EVALUATION OF MICROCRYSTALLINE CELLULOSE DERIVED FROM CASSAVA PEEL AS DISINTEGRANT IN PARACETAMOL TABLET FORMULATION

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Agricultural wastes can be harnessed as raw materials for other products thereby creating wealth, preventing environmental degradation and ultimately ensuring the achievement of the sustainable development goals. The purpose of this study is to investigate the disintegrant property of microcrystalline cellulose extracted from cassava peel in paracetamol tablet formulation. Cellulose was extracted from cassava peel using the Sodium hydroxide method and subsequently hydrolysed to obtain cassava peel microcrystalline cellulose (CP-MCC). The CP-MCC was used as disintegrant in the formulation of paracetamol tablet. The formulated tablets were evaluated using the following parameters: uniformity of weight, hardness, friability, disintegration time and dissolution rate test. Batches CP1, CP2, and CP3 failed the weight uniformity test while batch CP4 complied with the test having a deviation of less than 5% (3.99%). All batches had fairly good tablet hardness with batch CP1 having the lowest hardness of 4.3 kg. Batches CP1 and CP2 complied with the official test for friability with values of 0.85% and 0.58% respectively, while CP3 and CP4 did not comply having values of 1.10 and 1.20% respectively. Tablets from all batches disintegrated within 15 min with batch CP2 showing the best disintegration time of 5.29 min; however batch CP2 released only about 55% of the paracetamol in 45 min while batch CP3 released over 80 % of paracetamol in 45 minutes. It can be concluded that CP-MCC obtained from cassava peel could be used as disintegrant for the formulation of paracetamol tablets.

Key words: Cassava peel, disintegrant property, microcrystalline cellulose, paracetamol.

INTRODUCTION

Agricultural wastes can be harnessed as raw materials for other products thereby creating wealth, preventing environmental degradation and ultimately ensuring the achievement of sustainable development goals. Most of our local agricultural wastes are directly disposed in river; consequently, the leaching fertilizers and pesticides could cause serious problems of salinity and biodiversity degradation in the river (Lamikanra, 1999). Therefore, an efficient utilization of such agricultural wastes is of great importance not only for minimizing the environmental impact, but also for obtaining a higher profit (Nuruddin et al., 2011).

Cassava (*Manihot esculenta*) is the third-largest source of food carbohydrates in the tropics (Farias et al., 2014) and a major staple food in Nigeria; it is a major economic sustenance crop and therefore produces large volumes of wastes in form of peels, capable of creating environmental nuisance (Claude and Fargette, 1990; Horsfall et al., 2003; Adeniji et al., 2005).

Cellulose is the structural component of the primary cell wall of green plants, many forms of algae and oomycetes. Some species of bacteria secrete it to form biofilms. Cellulose is the most common organic compound on Earth. About 33% of all plant matter is cellulose (the cellulose content of cotton fiber is 90%, that of wood is 40–50% and that of dried hemp is approximately 75% (Crawford et al., 1981; Decriaud et al.,1998;

Klemn et al., 2005).

Microcrystalline cellulose is a purified, potentially depolymerized cellulose prepared by treating Alpha cellulose obtained as pulp from fibrous plant material with mineral acid. Microcrystalline cellulose is basically cellulose and can only be derived from a specialized grade of Alpha cellulose from fibrous plant, treated with mineral acid. Microcrystalline cellulose has many uses in both food, cosmetics and pharmaceutical industries as an anticaking agent, emulsifier, stabilizer, dispersing agent, thickeners and gelling agent and one of the most used filler-binders in direct tablet compression due to its excellent binding properties, where it is used as a dry binder (Achor et al., 2014). The purpose of this study therefore is to convert cassava peel, an agricultural waste to microcrystalline cellulose, a pharmaceutical excipient and evaluate its suitability as a disintegrant in the formulation of paracetamol tablets.

