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EVALUATION OF THE POWDER AND COMPACTION PROPERTIES OF MICROCRYSTALLINE STARCH (MCS) DERIVED FROM CASSAVA (MANIHOT ESCULENTA CRANTZ) STARCH BY ENZYMATIC HYDROLYSIS

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ABSTRACT

The aim of this study was to investigate and determine the powder and compaction properties of microcrystalline starch (MCS) and compare with the properties of a well known direct compression filler-binder, microcrystalline cellulose (MCC).
Cassava starch was extracted from the freshly harvested tubers of *Manihot esculenta* Crantz and subjected to 5hours of enzymatic hydrolysis to yield microcrystalline starch. The powder and compaction properties were evaluated and compared with MCC 101, a commercial brand of microcrystalline cellulose.
Results of the powder properties of MCS revealed differences in the particle size, angle of repose, flow rate, bulk density, tapped density, true density, Hausner's ratio, Carr's index and powder porosity when compared to MCC. The compaction studies of both materials revealed that MCS had a faster onset of deformation and a greater extent of deformation in comparison to MCC. These results suggest that MCS has the potential of being used as a filler-binder in direct compression tableting.

Key words: Microcrystalline starch (MCS), Microcrystalline cellulose (MCC), Powder properties, Compaction properties, Direct compression tableting and Filler-binder.

INTRODUCTION

Tablet manufacturing by direct compression has advanced steadily over the years and has become the most preferred because of its simplicity, rapidity, being economical and of higher stability when compared to other dosage forms (5). This technology consists of compressing powdered blends of materials into tablets directly rather than going through the conventional granulation process which in turn avoids any change in the physical nature of the powdered material to be compressed (4).
The success of a direct compression process is influenced to a large extent by the functionality of the excipient chosen and this is determined greatly by its fundamental properties (powder and compaction properties). It therefore becomes necessary to characterize an excipient intended for use as a direct compression excipient before developing any formulation with that material by studying its powder and compaction properties in order to ascertain its functionality.
Starch is a versatile, cheap and readily available material obtained from renewable sources that has found wide application in tableting as a binder, disintegrant, diluent, lubricant and glidant. Unfortunately, it is not suitable for direct compression formulation due to its poor compressibility and flow characteristics. There is a need therefore to impart these properties requisite for direct compression by modifying starch. Several authors have employed physical and chemical methods as well as coprocessing to develop excipients suitable for direct compression. The objective of this study is to modify starch by enzymatic hydrolysis using α-amylase enzyme in order to produce microcrystalline starch, a multifunctional excipient adaptable for direct compression tableting. The powder properties will be determined by evaluating the flow and compressibility profiles while compaction studies will be carried out using the models of Heckel and Kawakita equations. These properties will be studied in comparison to microcrystalline cellulose as a reference.

MATERIALS AND METHODS

MATERIALS

The following materials used were all of pharmaceutical grade; Hydrochloric acid, A7595 α-amylase enzyme (Sigma-Aldrich laborchemikalien GmbH Germany), Xylene, Ethanol (95%$^{v}/_{v}$) (BDH Chemicals Ltd Poole, England), Sodium Hydroxide (Avondale laboratories Ltd Banbury, England) and Microcrystalline cellulose (MCC PH 101) (ATOZ

Pharmaceuticals Ltd Ambaltur, India). Cassava starch was extracted in the Process laboratory of the Department of Pharmaceutics & Pharmaceutical Microbiology, Ahmadu Bello University, Zaria.

METHODS

Synthesis of Microcrystalline starch

Cassava starch was extracted from freshly harvested tubers of *Manihot esculenta* Crantz using a method described in literature (3). The method described by Buwalda and Arends-Scholte (6) was adopted in the synthesis of microcrystalline starch.

One hundred grams (100g) of starch slurry was prepared containing 40%$^{w}/_{w}$ of cassava starch. It was then placed in a water bath (Digital thermostatic water bath) and the temperature set to 56ºC. The pH of the reaction medium was adjusted to 6 using 0.1N and 0.2ml of α-amylase (BAN 240L) was dosed into the reaction mixture. The hydrolysis was allowed to run for 5hr with constant stirring.

After 5hr, the activity of the enzyme was terminated by lowering the pH to 3 with 0.1N HCl and subsequently neutralized by raising the pH to 7 with 0.1N NaOH. The reaction mixture was allowed to settle and the supernatant decanted. It was then washed several times with distilled water before adding 500ml of ethanol (95%$^{v}/_{v}$) to dehydrate the microcrystalline starch (MCS) formed. The MCS was recovered by decanting the ethanol and then air-dried. It was then homogenised using a blender.

