Journal of
PHARMACEUTICAL
RESEARCH AND
DEVELOPMENT

Journal of Pharmaceutical Research and Development 5:1 (2000) 43-49

Isolation and Physiotechnical Properties of Grades of Cellulose Derived from a Novel Source, *Sorghum bicolor.*

J. Alfa.[b]*, A. Chukwu[b], O.K. Udeala[b], R.N. Nasipuri[a], C.O.N. Wambebe[a]
[b]Department of Pharmaceutical Technology and Industrial Pharmacy,
University of Nigeria Nsukka.

[a] National Institute for Pharmaceutical Research and Development, Idu, Abuja, Nigeria.

Abstract

Sodium hydroxide de-lignified α-Cellulose obtained from *Sorphum bicolor* was modified to the microcrystalline form by appropriate treatment with a mineral acid. The grades of cellulose were subejcted to preliminary evaluation for disintegrant or binder property. Compacts resulting from these polymers and their mixtures with dicalcium phosphate dihydrate (DCP) were found to be sufficiently hard, having disintegration times of between 6.5 to 9.5 m while pure DCP compacts had lower strength and disintegration time (DT) of over 50 m. Acetaminophen tablets formulated with SOMCC exhibited better disintegration profiles than those prepared using SC. The disintegrant activities of these polymers are most likely due to wicking and swelling effects with the former playing a dominant role. Swellability (S_b) of the polymers obeyed a derived equation; $S_b - (d_t/m \, .V_c) - 1$ where d_t is true density, m is weight of dry powder and V_c = volume of swollen material. The ratio of swellability of SC to SOMCC was approximately 2:1.

Key Words: Disintegration, hardness, swellability, sorghum cellulose (SC), sorghum microcrystalline cellulose (SOMCC)

Introduction

Cellulose and its derivatives have been used largely in paper, textile, paints, oil or pharmaceutical industries. Examples of those frequently encountered in pharmaceutical formulations include carboxymethylcellulose (CMC), mirocrystalline cellulose (MCC), powdered cellulose, sodium carboxymethylcellulose (SCMC), methylcellulose (MC), and hydroxpropylmethylcellulose (HPMC). While some of these serve as dispersants, protective colloids or thickeners in liquid systems, others are employed as disintegrant, filler-binder, or lubricant in tablet matrix (1) Purified cotton linters initially served as raw material for cellulose and its derivatives and thereafter wood pulp having high content of alpha cellulose was used (2). A brand of MCC, Avicel has been available since 1962 (3) and is derived from wood pulp obtained from plantation, specifically grown in the temperate climate. Though versatile as pharmaceutical aid, its production is expensive and the need for exploring other sources of MCC becomes imperative.

* Corresponding author

Cellulose extracted from rice husk, groundnut shell, or maize have been evaluated. They are found to be useful as disintegrant or filler-binder in tablet formulations (4,5,6). The present study involves evaluation of a plant whose stalk is highly fibrous, *Sorghum bicolor,* (family *Graminae*) as a possible source of cellulose.. Extraction and modification of the cellulose from this plant was carried out and the physico-technical properties were studied including preliminary evaluation as binders or disintegrants.

Sorghum is dietary staples of millions of people in the Sahel region of Africa, the near east, middle est, India and China (7). It is cultivated extensively within the northern and middle belt areas of Nigeria. The stalks from this plant are used in coarse matting for fencing (Hausa zana), hut enclosures, sheep pens and bands of conical thatch roof, but the greater percentages constitute wastes. Extraction and modification of the cellulose from this plant was carried out and the physico-technical properties were studied including preliminary evaluation as binders or disintegrants.

Materials and Methods

Materials

Sorghum stalk (as collected from a farm in Abuja after harvest); hydrochloric acid, sodium hydroxide (BDH chemicals, Poole, England); sodium hypochlorite as "JIK" (Reckitt and Colman Ltd, Nigeria); ammonia solution, magnesium stearate (Fissons Plc., England); acetaminophen (Vision Pharmaceutical Co. Ltd., China).

Methods

Preparation of plant material, extraction and modification of cellulose

Plant stalks were properly air dried until they became brittle and pulverized using a mill powered by an electric motor (Alzico Ltd., England) with capacity of 3.7kw/220v. A fraction of the powdered material passing through sieve of 599 micrometer aperture was used for the extraction of α-cellulose.