MATERIALS AND METHODS

Paracetamol powder was a gift from Emzor Pharmaceutical Ltd., Lagos, Nigeria; Sodium hydroxide pellets from Loba Chemie Laboratory Reagents and Fine Chemicals, Murshidabad; Sodium hypochlorite and Hydrochloric acid from JHD Gunsgdong Guandgua Chemical factory Co. Ltd, China; Talc from Premodecia Pharm. Lab, France; lactose from BDH, Poole, England; Magnesium stearate from Peter Graven Pharmaceuticals, Netherland. All other chemicals and reagents used were of analytical grade.

Extraction of cellulose from cassava peel

The cassava peels were collected from a local cassava processing plant at Abraka in Ethiope East local Government Area of Delta State, Nigeria. The peels were washed thoroughly and sundried; they were milled to very fine particles.

The method of Kopania et al. (2012) was used for the extraction, with some modification. A 250 g quantity of the milled cassava peel was treated with 2.5 L of 2% w/v aqueous solution of sodium hydroxide in a plastic vessel immersed in a water bath at 100°C for 3 h for delignification. Complete removal of lignin, as well as removal of b- and g- cellulose was carried out by further digesting the material with 2 L of 17.5% w/v of aqueous solution of sodium hydroxide for 1 h at 80°C. After thorough washing with distilled water, the remaining solids were filtered and dried in an oven at 60°C for 1 h.

The cellulose obtained was bleached with 3.2% w/v aqueous solution of sodium hypochlorite at 40°C for 1.5 h. The bleached sample was thoroughly washed several times with distilled water and dried in an oven at 60°C. The obtained cellulose was then hydrolysed with 2.5 N hydrochloric acid at boiling point for 30 min; subsequently the hot mixture was poured into cold water and stirred vigorously with spatula and allowed to stand overnight. The microcrystalline cellulose obtained was washed thoroughly with distilled water, dried in an oven at 50°C and stored in a labelled airtight container for further study.

Preparation of paracetamol granules

Paracetamol granules were prepared by wet granulation method. For each batch, quantities of paracetamol, lactose, and half the quantities of CP-MCC as specified in Table 1 were mixed together in a mortar with a pestle. The mix was granulated with the binder, starch mucilage and the wet mass was passed through a 1.8 mm sieve and then dried at 60°C in a hot air oven. The dried mass was further sieved through a 710 µm sieve to obtain paracetamol granules.

Determination of flow rate of CP-MCC and paracetamol granules

A 20 g sample of CP-MCC and paracetamol granules respectively were allowed to flow through the orifice of a funnel at a fixed height; the time taken for the material to flow out completely from the orifice was recorded and the flow rate was computed using the equation below,

$$Flow\ rate = \frac{Weight\ of\ powder\ or\ granule\ (g)}{Time\ (s)} \quad (1)$$

Determination of bulk and tapped densities of CP-MCC and paracetamol granules

A 20 g quantity of CP-MCC powder or paracetamol

granules from each batch were weighed and packed into a 50 ml graduated cylinder. The powders and granules were carefully levelled without compacting and the unsettled apparent volumes (V_o) were read and recorded as the bulk volumes. Thereafter, the cylinder was tapped to constant volume and recorded as the final tapped volumes (V_f). The process was done in triplicate and then the bulk densities and tapped densities in g/ml were calculated using Equations 2 and 3 (Bharadia et al., 2004).

$$Bulk\ density = \frac{M}{V_0} \quad (2)$$

$$Tapped\ density = \frac{M}{V_f} \quad (3)$$

Where, M = mass of the powder, V_0= bulk or unsettled apparent volume of the powder,
V_f= final tapped volume of the powder.

