

Research Article

Physicomechanical Behaviour of Novel Directly Compressible Starch-MCC-Povidone Composites and their Application in Ascorbic Acid Tablet Formulation

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ABSTRACT

The goal of this research was to provide critical evaluation of the physicomechanical performance of Starch-MCC-Povidone (SMP) composites engineered via co-processing strategy. Aqueous dispersions of the primary excipients at predetermined combination levels were subjected to physical agglomeration at controlled subgelatinization (55 °C) temperature followed by drying at 60 °C for 48 h. Under scanning electron microscope, the materials appeared as enlarged porous composites of starch-MCC bound by solid bridges of povidone. Powder fluidity indicators suggested acceptable flow properties (Angle of repose < 29°; Mass flow rate > 5 gs⁻¹). Compact weight variation studies revealed reproducible volumetric die filling capacity. Analysis of powder compaction indices shows appreciable densification and total volume reduction in both Heckel and Kawakita models. The dilution capacity of the composites was up to 40% using L-ascorbic acid as the model drug. Analysis of post compression tablet properties indicated extensive elastic recovery at low MCC content. All the novel composites were characterised by rapid *in-vitro* disintegration and efficient *in-vitro* drug release (t_{50%} < 1 min; t_{80%} < 2 min). In comparison to Ludipress® and Prosolv®, moderate to high MCC containing Starch-MCC-Povidone composites (SMP3 and SMP5) could be employed as alternative cost effective direct compression diluents in tablet formulation.

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INTRODUCTION

The wide therapeutic coverage of tablets as drug delivery systems coupled with the dynamic nature of tablet technology have prioritized considerable attention on development of novel materials required to meet up the 21st century's expectations in formulation design and manufacture with special focus on excipients development and optimization. Production of tablets via direct compression (DC) method, which involves only mixing and

compression, confers myriads of merits because it bypasses preliminary granulation stages which are associated with multiple unit operations, complex manufacturing challenges and huge economic implications (Armstrong, 2007; Alderborn, 2013). Limited availability of cost effective ready-to-compress raw materials (both active therapeutic agents and excipients) that possess the requisite critical physicomechanical functionalities has been a major setback to DC tableting (Augsburger, 2007; Thoorens *et al.*, 2014; Li *et al.*, 2017).

Starch and its derivatives are well known in tablet formulation for their stability, cheapness and availability (Rowe *et al.*, 2006; Newman *et al.*, 2007). In DC, these excipients suffer numerous setbacks that hamper their applicability as cost efficient raw materials in tableting. The poor fluidity and compressibility, low dilution capacity, production of friable tablets, low mechanical quality and high chances of wear and tear to press are among the myriads of mitigating factors that limits the usefulness of starch when it comes to direct compression tableting especially in modern high speed tablet press (Bolhuis and Armstrong, 2006).

A product of partial acid depolymerisation of α -cellulose units, microcrystalline cellulose (MCC) has been regarded as one of the best direct compression binders for over five decades (Pifferi *et al.*, 1999; Albers, 2006). MCC has broad compatibility with drugs and appears to possess high dilution propensity making it one of the most suitable diluent for poorly compressible actives (Carlin, 2008; Saigal *et al.*, 2009). However, the high cost of production, development and functional modification of MCC renders it quite expensive compared to other tablet excipients such as starch or α -lactose monohydrate.

To streamline manufacturing and accelerate development of cost effective novel materials for direct compression, existing established pharmacopoeial excipients are utilised in fabricating tailor-made diluents via co-processing strategy, which involves integration of two or more excipients by physical methods (Gohel & Jogani, 2005; Gonnisen, 2008; Apeji *et al.*, 2017). In recent years, co-processing provides a promising channel by which high-performance multifunctional diluents with requisite physicochemical attributes are developed (Gupta *et al.*, 2006; Desai *et al.*, 2012). In coprocessed materials, the undesired behaviour of the individual (primary) excipients could be masked to a great extent, while simultaneously improving the desired functionality (Rojas *et al.*, 2012). By significantly reducing development time and cost, co-processing of excipients could be an accelerated means by which novel direct compression excipients for

pharmaceutical industries could emerge (Saha & Shahiwala, 2009; Ambore *et al.*, 2014).

Several efforts have been made in developing starch-MCC based co-processed diluents exploited as potential direct compression candidates (Limwong *et al.*, 2004; Builders *et al.*, 2010). The goal of this research was to design, formulate and characterise the physicochemical properties of novel direct compression materials designed via co-processing strategy using maize starch (MS), MCC and PVP (primary excipients) at various combination levels.

Table 1: Materials used in the study.

Material	Role	Manufacturer/source
Maize starch	Primary excipient	BDH Chemicals, England
Microcrystalline cellulose (<i>Avicel PH101</i>)	Primary excipient	FMC Corporation, United Kingdom
Polyvinyl pyrrolidone (PVP), molecular weight: 700000	Primary excipient	BDH Chemicals, England
Ludipress®	*Co-processed excipient	BASF, Germany
Prosolv®	*Co-processed excipient	JRS Pharma, GmbH and Co., Rosenberg, Germany
L-ascorbic acid	Poorly compressible active drug	BDH Chemicals, England

*for comparison

MATERIALS AND METHODS

The materials used and their respective roles were enlisted in Table 1.