The extraction process involved the use of sodium hydroxide as the only reagent for delignification/digestion process in place of multiple reagents in an earlier method (5). A 300g weight of the powdered and sieved material was placed in a suitable vessel and treated with 2% NaOH. The hollow cellulose was washed, filtered and macerated using 17.5% w/v NaOH (2). The resulting α-cellulose was washed several times with deionised water, filtered and bleached using sodium hypochlorite solution. It was then thoroughly washed with deionised water, filtered, pressed and dried at 29 ± 0.5°C for 48 h then at 60°C for 2 h. Pulverization of the polymer was done using a Kenwood blender, model BL 350 (Kenwood Ltd. UK). Modification of the powdered cellulose to the microcrystalline form was carried out using 2.5 N hydrochloric acid (8). The final product was dried and pulverized as earlier described and the fraction, which passed through sieve of size 250 microns was collected and stored in a desicator at 28°C.

Identification, microscopy, Alkalinity or acidity tests

These were carried out in accordance with the method described in the B.P (9) for powdered and microcrystalline cellulose. Appearance or shape of the polymers was examined using an optical Nikon microscope Model Larbphot-2 (Japan) and the pH of each cellulose grade was determined using the Corning *p*H meter Model 215.

Physico-technical properties

Flow of powder: The angle of repose method (10) was used as expressed below:

$$\theta = \tan^{[h/r]} \quad \ldots\ldots\ldots\ldots\ldots\ldots [1]$$

where θ is the angle of repose, h and r are height and radius of the cone respectively.

Bulk density: This was determined using the Stampfvolumeter Model STAV 300 (JEF, Germany) and the bulk density (D_b) was calculated as;

$$D_b = w / v \quad \ldots\ldots\ldots\ldots\ldots\ldots [2]$$

e ; w is weight of powder and v = tapped a.. volume.

...ific volume (V_s): This was determined ... inverse of the bulk density (7), D_b.

$$Vs = 1 / D_b \quad \text{.....[3]}$$

...rosity (ϵ): This was calculated using the ...pression $\epsilon = (1-[d_b / d_t]) \cdot 100$ where d_b and ... present the bulk and true densities ...pectively.

... density: The specific gravity method ...10) was used and true density (D_t) was ...lated as;

$$D_t = (w.SGS)/ ([a + w] - b) \quad \text{.....(4)}$$

...re w = weight of powder, a = weight of ... e + solvent and b = weight of bottle + ...lvent + powder that is total weight of the ...le containing both the solvent and the ...der at the same time. SGS is specific ...ravity of the solvent, which in this instance ... ylene.

...oisture content: This was determined ... ng the Ohaus moisture balance model MB ... 0. The percentage loss after drying for 3 h ...t 105° was taken as the moisture content

... dration capacity: A slightly modified ...ethod of Kornblum and Stoppak (11), which ... s been used, by Odusote and Nasipuri (12) ... s applied here. The average of three determinations was used for calculting the ... dration capacity (H_c) using the expression;

$$H_c = \frac{\text{(weight of tube + hydrated sediment)-(weight of tube)}}{\text{Weight of sample (dry basis)}} \quad \text{...[5]}$$

...wellability (S_b): This was measured at the same time as hydration capacity (5). The ...aterial was tapped to a constant volume and ...oted. The volume of the swollen material (V_c) was also noted at the end of the ...xperiment. Swellability was calculated ...sing a derived expression;

$$Sb = \frac{(d_t . V_c) - 1}{m} \quad \text{.....[6]}$$

Where d_t is true density and m = weight of sample (dry basis).

Preparation of compacts

SC and SMCC compact: These were prepared to contain 300 mg of the material, compressed at fixed compression force of 8.5 dial units using a basket type tablet machine (model THP, Shangai) fitted with a punch of 10 mm diameter. A total of 50 tablets were produced per batch.

Dicalcium phosphate dihydrate (DCP) compacts; Compacts of this filler were made containing SC or SMCC as disintegrant, at fixed compression force dial of 8.5 units with above machine and punch. A general formular was used as follows:

Table 1: Formula for incorporating grades of cellulose in DCP.

Material	Weight per compact (mg)
Dicalcium phosphate Dihydrate (DCP)	268.5
Cellulose	30.0
Magnesium stearate	1.5
Total weight of compact	300.0

One batch contained SC whle the other was prepared using SOMCC. The materials were geometrically mixed in a bottle for 5 m in each batch after which the resulting blend was compressed.

