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Compression and Compaction Behaviour of Microcrystalline Cellulose from Sorghum and Andropogon Stalks

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Authors' contributions

This work was carried out in collaboration between all authors. Author JA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors AC and OKU managed the analyses of the study as well as the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Sources and processing techniques could affect performance of Microcrystalline Cellulose (MCC). This study therefore evaluated the suitability of some agricultural wastes as novel sources of MCC; Sorghum Bicolour and *Andropogon gayanus*. The physics of compaction of the new grades of cellulose; Sorghum MCC (SOMCC) or Andropogon MCC (AMCC) was compared with Avicel PH101. The SOMCC and AMCC were isolated from mineral acid hydrolysed de-lignified α-cellulose of the plant stalks. Particle size distribution was analysed. The carver hydraulic press was used for compaction study. Heckle plots, tensile strength, reworking potentials (RWP), disintegration and friability profiles were used as basis for assessment. The median particle size was 52.5 or 80 µm for AMCC and SOMCC with interquartile coefficient of skewness (IQCS) of 19.2 and

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21.5%.respectively. Particle size fractions of 125-250 µm produced compacts with similar strength profiles. The polymer grades, AMCC, SOMCC and Avicel PH101 at fixed compression pressure of 62.4 N/mm^2 exhibited similar tensile strength in the range of 2.7- 2.8 N/mm^2. Heckel plot analysis showed similarity in yield pressure of 152.3 N/mm^2 or 151.5 N/mm^2 for Avicel PH101 and SOMCC with notable higher value in AMCC at 192.1 N/mm^2. The degree of packing achieved by the particles at low compression pressure was 1.23, 1.39 and 1.12 for SOMCC, Avicel PH101 or AMCC while the extent of particle rearrangement at initial compression vide the relative densities (D_B) was in the order 0.519, 0.539 and 0.454 respectively. The results are heavily suggestive of deformation by plastic flow mechanism for the new polymers. In ranking, the degree of compaction and consolidation of SOMCC ≈ Avicel PH101 > AMCC. The reworking potential was in the order AMCC < SOMCC ≈ Avicel PH101.
The indication is that SOMCC and AMCC could find application as excipients in the pharmaceutical and allied industries.

Keywords: Andropogon; compaction; microcrystalline cellulose; sorghum.

1. INTRODUCTION

Microcrystalline cellulose (MCC) is a versatile pharmaceutical aid that could be used as filler-binder, disintegrant or dispersant. It is commercially available in grades produced by different manufacturers. MCC was discovered in 1955 by Battista and Smith and was first commercialized under the brand name Avicel® [1,2], introduced to the pharmaceutical market in 1964 [3]. Direct compression tableting is most economical technique in the production of large number of tablets. However excipient selection needs to be critically done to ensure optimum performance of the products. This requires art and science. Problem of inter-lot and inter-manufacture variability among microcrystalline cellulose grades has been studied [3,4,5,6,7] and [8] with Source of pulp and techniques of manufacture being largely accountable. Other factors include subsequent mechanical or chemical treatments (milling, hydrolysis, etc). Hydrolysis technique has been reported to affect such properties as crystallinity, degree of polymerization, water sorption capacity, particle size and specific surface area [4,9,6,7] and [8]. Studies on three batches of MCC supplied by the same manufacturer but differing in the manufacturing process and/or source of wood pulp have been done [8]. Significant differences were noted as regards lignin and hemicelluloses content, percentage crystallinity and capacity for moisture absorption. Although the differences did not significantly affect parameters such as compressibility and mean yield pressure, the authors noted that they could be potential causes of differences in behaviour of pharmaceutical products. Care therefore must be taken in changing from one cellulose product to another in an optimized tablet formulation. Compacts produced using different batches of MCC and micro fine cellulose powders at constant force disintegrated in different times. Although various agricultural by-products could serve as sources of cellulose [4,10,11], nonetheless performance evaluation must be done so as to determine the relative behaviour of such new products to official reference standard and commercially available grades.