METHODS

Formulation of Starch-MCC-Povidone Composites

The mixing formula for the preparation of the composites was given in Table 2. The proportions of maize starch (MS) and microcrystalline cellulose

Table 2: Composition of Starch-MCC-Povidone composites.

Composites*	Primary Excipients			Classification
	Maize starch (%)	MCC (%)	PVP (%)	
SMP1	87.75	9.75	2.5	High starch- low MCC composites
SMP3	68.25	29.25	2.5	High starch –moderate MCC composites
SMP5	48.75	48.75	2.5	High starch-high MCC composites

* Abbreviations used throughout text

(MCC) were varied, while the concentration of polyvinyl pyrrolidone was kept constant at 2.5% in all excipients combinations. For rapid dispersion, the dry PVP powder was initially heated over a regulator hot plate (Model HL-052 Gallenkamp, England) at 130 °C and then mixed with MS/MCC aqueous dispersion. The slurry was heated over a digital thermostatic water-bath (HH-S McDonald International) at a controlled subgelatinization temperature (55 °C) with constant and vigorous stirring for 15 min. The slurry was sufficiently exposed to oven (at 60 °C) for 24 h. The dried mass was micronised using pestle and mortar, screened through 250 µm sieve diameter and subjected to another drying cycle over 24 h (Olowosulu *et al.*, 2011; Apeji *et al.*, 2017).

Scanning Electron Microscopy (SEM)

The surface morphology of the physical mixture of the primary excipients and the composites were studied under scanning electron microscope (Phenom ProX, Netherlands). Samples were evenly mounted onto aluminium stubs with the aid of carbon adhesive and photographs acquired at an acceleration voltage of 15 kV.

Particle Size Analysis

Sieve method was employed for particle size analysis. Nest of sieves were arranged in descending order of mesh size (500, 250, 180, 90, 75 µm) on top of a collecting pan. Co-processed powder (30 g) placed on top of the coarsest sieve was set into 10 min vibration on a sieve shaker (Endecotts, England). The cumulative percent of the fractionated samples retained on the surface of each sieve was plotted against the mesh size (particle diameter) using Graphad Prism (Version 6.0). The d_{10} , d_{50} , and d_{90} corresponding to the particle sizes at 10%, 50% and 90% of the distribution, respectively, were determined.

Powder Flow Rate, Angle of Repose and Weight Variation

The mass flow rate (MFR) of the composites was determined by allowing 10 g of the powder to flow in a vibrating metal funnel of Erweka flow rate machine (Type GDT, Germany). The time taken for the sample to evacuate the funnel was recorded. Angle of repose (θ_r) was measured by allowing 10g quantity of the powder sample to flow freely from the base of a glass funnel perpendicularly fixed to a retort stand. The angle made by the inclined plane of the powder heap with the horizontal was calculated according to the relationship below (Train, 1958).

$$\theta_r = \tan^{-1}(h/r) \quad (1)$$

where h and r are the height and radius of the powder heap, respectively.

Die filling reproducibility of composites was evaluated by compressing the powder samples (500 mg) at 250 MNm⁻² in Erweka tablet press (Type AR 400 GmbH, Germany) equipped with round flat-faced (diameter: 12 mm) punch tooling. The percentage weight variation of the tablets was determined.

Moisture Content and Swelling Capacity

The moisture content of the composites was determined using loss on drying method in which samples (2g) were dried in hot air oven at 100 ± 2 °C until a constant weight was established. The percentage weight loss was calculated. Swelling capacity (SC) was determined by monitoring water imbibition tendency of 5 g of the materials in 50 ml deionised water. The graduated cylinder (22.5±0.02 mm in diameter) was agitated vigorously for 5 min and the dispersion was allowed to settle for 20 h. SC was calculated as the percentage volume expansion of the sedimented mass.

$$SC = 100\% \times [(V_2 - V_1) / V_1] \quad (2)$$

V_1 and V_2 were the initial and final volume of the sediment, respectively.

Water Retention and Moisture Sorption Capacity

The residual water retained within the composite structure after centrifugation was obtained as described by Rashid *et al.*, 2011. Moisture sorption capacity (MSC) was calculated as the percentage net increase in powder weight after 5 days of exposure in the upper compartment of desiccator containing distilled water in the lower chamber (RH=100%, 28 ± 2 °C) (Olowosulu *et al.*, 2011).

Densities

Bulk density (ρ_1) was measured as the ratio of 10 g of the powdered material to its occupied loose volume (v_1) in a 50 ml cylinder. After subjecting the cylinder to manual tapping for 5 min until a constant volume (v_2) was reached, the tapped density (ρ_2) was calculated by dividing the initial powder weight to the final volume (Picker & Brink, 2006). Fluid displacement technique was used to determine the true density (ρ) of the powder (Ohwoavworhua *et al.*, 2007).

