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Original Article

Synthesis of Methylcellulose from the Bark of *Crescentia cujete*: Characterization and Tabletting Properties

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ABSTRACT

The methylcellulose is an important ingredient in pharmaceutical, food, cosmetic and other industries. In this study, the methylcellulose, synthesized from the bark of *Crescentia cujete*, was evaluated for its physical and tableting characteristic to assess its usefulness in pharmaceutical tableting. The methylcellulose, synthesized from the bark of *Crescentia cujete*, obtained by alkali pre-treatment, delignification followed by sodium hypochlorite bleaching and methylation was examined for its physicochemical and tableting properties in comparison with the well – known commercial methylcellulose and starch BP. The synthesis yield of this methylcellulose, obtained from the bark of *Crescentia cujete* was approximately 83.33 % (0.8333g/g). The true density was 1.25; the flow indices showed that the methylcellulose synthesizes from the bark of *Crescentia cujete* has good flow properties. The hydration, swelling capacity were 4.40 and 466, respectively. Tablets resulting from these methylcellulose materials were found to be without surface defects, improves the hardness as compared to covenant methyl cellulose and starch maize, and having disintegration time within 15 minutes. The study reveals that the methylcellulose synthesized from the bark of *Crescentia cujete* compares favourably with standard and conformed to the official requirement specified in the British Pharmacopoeia 2012 for methylcellulose.

Keywords: Characterization, *Crescentia cujete*, Methyl Cellulose, Tableting

1. INTRODUCTION

Cellulose is considered as an important base material for the production of cellulose derivative such as carboxyl methyl cellulose, methyl cellulose, hydroxy propyl methyl cellulose [1]. These derivatives are exploited by food and drug processors and other industries to meet a specific need. Daiyong [2] reported that wood had been the dominant

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resource of cellulose in the total global production of paper and paperboard. Wood is not available in sufficient quantities in many countries because of the increasing consumption of furniture, construction, paper, paperboard, and cellulose derivatives [3, 4, 5]. An alternative new non – wood raw material needs to be investigated and exploited for the potential substitution of wood. A scrap of *Crescentia cujete* fruit is therefore considered in this work to be one of the possible alternative sources of industrial cellulose.

Due to increasing demand in the market, studies and work to produce cellulose are still rapidly developing [6]. The conventional sources of cellulose for industrial use include cotton linter and wood pulp [7]. Which recently are discouraged on account of the cost of the former and environment conservative regulations associated with the latter. Moore [8] reported that the need for environment-friendly processes as well as the need to slow down the fast global deforestation had stimulated renewed interest in agro-fibre plants waste. It is against this background that the bark of *Crescentia cujete*, which occur as huge agricultural waste in Nigeria mostly in Northern part of the country, was investigated as a source for the production and synthesis of cellulose. Recently investigated alternative sources for cellulose production include agricultural wastes and other plants parts not traditionally used for cellulose [9-13].

Crescentia Cujete, commonly known as the calabash tree, is species of flowering plant that is native to Central and South America of the bignonia family. It is the national tree of st. Lucia. In Nigeria, specifically Northern part of it, it receives priority as it is often used as tensile and the tree is also valued for fencing. This work reports on the preparation, characterization and tableting properties of methylcellulose, prepared from α-cellulose content of the bark of *Crescentia cujete*. The properties compared with those of the well-known commercial methylcellulose and starch BP.

2. MATERIAL AND METHODS

All chemicals used other than expressly noted were of analytical grade. Distilled water was used. Few other materials include sodium hydroxide (BDH, England), sodium hypochlorite (Jik® Reckitt and Colman Ltd, Nigeria), xylene, phloroglucinol and iodine crystals (BDH, England) were used as obtained. All other instruments used were Electronic microscopic (Optika/303059B-131), pH meter (Jenway 3510), Sieve, hydraulic hand press tableting machine, Erweka GmbH hardness tester, model: HT (Germany), Erweka disintegration test apparatus ZT4 (Germany), Erweka double drum friabilator tester (Copley TAR Erweka, Germany).