Determination of angles of repose of CP-MCC and paracetamol granules

A sample of CP-MCC powder and paracetamol granules equivalent to 20 g were allowed to fall freely from a funnel clamped to a retort stand at a height of 7.5 cm from a horizontal surface. The diameters and the heights of the pile formed by the powders and granules were measured using a meter rule. The angles of repose for CP-MCC powder and paracetamol granules were calculated using Equation 4 (Chawla et al., 2003).

$$Angle\ of\ repose\ (\Theta) = tan^{-1}\left(\frac{h}{r}\right) \quad (4)$$

Determination of Carr's compressibility index and Hausner ratio values

The Carr's index and Hausner's ratio were calculated from bulk and tapped densities using Equations 5 and 6 (Aulton and Wells, 1988).

$$Carr's\ index\ (\%) = \frac{Tapped\ density - Bulk\ density}{Tapped\ density} * 100 \quad (5a)$$

$$Carr's\ index\ (\%) = \frac{V_0 - V_f}{V_0} * 100 \quad (5b)$$

$$Hausner\ ratio = \frac{Tapped\ density}{Bulk\ density} \quad (6a)$$

$$Hausner\ ratio = {V_0}/{V_f} \quad (6b)$$

Preparation of paracetamol tablets

The granules prepared above were mixed with 1% talc (glidant), 1% magnesium stearate (lubricant) and the remaining half of the disintegrant (CP-MCC) was added extragranularly and compressed into tablets of 620 mg weight using a single punch tableting machine (Manesty, type F3) at a load of 28 arbitrary units. The compressed tablets were stored in a well labelled glass container.

Evaluation of tablets

Weight uniformity

In order to carry out this test, twenty (20) tablets were randomly selected from each batch of tablets and weighed individually. The average weights as well as percentage deviations were computed. The tablets meet the USP test if not more than 2 tablets are outside the percentage limits and if no tablets differs by more than 2 times the percentage limit (USP, 2004).

Tablet thickness, diameter and hardness

Five tablets were picked from each batch and their individual weights were determined. Thereafter the thickness, diameter and hardness of each tablet were determined by placing them into the digital tester machine (Veego digital hardness tester Mumbai India. Model no: VDIGITAB-1).

Tablets friability test

Ten tablets were selected at random and weighed. The tablets were placed in the drum of a friabulator (Erweka friabulator) and subjected to cascading and free falling stress for 4 min at 25 rpm. The tablets were removed from the friabulator, dedusted and reweighed. The difference between the initial weight and final weight expressed in percentage was taken as

percentage weight loss (friability percentage) (USP, 2004).

Disintegration test

The test was done using Manesty disintegration apparatus. Water maintained at 37 ± 0.5°C was the disintegration medium. Six tablets were selected at random from each batch and the procedure was as described in the British Pharmacopeia (1998).

Dissolution test

The *in-vitro* dissolution profile for each batch of the tablets was determined using a stirred beaker method as described by Iwuagwu and Onyeonwu (2002). The dissolution medium was made of 900 ml freshly prepared 0.1 N hydrochloric acid solution maintained at 37 ± 0.5°C. A tablet from each batch was placed in the dissolution medium and at interval; samples equivalent to 5 ml were withdrawn and the fluid replaced with fresh dissolution medium to maintain sink condition. The samples were analyzed with a UV - Visible spectrophotometer (PG. Instrument) at a wave length of 245 nm (Table 1).

Table 1. Composition of paracetamol tablets.

Ingredients (mg)	Formulation batches			
	CP1	CP2	CP3	CP4
Paracetamol	500	500	500	500
CP-MCC	15	30	45	60
Lactose	63	48	33	18
Maize starch	10	10	10	10
Talc	6	6	6	6
Magnesium stearate	6	6	6	6
Total weight	600	600	600	600

CP-MCC = Cassava peel microcrystalline cellulose. CP1 (2.5% w/w CP-MCC), CP2 (5% w/w CP-MCC), CP3 (7.5% w/w CP-MCC) and CP4 (10% w/w CP-MCC).

RESULTS AND DISCUSSION

The percentage yield of CP-MCC was 7.2% as presented in Table 2. The low yield may be due to the source (cassava peel), the experimental conditions such as reaction temperature, reaction time, agitation, concentration of sodium hydroxide, concentration of acid for hydrolysis and acid to cellulose ratio e.t.c

Table 2. Percentage yield of cassava peel microcrystalline cellulose (CP-MCC).