1.1 Sources of Microcrystalline Cellulose

Most pharmaceutical grade MCC are obtained from wood pulp; both evergreen conifers and deciduous greens [1]. This product, though not originally designed as filler-binder, brought about a revolution in direct compression tableting. The success story of FMC in launching this polymeric material stimulated other manufacturers to develop MCC from their novel sources, some of which have been evaluated and their tableting qualities compared with those of Avicel [6]. Other fibrous plant materials and agricultural residues or wastes have been explored. These include bagasse, rice straw, banana stem, water hyacinth and papyrus reeds [10,12] and [13]. Preliminary studies have been done on Sorghum bicolour isolated de-lignified α-cellulose and corresponding acid hydrolysed MCC product [14].

Sorghum bicolour (Guinea corn) is a dietary staple of millions of people in the Sahel region of Africa, the near east, Middle East, India and China [15]. The grain from guinea corn is used in a variety of meals such as pap, porridge, solid pudding or cakes [16]. The stalk largely constitutes a waste, after the grains are harvested. *Andropogon gayanus*, a specie of

grass which grows wildly and abundantly within the various vegetation belts of Nigeria is popularly referred to as 'elephant grass'. The young shoots serve as good fodder, up to the period of flowering. The stalk or stem of this grass predominantly constitutes wastes at end of the raining season. Scientists and researchers are constantly seeking opportunities for adding value with most cost effective means. The aim of this study is to evaluate the compaction and compression characteristics of MCC derived from Sorghum and Andropogon stalks with the hope of identifying alternative source of this versatile polymer.

2. MATERIALS AND METHODS

The grades of microcrystalline cellulose SOMCC and AMCC were derived from mineral acid (HCl) hydrolysed α-cellulose following de-lignification/ digestion with sodium hydroxide as previously described (14). The resulting slurry was neutratrilized with dilute ammonia solution, washed, air dried, pulverized, screened and stored in a desiccator. Pulverization was done using the Kenwood Blender model BL 350 (Kenwood Ltd, UK). Avicel PH 101 (FMC Corporation USA) and dicalcium sodium diphosphate as Emcompress (Mendel Patterson NY, USA) were used as obtained from the manufacturers. The particle size distribution was studied using the sieve method with the Endecott Test Sieves/Shaker (Endecotts Ltd England). The Tablet machine Model THP ('basket' type) made by Shanghai Tianxiana and Chentai (STC) Pharmaceutical Machinery Co. Ltd. China was used for tableting work. The Carver hydraulic hand press Model C (Carver Inc. USA) was used in the compaction study. SOMCC and AMCC were obtained as previously described [14] while Avicell PH101 and Dicalcium sodium Diphosphate (DCP) were used as gotten from the supplier. Preliminary experiments were carried out to assess the potentials of the newly derived cellulose as filler binders or disintegrant. Compacts of the polymers; SOMCC or AMCC were produced at optimum compression pressure setting of 8.5 units, using the single station tablet machine fitted with a biconcave punch of 10 mm diameter. Avicel PH101 served as reference material. Compacts of Dicalcium sodium diphosphate were similarly made containing 10% w/w SOMCC, AMCC or Avicel PH 101 as disintegrant with magnesium stearate as lubricant at 0.5% w/w. Effect of particle size fraction on compressibility of the polymers was determined. Particle size fractions screened through apertures of 250, 150 and 125 um were used. Compacts of these fractions were then made with Carver hydraulic hand press fitted with flat-faced punch of 10 mm diameter at compression pressures of 62.4, 93.6 and 124.8 N/mm2. Diameter and thickness of the compacts were measured 24 h following production. Crushing strength was determined using Erweka hardness tester, Model MT and tensile strength was calculated accordingly.

Compaction properties of SOMCC and AMCC were investigated with hydraulic hand press. Compacts were made at compression pressures of 31.2, 62.4, 124.8, 156.0 and 218.4 N/mm^2. Avicel PH 101served as reference standard to AMCC and SOMCC. Using Heckel plots with regression analysis, the yield pressure P_y and material constants were determined. The relative density D_A was calculated using the expression $D_A = 1\text{-}e^{-A}$ and the extent of particle rearrangement $D_B = D_A - D_0$.

