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EFFECT OF DRYING METHODS ON THE POWDER AND COMPACTION PROPERTIES OF MICROCRYSTALLINE CELLULOSE DERIVED FROM *BAMBUSA VULGARIS*

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ABSTRACT

Processing methods, besides the pulp source, is one of the major factors that contribute to variations in the characteristics of microcrystalline cellulose (MCC). The effect of drying method on the powder and compaction properties of MCC obtained from the acid hydrolysis of α-cellulose derived from *Bambusa vulgaris* (BV) was investigated. A portion of the wet MCC was fluid bed dried at 60 ± 1˚C for 2 h (coded MCC-BVF). The second portion was lyophilized at –45 ± 1˚C for 2 h (coded MCC-BVL). The MCCs were evaluated using standard methods. Avicel® PH 102 (MCC-AVC) was used as standard. Physicochemical properties and X-ray diffractometry results of MCC-BVF and MCC-BVL were consistent with MCC. The flow indices showed flowability. Assessment of the compaction properties of the MCCs using Kawakita and Heckel models showed good densification and compactibility. Compacts formed showed good weight uniformity (300 mg ± 5%), disintegration time (< 15 min) and friability (< 1%). The hardness and tensile strength of MCC-BVL were higher (176.79 – 551.77 kg/m^2) than MCC-BVF (28.04 – 232.44 kg/m^2). Heckel analysis showed good plasticity and slippage. MCC-BVL compacts had significantly ($p < 0.05$) better mechanical properties than MCC-BVF compacts. Lyophilization produced stronger compacts than fluid bed drying.

KEYWORDS: *Bambusa vulgaris*, microcystalline cellulose, drying methods.

INTRODUCTION

It is desirable that a pharmaceutical excipient should possess certain characteristics such as purity, inertness, compatibility, good compressibility and flowability before it can be considered for use in pharmaceutical formulations.[1] Microcrystalline cellulose is a purified, partially depolymerized cellulose prepared by the acid hydrolysis of alpha (α) cellulose obtained as pulp from fibrous plant material and marine (algae, bacteria) sources.[2] Cellulose and its derivatives have continued to attract the attention of researchers because of its natural abundance, biodegradability, eco-friendliness and ease of processing. It has remained one of the most used filler–binder in direct compression formulation. However, the use of MCC in direct compression is limited by a number of factors amongst which are low bulk density, high sensitivity to lubricants, poor flowability and compressibility.[3] especially when active pharmaceutical ingredients (APIs) with low bulk density and poor compressibility such as paracetamol and ibuprofen are involved.

In order to overcome some of the shortcomings of MCC which affects its functionality, various modifications have been made to enhance its properties. For instance, Avicel® PH, a foremost commercial brand of MCC which was introduced into the market by FMC Biopolymers, USA in 1964[4] has evolved from a single brand to many other brands such as PH 101,102,103,105, 112, 113, 200, 301 and 302 over the years in a bid to have variations of products with different characteristics aimed at meeting with the different formulation requirements that may have arisen because of the emergence of newer APIs and formulation techniques. Similarly, other manufacturers have introduced various brands of MCC such as Emcocel®, Comprecel®, and Microcel® into the market. Each brand's manufacturer has a unique product that is prepared in a unique way with an aim to impart the characteristics desired by the manufacturer to the product. These characteristics could be in terms of morphology, particle size, physicochemical property, or degree of crystallinity. These differences usually arise as a result of the

processing steps or source of pulp.[5] Brands of MCC that possess large particle sizes and high density have been introduced into the market in a bid to enhance its properties and use. Drying method and moisture content of the product are amongst the processing variables that could modify and determine the quality/characteristic of the MCC besides the source of pulp.[6] Spray drying technique has been reported as the most commonly used drying technique for most commercial MCC. It allows the wet MCC to dry as aggregates with a high porous inter-particulate structure.[3] Lyophilization has also been reported to cause materials to have a high porous structure[7] while fluidized drying leads to formation of discrete particles with low inter-particulate voids. Other methods that have also been reported to have improved the functionality of MCC include co-processing with other materials such as silicon dioxide. Silicification of MCC has been reported to improve both its flow and tabletability as a direct compression excipient.[8,9] This was achieved by the modification of the external as well as any internally exposed surfaces of such MCC particles.[10] Dry particle coating, a technology that does not use any solvent has also been reported to be useful in enhancing the bulk density, flow and compactibility characteristics of MCC.[11]

Microcrystalline cellulose is known as one of the best strong dry binders, tablet disintegrant, absorbent, filler or diluent, lubricant and anti-adherent.[3] It has also been reported as a good thickener and viscosity enhancer in liquid formulations.[12] Many other sectors such as the food, cosmetic, paint and energy sectors have also found it useful.[13]

Bambusa vulgaris (Poaceae), most commonly known as Indian bamboo is a perennial plant that is fast growing and grows best under humid conditions. It is found growing well on river banks, roadsides, wastelands or open grounds with low altitudes.[14] It is native to the Himalayas but is now found growing wild or cultivated in Asia, America, Europe and Africa. In Nigeria, it grows in almost all the southern parts except Lagos.[15] In Asia, its young shoots are boiled and eaten.[16] Its extracts have been used to treat inflammatory conditions, menstrual pains and as an abortifacient.[17] Its resin has been used for its astringent, expectorant, constipating, cardiotonic, hemostatic, aphrodisiac and diuretic properties.[18] Although many workers have previously worked and reported success in the extraction of MCC from BV, the need to improve on the powder and tableting quality of the MCC obtained gave birth to this work. The effect of method of drying as a process variable on the powder and tableting quality of MCC from *Bambusa vulgaris* was investigated. Fluid bed drying and lyophilized methods were used and the effect of the two variables on the powder and tableting properties of the resultant MCCs was compared with MCC-AVC which is popularly prepared by spray drying.

MATERIALS AND METHODS

Materials

Sodium hydroxide (Merck, Germany), Hydrochloric acid, Magnesium nitrate and Corn starch (BDH, Poole England), Sodium hypochlorite 3.5 % w/v (JIK®, Reckitt and Colman Nig. Plc), Avicel® PH 102, a generous donation by FMC Biopolymers, Brussels sales office, Belgium, potassium sulphate, sodium chloride (J.T. Baker, New Jersey, USA), talc, magnesium stearate (Sigma, USA) and distilled water (generated in the Pharm. Tech. Lab., Uniport). Dried chips of semi-matured BV stem bark.

METHODOLOGY

Isolation of alpha (α) cellulose

The method of Ohwoavworhua *et al*[19] with slight modification was adopted. Eight hundred grams (800 g) of the dried cut chips of *Bambusa vulgaris* was digested with 10 L of 3.5 % w/v solution of sodium hydroxide (NaOH) at a boiling temperature of 100˚C on a sand bath for 3.5 h. The resultant pulp was washed thoroughly with distilled water until neutral to litmus. The excess moisture was removed by squeezing through a muslin cloth. The damp mass was initially bleached by heating at 80 ± 1˚C for 30 min using 8.0 L of 0.4 % w/v solution of sodium hypochlorite. After washing with water until neutral to litmus, further alkaline treatment (delignification) was done with 8.0 L of 17.5 % w/v NaOH at 100˚C for 1 h, followed by further washing with distilled water until neutral to litmus. A second bleaching of the material was done with another 8.0 L of 0.4 % w/v solution of sodium hypochlorite. The material (α-cellulose) was washed with distilled water until neutral to litmus. The wet α-cellulose was squeezed with a muslin cloth, and dried at 60 ± 1˚C for 2 h in a hot air oven (Memmert®, England).

Acid hydrolysis of α-cellulose obtained from *Bambusa vulgaris*

A quantity of 60 g the dry α-cellulose obtained from *Bambusa vulgaris* was heated with 2.5 N Hydrochloric acid (HCl) solution at 105 ˚C for 30 min to obtain MCC. The mixture was poured into 5 L of cold distilled water and intermittently vigorously stirred until it became cold. On settling, the MCC was washed severally with copious amounts of distilled water until it became neutral to litmus. Excess water was squeezed out using a fine muslin cloth and the resultant lumps separated into two portions. One portion was dried using a fluid bed dryer (Sherwood® Tornado model, China) set at a temperature of 60 ± 1 ˚C and inlet air of 30 m^3 min^{-1} for 2 h and coded MCC-BVF. The second portion was lyophilized in an LGT 18 freeze dryer (Gallenkamp®, England) set at a temperature of - 45˚C for 2 h and coded MCC-BVL. Each of the material was milled using a domestic blender (Binatone®, Japan) and screened through a 250 µm stainless steel sieve (Retsch®, Germany). The microcrystalline cellulose obtained was stored.