Weight of dried cassava peel (g)	Method of extraction	Actual yield of cellulose after hydrolysis (g)	Percentage yield
250	Sodium hydroxide method	18	7.2

(Table 3). The results of the micromeritic properties of CP-MCC and paracetamol granules prepared using CP-MCC revealed that the CP-MCC powder exhibited good flow while the paracetamol granules exhibited excellent flow properties with angle of repose, Carr's index and Hausner's ratio values of 26.5° , 14.2% and 0.86 respectively for CP-MCC and 26.6°, 7.14% and 1.08 respectively for paracetamol granules.

The results of the physical properties of paracetamol tablets formulated with CP-MCC are presented in Table 4. Batches CP1, CP2, and CP3 failed the weight uniformity test while batch CP4 complied with the test having a deviation of less than 5% (3.99%). All batches had fairly good tablet hardness with batch CP1 having the lowest hardness of 4.3 kg. Batches CP1 and CP2 complied with the official test for friability with values of 0.85 and 0.58% respectively, while CP3

Table 3. Micromeritic properties of CP-MCC powder and paracetamol granules.

Parameter	Values obtained	
	CP-MCC powder	Paracetamol granules
Angle of repose (^{0})	26.5	26.6
Bulk density (g/ml)	0.70	0.39
Tapped density (g/ml)	0.92	0.56
Flow rate (g/s)	2.49	2.25
Carr's index (%)	14.2	7.14
Hausner's ratio	0.86	1.08

Table 4. Physical properties of paracetamol tablets.

Batch code	Thickness Mean ± SD (mm)	Diameter Mean ± SD (mm)	Hardness Mean ± SD (Kg)	Weight uniformity Mean ± SD (g)	Friability (%)
CP1	4.05 ± 0.02	13.88 ± 0.04	4.3 ± 1.16	0.624 ± 0.04	0.85
CP2	4.38 ± 0.42	13.86 ± 0.04	5.6 ± 1.32	0.5910 ± 0.05	0.58
CP3	4.09 ± 0.05	13.84 ± 0.01	6.4 ± 0.85	0.614 ± 0.04	1.10
CP4	4.46 ± 0.43	13.88 ± 0.02	6.6 ± 0.77	0.6086 ± 0.02	1.20

and CP4 did not comply having values of 1.10 and 1.20% respectively. Figure 1 depicts the disintegration times of all the batches. Tablets from all batches disintegrated within 15 min with batch CP2 (containing 5% w/w of CP-MCC) showing the best disintegration time of 5.29 min. The drug release profile in Figure 2 reveals that CP1 released over 60% of paracetamol in 45 min, CP2 released only about 55% of the paracetamol in 45 min while batch CP3 released over 80% of paracetamol in 45 minutes and CP4 released over 60% of paracetamol.