Polymers reworking potential was studied as ratio of area under the curve (AUC) for compressed (C_1) and re-compressed (C_2) tensile strength profile. Friability and in-vitro disintegration times were determined using Erweka dual drum friabilator and disintegration tester Model EP4-4.

3. RESULTS AND DISCUSSION

The particle size distribution of the derived MCC from stalk of sorghum and Andropogon plant is presented in (Fig. 1). The particles in both cases represent typical examples of positively skewed distribution [17]. The powders therefore have a narrow range of spread of equivalent diameters compared to larger range of spread in a normal distribution.

The cumulative frequency distribution is shown in (Fig. 2) and from this the median particle diameter, ($D_{50\%}$), the lower quartile point, ($D_{25\%}$) and the upper quartile, ($D_{75\%}$) were determined [17,18].

The degree of skewness, termed interquartile coefficient of skewness, IQCS, was calculated [17] as follows:

$$IQCS = \frac{(D_{75\%} - D_{50\%}) - (D_{50\%} - D_{25\%})}{(D_{75\%} - D_{50\%}) + (D_{50\%} - D_{25\%})}$$

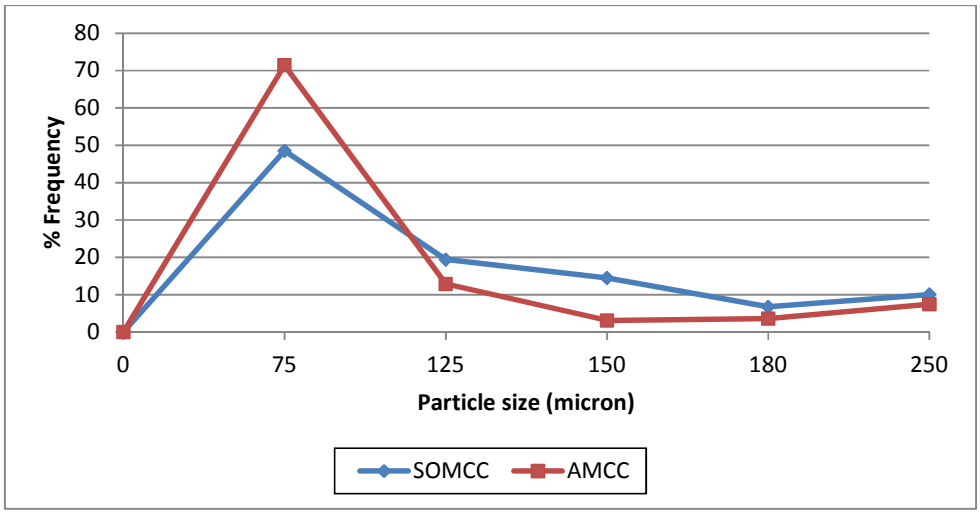

Fig. 1. Frequency distribution of different types of MCC

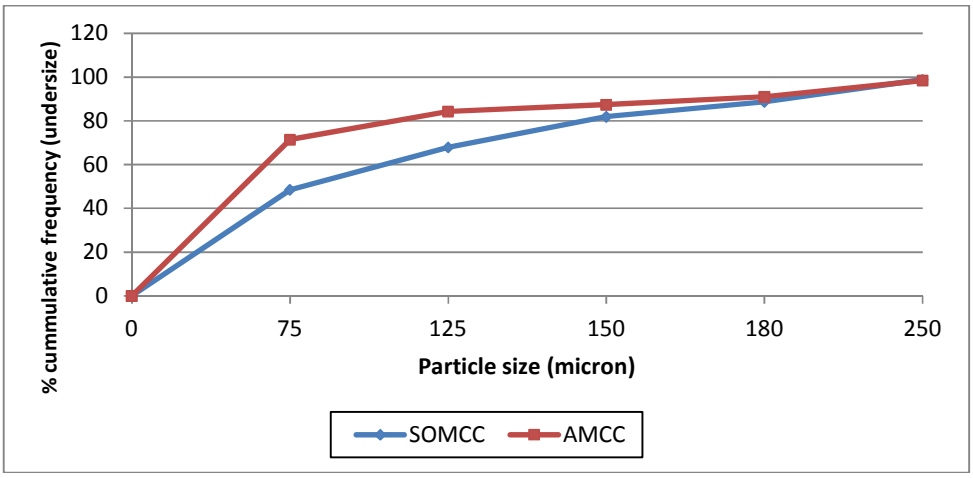

Fig. 2. Cumulative frequency distribution of SOMCC and AMCC

These determined quartile sizes and IQCS are presented in (Table 1). The AMCC had smaller particle diameter at all levels, the median particle size is 52.5microns while that of SOMCC is 80.0 µm. Although SOMCC consist of bigger size particles than AMCC, there is closeness in the degree of skewness; 21.5 and 19.2% respectively.