Physicochemical evaluation

Identification

Observations on the color, odor, taste and texture of the MCC powders were made and recorded. One (1.0) g of the MCC was soaked in an iodine solution for 5 min. Any excess iodine was drained off the wet MCC and visual observations for possible changes in color was made and recorded. Besides the iodine treatment, 2 drops of 60 % v/v of sulphuric acid solution were added to a fresh portion of the MCC dry powder and observation for possible change in color of the MCC was also made and recorded.[20] The test was done on all the MCC powders.

Solubility determination

One (1.0) g each of MCC-BVF, MCC-BVL and MCC-AVC was submerged in each of these solvents: distilled water, acetone, 0.1 N HCl and ethanol. They were shaken to mix properly and visual observations for solubility of the MCC in the solvent noted.

Hydrogen ion concentration (pH) determination

The hydrogen ion concentration (pH) determination of the MCC powders was done by shaking a dispersion of 2 g of each of the MCC in 100 ml of distilled water for 5 min. The mixture was allowed to settle and the pH of the supernatants determined[20] using a pH meter (PHS® 25, India). Three replicate determinations were made.

Total ash content determination

Three (3.0 g) of the MCC obtained from BV and MCC-AVC was combusted individually in a furnace at 550˚C for 3 h. The total ash content was determined by measuring the residue left after the combustion.

Determination of elemental / heavy metals

The presence of heavy metals such as lead (Pb), iron (Fe), zinc (Zn), manganese (Mn) and arsenium (As) were investigated by the aid of a flame Atomic Absorption Spectrophotometer (AAS) (Model AA-7000, ROM version 1.01, S/N A30664700709, SHIMADZU, Japan) at wavelengths of 283.33, 248.30, 213.90, 279.50 and 197.3 nm for Pb, Fe, Zn, Mn and As respectively. A quantity of 1.0 g of the MCC was digested using a 10 ml mixture of a 1:3 medium of concentrated nitric acid (HNO_3) and HCl solution. The filtrate obtained was diluted up to 50 ml using distilled water. The pure/standard samples of the heavy metals being investigated were diluted serially to enable determination of the maximum wavelengths of absorption and standard calibration plot (Beers plot) of the elements. All the determinations of absorbance of the samples taken were converted to concentrations using the standard calibration plot earlier determined.

X-ray Diffraction (XRD) determination

One hundred and fifty (150) mg of each of the MCC-BVF, MCC-BVL and MCC-AVC was tightly packed in the sample holder of the XRD equipment and was exposed to the X-ray radiation using an X-ray diffractometer (D/MAX-1200, Rigaku, Japan), which was powered by a 45 kilovolt (kv) X-ray generator (RINT 2000, Rigaku, Japan) at an input of 35 milliAmpere (mA) and set at 0.020˚ and step time of 29.10 sec (Cu Kα radiation) and a scan speed of 2˚ per sec at a 2 theta (Θ) range of 3 - 80˚. Diffractograms of the samples were made and the degree of crystallinity of each sample was calculated from Equation 1.[21]

Crystallinity index (CI) = $[(I_{002} - I_{am})/I_{am}]x100$ …… 1

Where I_{002} is the highest peak intensity of the crystalline fraction and I_{am} is the low intensity peak of the amorphous region.

Scanning Electron Microscopy (SEM) determination

This test was done independently with quantities ranging from 3-5 mg of MCC-BVF, MCC-BVL and MCC-AVC samples placed in appropriate containers in the sample chamber of the SEM equipment (Phenom Prox, Model no MVE016477830) and covered with a coating/sputter of gold. The equipment was switched on and readings were taken. Micrographs of the scanned samples showed the morphology, particle shape and size of each sample.

Swelling capacity determination

The swelling capacity of the microcrystalline cellulose samples MCC-BVF, MCC-BVL and MCC-AVC were determined by using the method of Bowen and Vadino[22] with slight modification. A quantity of 3 g of the sample was placed in a 100 ml graduated glass measuring cylinder and tapped to obtain the tapped volume, V_t. A 100 ml volume aqueous dispersion of the powdered sample was made using distilled water. The mixture was shaken thoroughly and was allowed to stand undisturbed for 24 h on a flat surface and the volume of the sediment formed, V_v noted. Triplicate determinations were done for each of the samples and the swelling capacity calculated as a percentage using Equation 2.[23]

Swelling capacity (S.C.) = $\frac{Vv - Vt}{Vt}$ x 100 …… 2

Hydration capacity determination

One (1) g of each of the MCCs was weighed into a 15 ml plastic centrifuge tube and 10 ml of distilled water was added to it. Each tube was shaken intermittently over a period of 2 h and left to stand for 30 min. Centrifugation at 1000 revolutions per minute (rpm) was done for 10 min using a table top centrifuge model TX 150 (ThermoFisher Scientific, UK). The supernatant was carefully decanted and the wet sediment weighed. This procedure is a slight modification of Kornblum and Stoopaks method.[24] Triplicate determinations were done. The hydration capacity was calculated from Equation 3.

Hydration capacity (H.C.) = $\frac{x}{y}$ …… 3

Where x is the weight of the wet sample/ powder sediment and y is the weight of the dry sample/powder.

Moisture content determination

A quantity of 5 g each of MCC-BVF, MCC-BVL and MCC-AVC was placed in a tarred white porcelain crucible and dried in a hot air oven (Mermmet®, England) at 105˚C until a constant weight was obtained. The percentage moisture content was determined using Equation 4.[25]

$$\text{Moisture content (M.C.)} = \frac{Wi - Wf}{Wi} \times 100 \quad \ldots\ldots\ldots\ldots 4$$

Where W_f is the final weight of powder after drying, and W_i is the initial weight of powder before drying.

Moisture sorption test

Two (2) g each of MCC-BVF, MCC-BVL and MCC-AVC were weighed into a tarred 7 mm Petri dish and placed in desiccators of relative humidity of 52, 75, 84 and 96 % respectively at room temperature of 29 ± 1˚C. The weight gained by each powder over a period of five (5) days was calculated for each sample from Equation 5. Triplicate determinations were done.

$$\text{Moisture gained (M.G.)} = \frac{W2 - W1}{W1} \times 100 \quad \ldots\ldots\ldots\ldots 5$$

Where W_1 is the weight before exposure and W_2 is the weight after exposure.

Particle size determination/analysis

The particle size analysis was done using the nest of sieves method. Seven stainless steel sieves (Retsch®, Germany) ranging from 1 mm to 45 µm arranged in descending order with a collection pan underneath the sieves was placed on a sieves shaker (Endicott® Ltd, UK). The sieves were weighed empty and to the topmost sieve a 25 g quantity of MCC-BVF, MCC-BVL or MCC-AVC was placed and agitated for 5 min at amplitude of 1.5 mm/g. The weight of material retained on each of the sieves was obtained by deducting the weight of the empty sieves from its weight with the powder sample retained. The percentages of the samples retained were calculated. Triplicate determinations were done and the mean weight at each determination calculated from Equation 6.[26]

$$\text{Average diameter} = \frac{[\Sigma\ [\%\ \text{retained x mean apperture}]}{100} \ldots 6$$

Degree of polymerization and Molecular weight determination

The solution viscometry method[27] using a U-tube viscometer (Technicu size C100) was employed in determining the degree of polymerization and molecular weight of MCC-BVF, MCC-BVL and MCC-AVC. Stock solutions of 2 % w/v of MCC-BVF, MCC-BVL and MCC-AVC were separately made using an ammoniacal solution of copper. Serial dilutions of 1 %, 0.5 %, 0.25 %, 0.125 % w/v was made from each MCC stock solution. Using the U-tube viscometer, the flow time of each of the MCC solutions at the different dilutions available were made. This enabled the determination of the flow rates of the solutions. The MCC solutions were considered to be adequately diluted when their flow time measurements become close or equal to that of the solvent (ammoniacal solution of copper). The experiments were conducted at ambient temperature (29 ± 1˚C). Determination of the densities of the different MCC solutions was done using pycnometric method. From the relative viscosity (viscosity ratio), the reduced viscosity (viscosity number) was measured. A plot of the reduced viscosity versus concentration was made and the intrinsic viscosity determined as the intercept of the y-axis of the plot of either MCC. From the value of intrinsic viscosity, the degree of polymerization was calculated from Equation 7.[27]

$$(DP)^{0.85} = 1.1 \times \eta \quad \ldots\ldots\ldots\ldots 7$$

where η is the intrinsic viscosity.