The bark of the *Crescentia cujete*, properly identified in the Department of Pharmacognosy and Ethnopharmacy, Usmanu Danfodiyo University Sokoto, Nigeria, were collected from Kara market Sokoto and the extraction and synthesis of the cellulose were prepared in formulation laboratory of Faculty of Pharmaceutical Science, Usmanu Danfodiyo University Sokoto, Nigeria.

Extraction of α-Cellulose

The dried back of the fruit of the plant *Crescentia cujete* was obtained and milled into powder for extraction. The method of Achor *et al.* [14] was adopted with modification. Fifty-gram quantity of this material was placed in a stainless steel container to which 1.0 L of 2 % w/v sodium hydroxide was added and digested effected for 5 hours at 80^0 C in a water bath. Followed by washing and filtration, and then bleached with 1.0 L of a 1:1 aqueous dilution of sodium hypochlorite for 15 minutes at 80^o C. The material was then washed sufficiently with water and treated with 1.0 L of 17.5 % w/v sodium hydroxide at 80^o C for 1 hour. The resulting cellulose was washed repeatedly with double distilled water.

Bleaching

The extraction process was completed made whitening with a 1:3 aqueous dilution of sodium hypochlorite for 60 minute at 80^o C and 1:1 for 24 hours and washed with water until neutral; the procedure was repeated for the remaining samples. The material was filtered, and the water was manually squeezed out using calico cloth to obtain small lumps, which was dried in a hot air oven at temperature of 45^o C for 1 hour.

Methyl Cellulose Synthesis Using Dimethyl Sulphate

The methylation of *Crescentia Cujete* cellulose was made according to the method described by Vieira *et al.* [15] with modification. The procedure is described as follows: 5 g of cellulose was initially mercerized using 100 ml of sodium hydroxide (15 %) solution for 1 hour at ambient temperature. After this time, the mixture was filtered to remove the excess of sodium hydroxide. 10 ml of acetone and 4 cm^3 of dimethyl sulphate were added to the mixture. It was left to react for 4 hours at 50^o C by shaking in a closed system, and the reaction mixture was change hourly. Finally, the mixture was neutralized with acetic acid at 10 % [v/v] solution and filtered in a synthesized plate funnel and was washed with three successive portions of acetone. The final product obtained {methylcellulose} was dried in an oven at 50^o C for 6 hours.

Determination of the Degree of Substitution and Methoxyl Groups

The determination of the degree of substitution and the methoxyl groups content was made through the modified procedure of Viebock and Schawappach, described by Chen *et al.* [16]

Determination of Reaction Efficiency

Reaction efficiency was determined using the following equation as suggested by Wurzburg [17].

Physicochemical Analysis

The organoleptic characteristic, identification tests, and presence of organic impurities were carried out following BP specifications [18]. pH determination was carried out by mixing the two gram of the powder material with 100 ml of distilled water for 5 minutes and the pH of the supernatant

liquid determined using a pH meter. The total ash content was estimated by measuring the residue left after combustion in a furnace at 550^{o} C [11].

Powder Properties

The extracted and synthesized cellulose were evaluated for density, compressibility index, powder porosity, moisture sorption capacity, moisture content and swelling capacity [11], angle of repose [19], hydration capacity [20].

True Density

True density, Dt of both the native and synthesized cellulose powders were determined by the liquid displacement method using xylene as the immersion fluid [11] and computed according to the following equation.,

Dt = w/[(a+w)-b] x SG……. (1)

Where w represents the weight of powder, SG represents specific gravity of solvent; a represents the weight of bottle+solvent and b represents the weight of bottle+solvent+powder.

Angle of Repose

The angle of repose, Θ, was measured according to the fixed funnel and free-standing cone method [19]. A funnel was clamped with its tip 2 cm above a graph paper placed on a flat horizontal surface. The powders were carefully poured through the funnel until the apex of the cone thus formed just reached the tip of the funnel. The mean diameters of the base of the powder cones were determined and the tangent of the angle of repose calculated using the equation

$\tan\Theta = 2h/D$…….. (2)

Where h is the height of the heap of powder and D is the diameter of the base of the heap of powder.