Spray drying of neutralized slurry from hydrolysis of cellulose is often applied in the manufacture of MCC. Controlling the conditions of this process results in different degrees of agglomeration and consequently varied particle size distribution. Different moisture removal measures and screening could also be used as means of controlling distribution of particle size. The use of specific cellulose pulps as starting processing material and controlled milling may result in median particle sizes below 50 µm of MCC [19]. Slurry in the current work was air dried at ambient temperature and thereafter pulverized. This may account for the lower median particle sizes of SOMCC and AMCC compared to 90µm in spray dried Avicel PH101.

3.1 Disintegration Profiles of SOMCC and AMCC

Dibasic calcium phosphate dihydrate (DCP) is a free flowing material having no disintegrant property [20]. In (Table 2), the effect of SOMCC or AMCC on disintegration of compacts of this filler-binder is shown. Dicalcuim phosphate

dihydrate matrixes containing either of these polymers disintegrated below 10 minutes whereas that made without any cellulose product failed to break down after 50 minutes. The indication is that these polymers possess some disintegrant characteristics in addition to the dry binding potential. This observation is consistent with report that powdered cellulose and microcrystalline cellulose grades have some disintegrant properties [21,22] and [23].

The strength of the dicalcium phosphate dihydrate compact is seen to be enhanced by incorporation of the cellulose polymers. This is similar to the report of Wells and Langride [20] who observed that there was strength enhancement of DCP compacts containing low concentration of MCC. This has been 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.

The disintegration profile of acetaminophen tablets containing the new cellulose grades is presented graphically in (Fig. 3). Microcrystalline cellulose has both water sorption and wicking properties but the latter effect plays a dominant role in the disintegration process [21]. Caramella et al. [24] described starch and cellulose as limited swelling agents which implies that the mode of disintegration involves swelling in the presence of water and a capillary mechanism due to their hydrophilic nature. The mode of action of SOMCC and AMCC as disintegrant may thus be attributed to wicking as well as swelling effects with the former playing the greater role.

The trend observed with formulations containing SOMCC or AMCC may be explained on the basis of force development. The building up of disintegrating force responsible for breakdown of the compacts might have increased with concentration of the MCC grades up to a level of 15% w/w concentration where DT of 3.4 and 3.6 minutes were recorded for SOMCC or AMCC respectively. At higher concentration no appreciable alteration in DT was noticed and it may as well be that disintegration force reached a maximum at concentration of 15 to 20% w/w. Wicking activity might have increased with concentration and reached a maximum at incorporation level of 15 to 20% in the experimental range used here. The use of SOMCC or AMCC at 10 to 20% w/v may be necessary to produce optimum disintegrating effect in acetaminophen tablets. Interestingly however, all the formulations containing the new polymers disintegrated below 10 minutes, which is within the acceptable limit for uncoated tablets.

3.2 Effect of Particle Size on Compressibility of the Derived Polymers

Particle size and shape could have significant effect on compacts [25]. The compaction profile of different particle size fractions of SOMCC and AMCC has been studied and the result is presented in (Fig. 4). It shows that fractions of the products used within the experimental limit of 125 to 250 µm exhibited similar strength profiles. Usually, a decrease in particle size results in an increase in surface area available for bonding which eventually leads to increased tensile strength [26]. It has also been reported that new surfaces created during consolidation process cannot be utilized for establishment of inter-particulate bonds in all materials [27]. In the AMCC powder, about 75% of the particles size fraction was found to be within 0 to 91.25 micron range whereas that of SOMCC was within 0 to 140 µm. The median diameters were 52.50 µm and 80.0 µm for AMCC and SOMCC respectively. This analysis shows that both powders consisted of high proportion of fines, which may account for the similar strength profile exhibited. It is suggested that the effective bonding surfaces created within the different size fractions are predominantly due to the composition of the fine particles.

