable tablets would give a reading of lower value while well-compacted tablets would give up to 6 kgf or more[23]. The tablets all showed satisfactory crushing strength with no significant difference ($p>0.05$). The crushing strength of tablets containing the corn starch, M_6, M_5 showed a clear reduction in crushing strength with an increase in starch concentrations. There was no effect of disintegrant concentration on M_3. This trend has been reported before[19]. Starch disintegrants generally tend to lower the tensile strength of the tablet structure when used at high concentrations[23,24]. Tablets should have strong tensile strength to withstand pressure due to handling, packaging and film-coating but must allow drug release after administration[17]. There was no significant difference ($p>0.05$) between the tensile strength of the tablets containing the modified starches, native starch and corn starch.

Table 5: Physical properties of ibuprofen tablet

Batch	Weight uniformity (g)	Thickness (mm)	Diameter (mm)	Crushing strength (kgf)	Friability (%)	Disintegration time (min)	CSFR	Tensile strength (K Fcm^{-2})
B_1	0.39±0.02	2.81±0.06	12.59±0.02	7.00±1.41	1.20	25.10±2.08	5.8	12.60
B_2	0.39±0.02	2.73±0.04	12.56±0.01	5.67±0.94	1.70	7.68±2.43	3.3	10.53
B_3	0.38±0.01	2.67±0.03	12.59±0.0	6.00±0.0	1.90	29.75±0.47	3.2	11.36
B_4	0.39±0.01	2.72±0.07	12.58±0.01	5.67±0.87	0.50	20.73±0.28	11.3	10.55
B_5	0.37±0.01	2.56±0.04	12.57±0.01	6.00±0.82	0.70	19.72±0.64	8.6	11.87
B_6	0.41±0.01	2.75±0.06	12.55±0.02	5.67±0.47	1.80	14.27±2.09	3.2	10.44
B_7	0.41±0.01	2.69±0.08	12.53±0.02	7.33±0.47	2.50	18.85±0.47	2.9	13.84
B_8	0.41±0.01	2.77±0.07	12.56±0.01	7.67±0.47	1.80	16.24±0.01	4.3	14.03
B_9	0.41±0.01	2.56±0.04	12.55±0.01	8.00±0.82	2.29	29.09±0.06	3.5	15.85

CSFR: Crushing strength friability ratio

Table 6: Indicators of disintegration efficiency for the tablets using starches of native and modified *Dioscorea bulbifera* and corn starch, respectively

Batch	DER	DERc
B_1	0.23	-
B_2	0.43	-
B_3	0.11	0.48
B_4	0.55	1.27
B_5	0.44	1.91
B_6	0.22	0.51
B_7	0.15	0.65
B_8	0.26	0.60
B_9	0.12	0.52

DER: Disintegration efficiency ratio and DERc: Disintegration efficiency ratio constant

The disintegration of a tablet is affected not only by the nature and amount of disintegrants used apart from those of binder and temperature of the disintegration medium but also by how the disintegrant is incorporated[17]. The disintegration assesses how long it takes a tablet or capsule to break up into granules and de-aggregate into individual particles in a physiological media. This process is a necessary step for drug release and the onset of therapeutic action[23]. While the British Pharmacopoeia stipulates disintegration of uncoated tablets to be within 15 min the USP prescribes $\leq$30 min[20]. The results presented in Table 5 therefore indicate that an increase in the disintegrant concentration resulted in a decrease in disintegration time for tablets formulated with corn starch, M_5 and M_3. There was no reduction in the tablets formulated with M_6. No significant differences ($p>0.05$) were observed between tablets in the different batches.

The crushing strength-friability ratio (CSFR) is a better measure of the mechanical strength of tablets than crushing strength as it removes the weakness of the tablet as related to friability of a tablet[25]. Tablets in B_4 had the highest CSFR value indicating it has a strong mechanical strength (Table 5). There was no significant difference ($p>0.05$) in the tablets from different batches.

A disintegration efficiency ratio (DER) is an assessment of the balance between the mechanical strength of tablets to their disintegrant properties. The DER is a step further than the CSFR in assessing tablet quality for the DER evaluates the mechanical strength of a tablet, incorporating parameters that relate to mechanical strength, disintegration time and weakness related to friability. Generally, tablets having higher DER values reflect a better balance between disintegration time and binding properties[19]. From Table 6, the DER values of tablets increased with an increase in concentration of the starch except for tablets in B_5 and B_6 which were formulated with M_5. Tablets formulated with the corn starch appeared to produce a better balance between their disintegration and mechanical properties than tablets produced from many of the modified starches and native starch at concentrations used for the study except in batches B_4 and B_5. It had been reported that when compared with other starch sources such as cassava and potato, corn starch showed better disintegrant properties at similar concentrations[23]. There were no significant differences ($p>0.05$) from tablets in each batch.

Since B_4 and B_5 are modified forms of *D. bulbifera* starch of M_6 at 7.5 and M_5 at 5%, respectively, modified *D. bulbifera* starch M_5 and M_6 provide a better alternative to corn starch as a disintegrant in tablets. Further chemical modification such as carboxymethylation is a good option to improve the properties of disintegrants.

The carboxymethylation of *Dioscorea bulbifera* starch showed promising use as a disintegrant than the native starch and B_4 and B_5 even had better disintegration efficiency ratios than the standard corn starch disintegrants. Further, work on *in vitro* and *in vivo* dissolution studies using these promising disintegrants will give further information on their functionalities and possible application for industrial use as alternative excipients in drug manufacture.

CONCLUSION

Carboxymethylation of *Dioscorea bulbifera* starch carried out in this work significantly improved water interaction properties (swelling power, hydration capacity) and particle size of the starch. These properties showed its potential usefulness as a disintegrant in oral immediate release tablets. Disintegration as a necessary preliminary step towards drug release, this research has identified a new effective disintegrant in modified starch of *Dioscorea bulbifera,* a vital finding to achieve optimal drug release and therapeutic outcome in oral immediate release tablets and as a viable alternative with economic advantage to the expensive imported disintegrant brands.

SIGNIFICANCE STATEMENT

This work modified *Dioscorea bulbifera* starch by carboxymethylation, improving its properties and functionalities for use as an alternative disintegrant in tablet formulations. Carboxymethylation significantly improved the flow properties, water interaction properties (swelling, hydration capacity) and particle size of native starches, necessary excipient parameters that influence disintegration. This study's results showed the potentials of carboxymethylation of *Dioscorea bulbifera* starch as an alternative source of disintegrant in tablet formulations.

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