Formulation of acetaminophen tablets

Tablets of acetaminophen were produced according to the formular in table 2:

Table 2: General formular for preparing acetaminophen tablets.

Acetaminophen	500mg
Starch paste (10% w/v)	Qs
Disintegrant	x% w/w
Magnesium stearate	0.75%

The concentration of SC or SOMCC was such that $5 \leq x \leq 20$. The tablets were produced using the wet granulation method with starch

paste as binder. Fifty percent of the cellulose was incorporated intragranularly while the rest 50% was incorporated extragranularly, in each batch. Magnessium stearate was appropriately mixed with the granule and the final blend was compressed at fixed compression pressure of 12.0 mm using the machine earlier described, which was fitted a flat faced punch of 12 mm diameter.

Evaluation of compacts

Compact strength: Crushing strength of the compact or tablet was determined using the Mosanto hardness tester. A total of 10 tablets or compacts was used per batch and the mean was taken as the hardness.

Disintegration time: The disintegration time of various batches of acetaminophen or DCP compacts were determined using the Erweka disintegration apparatus, distilled water being the immersion fluid at $37^{o} \pm 0.5$. The mean of three determinations was taken as the disintegration time.

Results and Discussion

The results of the preliminary experiment presented in Table 3 indicates that the derived polysacharides could be grades of powdered and microcrystalline cellulose as the observations are in conformity with the BP specifications (9). The new cellulose products compressed directly without the addition of any binder as shown in Table 4, which indicates that the particles posses inherent binding property. The relative strength of the compacts shows that the performance of SOMCC is close to that of a commercial brand of microcrystalline cellulose, Avicel PH101, a direct compression filler-binder (3,4). Avicel produced compacts with an average hardness of 10.2 ± 0.5kgf while that of SOMCC was 8.0 ± 0.5 kgf. Powdered or microcrystalline cellulose are useful as direct compression excipients [1,3] and these derived polysaccharide products, SC and SOMCC may be new grades of direct compression cellulose materials.

Table 3: Some physicochemical properties of the new polymers

Test	Index of assessment	Observation	
		SC	SOMCC
Identification	Treatment with iodinated zinc oxide solution.	Colour change	Violet-blue	Violet-blue
Microscopy	Microscope	Particle appearance	Coarse, elongated fibres	Fine, aggregated particles
Alkalinity or acidity	*p*H meter	*p*H	6.3	5.6

Table 4: The filler-binder and disintegrant properties of cellulose

Direct compression Filler-binder	Hardness(kgf)	Disintegration time (minutes)
SC	6.2 ±0.5	9.5
SMCC	8.0 ± 0.5	6.5
Avicel PH101	10.2 ±0.5	6.2
DCP + SC	5.7 ± 0.5	7.4
DCP + SMCC	7.1 ± 0.5	6.9
DCP (control)	3.2 ± 0.5	> 50

Dicalcium phosphate dihydrate is a free flowing material having no disintegrant properties (13). Table 4 shows the effect of SC or SOMCC on the disintegration of compacts of this filler-binder. The matrixes containing either of these polymers disintegrated in less than 10 minutes while the disintegration time of DCP compacts made without any cellulose was over 50 minutes. The result shows that these polymers have some disintegrant characteristics in addition to the dry binding potential. This is

consistent with reports that powdered and microcrystalline cellulose have some disintegrant properties (1,3,13). The strength of dicalcium phosphate dihydrate compact was seen to be enhanced by incorporation of the cellulose grades just as Wells and Langridge (13) observed an enhancement in compacts containing low concentration of microcrystalline cellulose. This was attributed to larger bonding surfaces created by plastic deformation of the cellulose particles at low compression force with infiltration of the fragmented particles of DCP, resulting in improved bonding.

Some of the physico-technical characteristics of the derived polymers are shown in Table 5. The grade of cellulose, SC was found to be much more bulkier than the corresponding SOMCC. This may be due to the irregular geometrical arrangement of the coarse, elongated particles in SC, compared to the more orderly configuration in the agglomerated crystalline structure of SOMCC in which the particles are smaller, having regular shape and more closely packed. The ratio of hydration capacity of SC: SOMCC is approximately 2:1 and this may be due to the highly amorphous state of the alpha cellulose, since water sorbed by a polymer is proportional to the fraction of the amorphous material present (14). Moreover microcryatalline cellulose is approximately 63% crystalline (13,14), which accounts for the lower moisture uptake in SOMCC where Hc is 2.7, compared to 6.0 in SC.

