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Microcrystalline cellulose obtained from corn stalk as a potential pharmaceutical excipient: extraction and characterization

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Abstract

In this study, microcrystalline cellulose coded MS-MCC, was obtained from Corn (*Zea mays)* stalk by a two-stage sodium hydroxide delignification process followed by sodium hypochlorite bleaching and acid hydrolysis. MS-MCC was examined for its physicochemical and powder properties. The powder properties of MS-MCC were compared to those of best commercial microcrystalline cellulose grade, Avicel PH 101. The extraction yield of MS-MCC was approximately 15%. The cellulose material was composed of irregularly shaped fibrous cellulose particle with a moisture content of 5.8% and total ash of 0.28%. The true density was 1.6. The flow indices showed that MS-MCC has good flow. The hydration and swelling capacities were 3.1 and 36.4% respectively. The study revealed that the cellulose material compares favourably with Avicel PH 101 as well as official requirement specified in the British Pharmacopoeia 1993 for microcrystalline cellulose.

Keywords: Corn stalk, *microcrystalline cellulose,* extraction, characterization.

Introduction

Microcrystalline cellulose, (MCC), is described as a purified, partially depolymerised cellulose prepared by treating á-cellulose, obtained as a pulp from fibrous plant with mineral acids. MCC is one of the most used filler-binders in direct compression. Its popularity in direct compression is because of its extremely good binding properties as a dry binder. It also works as a disintegrant and a lubricant and has a high dilution potential in direct compression formulations. In addition to its use in direct compression formulations, MCC is used as a diluent in tablets prepared by wet granulation, as a filler for capsules and for the production of spheres (1).

Commercially available MCC is derived from both gymnosperms (generally conifers) and other softwoods, and from hardwood dicotyledons. These woods differ considerably in chemical compostion (proportions of cellulose, hemicelluloses and lignin) and structural organization which affect the compostion of the á-cellulose extracted and the compostion and crystallinity of MCC finally produced (2). Besides the wood pulp as a source of cellulose and its derivatives, the purified cotton linters obtained from *Gossypium* species are also a common source (3). Purified cotton linters and wood pulp are obtained from plantations specially grown in temperate climates, as such its production is expensive and the need for exploring other sources for MCC becomes imperative. Alternative sources for MCC recently investigated include agricultural wastes and other plants parts not traditionally used for MCC production (4-9). Corn is annual plant of the grass family (Gramineae) that probably originated in tropical South America. Corn is considered the most important cereal in the Western Hemisphere and it is the largest of the cereals, reaching 3 to 15 feet (1 to 4.5 meters) or more in height. The plant has a solid, jointed stalk or stem and large but narrow, wavy-margined leaves. The commonly recognized types of corn, distinguished largely by the type of endosperm and the shape of the grain, include dent, flint,

flour, pop, sweet, pod, and waxy. At one time these types were given scientific names; but since the genus *Zea* is fully domesticated, and all of these types are cultivated forms that interbreed freely, there is little valid basis for taxonomic distinctions (10). Corn starch and corn oil are products from corn (*Zea mays)* plant, from the grains, which are popular with pharmacy in that they find use as pharmaceutical aids (3). Beside these, alpha- and microcrystalline- cellulose, have been obtained, most recently, from degrained corn cob (8, 5) and they function as disintegrants, diluents and dry binders in tablet formulations. Stalks of some species in the family of Gramineae like wheat *(Triticum spp),* guinea corn (*Sorghum bicolour),* and sugar cane *(Saccharum officinarum),* have been reported in the literature as sources of cellulose and or its modified form, MCC, (9, 4, 8). Work on corn stalk as a source of either alpha- or microcrystalline- cellulose has not been reported in literature to the best of our knowledge. As part of the continuous search for locally available pharmaceutical raw materials a grade of microcrystalline cellulose, coded MS-MCC, was prepared from alpha cellulose content of corn stalk which exist as huge waste after harvesting of the corn cobs. MS-MCC was assessed for its physicochemical and functional properties. Its functional properties were however compared with those of the widely used microcrystalline cellulose, Avicel PH 101.

