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Effect of polymorphic form on the functional properties of cellulose: A comparative study

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ABSTRACT

The powder and tableting properties of cellulose II powders (MCCII) and (SDCII) were evaluated and compared with common direct compression binders. The cellulose II polymorphs offered more benefits in terms of functionality as compared with cellulose I (Avicel® PH-102) spray dried lactose and starch. Spray dried cellulose II (SDCII) had a better disintegrant ability, but a lower compactibility than microcrystalline cellulose I (Avicel® PH-102). However, when mixed and compressed with acetaminophen, SDCII was as compactable as cellulose I. Further, unprocessed cellulose II has a comparable compressibility to that of cellulose I. SDCII was found to be less friable, less sensitive to magnesium stearate, and possessed better acetaminophen loading capacity than unprocessed cellulose II and comparable to that of cellulose I. The cellulose II materials showed potential for use as a direct compression excipient.

1. Introduction

Spray drying is a single-step continuous process to produce dried particles from their dispersions or solutions, preferably, in water. This process is achieved in four stages: atomization of the feed dispersion by a pneumatic system, contact of the sprayed droplets with hot air, fast drying of the sprayed droplets, and separation of the dried particles from the drying air (Master, 1991). This technique has been extensively applied in the to prepare free flowing granules, agglomerates, or spherical particles in a narrow particle size range as well as to develop new excipients for direct compression (Bolhuis, Kussendrager, & Langridge, 2004; Limwong, Sutanthavibul, & Kulvanich, 2004; Te Wierik et al., 1996). It has also been used to modify the physicochemical properties of carbohydrate. For example, spray-dried lactose shows better flow and compactibility than the non-spray-dried material (Corrigan & Crean, 2002; Elversson & Millqvist-Fureby, 2005; Sebhatu, Elamin, & Ahlneck, 1994).

Cellulose is known to exist in four different allomorphs (Klemm, Philipp, Heinze, & Heinze, 1998). Microcrystalline cellulose (MCC), the most commonly and widely used direct compression excipient today, contains the cellulose I lattice. It is prepared from cellulose sources, such as wood pulp and cotton linter, by hydrolysis using dilute mineral acids at elevated temperatures (Battista & Smith, 1961). Recently, cellulose II powders, prepared from hydrocellulose and commercial MCCs by treatment with sodium hydroxide solutions at room temperature, have been found to be useful filler/binder (Reus & Kumar, 2007). In general, cellulose II powders show lower crystallinity and higher bulk and tap densities, compared to the starting cellulose I counterpart. They are less ductile and their compacts, irrespective of the compression force used to prepare them, disintegrate rapidly (Kumar, Reus, & Yang, 2002).

In this study, the effect of spray drying on the functionality of cellulose II was evaluated. The particle and mechanical properties of the spray dried product (SDCII) were evaluated and compared with those of the parent material (MCCII) and carbohydrate excipients, namely, Avicel® PH102 (spray-dried cellulose I; FMC Bipolymers, Newark, DE), Starch 1500® (pregelatinized starch; Colorcon, Indianapolis, IN) and Fast Flo® 316 (spray-dried lactose; DMV International Pharma and Foremost Farms, Baraboo, WI).

2. Materials and methods

2.1. Materials

Cotton linter (grade #R270) was received from Southern Cellulose Products, Inc., Chattanooga, TN. Avicel® PH-102 (lot 2339), starch (Starch 1500, lot IN504089), spray-dried lactose (Fast Flo® 316, lot 8596021361), and sodium hydroxide (97.5%; lot 051758) were obtained from FMC Biopolymers (Newark, DE), Colorcon (Indianapolis, IN), DMV International Pharma and Foremost Farms (Baraboo, WI), and Fisher Scientific (Fair Lawn, NJ), respectively. Concentrated hydrochloric acid (37%; lot 2612KLHV) and

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magnesium stearate (Powder Hyqual®, lot #2256KXDS) were purchased from Mallinckrodt Specialty Chemicals Co. (St. Louis, MO). All other chemicals were of analytical reagent grade.