Table 5: Some Physico-technical properties of SC and SMCC.

Parameter	SC	SOMCC
Bulk Density (g/ml)	0.14	0.47
Particle Density (g/ml)	1.8	1.6
Porosity (%)	92.2	70.6
Specific volume (ml/g)	8.30	2.10
Angle of repose (deg)	No flow	43°
Moisture content (%)	6.2	4.7
Hydration capacity (Hc).	6.0	2.7
Swellability (S_b)	6.5	3.0
*p*H	6.3	5.6

A derived equation, which is a modification of that used by Okhamafe et al (5) was applied in the determination of swellability (S_b) of the polymer grades. Swellability has been defined as:

$$S_b = \frac{\text{Change in volume of swollen material}}{\text{Initial volume of dry material}} \quad \ldots [7]$$

Let the change in volume be represented by ΔV and the initial volume, V, then equation 7 can be stated as:

$$S_b = \frac{\Delta V}{V} \quad \ldots [8]$$

If the weight of dry material is represented by *m* and true density, dt, then the initial volume, V becomes m / dt. Substituting this in equation 8 gives:

$$S_b = \frac{dt \cdot \Delta V}{m} \quad \ldots [9]$$

Let the volume of the swollen material after centrifuge be V_c, then $\Delta V = V_c - V$ which can also be expressed as

$V_c - \frac{m}{d_t}$. Substituting this in equation 9 0 gives the relationship:

$S_b = d_t \cdot \left(\frac{Vc}{m} - \frac{m}{d_t}\right)$ and we finally have;

$$S_b = \left(\frac{d_t}{m} \cdot Vc\right) - 1 \quad \ldots [10]$$

Swelling potential was thus determined using equation 10 and the result is shown in table 4.

Swelling in polymers takes place within the amorphous region (17) where the interchain bond is replaced by water–polymer bonds and the resulting structure held by the non swelling crystalline domain. SC exhibited higher swelling strength than SOMCC. The result obtained using the derived expression is in agreement with the experience and work of other investigators (4, 14, 15, 16, 17). In the application of this novel equation, determination of the initial volume of material

is unnecessary and its use is independent of the porous state of materials.

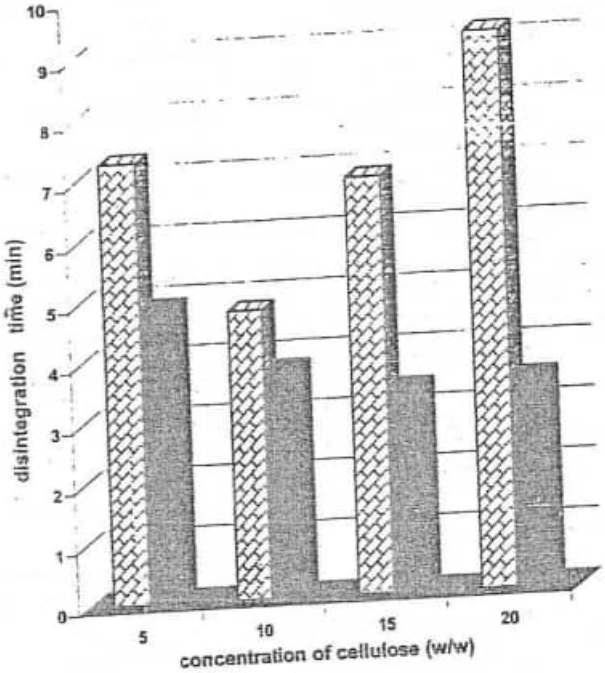

Figure 1: Effect of concentration of cellulose on the disintegration of acetaminophen tablets

The disintegration time of acetaminophen tablets containing the new cellulose grades is presented and graphically shown in figure 1. Tablets containing SOMCC disintegrated faster than those formulated with SC at equivalent concentrations. DT decreased with increased concentration of SOMCC whereas a minimum DT of 4.5 minutes was recorded at 10% w/w concentration of SC. The result shows that swelling does not play the dominant role in the disintegrating action of these polymers, which is in consonance with Kornblum and Stoopak's (11) observation that swelling may not be the major mechanism of action in the disintegrant characteristics of some polymers.