The molecular weight can be calculated from Equation 8

$$D_p = \frac{M}{Mo} \quad \ldots\ldots\ldots\ldots 8$$

Where M is the molecular weight of the material or polymer, and M_o is the molecular weight of glucose. Calculations and plots to determine the intrinsic viscosity, relative viscosity, the molecular weight and degree of polymerization were done for each MCC sample.

Bulk and Tapped density determination

A quantity of 10 g of each MCC powder was poured freely under gravity into a 50 ml clean, dry, graduated measuring cylinder and the volume occupied by the sample noted as the bulk volume (V_b). The bulk density, D_b was obtained from Equation 9.[26]

$$D_b = \frac{M}{Vb} \quad \ldots\ldots\ldots\ldots 9$$

Where M is the mass of the MCC powder.

The cylinder was tapped on a flat wooden platform by dropping the cylinder from a height of about 2 – 3 cm at 2 – 3 sec intervals until there was no further reduction in the volume of the material. The tapped density, D_t was calculated using Equation 10

$$D_t = \frac{M}{Vt} \quad \ldots\ldots\ldots\ldots 10$$

Where V_t is tapped volume

Particle density determination

The determination of the particle density of the MCC powders was done by the liquid displacement method using xylene as the immersion fluid. A 25 ml volume capacity pycnometer was weighed empty, and later was filled with xylene. It was stoppered, wiped of any spilled xylene on its body and weighed. One gram (1 g) of the powdered sample was weighed into the pycnometer. The pycnometer was stoppered, wiped clean of excess xylene and reweighed. The particle density was calculated from Equation 11.[28]

$$P_d = \frac{Wp}{(a + Wp) - b} \times \text{S.G.} \quad \ldots\ldots\ldots\ldots 11$$

Where P_d is the particle density, S.G. is specific gravity of solvent, a is the weight of pycnometer and solvent, W_p is the weight of powder and b is the weight of pycnometer + solvent + powder. Triplicate determinations were made for each powder sample.

Flow rate and angle of repose determination

The dynamic angle of repose was measured using the funnel and free-standing cone method. A quantity of 10 g of microcrystalline cellulose powder was poured into and allowed to flow freely from a clamped stoppered clean glass funnel whose orifice was 4 cm above a flat surface. The time taken to flow, the diameter and height of the powder heap formed were measured and recorded. The flow rate and tangent of the powder heap were calculated from Equation 12

$$F.R. = \frac{M}{F.T.} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ 12.$$

Where F.R. is the flow rate, F.T. is the flow time and M is the mass of powder used. The angle of repose is calculated using Equation 13

$$\text{Angle of repose } (\Theta) = \tan^{-1}\left(\frac{2h}{D}\right) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ 13$$

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

Hausner's quotient (ratio) and Carr's index determination

The Hausner's quotient and Carr's index for MCC-BVF, MCC-BVL and MCC-AVC were calculated from Equations 14 and 15 respectively.[27]

$$\text{Hausner's quotient (H.Q.)} = \frac{Dt}{Db} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ 14$$

$$\text{Carr's Index (C.I.)} = 1 - \left(\frac{Db}{Dt}\right) \times 100 \quad \ldots\ldots\ldots\ldots\ldots 15$$

Powder porosity determination

The powder porosity, ϵ is obtained using Equation 16.[29]

$$\epsilon = 1 - \left(\frac{Db}{Pd}\right) \times 100 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots 16$$

where P_d is the particle density and D_b bulk density.

Compactibility and powder cohesion determination

The Kawakita plots of the tapped density and the reduction in volume of the powder bed during quantified tapping were used in deriving the cohesion and compactibility of the microcrystalline powders. The relationship between the volume reduction of powder column and the applied pressure is described by the Kawakita Equation. A 50 ml clean, dry, graduated, glass measuring cylinder kept on a flat platform was filled with 10 g of the MCC that was freely poured into it. The bulk volume, V_o was noted and the cylinder was mechanically tapped at determined incremental number of taps, N and the volumes occupied by the powder noted each time until there was no further decrease or reduction in volume, V. The degree of volume reduction, C was calculated from the values of V and V_o. The degree of cohesion and compactibility of the powder was calculated using Equation 17 known as the Kawakita Equation.[30]

$$\frac{N}{C} = \frac{N}{a} + \frac{1}{ab} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ 17$$

The degree of volume reduction, C, is derived from $(V_o - V)/V_o$. The cohesiveness of the powder sample is described by '1/b' while 'a' is considered as the compactibility of the powder. When the volume of powder reduction based on the number of taps, N/C is plotted against N in a graph, the slope of the graph would be '1/a' while the intercept would be '1/ab'. The procedure was carried out on the three samples of microcrystalline cellulose: MCC-BVF, MCC-BVL and MCC-AVC.

Compaction of microcrystalline powders

Each of the different samples of microcrystalline powders: MCC-BVF, MCC-BVL and MCC-AVC were compressed at different compression loads ranging from 4.90 to 14.71 mPa (megaPascal). The MCC powder was manually fed into a single punch hydraulic tablet press (Model C, Carver Inc., Wisconsin, USA) fitted with a flat faced set of punches of 10 mm diameter to make 100 compacts of 300 mg weight each. The compression time for each compact was 30 sec. The punches and dies were lubricated with a 2 % w/v dispersion of stearic acid in acetone before each compaction cycle.

Evaluation of microcrystalline cellulose compacts

The batches of the compacts were each allowed a 24 h post compression-relaxation time before evaluation for wholesomeness, uniformity of weight, thickness, hardness, friability, disintegration time and tensile strengths.

Wholesomeness determination

The compacts were visually and physically inspected to see whether defects such as capping, chipping, staining or breaking existed.

Weight uniformity test

Twenty compacts were randomly selected from each batch of MCC-BVF, MCC-BVL and MCC-AVC and individually weighed. The mean, standard deviation and coefficient of variance were determined. Acceptance or rejection of compacts was based on the British Pharmacopoeia (BP) coefficient of variance tolerance limits for uncoated tablets of 300 mg which is ± 5 % for tablets > 250 mg.[20]

Hardness test

The hardness of ten compacts that were randomly selected from each batch of MCC-BVF, MCC-BVL or MCC-AVC was determined using an Erweka TBH 200 hardness tester (Erweka®, Germany). The mean, standard deviation, and coefficient of variation were determined.

Disintegration test

Six compacts that were randomly selected from each batch were used for the test. The test was carried out using an Erweka®ZT-3 double basket disintegration tester (Erweka®, Germany) and each compact was held in place with a glass disc inside each cylindrical glass hole. Each of the beakers was filled with 500 ml of 0.1 N

HCl and heated up to 37 ± 1˚C in the equipment's water bath. The time taken for each compact to completely break up and pass through the mesh was noted. Triplicate determinations were done.

Friability test

Ten tablets randomly selected from each batch of the compacts were de-dusted. They were collectively weighed and put in one of the drums of a model TAR 200 (Erweka®, Germany) twin drum electronic friabilator programmed to revolve at 25 rotations per minute (rpm) for 4 min. At the end of the exercise the tablets were collected and re-dedusted and any broken tablets rejected. The tablets were reweighed and the percentage friability (F) calculated from Equation.[31]

$$F = 1 - \left(\frac{Wo}{Wf}\right) \times 100 \quad \ldots\ldots 18$$

Where W_o is the initial weight and W_f is the final weight.

Thickness/height and diameter test

Using a micrometer screw gauge, ten compacts that were randomly selected from each of the batches of the MCC was measured for thickness and diameter. The mean and standard deviation were calculated and recorded for each batch.

Tensile strength

The tensile strength of the compacts was determined based on hardness, thickness and tablet diameter using Equation.[32]

$$\text{Tensile strength } (T_S) = \frac{2P}{\pi dt} \quad \ldots\ldots 19$$

Where P is the breaking force, d is the tablet diameter, t is the tablet thickness.