Compression Analysis

Compacts (500 ± 3 mg) were formed on hydraulic press (Model 184, Apex Construction Ltd, England) using 5 different compression pressures (50, 100, 150, 200, 250 MNm⁻²) with a dwell time of 30 seconds. The punch (12.5 mm) was pre-lubricated with 2% magnesium stearate in acetone for each compression cycle (Odeku *et al.*, 2005). The weight (w), thickness (h) and diameter (d) of each compact were measured 48 h after compaction to allow for sufficient elastic recovery and prevent false yield values (Adedokun and Itiola, 2010). The relative density (D) was measured as the ratio of the apparent compact density ($\rho' = \text{mass/volume}$) to true density (ρ).

$$D = \rho' / \rho = 4w / \rho \pi d^2 h \quad (3)$$

Densification of the composites at the stated pressures was studied using Heckel compression model given by Eqn 4 (Heckel, 1961).

$$\ln(1/1-D) = P\sigma + A \quad (4)$$

P is the compression pressure, the constants σ is the slope while A is the intercept of the linear region of Heckel plot (Sonnergaard, 1999).

Densification at zero and low pressures (D_a , D_b), and during phase-rearrangement (D_0) were computed using Eqn 5 (Odeku & Itiola, 2007).

$$D_a = 1 - e^{-A} = D_b + D_0 \quad (5)$$

The degree of volume reduction (C) of the composites as a function of applied pressure (P) was analysed using Kawakita model (Kawakita and Ludde, 1971) expressed in Eqn 6.

$$P/C = (1/a b) + (P/a) \quad (6)$$

The constant a measures the volume reduction propensity (compressibility) and b relates to the total plasticity of the powder, respectively (Nordström *et al.*, 2008).

Table 3: Formula for L-ascorbic acid tablet formulations

Ingredients (mg)	F1	F2	F3	F4	F5
L-ascorbic acid	200	200	200	200	200
SMP1	295	-	-	-	-
SMP3	-	295	-	-	-
SMP5	-	-	295	-	-
Prosolv	-	-	-	295	-
Ludipress	-	-	-	-	295
Talc	3.75	3.75	3.75	3.75	3.75
Stearic acid	1.25	1.25	1.25	1.25	1.25
Tablet weight	500	500	500	500	500

F1 (SMP1), F2 (SMP3), F3 (SMP5), F4 (Prosolv), F5 (Ludipress)

Dilution potential

L-ascorbic acid powder, a poorly compressible drug was used to evaluate the loading-capacity of the novel materials. Compression of the composite-drug mixture containing variable concentration of ascorbic acid (10, 20, 30, 40, 50, and 60%) was conducted on single-punch Erweka tablet press (Type AR 400, Apparatebau-GmbH, West Germany) equipped with 12 mm circular flat-faced punch at 300-400 MNm⁻². The crushing strength CS of the tablets ($n=5$) was determined using tablet breaking force tester (Monsanto hardness tester, England) as the load required to cause diametral fracture. The friability

(Fr) of the compacts ($n=5$) was tested in a friabilitor (Type TA3R Erweka, Germany) operated at 25 rpm for 4 min (USP29-NF24). The fractional weight loss was computed as:

$$Fr = [(m_i - m_f)/m_i] \times 100 \quad (7)$$

where m_i and m_f are the initial and final tablet weight, respectively.

Formulation of L-ascorbic Acid Tablets

Tablets containing the model drug at 40% dilution (200 mg) were formulated using the formula in Table 3. Formulations F1, F2 and F3 contain the novel composites SMP1, SMP3 and SMP5, respectively, while batch F4 and F5 contain Ludipress® and Prosolv®. The drug was premixed with the excipients for 5 min in a glass jar. Talc and stearic acid were successively blended just prior to compression. The powder was compressed as previously described under dilution potential studies.

Elastic Recovery

The thickness of the tablets ($n=10$) immediately after ejection (h_0) and after 10 days of production (h_{10}) were measured using digital calliper (Denver Instruments, USA). The elastic recovery ER was derived from Eqn 8 (Armstrong and Haines-Hutt, 1972). Radial tensile strength (T) was calculated using Eqn 9.

$$ER = [(h_{10} - h_0)/h_0] \times 100 \quad (8)$$

$$T = 2F/\pi dh \quad (9)$$

Where F is the force required to cause diametral tablet fracture measured using Monsanto hardness tester, d and h are the diameter and thickness of the tablets, respectively (Fell and Newton, 1970).

In-vitro Disintegration and Drug Release Studies

In-vitro disintegration time (t_d) of L-ascorbic acid tablets ($n=6$) was monitored using USP apparatus (Type ZT3 Erweka, Apparatebau-GmbH, Germany). The period over which the entire compacts deaggregate and passed through the mesh was recorded as t_d . *In-vitro* dissolution rate studies were conducted using the basket method (USP apparatus 1). The tablet was centrally stationed in the basket

and lowered into the vessel containing 900 ml of 0.01M HCl maintained at $37 \pm 0.5^\circ\text{C}$ with rotation speed of 100 rpm. For each formulation, samples of 5 ml were withdrawn and simultaneously replaced with fresh volume of the medium at 0.25, 0.5, 0.75, 1, 2, 3, 5 and 10 min. Spectrophotometric analysis of the drug released was conducted using UV spectrophotometer (UV-1800 Shimadzu, England) at 244 nm wavelength.

Statistical Analysis

Comparison of means was conducted by one-way analysis of variance (ANOVA) using GraphPad Prism (Version 7). Differences were considered significant for $P < 0.05$.