Investigation of Powder Properties

Moisture Content

Five grams (5g) of each powder sample was accurately weighed and dried at 105°C in the oven to constant weight. The sample was reweighed and weight loss calculated.

Angle of repose and Flow rate

The method described by Alebiowu (2) was adopted. Twenty grams (20g) of each powder sample was weighed and placed in a standing cylindrical tube. The cylinder was gently raised to leave a free heap of the powder. The circumference of the base of the heap was outlined and its radius, r, measured. The height of the heap, h, was also measured and the angle of repose calculated using the equation,

$$\theta = Tan^{-1}\frac{h}{r} \ldots\ldots\ldots\ldots\ldots 1$$

The mean of three determinations was recorded. Flow rate of was determined by placing twenty grams (20g) of the powder in an Erweka flow apparatus (Type GDT, Erweka Apparatebau GmbH, West Germany) and allowed to flow through the funnel orifice. The time taken for the powder to flow through the orifice was noted and the flow rate was determined as the ratio of weight (g) to time (seconds). The mean of three determinations were recorded.

True Density

The true density of the material was determined using a method described elsewhere (18). Xylene was employed as the displacement liquid using the pycnometer bottle.

Bulk and Tapped Densities

Exactly 50 gm of each powder sample was weighed and poured through a glass funnel into a 100 ml measuring cylinder at an angle of 45º. The cylinder was dropped on a wooden platform from a height of 2.5 cm three times at 2 second interval. The volume occupied by the powder recorded as the bulk volume. The cylinder was then tapped on the wooden platform until the volume occupied by the powder remained constant. This was repeated three times for both powders. The data generated were used in computing the Carr's index and Hausner's ratio for both powders.

Compressibility Index

The compressibility indices of Carr's index and Hausner's ratio were computed using the formulas below;

Carr's index=.....2

Hausner'sratio=.....3

Swelling, Hydration and Moisture sorption capacities

The swelling capacity of the powder was estimated by a method described by Iwuagwu and Onyekweli (12). The tapped volume occupied by 5 g of the powder, V_X, was noted. The powder was then dispersed in 85ml of water and the volume made up to 100 ml with more water. After 24 h of standing, the volume of the sediment, V_V, was estimated. The swelling capacity was determined using the formula, V_X/V_V. The method of Kornblum and Stoopak (15) was used to determine the hydration capacity. A 1g sample was placed in each of four 15ml plastic centrifuge tubes to which 10ml distilled water was added and then stoppered. The contents were mixed on a vortex mixer for 2min. The mixture was allowed to stand for 10min and then centrifuged at 1000rpm for 10min on a bench centrifuge. The supernatant was carefully poured out and the sediment weighed. The hydration capacity was determined as the ratio of sediment weight to the dry sample weight. Moisture sorption test was carried out using 2g of each material. It was weighed and evenly distributed over the surface of a 70mm tarred Petri-dish. The samples were placed in a dessicator containing distilled water in its reservoir (RH = 100%) at room temperature and the weight gained by the exposed samples at the end of the five day period was recorded and the amount sorbed was calculated from the weight difference.

Compaction Studies

Compacts of each material weighing 500mg were prepared by compressing them for 30s at various

compression loads (28.3-141.6MN/m^2) using a Carver hydraulic hand press (Model C, Carver Inc., Menomonee Falls, W.I). Before each compression, the 10.5mm die and flat-faced punches was lubricated with 2% $^{w}/_{v}$ dispersion of magnesium stearate in ether – ethanol (1:1) solution. After ejection, the compacts were stored over silica gel in a dessicator for 24hrs to allow for elastic recovery and hardening preventing false low yield values. Their weights (W) and dimensions (diameter and thickness) were then determined to within ± 1mg and 0.01 mm respectively, and their relative densities (*D*) were calculated using the equation:

D = ... 4

Where W is the weight of the compact, Vt is the volume of the compact and ρs is the particle density of the material. The plots constructed according to Heckel (9) and Kawakita (14) equations were used to characterize the consolidation behaviour of the material.

RESULTS AND DISCUSSION

The results for the study are presented in Tables and Figures. The powder and compaction properties of a material determine its functionality in a formulation. For a material to meet the requirements of a good directly compressible excipient, it should possess good flowability, compressibility and high dilution capacity among other requirements. These properties are usually evaluated by measuring the angle of repose, bulk, tapped and true densities, Hausner's ratio, Carr's Index (Powder properties) while Heckel and Kawakita analysis of the compact parameters are investigated for compaction properties.