Materials and methods

Materials

Sodium hydroxide (BDH, England), sodium hypochlorite as 'Jik' (Reckitt and Colman Ltd, Nigeria), hydrochloric acid (Fisons, UK), Avicel PH 101 (FMC corporation, USA), xylene, phloroglucinol and iodine crystals (Hopkin and Williams, London) were used as obtained. All other chemicals used were of analytical of reagent grade and water was double distilled. Matured corn stalks were collected from a farm in Abuja after the cobs were harvested. The microcrystalline cellulose, MS-MCC, was prepared in our laboratory by the following method.

Methods

Extraction of á- cellulose

Plant stalks were properly air dried until they become brittle and pulverized using a mill powered by an electric motor with capacity of 3.7 kw/220 v. A fraction of powdered material passing through sieve of 2.0 mm aperture was used for extraction of alpha cellulose in accordance with method described in an earlier study (7).

Production of microcrystalline cellulose (MS-MCC)

The procedure reported earlier (7) with slight modification was used. A 50 g quantity of the alpha cellulose obtained was placed in a glass container and hydrolyzed with 0.8 L of 2.5 N hydrochloric acid at boiling temperature for 15 min. The hot acid mixture was poured into cold tap water which was followed by vigorous stirring with a glass rod and allowed to stand overnight. The microcrystalline cellulose obtained by this process was filtered, washed with water until neutral, filtered, pressed and dried in a fluid bed dryer at an inlet air temperature of 57 60 °C for 60 min. Following further milling and sieving, the fraction passing through 1.0 mm sieve was obtained and stored at room temperature in a desiccator.

Physicochemical properties of MS-MCC

The organoleptic characteristic, identification, organic impurities, starch and dextrin, solubility, total ash and water-soluble substances were carried out in accordance with BP (11) specifications. An optical microscope, Nikon model Larphot 2 (Nikon Inc. Japan) was used for preliminary assessment of the nature of particles in MS-MCC. The combination of

low and high power objective lenses of 100 and 400 times magnification was used.

pH determination: This was done by shaking 2 g of the powder material with 100 ml of distilled water for 5 min and the pH of the supernatant liquid was determined using a pH meter (Corning, model 10 England) (7).

Total ash determination: The method described in an earlier study (7) was adopted.

Powder properties

Particle size analysis
An Endicott's sieves shaker, (Endicott's Ltd UK) was used for this. Test sieves ranging from 1.18 mm to 75 µm were arranged in a descending order. A 20 g quantity of MS-MCC powder was placed on the top sieve and was shaken for 5 min. and the weight of material retained on each sieve determined.

True Density
The densities of cellulose powders were determined by the liquid displacement method using xylene as the immerse fluid (12).

Flow Properties

Angle of Repose
The static angle of repose, *a*, was measured according to the fixed funnel and free standing cone method (13). 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:

$$\text{Tan } a = 2h/D \ldots . 1$$

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

Bulk and Tap Densities
A 10 g quantity of powder samples were each, placed into 50 ml clean, dry measuring cylinder and the volume, V_0, occupied by each of the samples without tapping was determined. After 500 taps using Stampfvolumeter (Model STAV 2003 JEF, Germany), occupied volumes, V_{500} were determined. The bulk and tap densities were calculated as the ratio of weight to volumes (V_0 and V_{500}respectively) (7).

Hausner and Carr's compressibility indices
These were calculated as reported earlier (7).

Powder Porosity
This was derived from the values of true and bulk densities when fitted into the equation:

$$e = 1\text{-}B_b/D_t \times 100 \ldots . 2$$

Where B_b is the bulk density, D_t is the true density and e is the porosity (7).

Hydration Capacity
The method of Kornblum and Stoopak (14) was used. A 1.0 g each of the samples was placed in each of four 15 ml plastic centrifuge tubes and 10 ml distilled water was added from a 10 ml measuring cylinder and then stoppered. The contents were mixed on a vortex mixer (Vortex-Gennie Scientific Industry, USA) for 2 min. The mixture was allowed to stand for 10 min. and immediately centrifuged at 1000 rpm for 10 min. on a Gallenkamp bench centrifuge (Gallenkamp, England). The supernatant was carefully decanted and the sediment weighed. The hydration capacity was taken as the ratio of the weight of the sediment to the dry sample weight

Swelling capacity
This was measured at the same time as the hydration capacity determination using the method of Okhamafe et al (12).