Heckel Equation

The Heckel Equation is used in relating the relative density of a powder bed to the applied compression pressure it receives during tableting. It gives a description of the densification behavior of the powder bed from the point the die is filled to the time a quantified pressure is applied. It also describes the deformation mechanism of the powder in forming the compact. The Equation is stated as Equation.[33]

$$\ln\left(\frac{1}{1-D}\right) = KP + A \quad \ldots\ldots 20$$

where:

D is the relative density of a powder compact at pressure P, K is a constant, to measure the plasticity of the compressed material, A is the Y-axis intercept, related to die filling and particle rearrangement before deformation and bonding of the separate particles.

Reworking potential of microcrystalline cellulose

This is achieved by randomly selecting compacts of the microcrystalline cellulose compressed at the different compression loads, crushing them to fine particles, screening through a 250 µm stainless steel sieve and recompressing at the same compression loads and target compact weights of 300 mg each using 10 mm flat faced punches and the same tablet press. Reworked compacts were evaluated 24 h post-compression for uniformity of weight, thickness, hardness and friability. Plots of hardness against compression pressure were made for the initial compacts and the reworked compacts of each sample. The area under the curve (AUC) of each plot was determined using Wolfram/Alpha Widget software. The reworking potential was calculated as the percentage of the AUC of the reworked MCC (AUC_r) against the AUC of the initial MCC (AUC_i) compact as shown in Equation 21.

$$\text{Re-workability} = \left(\frac{AUCr}{AUCi}\right) \times 100 \quad \ldots\ldots 21$$

Statistical evaluation

The data obtained were statistically analyzed using Analysis of Variance (ANOVA) and students t-test (IBM SPSS version 21). At 95 % confidence interval, p values less than or equal to 0.05 ($p \leq 0.05$) were considered significant.

RESULTS AND DISCUSSION

The yield of α-cellulose and microcrystalline cellulose were 24.0 % and 6.8 % respectively with reference to the dry BV starting material.

Physicochemical properties

Identification

Results of organoleptic tests showed MCC-BVF and MCC-BVL as a fine, white, odorless, and tasteless powder that possessed similar organoleptic characteristics with MCC-AVC. These and some other physicochemical test results are shown in Table 1. Identification test results using iodine gave a reddish brown color indicating the absence of starch. The sulphuric acid test gave a blue color which confirmed that the sample is MCC[20] (Table 1). Amongst cellulose materials, only MCC would show a blue color on the addition of sulphuric acid.[20]

Solubility

The solubility profile results show that the materials were insoluble in water and some organic solvents (acetone, ethanol and 0.1 N HCl) as a result of their high crystalline structure (Table 1).

pH result

The results of the acidity and alkalinity of the samples were near neutral as shown by the pH values obtained (6.36 ± 0.08 to 6.80 ± 0.07) (Table 1). Both acidic and basic drugs can be formulated with these MCCs because of their near neutral pH characteristics.

Total ash content result

The ash content of the MCC from BV was 1.85 % while that of MCC-AVC was 1.95 % (Table 1). These low values show that the MCCs were properly prepared and they also have a low degree/content of organic matter.

Elemental / Heavy metal analysis result

The elemental analysis results show that the samples were safe for heavy metals (Table 1). Some of the heavy metals such as lead (Pb) and arsenic (As) were absent whereas others such as zinc (Zn), manganese (Mn), iron (Fe) and sodium (Na) were present within the British Pharmacopoeia and World Health Organization (WHO) tolerance limits.[20,34]

X-Ray Diffraction (XRD) result

Diffractograms obtained from XRD tests of the samples (Fig. 4 and 5) showed diffraction patterns that were similar to the diffraction pattern of MCC-AVC (Fig.6). Peaks were observed at 22.11˚ and 15.90˚ of 2 theta (θ) for the crystalline and amorphous regions respectively for MCC-BVF and at 22.26˚ and 17˚ of 2θ for MCC-BVL. Double peaks were observed for MCC-BVF and MCC-BVL at the 22° range of 2θ while a single peak was observed at the same point for MCC-AVC. Such peaks can be attributed to the existence of cellulose II crystalline structure for the BV MCCs.[36,37] These gave percentage crystallinity values of 85.51 and 90.31 % for MCC-BVF and MCC-BVL respectively (Table 1). These values were also comparable to that obtained from MCC-AVC which was 80.15 % at 23.32˚ and 16.24˚ of 2θ. Literature has reported crystallinity values of 60 – 80 % for MCC.[38,39] Besides the mechanical properties, the physicochemical behavior of cellulose is strongly related to its degree of crystallinity which would directly influence the extent of its accessibility for chemical modification, swelling and water-binding abilities.

Scanning Electron Microscopy (SEM) result

The micrographs from SEM test (Fig.1 and 2) for MCC-BVF and MCC-BVL showed strands whose morphology and size resembled MCC-AVC (Fig.3). The particles of MCC-AVC appear to be more clustered than MCC-BVF and MCC-BVL. The clustering or aggregation may imply that the particles are more closely bonded and may translate to increased mechanical strength when compressed into compacts than would be obtained from MCC-BVF and MCC-BVL. However, the features of these micrographs are similar or consistent with SEM micrographs of MCC.[35]

Swelling capacity result

The swelling capacity describes the swellability and this depicts/indicates an increase in the volume of water taken up after absorption by the material.[3] The swelling capacity value of MCC-BVF was (124.32 ± 1.60 %). This is about half the value obtained for MCC-BVL (267.38 ± 1.76) and MCC-AVC (255.57 ± 1.53 %) powder samples respectively (Table 1). A high swellability is a good index that the material would serve as a good disintegrant in tablet formulations. This implies that both MCC-BVL and MCC-AVC would be better disintegrants than MCC-BVL when used in tablet formulations.

Hydration capacity result

The hydration capacity indicates the amount of water a material is able to absorb on hydration.[40] The hydration capacity of MCC-BVF powder was 2.35 ± 0.23 (Table 1). This value is significantly lower ($p < 0.05$) than that of MCC-BVL powder (3.38 ± 0.33). The hydration capacity of MCC-AVC was 3.55 ± 0.07 and is similar to the value obtained for MCC-BVL powder. Both the hydration capacity and swelling capacity characteristics play a role in the disintegrant properties associated with MCC.[3]

Moisture content result

The moisture content of MCC-BVF, MCC-BVL and MCC-AVC were below 7 % and thus met with the British Pharmacopoeia (BP) specification which stipulates 5 – 7 % as the moisture content.[20] This residual moisture is necessary in the MCC as it aids formation of strong bonds in the compacts thereby increasing their tensile strengths.[41] The residual moisture can also aid lubrication of the particles and this would improve its flow from the hopper to die[42] and also its easy ejection from the punch and die surfaces of the tablet press after compaction.

Moisture sorption result

The moisture sorption evaluation results show that varying degrees of moisture was adsorbed at the different relative humidity the evaluations were done (Table 1). More moisture was adsorbed by each of the MCCs as the relative humidity increased. MCC-BVL adsorbed more moisture than MCC-BVF at similar relative humidity but had closer values to MCC-AVC. The ability of the material to adsorb moisture would depend on the proportion of the amorphous material to the crystalline material.[36] This is because the amorphous portion is the hydrophilic portion of the MCC. The rate of adsorption of water by a powdered material is always of interest to the formulation pharmacist as the stability of the drug or excipient would depend on the hygroscopicity of the excipient. For instance, the combination of a hygroscopic excipient with a hygroscopic drug would cause enhanced water adsorption rate which could cause instability of the product.

Particle size result

The results of the mean particle sizes of MCC-BVF, MCC-BVL and MCC-AVC were 148.95 ± 1.00, 145.31 ± 0.95 and 154.11 ± 1.20 µm respectively (Table 2). MCC-AVC had the largest mean particle diameter while MCC-BVL had the least mean particle size. There was a significant difference ($p < 0.05$) in the particle sizes of these MCCs. The differences in the particle sizes are expected to be impart positively on the flow behavior of the MCC powders as well as the mechanical strengths of the compacts.

Degree of polymerization and Molecular weight result

The results of evaluation of the degree of polymerization (DP) and molecular weight are shown in Table 1. The DP of 237.4 identifies the material as MCC as it falls within values of < 350 that is characteristic of MCC.[20] The molecular weight of MCC-BV (42,769.01) was also close to that of MCC-AVC (42,156.48) which is characteristic of processed cellulose (Table 1).

Table 1: Some physicochemical properties of MCC-BVF, MCC-BVL and MCC-AVC.