Table 1. Particle size distribution and degree of skewness

Cellulose grade	Particle sizes (µm)			IQCS
	$D_{25\%}$	$D_{50\%}$	$D_{75\%}$	
SOMCC	41.25	80.00	140.00	0.215
AMCC	26.25	52.50	91.25	0.192

Table 2. Hardness and disintegration time of compacts

Tablet property	Compacts					
	Avicel PH101	SOMCC	AMCC	SO/DCP	AM/DCP	DCP
Hardness kgf	9.5	8.5	8.5	7.1	6.9	3.2
Disintegration time (min)	6.2	6.5	5.9	6.9	6.8	>50

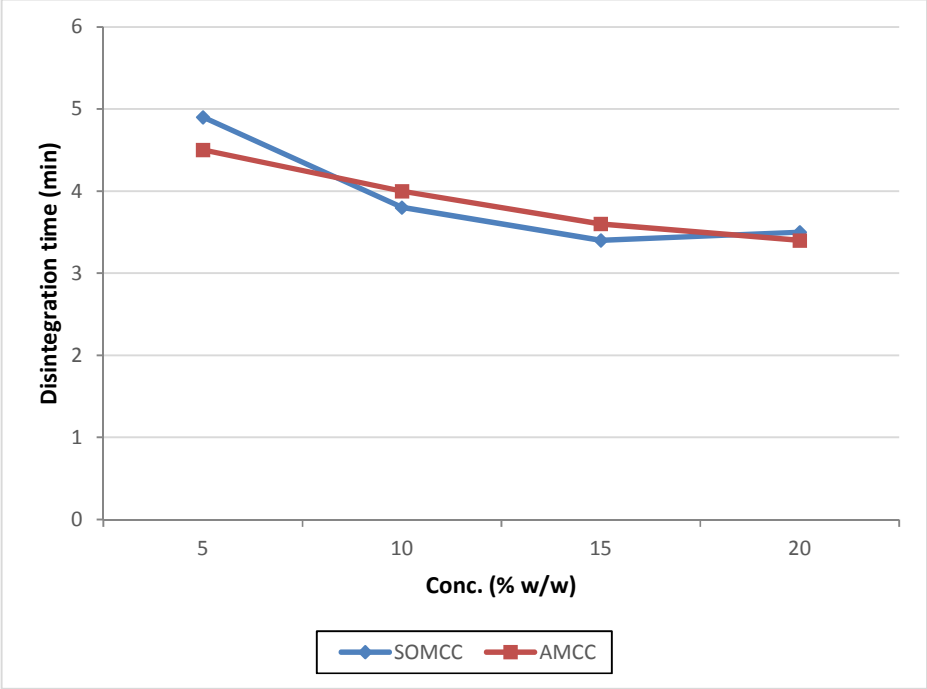

Fig. 3. Effect of concentration of MCC grades on DT of acetaminophen tablets

Sodium chloride, which deforms by plastic flow [28], has been reported by Aldolfsson et al. [29] to show an increase in tensile strength with particle size. This is attributed to predominance of weak distance forces between the particles in addition to solid bridges [29]. In the present study, the composition of the coarse particles in each case is low and probably might not have played the dominant role in the compaction behaviours of the particulate matters. However, the contributory effect of some weak distance forces due to the coarse particles cannot be ignored completely. Although AMCC had a lower median particle diameter than that of SOMCC, the degree of skewness appears to be somewhat close i.e. 19.2 and 21.5% respectively. The overall compact characteristics of these polymers could therefore be attributed to the combined effects of the characteristic poly-size particle distribution in each case. Compressibility profiles of the particle size fractions in these polymers are therefore rated as being similar.