2.2. Preparation of unprocessed (MCCII) and spray-dried (SDCII) cellulose II

A previously reported method was employed to prepare cellulose II powders (Rojas & Kumar, 2011). Spray dried cellulose II (SDCII) was prepared by spray drying ~5 L of a 3% MCCII dispersion using a Yamato Pulvis spray drier (Model GB22, Yamato Scientific America, Inc., Santa Clara, CA). The operational conditions were: inlet temperature 195 °C, feed spraying rate 2 mL/min, drying air rate 0.44 m^3/min, atomization air pressure 1.0 kg f/cm^2 and nozzle diameter 711 μm.

2.3. Particle size and particle size distribution analyses

The geometric mean diameter (d_g) was determined microscopically using a Hitachi S-4800 scanning electron microscope (Hitachi High Technologies America, Inc., Schaumburg, IL), operated at an acceleration voltage of 3 kV. The powder was fixed on an aluminum stub and coated with gold/palladium (3–5 nm) for 4 min at 30 W. The photographs were taken at a 35× magnification. Six hundred particles were randomly selected in each picture and their projected diameter (d_p) was calculated using the ImageJ software (v. 1.37, National Institutes of Health, Bethesda, MD) according to the relationship:

$$d_p = 2 \times \left(\frac{\text{projected area}}{\pi}\right)^{0.5}$$

The log-normal distribution plot was then constructed between d_g and cumulative percent frequency to calculate the geometric mean diameter, d_g, using the Minitab software (v.15, Minitab, Inc., State College, PA).

2.4. Degree of crystallinity (DC)

Powder X-ray diffractions (PXRD) measurements were conducted over a 5–45° 2θ range using a Siemens difractometer (Model D5000, Siemens Energy and Automation, Inc., Madison, WI), equipped with a monochromatic Cu Kα (α_1 = 1.5460 Å, α_2 = 1.54438 Å) X-ray radiation. The step width was 0.020° 2θ/min with a time constant of 0.5 s. The Difrac® plus Eva software, version 2.0 (Siemens Energy and Automatization, Inc., Madison, WI) was used to calculate the crystalline areas. The DC was calculated by separating the crystalline and amorphous scattering according to the relationship (Rabek, 1980):

$$\text{DC} = \frac{I_c}{(I_c + I_a)} \times 100\%$$

where I_c is the sum of all crystalline diffracted areas and I_a is the area of the diffuse halo due to the amorphous region.

2.5. Scanning electron microscopy (SEM)

SEM photographs were obtained on a scanning electron microscope (Model S-4800, Hitachi, Hitachi High Technologies America, Inc., Pleasanton, CA). Powders were fixed on aluminum stubs using a double-sided adhesive tape and coated with gold/palladium (60:40) using a sputter coater (Model K550, Emitech, Ashford, UK) for 4 min at 30 W. The acceleration voltage was 5 kV.

2.6. Powder properties

The moisture content was obtained by the gravimetric method described in the United States Pharmacopoeia/National Formulary 28/23 (US Pharmacopoeia, 2009). Briefly, lactose was heated at 80 °C for 2 h, starch at 120 °C for 4 h and cellulose samples at 105 °C for 3 h in a mechanical convection oven (Model STM 80, Precision Scientific, Inc., Chicago, IL).

True density was determined using a helium displacement micropycnometer (Model MPY-2, Quantachrome Corporation, Boyton Beach, FL). Approximately, 1 g of a dry sample was used for the analysis. It was calculated by dividing the mass of the material by its volume, obtained from the equation:

$$V_p = V_c - V_r \times \left[\frac{p_1}{p_2} - 1\right]$$

where V_p is the volume of the powder, V_c is the cell volume and V_r is the volume of the reference spheres. The test was carried out in triplicates of three independent samples. Bulk density (ρ_{bulk}) was determined using a 100 ml graduate cylinder filled with 20 g of sample. Bulk density was calculated by: ρ_{bulk} = mass/volume. Tap density was measured on a VanKel tap density analyzer (Model 50-1000, VanKel industries, Cary, NC) for 1200 taps. Testing was carried out in triplicate. Porosity (ε) was determined from the equation:

$$\varepsilon = \left[1 - \frac{\rho_{bulk}}{\rho_{true}} * 100\%\right]$$

where ε, $\rho_{bulk,}$ and ρ_{true} are the porosity, bulk density and true density of the powder, respectively. Hausner ratio was determined from the bulk and tap densities according to the relationship:

$$\text{HR} = \left[\frac{\rho_{tap}}{\rho_{bulk}}\right]$$

where ρ_{tap} and ρ_{bulk} are the tap and bulk densities, respectively. Powder flow was determined by the flow-through-an-orifice method. The test was executed on a custom-made flowmeter, which consisted of a stainless steel cylinder (2.5 cm × 20.0 cm), mounted on a metal block, and a replaceable set of steel plates with a hole in the center. Approximately 20 g of material that passed through the orifice and its weight was recorded as a function of time. The test was conducted in triplicate.

2.7. Tableting properties

Compacts of ~500 mg were made on a Carver press (Model C, Fred S. Carver, Inc., Menomonee Falls, WI) coupled with a load cell (Model LCGD-10K, Omega Engineering, Inc., Stamford, CT) of 30 s using a flat-faced 13 mm punches and die tooling. Pressures ranged from ~10 to ~260 MPa. Forces were measured on a on a strain gauge (Model DP25B-S, Omega Engineering, Inc., Stamford, CT) connected to the load cell. Compacts were stored in a desiccator containing drierite (RH = 15–30%) for 48 h.

2.8. Compressibility analysis

The natural logarithm of the inverse of compact porosity, ln(1/ε), was plotted against compression pressure (σ) to construct the Heckel plots (Heckel, 1961a, 1961b). The slope (m) of the linear region of this curve is inversely related to the material yield pressure (P_y), which is a measure of its plasticity (Alderborn & Nyström, 1996). Thus a low P_y (usually values <100 MPa) indicate a high ductile deformation mechanism upon compression. The Heckel model is given by:

$$\ln \frac{1}{\varepsilon} = m\sigma + A$$

where A is the intercept obtained by extrapolating the linear region to zero pressure. Other parameters useful in assessing compressibility are D_0, D_a, and D_b, which are related to initial powder packing/densification, total compact densification, and particle rearrangement/fragmentation at the initial compaction stage, respectively (York, 1992). D_0 was calculated by dividing the bulk density with the true density (Chowhan & Chow, 1980). D_a and D_b were obtained by the expressions:

$$D_a = 1 - \exp^{-A}$$
$$D_b = D_A - D_0$$

2.9. Compact crushing strength

It was performed using a Schleuniger Pharmatron tablet hardness tester (Model 8M, Dr. Scheleuniger Pharmatron Inc., Manchester, NH). The crushing strength (in kPa), was then recorded. The crosshead speed of the left moving platen was 3.5 mm/s.

2.10. Dilution potential

Tablets containing different levels of acetaminophen (25%, 50%, 75%, 85% or 95%), a poorly compressible drug, were prepared and their crushing strength was determined. Acetaminophen and the test excipient were mixed in a V-Blender (Model LB429, The Petterson Kelley Co. East Stroudsburg, PA) for 30 min and then compressed on a Carver Press at 120 MPa and a dwell time of 30 s. Samples were analyzed in eight replicates.

2.11. Lubricant sensitivity

Lubricant sensitivity was assessed by mixing powders with magnesium stearate in 99.5:0.5, 99:1, and 98:2 weight ratios in a V-blender (Model LB429, The Petterson Kelley Co. East Stroudsburg, PA) for 30 min. Tablets were prepared using a Carver press at 120 MPa and at a dwell time of 30 s. The lubricant sensitivity was expressed as the lubricant sensitivity ratio (LSR):

$$\mathrm{LSR} = \left[\frac{H_0 - H_{lub}}{H_0}\right]$$

where H_0 and H_{lub} are the crushing strengths of tablets prepared without and with lubricant, respectively. Samples were analyzed in triplicates.

2.12. Compact friability

The friability test was performed on a friabilator (Model 45-1000, Erweka, Cary, NC) at 25 rpm for 4 min. Briefly, 13 compacts (made at ~60, 120 and 200 MPa), each weighing ~500 mg, were placed in a VanKel friabilator. Compacts were then dedusted and reweighed. The percentage weight loss was taken as friability.