Moisture Sorption Capacity
Two grams of the cellulose materials were accurately weighed and evenly distributed over the surface of a 70 mm tarred *Petri* dish. The samples were then placed in a large desiccator containing distilled water in its reservoir (RH = 100%) at room temperature and the weight gained by the exposed samples at the end of a five-day period was recorded and the amount of water sorbed was calculated from the weight difference (6).

Moisture Content
Five grams of powder samples were transferred, each, into a *Petri* dish and then dried in an oven at 60 °C until a constant weight was obtained. The % moisture content was then determined as the ratio of weight of moisture to weight of sample expressed as percentage (6).

Results and discussion

The yield of alpha cellulose was about 18 percent w/w of the original material. The yield of the microcrystalline MS-MCC, obtained from alpha-cellulose was approximately 81 percent w/w. Thus the yield of MS-MCC was approximately 15 percent w/w of the starting dry plant material. The results of the physicochemical properties investigated are shown in Table 1. The results indicate a high level of purity of the cellulose material. The organoleptic qualities of the MS-MCC produced were good as the material was odourless, tasteless, white and granular in texture. The value obtained for the total ash was very low possibly because cellulosic materials are almost free of inorganic compounds. When vegetable plants are incinerated, they leave an inorganic ash which in the case of many drugs varies within wide limits. The total ash figure is of importance and indicates to some extent the amount of care taken in the preparation of the substance (3).

Powder properties

The powder properties of MS-MCC and Avicel PH 101 are presented in Table 2 while the particle size analysis of MS-MCC powder is as shown in Figure 1.

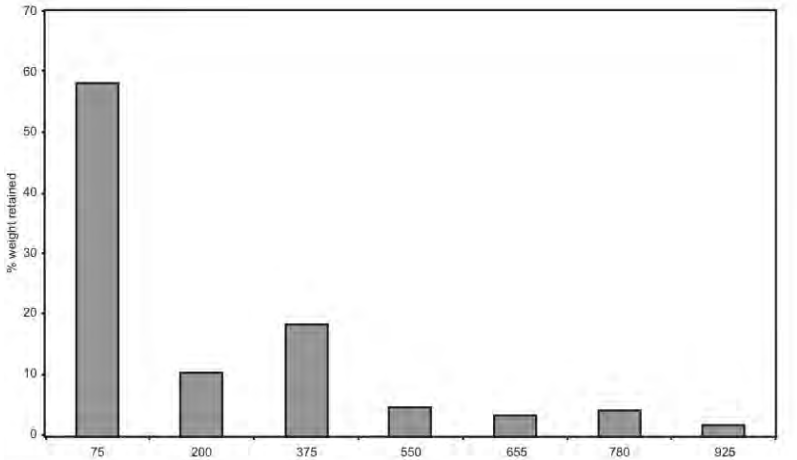

Figure 1: Particle size distribution of MS-MCC powder Mean sieve aperture (in microns)

The true density of 1.6 for MS-MCC (Table 2) is high when compared to 1.40 for Avicel PH 101. Stamm (15) had pointed out that a direct correlation exists between the degree of crystallinity of cellulose and its true density when determined in a non-polar liquid. Consequently, the slightly high true density value for MS-MCC is suggestive that it might have higher degree of crystallinity than Avicel PH 101.

Table 1: Some physicochemical properties of MS-MCC

TESTS	MS-MCC
Organoleptic	Odourless, white, tasteless, coarse powder
Identification	Turns violet-blue with iodinated $ZnCl_2$
Organic impurities	Nil
Starch and dextrins	Nil
pH	7.6
Solubility (in ammonical solution of copper tetrammine)	Complete and no residue
Water soluble substance	< 0.2%
Total ash (%)	0.21 (0.06)
Microscopy	Irregularly shaped fibrous particles which are mixture of primary particles and spherical aggregates.