Microcrystalline cellulose has both water sorption and wicking properties but the later effect plays a dominant role in the disintegration process (3). Caramella et al (18) described starch and cellulose as limited swelling agents which implies that the mode of disintegrant action involves swelling in the presence of water and a capillary mechanism due to their hydrophilic nature. The mode of action of SC and SOMCC as disintegrants may be attributed to wicking and swelling with the former playing the dominant role. The increase in DT noticed in SC formulated tablets at levels above 10% w/w may be as a result of excessive swelling which tends to narrow the wicking routs (capillary pores). The interparticulate water which predominantly causes the breaking of hydrogen bonds between adjacent bundles of the cellulose is thus, reduced. On the other hand, DT of tablets made with SOMCC decreased with concentration at the concentration range used. It may therefore, be said that capillary action is more pronounced in SOMCC than SC and the wicking activity increased with concentration of the MCC. Interestingly all formulations disintegrated below 10 minutes, which is within the acceptable limit for uncoated tablets (1).

Conclusion

The results of the preliminary evaluations indicate that grades of cellulose derived from sorghum stalk have good potentials as disintegrant or filler-binder and may be explored as local source of excipient for tabletting. Further work is going on in order to determine their compactio characteristics. Their tableting qualities ar also being compared with those c commercial brands of MCC such as Avic and will constitute separate reports.

References

1. United States Pharmacopoeia xxii NF XVII (1990) US Pharmacopoeial convention Inc. 12601 Twin brook, Parkway. 1852.

2. Noller, C.R. (1958) *Chemistry of Organic Compounds* 2 Ed W.B. Sounders Company, London. 398.

3. Liberman, H. A., Lachman, L., Schwartz, J.B. (1989) *Pharmaceutical Dosage Forms; Tablets* (2) Mercel Dekker Inc. N.Y. 210.

4. Florence, A.T., Attwood, D (1981) *Physicochemical Principles of Pharmacy*. I Ed. Macmillan Press Ltd. London. 293.

5. Okhamafe, A.O., Igboechi, A.C., Obaseki, T.O. (1991) Cellulose extracted from groundnut shell and rice husk I; Preliminary physicochemical characterization. *Pharm. World Journal 8* (4). 120 – 124.

6. Okhamafe, A. O., Ejike, E. N. Akinrinola, F., Ubuane-Inedegbo, A. (1995) Aspects of the tablet disintegrant properties of cellulose derived from bagasse and maize cob. *J. West African Pharm. 9 (1). 8 – 13.*

7. Kochhar, S. L. (1986) *Tropical Crops – a Textbook of Economic Botany,* Macmillan Publishers, India. 102 – 107.

8. *British Pharmacopoeia* (1993) HMSO, London. Vol. 1: 119 – 120.

9. Martin, A., Swabrick, J., Cammarata, A. (1983) *Physical Pharmacy* 3 ed. Lea and Fabiger, Philadelphia. 516 – 517.

10. Kornblum, P.S. Stoopak, B. (1973) A new tablet disintegrating agent: Cross-linked polyvinylpyrrolidone. *J. Pham. Sci.* 62 (1) 43 – 49.

11. Odusote, M. O., Nasipuri, R. N. (1987) Correlation between some properties of starches and disintegration behaviour of tablets. *Nigerian J. Pharm.* 18 (3). 28 – 31.

12. Wells, J. I. And Langridge, J.R. (1981) Dicalcium phosphate dihydrate-microcrystalline cellulose systems in direct compression. *Inf. J. Pharm. And Prod. Mfr.* 2 (2) 1 – 8.

13. Hoover, J.E., Osol, A. (1975) *Remington's Pharmaceutical Sciences.* 15th ed. Mack Publishing Company. New York. 88

14. Okansen, S.A. Zografi, G. (1990) The relationship between the glass transition temperature and water vapour absorption by polyvinylpyrrolidone. *Pharm. Res.* 7. 654 – 657.

15. Hollenback, R.G., Peack, G.E., Kilsig, D.O. (1978) Application of immersional calorimetry to investigation of solid-liquid interactions: microcrystalline – water system. *J. Pharm. Sci.* 1606 – 1610.

16. Nakai, Y., Fukuoka, E., Nkajima, S.N., Yamamoto, K. (1977), Crystallinity and physical characteristics of microcrystalline cellulose. *Chem. Pharm, Bull.* 25. 96 – 110.

17. Caramella., Colombo, P.C., Conte, U., LaManna, A. (1983). Swelling of disintegrant particles and disintegrating force of tablets. *3rd Conf. Pharm. Tech.* Vol. 5. 41 – 49.