3.3 Compressibility Profiles of Different MCC

The net characteristics of AMCC or SOMCC was compared with Avicel PH 101 as shown in (Fig. 4) using the 250 µm fractions. This particle size was selected based on comparable compactability with other fractions but better flow potential. The compact strength profiles of SOMCC and AMCC were observed to be similar and appear to be slightly better than Avicel PH 101 at all corresponding pressure levels. At compression pressure of 62.4 N/mm^2, 400 mg compact of Avicel PH 101 had an average tensile strength (ST) of 2.7 N/mm^2 while those of SOMCC or AMCC were 2.81 or 2.8 N/mm^2 respectively. Avicel PH 101 is reported to have an average particle size of 90 µm in aggregate form. Average medium particle size of 52.5 or 80 micron have been determined for AMCC or SOMCC respectively in this investigation. Spraying of the slurry in Avicel processing is said

to prevent crystal growth, resulting in aggregates of regular shape having good compressibility [30, 31]. The slurry in AMCC or SOMCC was on the other hand air dried at room temperature, then in the oven for a suitable time range. This may have resulted in predominantly fine particles and some low percentage of agglomerates. Prevalence of fines in the new polysaccharides may have resulted in creation of large bonding surfaces, culminating in high network of bonding with good compact strength profiles.

3.4 Compaction Behaviour of SOMCC and AMCC

Heckel plots [32,33] were used in characterizing the behaviour of the new cellulose products under compressive loads on the basis of equation; ln [1/ (1-D)] = KP = A. The compression pressure (P) was plotted against ln [1/ (1-D)] for SOMCC, AMCC or Avicel PH 101 respectively as presented in (Fig. 5). It shows that transition from curved to linear behaviour in SOMCC or AMCC is similar to that of Avicel PH 101. Densification in Avicel PH101 has been reported to occur by plastic deformation following application of a minimum level of pressure [21] which results in appreciable amount of interparticulate bonding.

The P_y, a measure of the ability of the material to consolidate by plastic flow was determined as reciprocal of the slope of the linear region of the graph while the values of A were determined by regression analysis using MS-Excel programme. Robert and Rowe's method [34] was used to determine the values of D_A and D_B as analysed and presented in (Table 3). The yield pressure of SOMCC is almost equivalent to that of Avicel PH101 i.e. 152.27 N/mm^2 and 151.54 N/mm^2 respectively while that of AMCC is much higher than either of the two i.e. 195.08 N/mm^2.