Table 1 displays results for the powder properties for both materials used for the study (MCS & MCC). The angle of repose is an index of flowability and therefore predicts the flow property of the formulation during tableting. Values for angles of repose less than 30º usually indicate a free flowing material while angles greater than or equal to 40º suggest a poor flowing material. Both materials had angles of repose greater than 40º indicating that they possess poor flow property. This can be attributed to the small particle sizes of both materials. Particle size is one of the principal determinants of powder behaviour such as packing and consolidation, flow ability and compaction (7). It becomes necessary therefore to add a glidant in order to improve the flow of the formulation during tableting. Bulk and tap density usually provide information on the flowability of the powders hence is used to calculate the parameters of Hausner's ratio and Carr's Index. The lower the Carr Index, the better the flowability of the powder (8). According to Carr, values of 5 to 10, 12 to 16, 18 to 21, and 23 to 28 represent excellent, good, fair, and poor flow properties respectively (1965). Hausner ratio and Carr's index are considered as indirect measurement of powder flowability (21). Hausner's ratios greater than 1.25 indicate poor flow. The values obtained for Carr's index fell within the range of 23-29% for both materials while Hausner's ratio recorded was greater than 1.25. These results obtained for Hausner's ratio and Carr's Index confirms the poor flowability of both materials. Carr's index and Hausner ratio are one-point determinations and do not always reflect the ease or speed with which consolidation of the powder occurs. Indeed, some materials have high indices, suggesting poor flow, but they consolidate rapidly and vice versa (22). Rapid consolidation is essential for uniform filling on tablet machines.

The swelling power, hydration capacity and moisture sorption capacity of both materials is presented on Table 1. The swelling capacity ranged from 1.31-1.50 with MCS having a larger value compared to MCC. This is likely to affect the disintegration potential of both materials since swelling plays a role in disintegration. The hydration capacity values for both materials were comparable not suggesting any significant difference. However, there is a marked difference in the moisture sorption capacities of MCS and MCC as displayed on Table 1. The values suggest that MCS is more hygroscopic with a tendency to absorb and retain moisture when exposed to a humid environment compared to MCC. Stability problems are therefore predictable with MCS and so storage precautions should be given due consideration with moisture sensitive drugs.

The compaction characteristics of both materials were studied using the Heckel and Kawakita Models. Heckel equation has been most widely used to describe the compaction of pharmaceutical powders (9). This equation, originally used to describe the densification of ceramics, is essentially a curve-fitting equation that provides correlation with the observed facts of porosity of compacts over a wide range of applied pressures. The Heckel equation which is applicable at the compression part of the porosity pressure plot, is given below;

ln (1/1-D) = KP + A 5

Where D is the relative density of the compact, K is the slope of the straight line portion of the graph, reflecting the reduction in porosity or the resistance to volume reduction and A is the intercept of the extrapolated linear region of the plot. The Heckel plot for both materials used for the study is displayed as Figure 1. The plot shows an almost linear relationship at all applied pressures for both materials suggesting that they deform principally by plastic deformation. Pharmaceutical powders do not produce perfect straight lines and the type of deformation provides information about the compaction behaviour of the material (16).

Heckel equation classifies powders based on their compaction behaviour into three types; A, B and C (23). Type A materials are characterised by a straight line plot occurring over a wide range of pressures. The Heckel plot obtained for the study confirms that both materials are type A in nature.

The yield pressure, P_Y, resolved from the slope of the curve is a measure of the plasticity and is considered as that pressure at which yielding occurs during compaction (16). In general, a low P_Y value reflects low resistance to pressure, good densification and easy compression (11). The P_Y value obtained for MCS as presented on Table 2 was significantly lower compared to MCC indicating that MCS has a faster onset of deformation at low pressures. The D_0 values presented on Table 2 was determined by the ratio of the powder's loose bulk density to its particle density (19). This parameter represents the phase of densification occurring during compaction as a result of die-filling. It is the relative density of the powder at the point when the applied pressure is equal to zero. The greater the value of D_0, the greater the degree of packing or consolidation of the powder bed. MCS was shown to have a higher D_0 compared to MCC indicating that it has a greater degree of packing as confirmed by its bulk and tapped densities. The relative density, D_A, was calculated from the intercept using the equation,

$D_A = 1 - e^{-A}$..... 6

While D_B is the relative density describing the phase of densification occurring during rearrangement of the powder bed at low pressure and is given as;

$D_B = D_A - D_0$..... 7

The values of D_A and D_B are presented on Table 2.