Bulk and Tap Density

Bulk and tap density determination were carried according to the method described by Ohwoavworhua *et al.* [11] a 500 mg quantity each of the powder samples were placed into a 50 ml clean, dry measuring cylinder and the volume, V_o, occupied by each of the samples without tapping was determined. After 500 manual tappings, the bulk and tap densities were calculated as the ratio of weight to volume (V_o and V_{500} respectively).

The Hausner index, compressibility index (C %) and powder porosity were calculated using equations

Hausner index = Tapped density/bulk density…… (3)

Compressibility index (C %) = Tapped density – bulk density)/Tapped densityx100 %..... (4)

Powder porosity = 1-(bulk density/true density) x100……. (5)

Hydration Capacity

The method of Kornblum and Stoopak [20] was adopted in the determination of hydration capacity. 500 mg each of the samples was placed in each of four 15 ml plastic centrifuge tubes and 10 ml of distilled water added and stoppered. The content was manually mixed for 2 minutes. The mixture was allowed to stand for 10 minutes on tube holder. The supernatant was carefully decanted, and the sediment was weighed. The hydration capacity was taken as the ratio of the weight of the sediment to the dry sample weight.

Swelling Capacity

Swelling capacity was measured at the same time as the hydration capacity determination using the method reported by Ohwoavworhua *et al.* [11] and calculated as follows:

$S = (V_2 - V_1)/V_1 \text{ X } 100$……. (6)

Where S is the % swelling capacity, V_2 is the volume of the hydration, or swollen material and V_1 is the tapped volume of the material before hydration.

Formulation of Tablets

Nine different batches of the tablet were prepared using wet granulation technique. The composition of a single tablet per batch was given as seen in Table 1.0. Calculated amount which is required to prepare 280 mg tablets, containing 200 mg ibuprofen powder, where binder [synthesized methylcellulose, standard methylcellulose and standard maize starch (BP) were used at various percent (3, 5 and 10 %) and others excipients (lactose, talc, magnesium stearate and sodium starch glycolate) were mixed uniformly. A sufficient amount of granulating agent (water) was added slowly to prepare wet mass. Granules were prepared by sieving method using a sieve with 20 size mesh.

Further, granules were dried at 45^{o}C for six hours. The required amount of granules was weighed and compressed using a tableting machine (single station). The compressed tablets of each batch were stored in airtight container at room temperature for further study. A total of 100 tablets were produced per batch.

Evaluation of Tablets

Uniformity of Weight

Sample tablets (20) from each of the nine batches were randomly selected, weighed together, and average weight determined. Each tablet was subsequently weighed individually on analytical weighing balance and percentage (%) deviation determined.

Friability Test

Ten tablets from each batch were randomly selected and weighed on the analytical balance. These tablets were put in an automated friabilator, spun at 100 rev/ 4 minutes to roll and fall within the rotating apparatus. After spinning, the tablets were reweighed after all loose particles were excluded by blowing off gently with a hand fan. The friability of the tablets was calculated as

% Friability = [(initial Wt- final Wt)/initial Wt] X 100……..XV

Tablet Strength (Hardness Test)

Sample tablets (5) of each batch were randomly selected, then placed between the spindle of the Erweka hardness tester machine and pressure was applied by turning the knurled knot just sufficient to hold the tablet in position. The pressure was uniformly increased until the tablet breaks, and the pressure required to break the tablet was then recorded.

Disintegration Test

The disintegration time of six randomly selected tablets from each batch was determined at 37^0C in distilled water using a multi-unit disintegration tester apparatus.

Assay of Ibuprofen Tablets

This was done according to BP [18] specification with modification. Twenty (20) tablets of each were weighed and made into powder. A quantity of the powder equivalent to 0.8 g of Ibuprofen was extracted with 20 ml of chloroform, filtered and washed with three quantities, each of 10 ml, of chloroform. The combined filtrates evaporated to dryness by gentle heating, with the aid of a current of air, the residue thus obtained in 100 ml of ethanol (96 %) previously neutralized to phenolphthalein solution was dissolved and titrate with 0.1M sodium hydroxide VS using phenolphthalein solution as indicator.