Sample/ Parameter		**MCC-BVF**	**MCC-BVL**	**MCC-AVC**
Iodine solution		Reddish brown color	Reddish brown color	Reddish brown color
Sulphuric acid (60% v/v)		Blue color	Blue color	Blue color
Solubility in water, alcohol, acetone, dilute mineral acid.		Insoluble	Insoluble	Insoluble
Solubility in ammoniacal solution of copper tetramine.		Completely soluble	Completely soluble	Completely soluble
pH		6.36 ± 0.08	6.80 ± 0.07	6.74 ± 0.31
Ash content (%)		1.85	1.85	1.95
% crystallinity		85.51	90.31	80.15
Molecular weight		42,769.01	42,967.18	42,156.48
Degree of polymerization		237.40	238.5	234.40
Hydration capacity		2.35 ± 0.23	3.38 ± 0.33	3.55 ± 0.07
Moisture sorption (%)	RH 96 %	7.50 ± 0.09	7.80 ± 0.55	7.80 ± 0.75
	RH 84 %	1.10 ± 0.15	1.60 ± 1.00	1.60 ± 1.50
	RH 75 %	0.50 ± 0.05	1.10 ± 0.25	1.10 ± 0.85
	RH 52 %	0.40 ± 1.00	0.60 ± 0.10	0.60 ± 0.50
Elemental analysis (ppm)	Pb	0.00	0.00	0.00
	Mn	0.02	0.02	NMT 10
	Zn	0.12	0.12	NMT 10
	Fe	0.10	0.10	NMT 10
	Na	299.90	229.90	NMT 10
	As	0.00	0.00	NMT 10
Swelling capacity (%)		124.32 ± 1.60	267.38 ± 1.76	255.57 ± 1.53
Loss on drying (%)		6.16 ± 0.60	6.52 ± 0.31	6.58 ± 0.25

NMT is Not More Than.

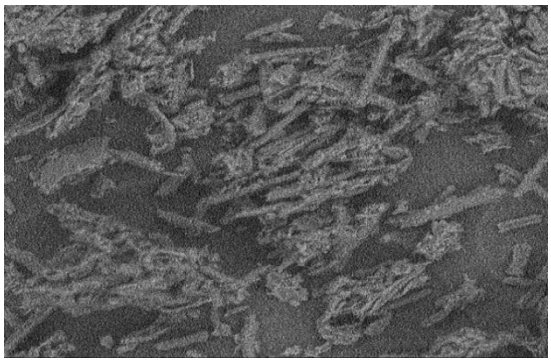

Fig.1: SEM of MCC-BVF (X1000).

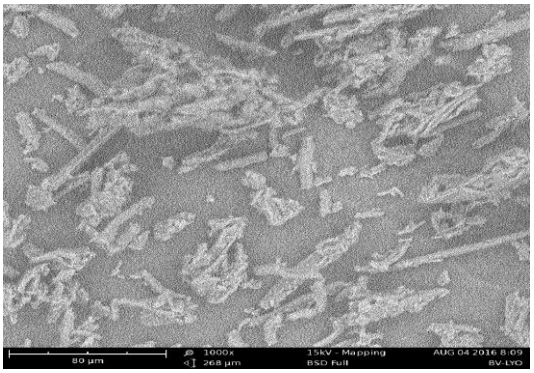

Fig.2: SEM of MCC-BVL(X1000)

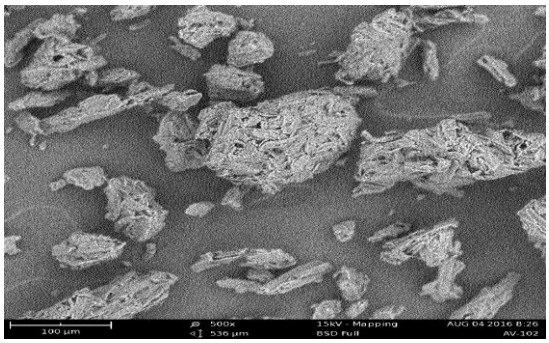

Fig.3: SEM of MCC-AVC (X500)

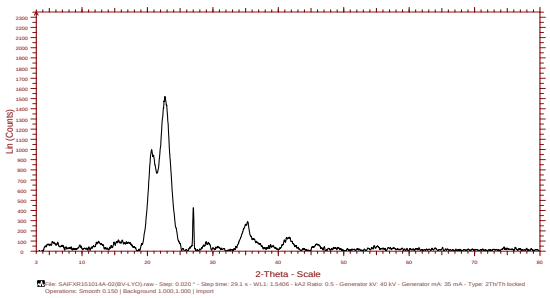

Fig.4: X-ray diffractogram of MCC-BVF.

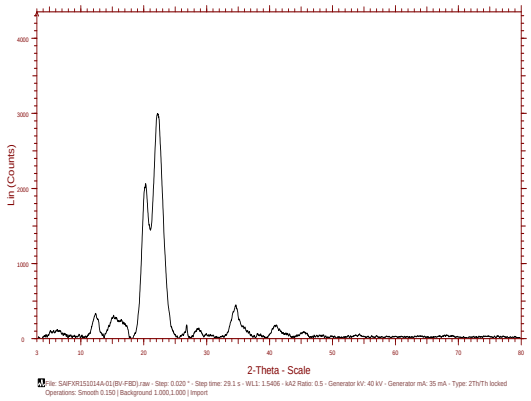

Fig.5: X-ray diffractogram of MCC-BVL.

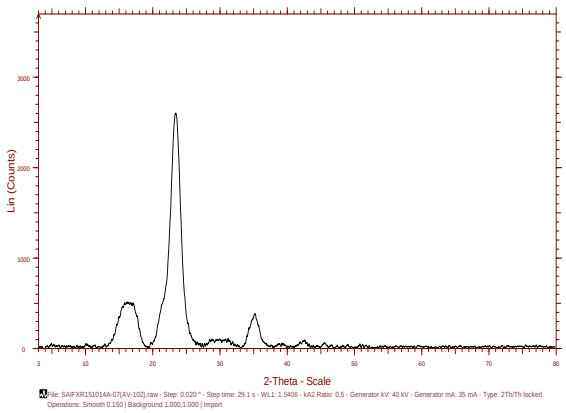

Fig.6: X-ray diffractogram of MCC-AVC.

Bulk and Tapped density result

The bulk and tapped density of the powders are shown in Table 2.The bulk and tapped densities of MCC-BVF powder were higher than those of MCC-BVL and MCC-AVC powders. The higher density values shown by MCC-BVF indicate that the powder is more intimately packed and therefore would be less bulky, easier to handle and transport than MCC-BVL and MCC-AVC. The British Pharmacopoeia states that powders have a better flowability when the difference between the bulk and tapped densities is very small.[20] Based on the bulk and tapped densities, MCC-BVF would have more flow as it has a narrower difference in both density values than MCC-BVL and MCC-AVC.

Particle density result

The particle densities of the powders ranged from 1.50 ± 0.01 to 1.56 ± 0.07 g/ml (Table 3). Both MCC-BVL and MCC-AVC were similar while that of MCC-BVF was slightly lower. Since particle density depicts the actual density of the MCCs devoid of any inter and intra particulate void spaces, it expresses the actual mass to volume relationship of powder devoid of the packing order of the powder particles within the powder bed.

Flow rate and angle of repose result

The flow rate is a parameter used to determine the ability of a powder to be discharged from an orifice of a funnel and it simulates powder discharge from the hopper during tableting operations. The angle of repose of a powder is used to qualitatively assess the internal and cohesive frictions that exist in the powder. The flow rates and angle of repose of the MCC powders are shown in Table 3. The order of flow was MCC-BVF > MCC-AVC > MCC-BVL. There was significant difference ($p < 0.05$) in the flow behavior of the MCCs. The angle of repose of MCC-BVF was 26.35 ± 2.35°, MCC-AVC was 30.52 ± 1.78 ° while MCC-BVL had a value of 53.04 °. Based on the BP and Unites States Pharmacopoeia (USP) classification of powders, both MCC-BVF and MCC-AVC have excellent flow whereas MCC-BVL has a poor flow.[20,41] The angle of repose results correlates with the flow rates obtained for the different MCCs (Table 3).