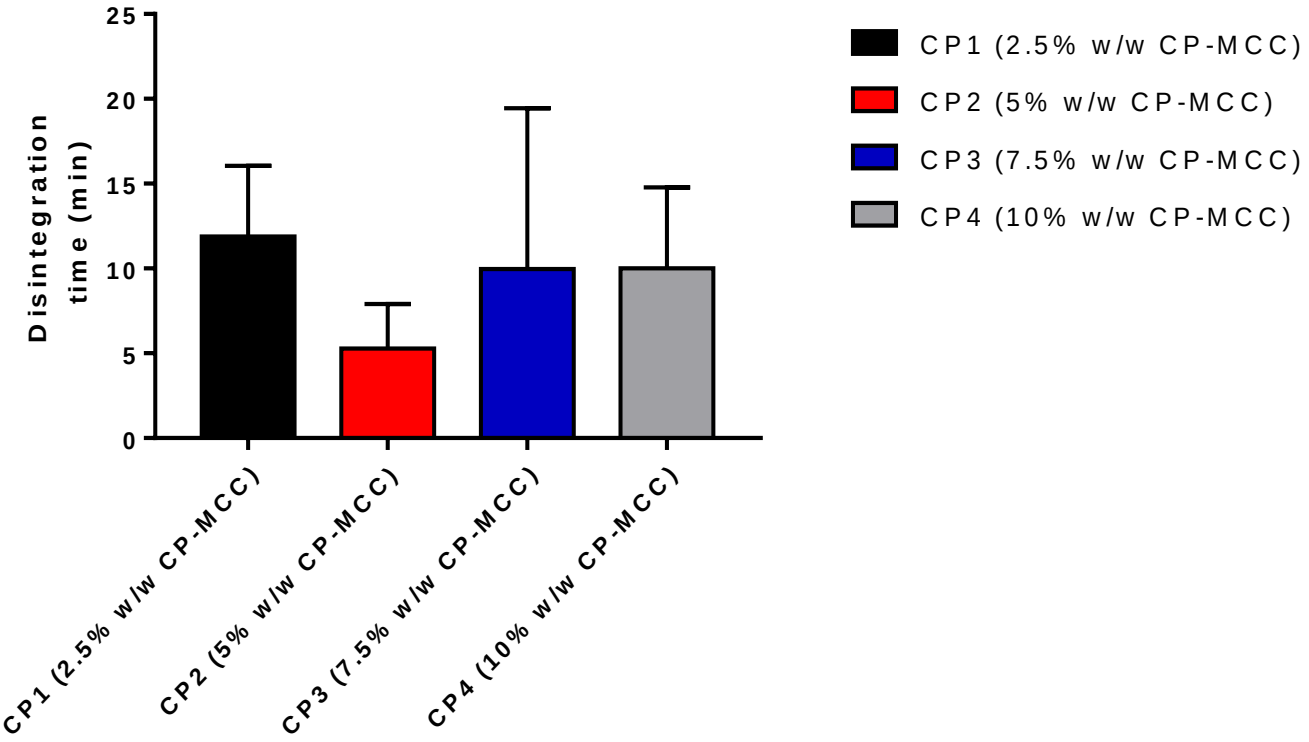

Figure 1. Graph of Disintegration time for the various batches of paracetamol tablet.

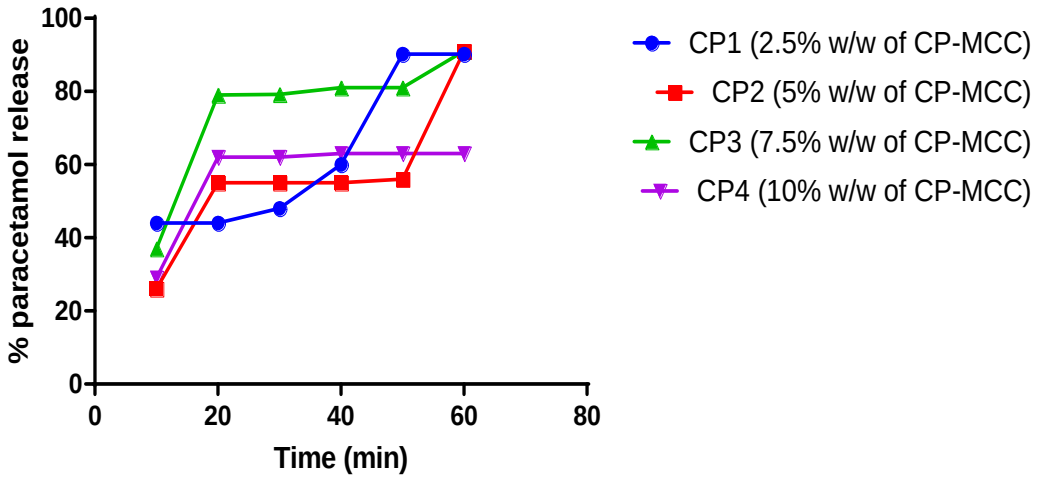

Figure 2. Drug release profile of the various batches of paracetamol tablets.

Conclusion

It can be concluded that CP-MCC obtained from cassava peel could be used as disintegrant for the formulation of paracetamol tablets. The optimized batch CP3, containing 7.5% w/w of CP-MCC had good flow properties, disintegrated within 15 min and released 80% of paracetamol in 45 min.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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