The Kawakita equation is a commonly used expression to linearize compression data. The equation describes the relationship between the degree of compression (C) of a bed of particles in a die and the applied pressure during compression (P) as follows;

$$\frac{P}{C} = \frac{P}{a} + \frac{1}{ab} \dots\dots\dots\dots\dots\dots\dots\dots 8$$

Table 1: Powder Properties of MCS and MCC

Property	MCS	MCC
Angle of repose (º)	45.4 ± 1.03	46.2 ± 1.77
Flow rate (g/s)	1.5 ± 0.08	0.71 ± 0.02
Bulk density (g/ml)	0.61 ± 0.02	0.39 ± 0.02
Tapped density (g/ml)	0.79 ± 0.02	0.55 ± 0.01
True density (g/ml)	1.38	1.48
Hausner's ratio	1.30	1.41
Carr's Index (%)	23	29
Swelling capacity	1.50	1.31
Hydration capacity	0.82	0.84
Moisture sorption capacity (%)	19	10

Table 2: Compact Parameters obtained from Heckel and Kawakita plots

	Heckel Parameters				Kawakita Parameters			
Material	**P_Y**	**D_0**	**D_A**	**D_B**	**a**	**b**	**D_I**	**P_K**
MCS	45.45	0.413	0.933	0.52	0.562	0.809	0.438	1.24
MCC	111.11	0.264	0.874	0.61	0.735	0.673	0.265	1.49

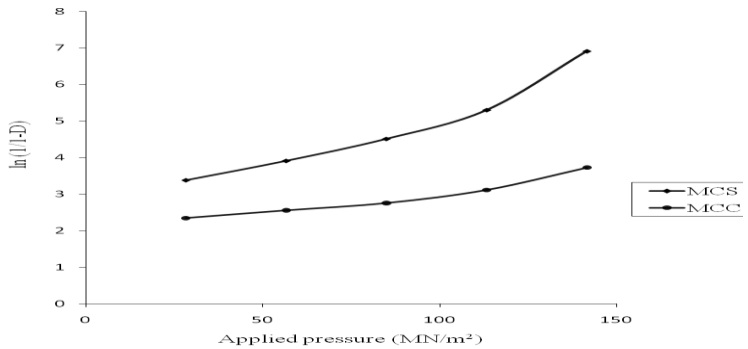

Figure 1: ln (1/1-D) against applied pressure for MCS and MCC compacts

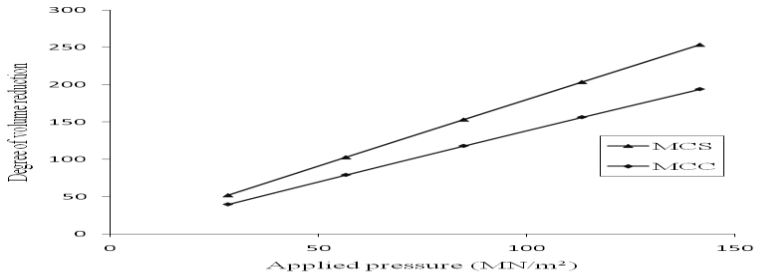

Figure 2: Degree of volume reduction against applied pressure (Kawakita plots for MCS and MCC)

The Kawakita plot is displayed as Figure 3 in the study. A straight line curve was obtained at all pressures linearizing the compression data. The compressibility parameters, a & b were obtained from the slope and intercept of the plot. The compression parameter, a, reflects the total degree of volume reduction of the powder at infinite applied pressure. The value recorded for MCS on Table 2 was greater when compared to MCC. This suggests that MCS achieves a closely packed structure with minimal porosity necessary for effective bonding compared to MCC. The reciprocal of the compression parameter, b (i.e. 1/b) denoted as P_K represents an indication of the stress/pressure at which particles deform or fail during confined compression (1, 13 and 17). The P_K values observed for both powders (Table 2) shows that MCS deforms at a lower pressure compared to MCC. Plastic deformation of the particles in the bed is brought in close proximity to each other facilitating bond formation resulting in tablets of sufficient mechanical strength. This is a common feature of many filler-binders in direct compression that they undergo plastic deformation during compaction (16).

CONCLUSION

The powder and compaction properties of MCS compared well with MCC as revealed by the study and so can be incorporated as a directly compressible excipient in tablet formulations but precautions should be taken with moisture sensitive drug formulations by including handy packs of dessicants.

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