Hausner's quotient and Carr's index result

The Hausner's quotient and Carr's index of MCC-BVF, MCC-BVL and MCC-AVC are shown in Table 2. The results obtained show that MCC-BVF powder has a greater tendency to flow than MCC-AVC and MCC-BVL powders.[20] While the MCC-BVF and MCC-AVC powders passed the BP set limits for good flowability, the MCC-BVL powders were poor flowing. Based on the BP classification of powders, Carr's index value of 16-20 % is classified as fair flowing, 26-31 % as poor while Hausner's quotient of 1.00-1.11 is classified as excellent flowing, 1.19-1.25 as fair and 1.35- 1.45 as poor flowing.[20,41] Thus, correlating the results of some other flow parameters such as bulk and tapped densities, flow rate and angle of repose, MCC-BVF powder consistently

showed better flow indices than MCC-AVC and MCC-BVL powders (Table 2).

Powder porosity and packing fraction result

Table 3 shows the porosity and packing fraction of the different powders. The porosity shows the level of inter and intra-particulate void spaces that exist between the different particles within the powder bed. The arrangement of the particles would depend on the particle shape, size and diameter. The porosity and particle size distribution will affect the rate of penetration of disintegration/dissolution solvents as well as the initial release of the active pharmaceutical ingredient from the compact/tablet when the powder is compacted.[43] The porosity and particle density values of MCC-BVL resemble those of MCC-AVC, implying comparable inter particulate distribution and densification behavior. The high porosity value of MCC-BVL powder confirms a high degree of inter-particle voids consisting of entrapped air which would be lost or reduced on agitation of the powder bed or the application of a quantified pressure on it. Its effect is that the flow of the powder would be impaired[5] The packing fraction of a powder is given as the ratio or percentage of total space filled by the particles and relates how the particles are packed in the consolidated powder bed.[44] The packing fraction of porous materials is dependent on the particle shape, and method of packing. The packing fraction was in the order MCC-BVF > MCC-AVC > MCC-BVL. There was a significant difference ($p < 0.05$) in the packing fraction of MCC-BVF, MCC-BVL, and MCC-AVC.

Compactibility and powder cohesion result

The Kawakita plots of the powders are shown in Fig. 7 and the compactibility and cohesiveness values derived therefrom are shown in Table 3. The compactibility 'a' which expresses the level of volume reduction of the given powder bed shows that all the MCCs were compactible. However, MCC-BVL powder exhibited higher compactibility value than the MCC-BVF powder implying that MCC-BVL powder would undergo greater densification on the application of stress or agitation by tapping of the powder bed.[32] Cohesiveness which is expressed as '1/b' describes the capability of the powders to adhere to each other leading to aggregation.[5] It is the resistance to flow of a powder as a result of attractive forces (charges) on the powder particle. High cohesiveness impairs flow of powders.[33] The MCC-BVL powder had a higher cohesive value than the MCC-BVF powder and thus would have a poorer flow (Table 3). Comparatively, MCC-BVL has a significantly ($p < 0.05$) higher compactibility and cohesiveness than MCC-AVC and MCC-BVF implying that it is more compressible and less flowable.

Table 2: Some micromeritic properties of MCC-BVF, MCC-BVL and MCC-AVC

Sample/Parameter	MCC-BVF	MCC-BVL	MCC-AVC
Bulk density (g/mL)	0.57 ± 0.01	0.32 ± 0.01	0.31 ± 0.04
Tap density (g/mL)	0.61 ± 0.01	0.44 ± 0.18	0.38 ± 0.02
Angle of repose (˚)	26.35 ± 2.35	53.04 ± 1.89	30.52 ± 1.78
Flow rate (g/s)	9.30 ± 1.42	0.28 ± 0.04	5.23 ± 0.22
Carr's index (%)	18.55 ± 1.28	27.36 ± 1.12	18.96 ± 0.67
Packing Fraction	0.93 ± 0.01	0.73 ± 0.02	0.81 ± 0.01
Hausner's quotient	1.07 ± 0.02	1.38 ± 0.04	1.23 ± 0.01
Porosity (%)	62.26 ± 0.59	79.61 ± 0.35	76.12 ± 0.36
Particle density (g/mL)	1.50 ± 0.01	1.56 ± 0.01	1.56 ± 0.07
Mean particle size (µm)	148.95 ±1.00	145.3± 0.95	154.11±1.20

Table 3: Compactibility and cohesiveness of MCC-BVF, MCC-BVL and MCC-AVC.

Sample	a	b	1/a	1/b(P_k)	1/ab (%)	R^2
MCC-BVF	0.22	0.11	3.39	9.09	12.42	0.992
MCC-BVL	0.41	0.21	4.56	4.76	35.22	0.992
MCC-AVC	0.14	0.07	6.99	14.29	20.00	0.998

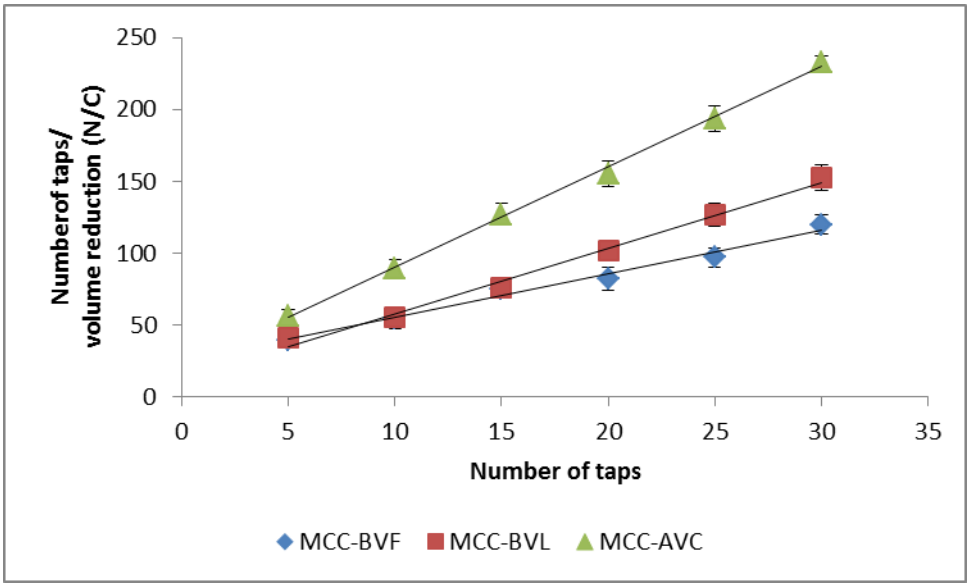

Fig.7: Kawakita plots of MCC-BVF, MCC-BVL and MCC-AVC.

Compact properties results

Wholesomeness

The compacts formed from MCC-BVF, MCC-BVL and MCC-AVC were white, strong, smooth and without any signs of physical deformation.

Weight uniformity

The compacts generally weighed between 294.65 ± 4.25 to 302.00 mg ± 2.60 % (Table 4) and can be categorized as of good quality in terms of weight variation since the coefficient of variation values are within the BP set limits of ± 5 % for tablets weighing above 250 mg.[20] Minimal variation in tablet weight would enhance uniformity of the thickness, size and the mechanical properties of the compacts.

Hardness

The hardness of the compacts is shown in Figure 8. There was a general increase in hardness as the compression load increased. All the compacts had values above 4 kgF except for MCC-BVF compacts at 4.90 and 7.35 mPa. The compacts that had hardness of ≥ 4 kgF could be considered strong enough to withstand intolerable stresses that may arise during handling and transportation.[20] These stresses can damage the physical features of the compact by abrasion or breakage. The MCC-BVL compacts were consistently significantly ($p < 0.05$) stronger at all compression loads than MCC-BVF compacts. However, the strongest compacts were made from MCC-AVC at all compression pressures.