RESULTS AND DISCUSSION

Material properties

Surface Morphology and Powder Properties

The surface morphology of excipients is a critical property that influences fluidity and tableability of materials (Liu *et al.*, 2008). Under scanning electron microscope, the simple physical mixture of the primary excipients shows loosely associated interactions between MCC fibres, starch granules and the needle-like particles of PVP (Figure 1a). Sequel to differences in particle properties, the physical mixture of the primary excipients would have high tendency of segregation during compression (Howard, 2007).

However, by co-processing, interparticular agglomeration resulted in size enlargement and the resulting coprocessed structure appeared as enlarged porous mass of maize starch-MCC composites synergized by PVP solid bridges at their interfaces (Figure 1b-1d). The shape of the composites was more spherical and similar in shape than their corresponding physical mixture at equivalent proportion. The surface characteristics of the composites were defined by starch-MCC ratio and this affected the nature of interaction with other molecules. The high starch-low MCC composite, SMP1 had more of starch granules and an intermittent appearance of MCC fibres on their surfaces (Figure 1b). The SEM photograph of SMP3 shows a moderate appearance of MCC particles than

in SMP1 (Figure 1c). The SMP5 had more of MCC particles predominating at the surface of the composite (Figure 1d).

It is evident that fine particles impair fluidity due to high cohesive forces. Co-processing resulted in agglomeration of primary excipients into larger entities and the size distribution of the composites

favours decrease interparticle cohesion resulting in the observed flow behaviour (Table 4). SMP1 and SMP3 composites were characterised by lower bulk densities than Prosolv, Ludipress and SMP5 ($P < 0.001$). Despite these differences in ρ_{bulk} , the powder fluidity indicators measured in terms of Θ_r and MFR suggested acceptable flow properties.

Table 4: Bulk density, size distribution and fluidity indicators for Starch-MCC-Povidone composites in comparison to Ludipress and Prosolv

Co-processed excipient	d_{10} (μm)	d_{50} (μm)	d_{90} (μm)	ρ_{bulk} (gcm^{-3})	Θ_r ($^\circ$)	MFR (gs^{-1})	Compact weight (mg)
SMP1	147	189	227	0.395 \pm 0.01	26 \pm 2.06	5.5 \pm 0.08	517 \pm 0.13
SMP3	105	184	235	0.385 \pm 0.02	24 \pm 0.96	5.6 \pm 0.29	497 \pm 0.10
SMP5	90.3	180	249	0.502 \pm 0.02	22 \pm 0.68	5.0 \pm 0.20	500 \pm 0.01
Prosolv	-	-	-	0.448 \pm 0.01	19 \pm 0.87	4.3 \pm 0.29	500 \pm 0.10
Ludipress	-	-	-	0.471 \pm 0.01	25 \pm 1.00	7.1 \pm 0.43	493 \pm 0.31

MFR: Mass flow rate, (-): Not determined

Table 5: Interaction of Starch-MCC-Povidone composites with water molecules.

Characteristics	SMP1	SMP3	SMP5
Moisture content (%)	3.7 \pm 0.44	3.5 \pm 0.09	3.2 \pm 0.76
Moisture sorption (%)	28.5 \pm 0.17	25.7 \pm 0.42	22.3 \pm 0.81
Swelling capacity	4.5 \pm 0.00	9.3 \pm 0.31	33.3 \pm 0.44
Water retention capacity	25.6 \pm 0.78	30.7 \pm 0.67	40.6 \pm 0.76

All the composites had $\Theta_r < 30^\circ$, which according to powder classification indicated acceptable flowability (Aulton, 2013). The extent of flow as indicated by the MFR, which measured the bulk rate of flow of powder under vibration, was ranked as Ludipress>SMP1>SMP3>SMP5>Prosolv. Similarly, the enhanced fluidity of the powder was reflected in the weight variation studies. The tableted powders demonstrated reproducible volumetric filling of the die cavities with variation within official limits, thus signifying efficient fluidity.

Composite Interaction with water molecules

The low moisture content (<4%) of the composites conforms to the monograph specification for directly compressible diluents making the materials suitable for tableting hygroscopic ingredients such as ascorbic acid powder (USP 37-NF28). However, because of the abundant -OH groups on the surface of the composites, a reasonable interaction with water molecules occurred via hydrogen bonding (Builders *et al.*, 2010). Thus, the novel composites were capable of absorbing significant moisture when exposed to 100% RH (Table 5). The porous nature of the composite structure provide channel for molecular diffusion of water within the matrix. Due to this property and the combined intrinsic swelling tendencies of starch and MCC, the composites could retain water molecules to a great extent and the corresponding swelling ratio was quite dramatic. Thus this study found that high MCC content (in SMP3 and SMP5 composites) synergistically promotes imbibition of water molecules through the composite matrix more than high starch content (in SMP1).