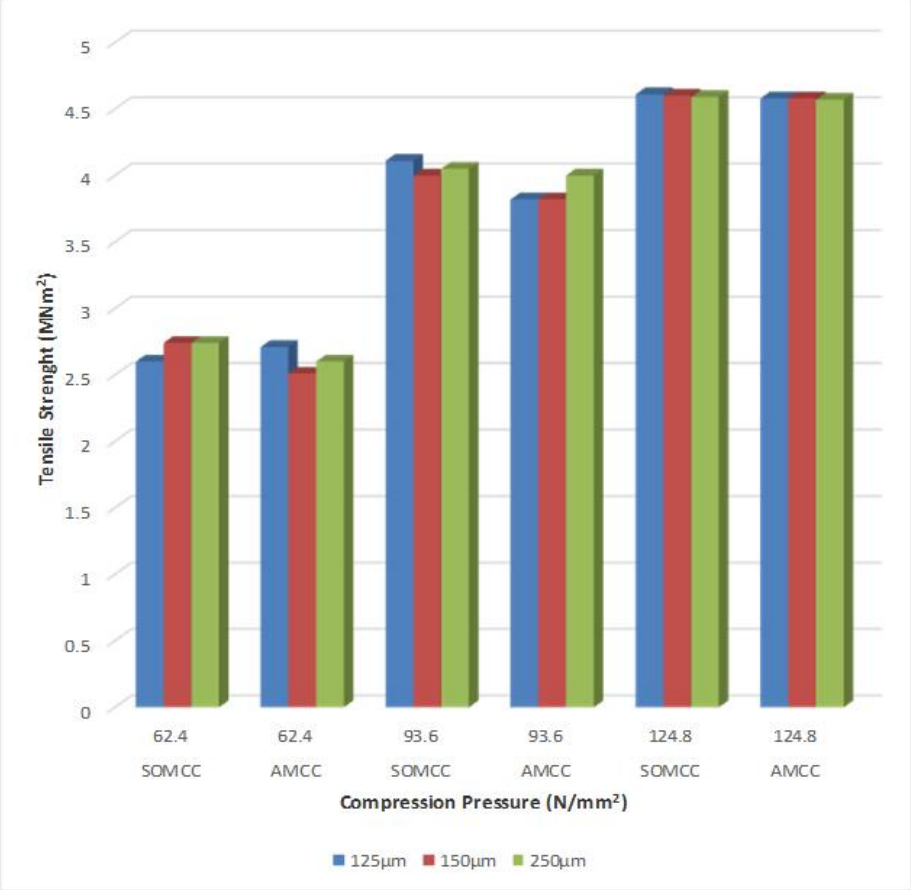

Fig. 4. Effect of particle size on compressibility of SOMCC and AMCC

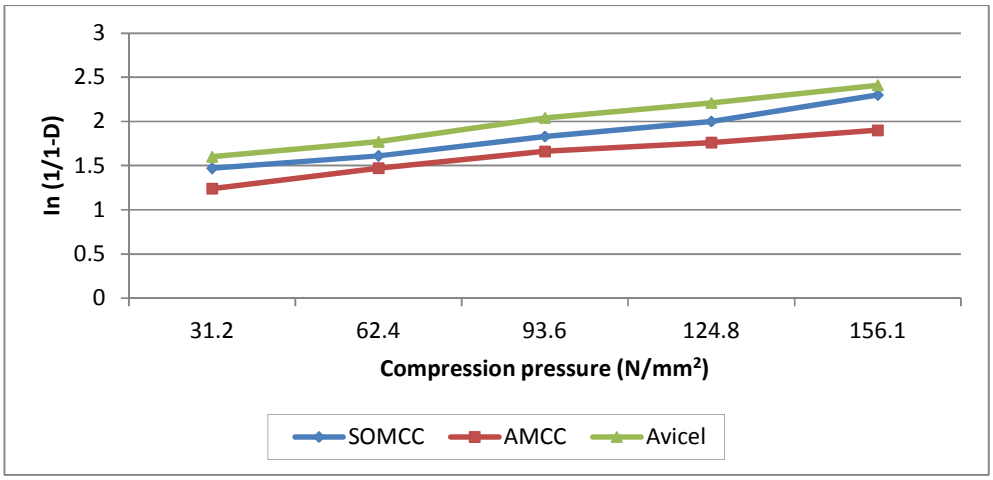

Fig. 5. Heckel plots for different MCC

Table 3. Compaction behaviours of different grades of MCC

Cellulose grade	K	P_y (N/mm^2)	A	e^{-A}	D_A ($I-e^{-A}$)	D_O	D_B ($D_A.D_O$)
SOMCC	0.0066	152.17	1.227	0.293	0.707	0.188	0.519
AMCC	0.0051	195.08	1.116	0.328	0.672	0.218	0.454
AvicelPH101	0.0067	151.54	1.388	0.250	0.750	0.22	0.530

The values of A, shows that the degree of packing achieved at low compression pressure were higher in SOMCC and Avicel PH101 than AMCC i.e. 1.227, 1.388 and 1.116 respectively. The phase of particle rearrangement represented during the initial stage of compression indicate the relative density D_B attained by SOMCC or Avice/PH101 as 0.519 or 0.530 respectively which is higher in either case than that of AMCC of 0.454. These results show that plastic deformation in SOMCC appears to be similar to that of AvicelPH101 and slightly lower in AMCC. On the basis of the result of compaction behaviours, York and Pilpel [28], Hersey and Rees [35] classified powders into three types referred to as type A, B, or C. The consolidation pattern exhibited by the new cellulose products indicates that they are most likely type A materials [20,21]. The linearity of the plots and relative density profiles are similar to the behaviours of Avicel PH101, an established plastically deforming MCC [20,21].

3.5 Reworking Potential (RWP)

Tensile strength (TS) of compacts made from different cellulose products at different compression levels were determined. Similarly, TS of compacts of the reworked materials made at similar compression pressures were determined and represented graphically in (Fig. 6).