Table 4: Uniformity of weight, thickness and friability of compacts

Parameter	Compression Load					
	Batch	4.9 (mPa)	7.35 (mPa)	9.81 (mPa)	12.26 (mPa)	14.71 (mPa)
Uniformity of weight [mg ± CV(%)]	MCC-BVF	296.15 ± 3.23	302.00 ± 2.60	294.65 ± 2.25	296.45 ± 1.94	299.35 ± 1.92
	MCC-BVL	299.00 ± 1.76	296.60 ± 2.94	297.40 ± 1.74	295.65 ± 1.55	298.90 ± 1.58
	MCC-AVC	296.85 ± 1.16	300.25 ± 2.28	301.60 ± 2.48	298.65 ± 0.06	301.40 ± 1.19
Thickness (mm)	MCC-BVF	3.36 ± 0.21	2.90 ± 0.43	2.64 ± 0.06	2.57 ± 0.08	2.33 ± 0.08
	MCC-BVL	3.45 ± 0.22	2.84 ± 1.16	2.79 ± 0.15	2.57 ± 0.12	2.30 ± 0.03
	MCC-AVC	3.16 ± 0.06	2.78 ± 0.14	2.65 ± 0.14	2.45 ± 0.45	2.40 ± 0.13
Friability (%)	MCC-BVF	1.86 ± 0.01	0.77 ± 0.03	0.65 ± 0.01	0.56 ± 0.14	0.49 ± 0.01
	MCC-BVL	0.57 ± 0.01	0.55 ± 0.06	0.52 ± 0.01	0.52 ± 0.02	0.51 ± 0.01
	MCC-AVC	0.95 ± 0.01	0.67 ± 0.05	0.56 ± 0.05	0.35 ± 0.01	0.21 ± 0.04

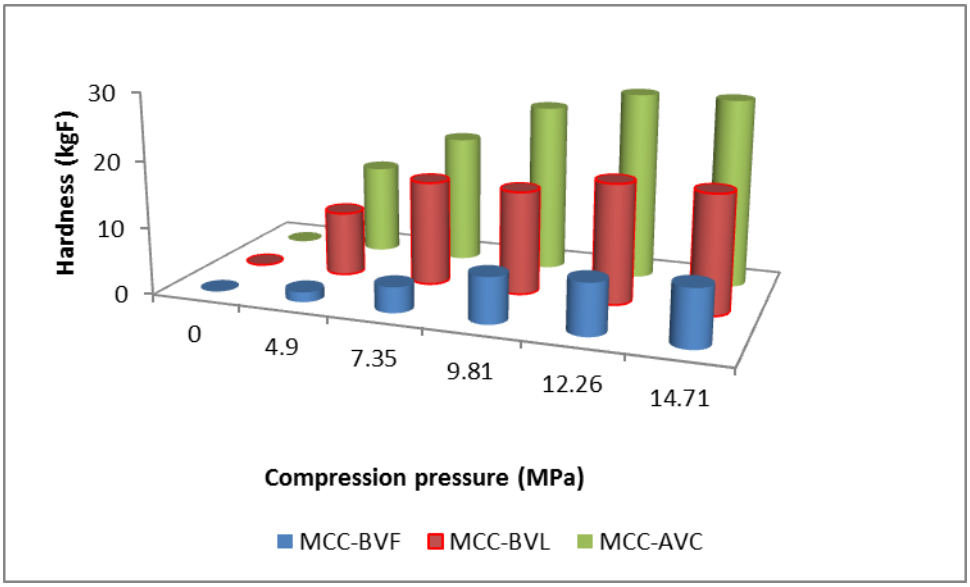

Fig. 8: Hardness against compression pressure of MCC-BVF, MCC-BVL and MCC-AVC.

Disintegration time

The disintegration test results of the compacts are shown in Fig. 9. The disintegration test results showed that all the compacts disintegrated within 13 min and complied with the BP set limit of ≤ 15 min for uncoated tablets[20] although the MCC-BVL compacts had disintegration times that were significantly ($p < 0.05$) higher than the MCC-BVF compacts (Fig. 9). This is a good attribute for the formulation of conventional release tablets. Conventional release tablets are expected to break up on hydration (*in vitro)* or oral ingestion and release their API content to enable its dissolution and absorbance *in vivo*.

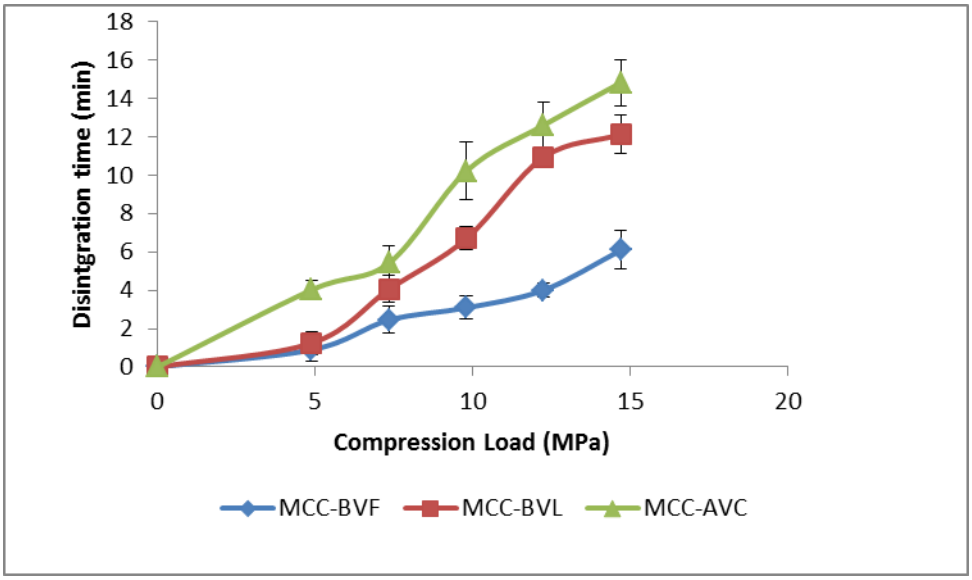

Fig. 9: Disintegration time of MCC-BVF, MCC-BVL and MCC-AVC.

Friability

The friability values of all the MCC compacts are shown in Table 4 and they were all below 1.00 % except for the batch of MCC-BVF compressed at 4.90 mPa which had a value of 1.86 ± 0.01%. The British Pharmacopoeia stipulates friability values of ≤ 1.00 % for uncoated tablets.[20] Generally, there was a decrease in friability of the compacts as the compression pressure increased. Compacts of MCC-BVL had friability values that were consistently lower than their corresponding MCC-BVF counterparts at similar compression pressures (Table 4). These could have resulted from the stronger bonding between the particles in the MCC-BVL compacts. Friability values of ≤ 1.00 % would imply retention of the integrity of both the API content and physical attributes at the surfaces of the compacts. All the compacts passed the friability test except MCC-BVF at 4.90 mPa compression pressure.

Thickness/height and diameter

The thickness/height of the compacts is as shown in Table 4. The thickness of these compacts was found to

decrease as the compression load increased while the diameter expectedly remained constant. This implies that increase in compression pressure caused increase in hardness as well as a decrease in size of the compact. This is applicable especially amongst compacts formed from the same batch of powders.

Tensile strength

The tensile strength values of the different compacts of MCC-BVF, MCC-BVL and MCC-AVC are shown in Fig.10. They were in the range of 28.04 – 232.44 kg/cm^2 for MCC-BVF powder compacts and 176.79 – 482.20 kg/cm^2 for MCC-BVL compacts. The MCC-BVL compacts were consistently significantly ($p < 0.05$) stronger than MCC-BVF at all compression loads. Values for MCC-AVC ranged from 274.11 – 745.43 kg/cm^2 implying that the tensile strength of the compacts were in the order MCC-AVC > MCC-BVL > MCC-BVF. The results obtained here correlates with the hardness pattern observed generally for the compacts which were seen to be increasing as the compression pressure was increased. Thus, a correlation existed between the tensile strength and the hardness of the different MCC compacts.