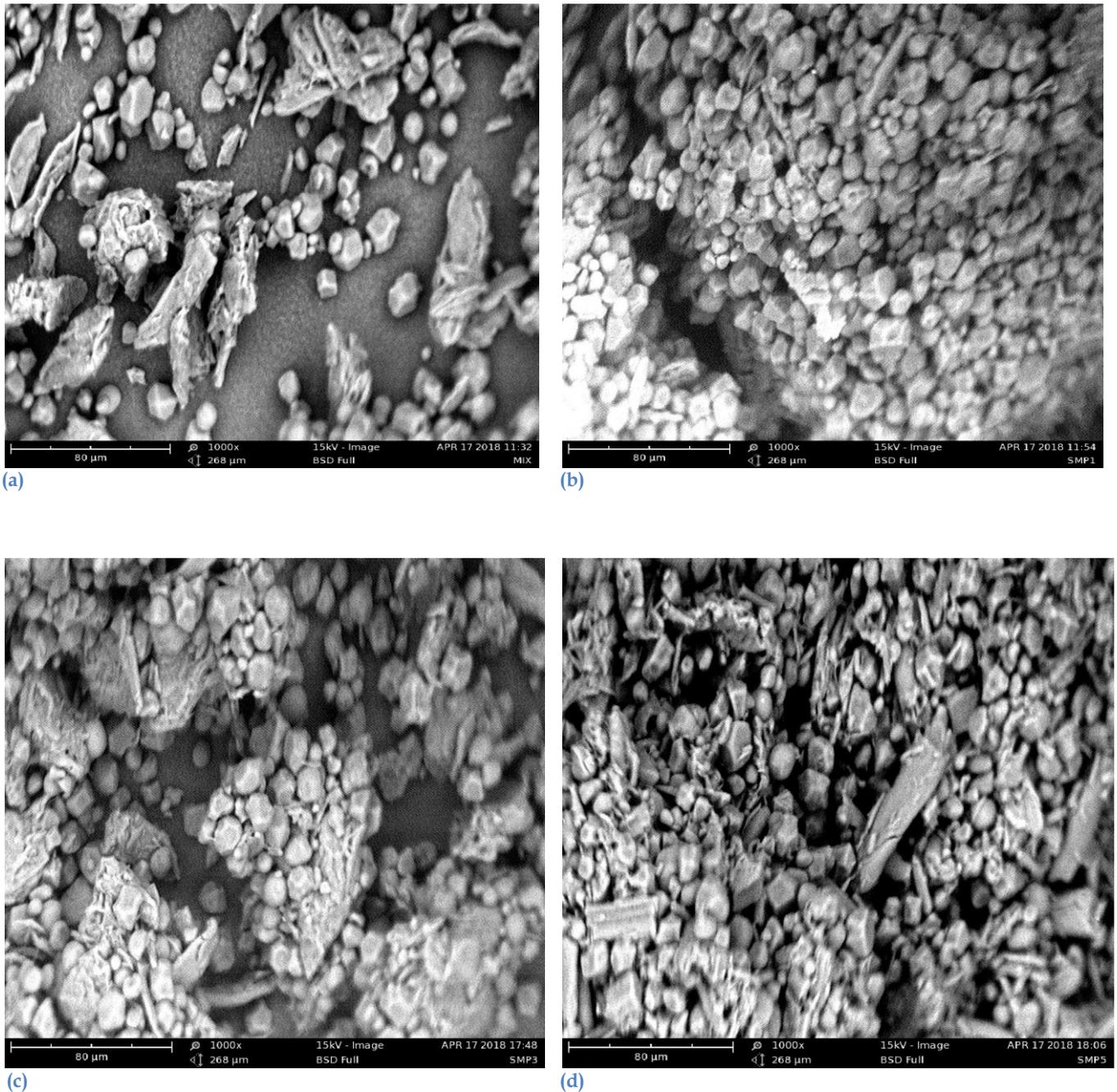


Figure 1: Scanning Electron Micrograph of (a) Physical mixture of maize starch, MCC and PVP, (b) SMP1, (c) SMP3, and (d) SMP5

Compaction Properties

Heckel analysis

The extent to which powder densification occurs during the compression stages is characteristically governed by the properties of the material and is of paramount importance in the design of novel diluents for tableting. Compression of a powder bed occurs in multiple, and often overlapping stages, during which application of pressure result in displacement of gaseous phase with subsequent

particle rearrangement, fragmentation, elastic and plastic deformations, and ultimately volume reduction (Nordström, 2008). These events could be quantitatively expressed using the Heckel mathematical compression model, which describes densification of powder bed as function of pressure in a similar pattern as first-order chemical reaction (Sonnergaard, 1999; Ghori & Conway, 2016).

The densification profiles of the novel composites were shown in Figure 2 and the corresponding constants derived from the regression equation were

presented in Table 6. The constant A relates to the particle rearrangement during die filling stage and it corresponds to the intercept of the Heckel plot (Adedokun & Itiola, 2010).

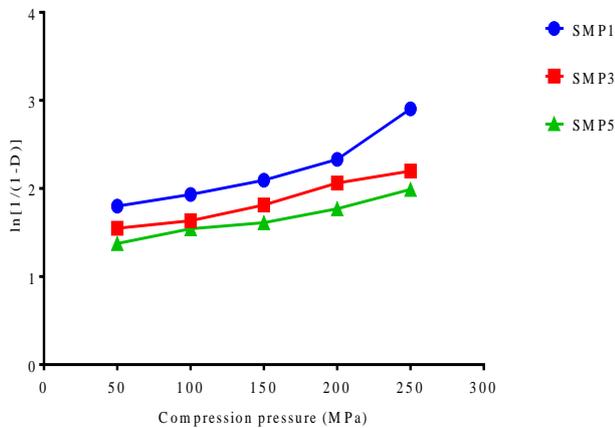


Figure 2: Heckel profile of novel Starch-MCC-Povidone composites.