*Value is mean and standard deviation is in parenthesis, Number of replicate =3

Table 2: Powder properties of MS-MCC and Avicel PH 101

Parameters	MS-MCC	Avicel PH 101
True density (g/ml)	1.6 (0.05)	1.40 (0.06)
Bulk density (g/ml)	0.21 (0.01)	0.31 (0.04)
Tapped density (g/ml)	0.32 (0.005)	0.42 (0.12)
Porosity (%)	86.9	78
Flow properties:		
(a) Angle of repose	48.3(3.5)	41.20 (0.46)
(b) Hausner index	1.52	1.35
(c) Compressibility index (%)	34.3	26
Hydration capacity	3.1 (0.19)	2.17 (0.01)
Swelling capacity (%)	36.4 (0.05)	21.4 (0.03)
Moisture sorption capacity (%)	15.0 (0.26)	16.6 (0.24)
Moisture content (%)	5.8 (0.12)	7.4 (0.4)

Values are mean and standard deviations are in parenthesis; Number of replicate, N=3

The moisture content of MS-MCC produced was about 5.8% which is well below the official limit of 8 % stated in British Pharmacopoeia, 1993 (11). This low value is indicative of the suitability of MS-MCC as a diluent in the formulation of hydrolysable drugs such as aspirin.

The flow properties of a powder is essential in determining the suitability of a material as a direct compression excipent. The angle of repose, Hausner index and Carr's percent compressibility are considered as indirect measurements of powder flowability (16) and the high angle of repose of MS-MCC (Table 2) is indicative of poor flow (17). While the Hausner index is indicative of interparticle friction, the Carr's index shows the aptitude of a material to diminish in volume (16). As the values of these indices increase, the flow of the powder decreases. In general however, Hausner ratio greater than 1.25 indicate poor flow and Carr's compressibility index below 16 % indicate good flowability while values above 35 % indicate cohesiveness (16). The flow indices showed MS-MCC and Avicel PH 101 powders as having poor flow. Consequently, a glidant will be needed when these materials are to be used in solid dosage formulations.

Swelling which is generally accepted as an indication of tablet disintegration ability (18) can be assessed by the determination of hydration capacity, swelling capacity and moisture sorption profile. The hydration capacity value obtained for MS-MCC, (Table 2), indicates that it is capable of absorbing more than thrice its own weight of water. The swelling capacity, which reflects the increase in volume of cellulose following water absorption was 36.4 % (Table 2). This is an indication that only a small portion of absorbed water actually penetrated the individual cellulose particles causing them to swell. The bulk of the absorbed water would exist in a 'free' state between the particles. Thus, if the cellulose was incorporated in tablet formulation as a disintegrant it would probably produce tablet disintegation by two mechanisms: capillary or wicking due to interparticulate water and

swelling. In addition, the slightly higher hydration and swelling capacities values observed for MS-MCC compared to Avicel PH101 could possibly be due to low moisture content and high powder porosity of MS-MCC.

The moisture sorption capacity is a measure of moisture sensitivity of material. The values for MS-MCC and Avicel PH 101 were similar. Stamm (15) reported that the crystallite portion of cellulose does not adsorb water and that the extent of water adsorption by cellulose should thus be proportional to the amount of amorphous cellulose present. Thus, the result is indicative of the high degree of crystallinity as well as suggestive of the comparable amount of amorphous cellulose in their unit fibrils. Also, study of water sorption is of importance since it reflects the relative physical stability of tablets made from MS-MCC when stored under humid condition. In all, this property showed that the cellulose powders are sensitive to atmospheric moisture and should therefore be stored in air tight container.

Conclusion

The cellulose product, MS-MCC, obtained from corn *(Zea mays)* stalk conformed to the official specifications in the British Pharmacopoeia (1993). The powder properties indicate that MS-MCC and Avicel PH101 are comparable, hence microcrystalline cellulose obtained from corn stalk, MS-MCC, is a potential tablet excipient.

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