Each ml of 0.1M sodium hydroxide VS is equivalent to 0.02063 g of $C_{13}H_{18}O_2$.

3. RESULTS AND DISCUSSION

The organoleptic properties carried out were good as the material was odourless, tasteless and granular in texture. The native *Crescentia cujete* gave a whitish (Table 2) colour similar to the cellulose obtained from *Lageriana siceriana* [14] while the modified *Crescentia cujete* cellulose gave a yellowish colouration (Table 2.0). Also according to Table 2.0, the identification of the native *Crescentia cujete* carried out show that it takes on a violet-blue colour indicating the presence of cellulose while for the organic impurity, no red colour with acidified phloroglucinol.

The yield of the alpha native *Crescentia cujete* according to Table 3 was 47.60 % w/w of the original material, which is higher than the cellulose obtained from *Lageriana siceraria* as reported by Achor *et al*. [14] that it contains approximately 29 % w/w of the original material. The cellulose obtained in this work is also found to be higher than the cellulose obtained from sugar cane bagasse as reported by Viera *et al*. [15] that it contains about 44.9 % of cellulose. And it's found to be less than the cellulose obtained from palm kernel cake with 65.66 % of cellulose [21]. While the yield of the modified *Crescentia cujete* cellulose as obtained in Table 2.0 is 0.8333g/g. According to Silva *et al*. [22], the yield is certainly a function of the amount of material lost during the dialysis step. Hence, more degradation occurred, and a larger amount of low molecular weight material was released when drastic reaction conditions (higher temperature, NaOH and DMS concentration) is applied. This will results in a smaller amount of methyl cellulose polymeric product remained to be recovered by drying.

From Table 3.0 the degree of substitution obtained was 0.325 of the methylated sample, these values evidence the methylation of the native cellulose obtained from the *Crescentia cujete*. The moisture content of the methylcellulose was 5.30 % , while that of the cellulose was 7.0 %, which is well below the official limit of 8 % stated in British Pharmacopoeia, 2010, this low value is indicative of the suitability of methylcellulose obtained from the bark of *Crescentia cujete* as a diluents in the formulation of hydrolyzable drugs.

Flow properties of a powder are essential in determining the suitability of a material as a direct compression excipient. The high angle of repose is indicative of poor flow — the result obtained in (Table 2). The Compressibility index gives an idea of how much powder can be compressed, while Hausner index measures/estimates cohesion between particles; the value of both varies inversely with particle flow. For Compressibility index values in the ranges 5 to 10, 12 to 16, 18 to 21 and 23 to 28 indicate excellent, good, fair and poor flow properties of the material, respectively [23]. The index obtained in this study is 5.70 while that of the cellulose was 16.67, indicating excellent and good flow property, respectively.

On the other hand, for the Hausner ratio value less than 1.2 indicate good flowability whereas, a value of 1.5 and above suggests poor flow properties. In our study, the Hausner ratio, lie around the threshold of 1.06 while that of the cellulose was 1.20 (excellent and good flow property respectively). Therefore, the value obtained for the Hausner ratio is consistent with that of Carr's index.

The swelling capacity, which reflects the increase in the volume of cellulose following water sorption, was 466.04 % (Table 3) and the hydration capacity obtained for the methylcellulose, (Table 3), indicates that it is capable of absorbing about four times its weight of water.

The tablets formed were good and acceptable as none had surface defects; all the batches passed the weight uniformity test since the variation (standard deviation) of the tablets in each batch was lower than 5 % of the mean value. This complies with the British Pharmacopoeia standard.

Friability is related to the strength of the tablets and its ability to withstand abuse during normal handling, packaging and shipping. All compacts had friability values less than 1 %, except batch F3. The friability values demonstrate the high compactibility of the batches tested.

Crushing strength measurements can also be a useful tool in the preliminary screening of potential direct compression excipient [24]. From the result of the hardness (Table 4), it shows that the mechanical strength of F1 (sample with methylated cellulose shows high mechanical strength compared to other batches).

The disintegration test for tablets determines whether tablets disintegrate within a prescribed time when placed in a liquid medium under the prescribed experimental conditions.