The observed differences in A values was attributable to the differences in spatial configurations of the composites which gave rise to variable packing geometries within the die cavity. Based on previous studies it was found that the extent of plastic deformation has direct link with the particle geometry; an oriented irregularly-shaped particles promotes mechanical interlocking of the entities which further augment the bonding contact area (Nyström *et al.*, 1993; Ohwoavworhwa *et al.*, 2007). The extent of particle rearrangement in the die cavity (A) also follows similar pattern as the P_y .

Table 6. Mean yield pressure and relative density derived from Heckel plot

Parameters	SMP1	SMP3	SMP5
Σ	0.0052	0.0035	0.0029
P_y	191.7	289.3	343.4
A	1.43	1.33	1.22
D_0	0.32	0.28	0.36
D_a	0.76	0.74	0.71
D_b	0.44	0.46	0.35
R^2	0.9002	0.9781	0.9728
Regression equation	$y = 0.005217x + 1.43$	$y = 0.03457x + 1.33$	$y = 0.002912x + 1.22$

The mean yield pressure (P_y) was obtained from the inverse of the slope (σ) and its low value corresponds to fast onset of plastic deformation. Thus, SMP1 deformed more readily than SMP3 and SMP5 despite the higher MCC content of the latter. From the SEM photographs of SMP1, the irregular projections and rough surfaces of the composites could account for its fastest onset of plastic deformation.

Additionally the values of D_b for the excipients were highest in SMP1, which implied that it had the highest fragmentation propensity (Rashid *et al.*, 2011; Widodo & Hassan, 2015). Likewise, D_b reflect the short-range densification at low pressures sequel to particle movement and rearrangement and the values were higher in SMP1 and SMP3.

Kawakita Analysis

The study of the extent of volume reduction of the composites as a function of applied pressure was graphically illustrated in Figure 3 and the various parameters derived from the regression equation were presented in Table 7.

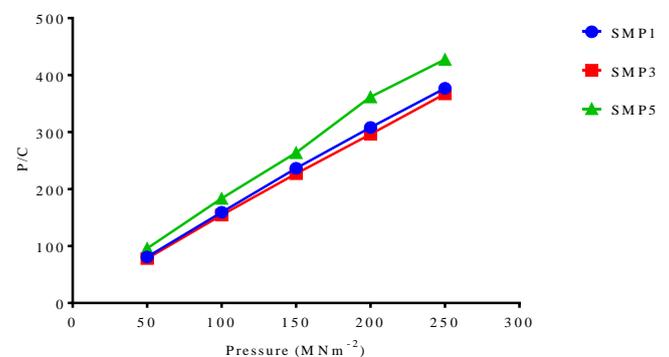


Figure 3: Kawakita compression profile of novel Starch-MCC-Povidone composites.

The extent of volume reduction of the materials under the applied compression load were denoted by the constant a , which measures the maximal engineering strain (Ghori and Conway, 2016). SMP1 and SMP3 have higher volume reduction tendency than SMP5. The P_k parameter provides a quantitative estimation of the pressure that is required to reduce the volume of the powder by 50% (Nordström 2008) and it correspondingly quantifies the inverse plastic deforming capacity of the composites (Adedokun & Itiola, 2010). This

shows that the onset of plastic deformation was more pronounced in SMP1 than in SMP3 and SMP5.

Table 7. Kawakita parameters for Starch-MCC-Povidone composites.

Parameters	SMP1	SMP3	SMP5
a	0.67	0.69	0.59
b	0.15	0.17	0.12
$b^{-1}(P_k)$	6.67	5.88	8.33
$D_i (1-a)$	0.33	0.31	0.41
R^2	0.9991	0.9997	0.9973
Regression equation	$y = 1.482x + 9.9968$	$y = 1.439x + 8.604$	$y = 1.682x + 14.15$

At low compression pressure all the composites can undergo significant volume reduction. Furthermore, P_k indicates the inverse plastic deforming propensity of materials under compression (Widodo & Hassan 2015). In this study it was found that composites containing moderate amount of MCC (SMP3) had the highest degree of plastic deformation.

Drug-loading capacity

Evaluation of drug-excipient mechanical properties

Drug-loading ability of a diluent is defined by the extent to which an active drug can be accommodated without loss in mechanical quality of the tablet (Habib *et al.*, 1996). Friability is used as an index to measure the drug-loading properties of materials. In this study, the friability curve indicated two distinct drug accommodation patterns (Fig. 4).