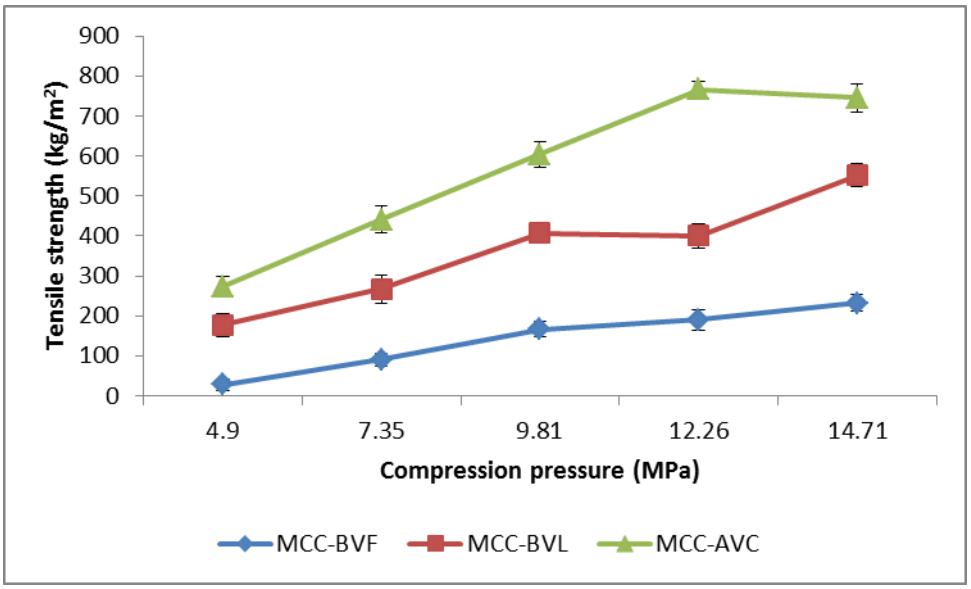

Fig. 10: Tensile strength against compression pressure of MCC-BVF, MCC-BVL and MCC-AVC

Heckel Equation

The Heckel parameters of the compacts (Table 5) were derived from the straight line portion of the Heckel plot (Fig.11) for MCC-BVF, MCC-BVL and MCC-AVC. The yield pressure, Py describes the tendency of the material to plasticize or fragment under an applied pressure which can be related to its compressibility.[33] The yield pressure of MCC-BVF and MCC-BVL were 0.30 and 0.21 respectively while that of MCC-AVC was 0.22. This implies that MCC-BVF exhibited a faster plasticity or onset of deformation than MCC-BVL and MCC-AVC. The MCC-BVL compacts had a plastic behavior almost equal to the comparing standard, MCC-AVC (Table 5). Initial packing in the die as a result of filling by powder is denoted as D_o . The D_o values of MCC-BVF was highest, followed by MCC-BVL while that of MCC-AVC was lowest, implying that MCC-BVF powder exhibited the highest degree of packing and re-arrangement on die filling while MCC-AVC exhibited the least. D_A represents the total degree of packing at zero and low pressures, while D_B represents the particle rearrangement phase in the early compression stage and shows the extent of particle fragmentation. It is obtained as the difference between D_A and D_O. The order of particle rearrangement at the early phase was MCC-BVF > MCC-BVL > MCC-AVC. Generally, all the powders had good compactibility and plasticity, MCC-BVL was more compactible than MCC-BVF.

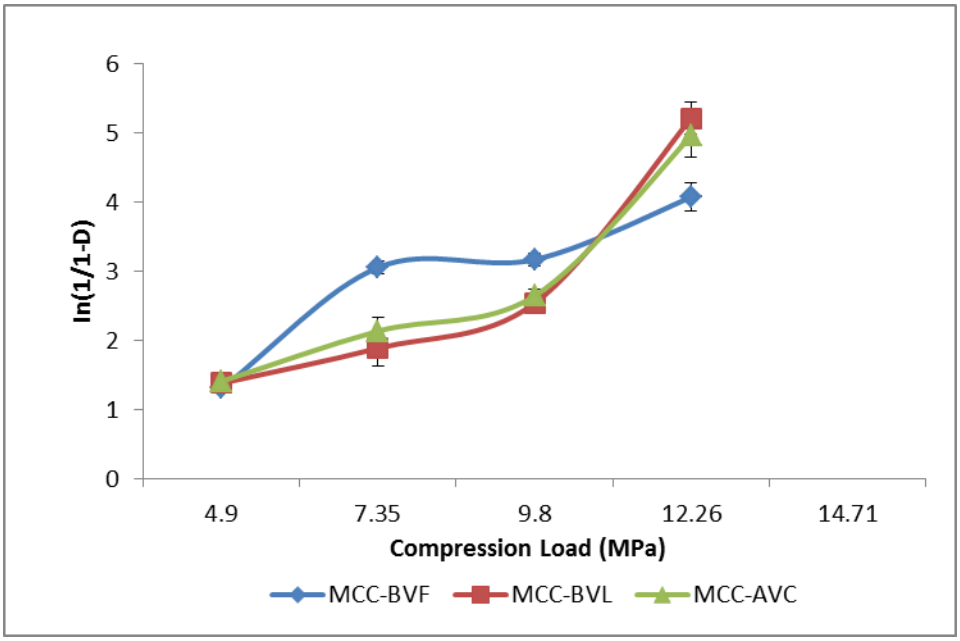

Fig.11: Heckel plots MCC-BVF and MCC-BVL and MCC-AVC.

Table 5: Parameters of Heckel plot

Sample/parameter	K	Py	D_o	D_A	D_B	A	R^2
MCC-BVF	3.37	0.30	0.38	0.93	0.55	0.11	1.000
MCC-BVL	4.70	0.21	0.21	0.19	0.37	0.87	0.997
MCC-AVC	4.46	0.22	0.19	0.91	0.17	0.17	0.989

Reworking potential of microcrystalline cellulose

The re-workability of the powders is shown in Fig. 12. All the MCC powders were re-workable implying that after compaction or subjection to similar stresses, the powders do not lose any appreciable compressibility and densification behavior. They could still be useful in the formulation of tablets that would have good mechanical properties.

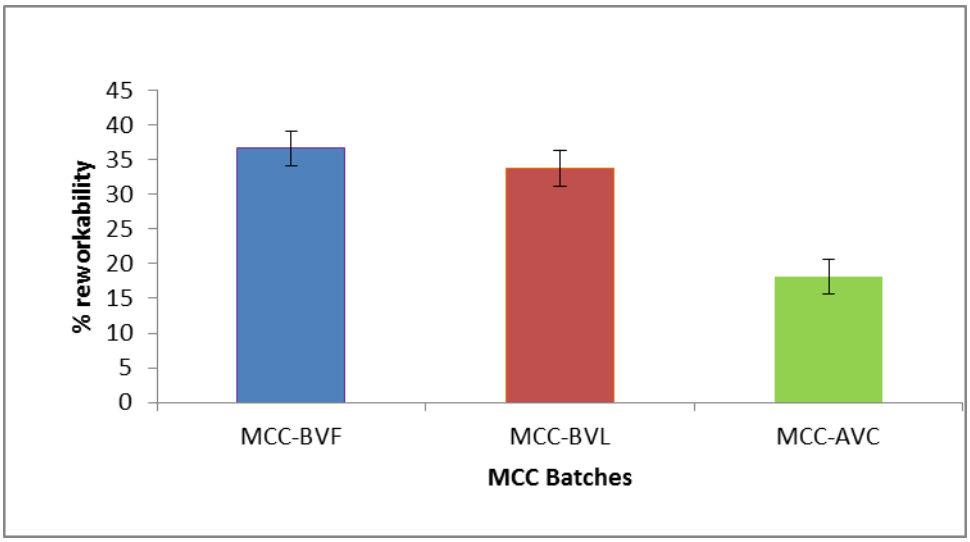

Fig. 12: Reworkability of MCC-BVF, MCC-BVL and MCC-AVC.

CONCLUSION

The micromeritic evaluation showed that drying method – a process variable significantly affected the characteristics of the derived MCC in terms of bulk and tapped density, angle of repose, powder porosity, Carr's index and other indices that affect flowability. The MCC-BVF powder flowed better than the MCC-BVL powder. The MCC-BVL powder samples had a lower bulk and tapped density, a higher porosity and swellability. The values obtained for these tests compared well with MCC-AVC which is usually dried or prepared by spray drying technique. Both powders showed good densification, volume reduction and compactibility based on the Kawakita model and have

flow properties that compared well with the standard. In terms of tabletability, the MCC compacts containing MCC-BVL powders were significantly ($p < 0.05$) stronger than the compacts containing MCC-BVF powder. This is a desirable feature in that the good mechanical strength of the compact imparts/influences positively the hardness, tensile strength, friability, and disintegration of the material. The Heckel model shows that on the application of stress or load, that the MCC powders undergo plasticity and slippage even at low compression loads. This enabled the formation of strong firm compacts. The compacts were fairly uniform in weight as values obtained conformed to BP specifications. The mechanical strength of the compacts formed from the lyophilized MCC obtained from BV were significantly stronger ($p < 0.05$) than those of the fluid bed dried MCC implying that lyophilization of the MCC aided the production of stronger compacts and is therefore a preferable method of drying than the fluid bed method of drying. However, compacts obtained from MCC-AVC were stronger than those of MCC-BVL and MCC-BVF.

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