The area under the curve (AUC) for the 1st compression (A) and the reworked profile (B) were determined using an ACAD Computer Programme. The reworking potentials (RWP) in percentage calculated using the expression RWP = B/A*100 and presented in (Table 4).

Aulton and Marok [36] noted that preformed tablets of sodium chloride (a, plastically deforming material) surprisingly exhibited brittle properties when subjected to diametral crushing tests. This, they suspected was due to work-hardening of inter-particulate bonds following extensive deformation at the points of contact. Earlier in the discussion on the consolidation pattern of the new polymers, plastic deformation was implied as the most probable mechanism of flow. Therefore the lower compact strength of the reworked material is most likely a result of reduced bonding due to work-hardening. The RWP is in the order SOMCC > AvicelPH101 > AMCC.

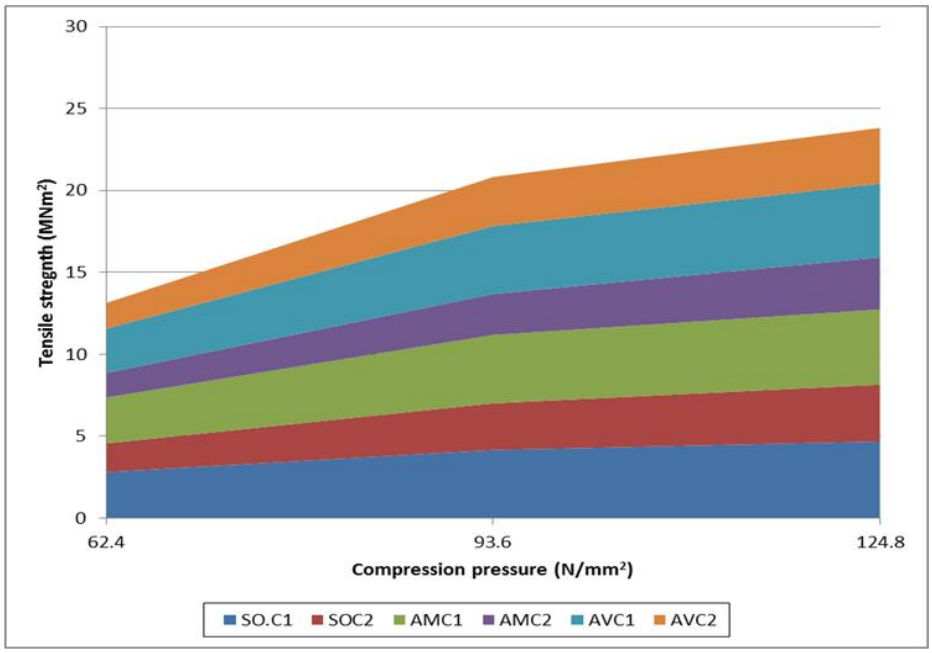

Fig. 6. Effect of reworking on the compressibility of different MCC

Table 4. Reworking potential of grades of MCC

Grade of MCC	AUC (units)		RWP (%)
	Compression 1 (A)	Compression 2 (B)	
SOMCC	333.84	224.84	67.38
AMCC	330.04	197.81	59.93
Avicel PH101	330.72	219.81	66.46

4. CONCLUSION

The polymers; SOMCC and AMCC compressed directly and exhibited high potential as disintegrant. Compacts of dicalcium phosphate dehydrate (a non-disintegrating diluent) disintegrated under 10 minutes when mixed with the derived cellulose in batches. Disintegration time (DT) of blends of these MCC grades in acetaminophen formulations was within acceptable limit for non-coated tablets. Heckel plots and analysis showed that consolidation behavior of SOMCC or AMCC is by plastic flow, similar to Avicel PH101.

The powder, compaction and tablet characteristics investigated here shows that the newly derived MCC from the novel agricultural wastes are comparable to an existing market grade filler-binder, Avicel®. Sorghum and Andropogon plants may therefore serve as alternative sources of pharmaceutical and cosmetic grade exceipient. Work on the bonding capacity and excipient – drug compatibility have also been looked into and currently undergoing internal review and would constitute separate reports.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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