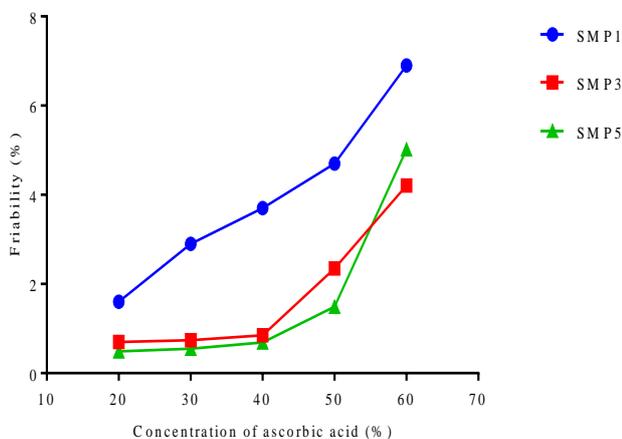


Figure 4: Friability composites at variable drug concentration.

Despite the high plasticity of SMP1, the bonding between the drug and composite particles was not appreciable and therefore the higher F_r values. Conversely, in SMP3 and SMP5 lower values were recorded to a certain critical value (40% dilution), beyond which saturation of interparticle bonding sites occurred with progressive increase in friability.

The diametral crushing strength was used to evaluate the drug-excipient bond strength (Fig. 5).

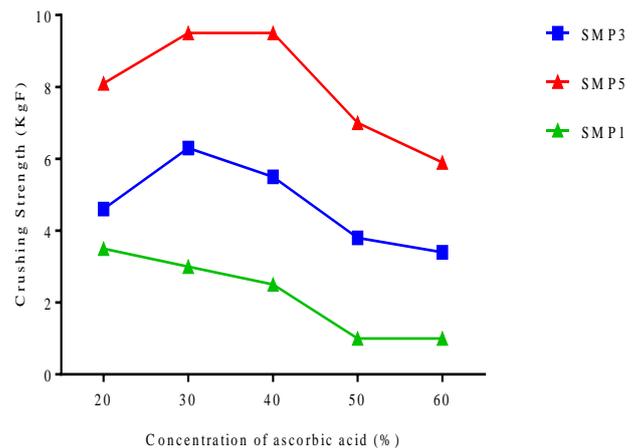


Figure 5: Crushing strength of ascorbic acid-coprocessed excipients compacts.

The high C_s values of SMP3 and SMP5 could be due to increasing MCC particles which have abundant hydrogen groups that participate in hydrogen bonding during compression and consolidation (Carlin *et al.*, 2008; Thoorens *et al.*, 2014). This shows that at Maize starch: MCC ratio of 7:3 (SMP3) and 5:5 (SMP5) considerable interparticle bonds held ascorbic acid particles to the composites at 20-40 dilution level to form mechanically stronger tablets. Therefore, the optimal drug accommodation capacity of the composites was up to 40% dilution level in the latter composites.

Properties of formulations containing optimum amount of ascorbic acid

Mechanical Characteristics

The mechanical behaviour of the tablet formulations containing ascorbic acid at 40% dilution level was further investigated in terms of elastic recovery (ER) and radial tensile strength as shown in Figure 6 & 7, respectively.

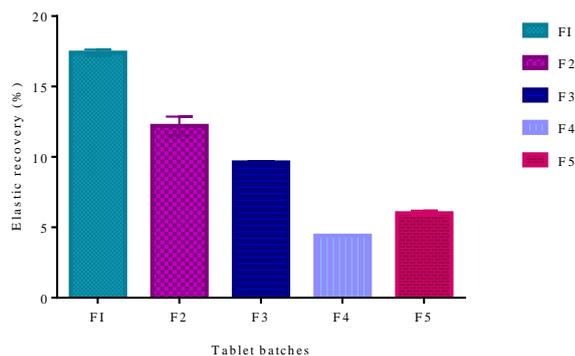


Figure 6: Elastic recovery (ER) of ascorbic acid tablets F1 (SMP1), F2 (SMP3), F3 (SMP5), F4 (Prosolv), F5 (Ludipress).

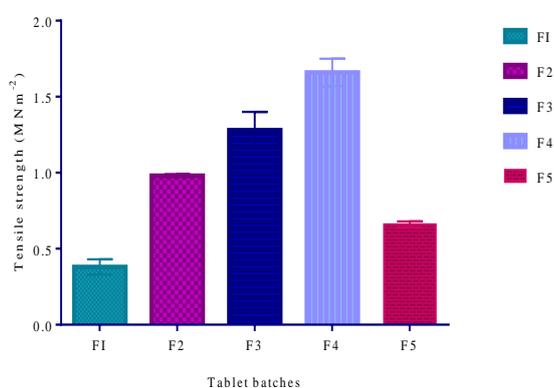


Figure 7: Tensile strength of ascorbic acid tablets. F1 (SMP1), F2 (SMP3), F3 (SMP5), F4 (Prosolv), F5 (Ludipress).