From the result of the disintegration test (Table 4), all the batches passed the test with all the tablets disintegrating less than 15 minutes, which compliance with the BP [18]. The disintegration time of a tablet can be affected by the pore structure and bonding structure within the tablet. All assay results achieved from analysis of active ingredients in the methylated sample, standard methylcellulose and standard

starch maize, as shown in the table (Table 4), were within BP limits which specify a range of 95 to 105 %.

Table 1: Formula for Ibuprofen Tablet Formulation with tablet total weight of 280 mg

Materials	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ibuprofen (mg)	200	200	200	200	200	200	200	200	200
Lactose (mg)	62.64	57.04	43.04	62.64	57.04	43.04	62.64	57.04	43.04
Modified methylcellulose	3 %	5 %	10 %	-	-	-	-	-	-
methylcellulose®-	-	-	3 %	5 %	10 %	-	-	-	
Starch maize®	-	-	-	-	-	-	3 %	5 %	10 %
Sodium starch glycolate (mg)	2.8	2.8	2.8	2.8	2.8	2.8	2.8	2.8	2.8
Talcum (Talc) (mg)	5.6	5.6	5.6	5.6	5.6	5.6	5.6	5.6	5.6
Magnesium stearate (mg)	0.56	0.56	0.56	0.56	0.56	0.56	0.56	0.56	0.56

Table 2: Results of some Physicochemical Properties of Native and Modified *Crescentia cujete* cellulose

Test	Native *Crescentia cujete* cellulose	Modified*Crescentia cujete* cellulose
Organoleptic	Odourless, whitish, tasteless, granular powder.	Odourless, yellowish and tasteless.
Identification	Turns violet blue with iodinated zinc chloride.	-
Organic impurity	No red colour with acidified phloroglucinol	-
Microscopy	Irregular shape particle	-
pH	6.8	7.13 -7.35
Yield	47.6 %	0.8333 g/g

Table 3: Powder Properties of Methyl Cellulose and Cellulose Obtained From *Crescentia Cujete*

Parameters	Methylcellulose	Cellulose
True density (g/ml)	1.25±0.01	1.23±0.01
Bulk density (g/ml)	0.50±0.01	0.50±0.01
Tapped density (g/ml)	0.53±0.01	0.60±0.01
Porosity (%)	60	59
Flow properties:		
(a) Angle of repose	57.15±0.0	
(b) Hausner index	1.06	1.20
(c) Compressibility index (%)	5.70	16.67
Hydration capacity	4.40±0.06	1.60±0.01
Swelling capacity (%)	466.04±2.10	136±1.10
Moisture content (%)	5.30±1.30	7.00±0.05
DS	0.325	-
R.E	10.275	-

Table 4: Tableting Properties of Formulated of Ibuprofen Tablets

Batches	Weight uniformity (%)	Friability (%)	Hardness (Kgf)	Disintegration time(minute)	Assay (%)
F1	0.311±0.006	0.60	5.44±0.49	7.42±0.23	95.82
F2	0.337±0.002	0.88	3.25±0.26	8.58±0.32	97.13
F3	0.333±0.001	1.20	4.85±0.13	10.26±0.36	99.50
F4	0.329±0.002	0.62	3.55±0.33	6.51±0.27	95.75
F5	0.316±0.001	0.94	2.67±0.09	13.35±0.38	98.43
F6	0.319±0.004	0.60	4.86±0.72	14.30±0.45	95.02
F7	0.351±0.001	0.85	4.66±0.45	14.27±0.47	95.31
F8	0.330±0.004	0.91	3.81±0.27	14.43±0.48	99.22
F9	0.338±0.001	0.89	3.49±0.31	14.57±0.50	100.21

4. CONCLUSION

In conclusion, the methylated cellulose obtained from the bark of *Crescentia cujete* conformed to the official specifications in the British Pharmacopoeia (2010). The powder and tableting properties indicate that the methylated cellulose is comparable to the standard methylcellulose and standard maize starch, hence the methylated cellulose, is a potential binder in wet granulation direct compression diluents in tableting.

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