ER measures the elasticity of compacts upon decompression and ejection of compacts from the die cavity (Rojas *et al.*, 2013). *ER* has direct influence on the mechanical stability of tablets because the dissipated potential energy upon decompression is often accompanied by decrease in interparticle bond strength (Armstrong and Haines-Hutt, 1972; Haware *et al.*, 2010). Generally, the axial expansion of the tablet formulations were more pronounced in low MCC containing composites. Tablets formulated with the SMP1 composites (batch F1) recorded the largest axial expansion and consequently exhibited the lowest radial tensile strength. This could be attributed largely to the high content of maize starch which dominated the surface of the composites. However, at higher MCC concentration (SMP5), there was significant ($P < 0.05$) decrease in *ER* values, which was partly responsible for better mechanical strength. The surface morphology of SMP5 indicated predominance of MCC particles which therefore confers the sufficient bonding sites during compaction. Conversely,

Ludipress and Prosolv show lower *ER* values ($P < 0.05$) and thus better tablet strength than SMP1 and SMP3. Prosolv is composed of MCC (98%) and colloidal silicon dioxide (2%), and therefore exhibited excellent binding property with very minimal elastic recovery (Hwang and Peck, 2001; Fraser *et al.*, 2004). Similarly, the lower *ER* values of Ludipress could be linked to the high content of the brittle excipients, α -lactose monohydrate which undergoes substantial fragmentation and large plastic deformation, hence mechanically stronger tablets (Henderson & Bruno, 1970; Hauschild & Picker, 2004).

Drug release efficiency

The drug release profile indicated in Figure 8 shows that all the tablets exhibited similar dissolution pattern. Disintegration time (t_d) and drug release indicators ($t_{50\%}$ and $t_{80\%}$) for the tablet formulations were summarized in Table 8.

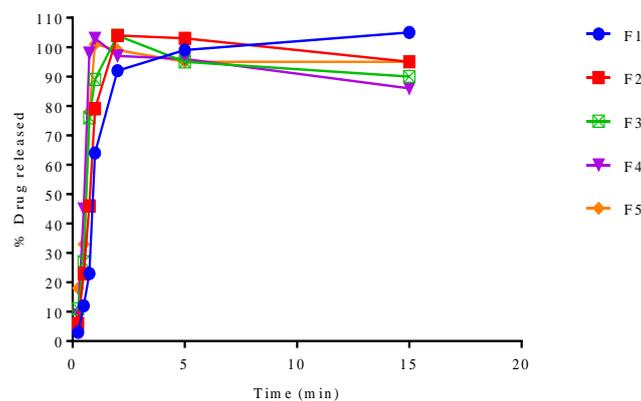


Figure 8: Drug release profile of ascorbic acid tablets formulated using various excipients. F1 (SMP1), F2 (SMP3), F3 (SMP5), F4 (Prosolv), F5 (Ludipress).

Tablets formulated with the novel composites were characterized by $t_d < 3$ min, while Ludipress and Prosolv formulated tablets had $t_d < 1$ min. Furthermore, the rapid disintegration of SMP1, SMP3 and SMP5 tablet formulations can be attributed to the synergistic potential of co-processing. The porous nature of the composites revealed by the SEM, the high swelling and water retention indices were responsible for the rapid imbibition of water molecules into the tablet matrix which subsequently causes structural collapse at a faster rate (Guyot-Hermann & Ringard, 1981).

Table 8: Disintegration time and drug-release indicators of L-ascorbic acid tablets.

Formulation	t_d (min)	$t_{50\%}$ (min)	$t_{80\%}$ (min)
F1	2.8 ± 0.16	0.92	1.5
F2	2.9 ± 0.24	0.83	0.96
F3	1.2 ± 0.06	0.61	0.79
F4	0.3 ± 0.14	0.53	0.70
F5	0.66 ± 0.09	0.57	0.75

F1 (SMP1), F2 (SMP3), F3 (SMP5), F4 (Prosolv), F5 (Ludipress)

The $t_{50\%}$ and $t_{80\%}$ are empirical indicators of onset of action with low values suggesting rapid drug release from the dosage form (Eraga *et al.*, 2015). Among the new coprocessed excipients, the $t_{50\%}$ decreased in the order SMP5 < SMP3 < SMP1. The rapid release could be related to the short t_d . L-ascorbic acid is a BCS (Biopharmaceutical Classification System) Class 3 drug and the *in-vitro* dissolution data implies that all the tablets formulated with the new coprocessed excipients have met with pharmacopeial criteria of 80% drug release from uncoated immediate-release tablets (USP 2011).

CONCLUSIONS

Directly compressible Starch-MCC-Povidone, (SMP) composites were engineered via coprocessing strategy. Under scanning electron microscope, the composites appeared as enlarged porous composites of starch-MCC bound by solid bridges of povidone at their interface. Powder fluidity predictors indicated acceptable flow properties (Angle of repose < 29°; Mass flow rate > 5 gs⁻¹). Weight variation studies indicated reproducible volumetric 'die' filling capacity. The interaction of the materials with water molecules was highly dependent on starch to MCC ratio. Analysis of the powder compaction indices indicated appreciable densification and total volume reduction in both Heckel and Kawakita models. The dilution ability of the composites was up to 40% using L-ascorbic acid as the model drug. Analysis of post compression tablet properties indicated extensive elastic recovery at low MCC content. All the novel composites were characterised by rapid *in-vitro* disintegration and efficient *in-vitro* drug release ($t_{50\%}$ < 1 min; $t_{80\%}$ < 2 min). In conclusion, moderate to high MCC

containing Starch-MCC-Povidone composites (SMP3 and SMP5) could be employed as cost effective direct compression diluents in tablet formulation.

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CONFLICT OF INTEREST

There is no conflict of interest associated with the content of this research.

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