2.13. Compact disintegration

Tablets, each weighing 500 mg, were made on a hydraulic Carver press (Model C, Carver Press, Menomonee Falls, WI) using a 13 mm round, flat-faced punches and die set at 260 MPa and a dwell time of 30 s. It was performed in five replicates in distilled water at 37 °C employing an Erweka GmbH disintegration apparatus (type 712, Erweka, Offenbach, Germany) at 30 strokes/min.

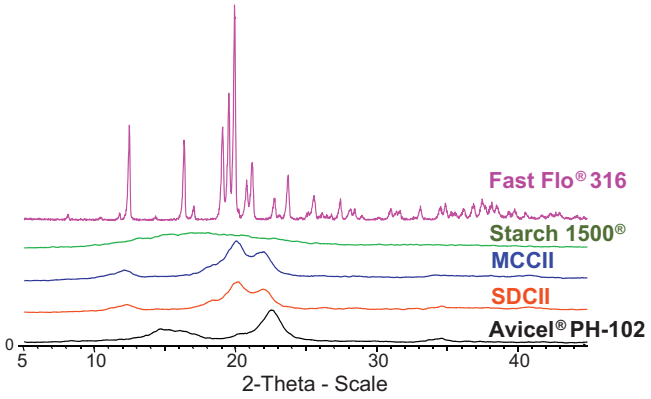

Fig. 1. Powder X-rays diffractograms of SDCII, MCCII and carbohydrate excipients.

3. Results and discussion

3.1. Powder properties

Fig. 1 shows the powder X-ray diffractograms of SDCII, MCCII, Fast Flo® 316, Avicel® PH-102 and Starch 1500®. The diffraction peaks appearing at 12°, 20°, and 22° 2θ for SDCII confirmed the cellulose II lattice attributable to 1 $\bar{1}$ 0, 1 1 0 and 2 0 0 reflections, respectively. Avicel® PH-102, in contrast, displayed characteristic diffraction peaks at 14.8°, 16.3° and 22.4° 2θ, corresponding to the 1 $\bar{1}$ 0, 1 1 0 and 2 0 0 reflections, respectively, of cellulose I. No difference in the diffractograms of SDCII and CII suggests that spray drying had no effect on the cellulose crystalline structure. However, the degree of crystallinity of the samples (from ~68% to ~63%). It is plausible that the rapid evaporation of water prevents alignment of some chains and results in crystallinity decrease. In the case of Starch 1500®, a diffuse amorphous halo is observed typical of spray-dried starch made from pregelatinized starch (Laovachirasuwana, Peerapattanaa, Srijesdarukb, Chitropasa, & Otsukac, 2010). Thus, the degree of crystallinity was very low (<7.5%). The characteristic crystalline peaks for Fast Flo® 316 (α-lactose monohydrate) were observed at 12.5°, 16.4° and 20° 2θ (Miao & Ross, 2005; Szepes, Fiebig, Ulrich, & Szabó-Révész, 2007). This material also showed the highest degree of crystallinity among all the materials evaluated (87%).

The selected powder properties of carbohydrate excipients, as produced or received, are presented in Table 1. Fig. 2 shows the SEM pictures depicting particle morphologies. MCCII consisted of fibers ($d_g = 89.9 \pm 5.0$ μm), while SDCII was a mixture of round to oblong shaped particles ($d_g = 52.5 \pm 3.0$ μm) with smooth surfaces. Fast Flo® 316, Avicel® PH-102, and Starch 1500®, in contrast, had irregularly shaped particles with rough surfaces and sharp edges ($d_g = 83.2 \pm 7.2$, 70.9 ± 7.0, and 47.2 ± 2.9 μm, respectively). The true density of SDCII was 1.554. Except for Starch 1500®, all materials showed comparable true density (1.538–1.551); in the case of Starch 1500®, the corresponding value was 1.500. The high bulk and tap density, smooth surface and semispherical shape led to SDCII to have better flow than MCCII. The flow of commercial materials was in between those of SDCII and MCCII.

3.2. Tableting properties

Although initially developed for metals, the Heckel analysis is widely used to assess the compressibility of pharmaceutical powders. Table 1 lists the Heckel analysis results. The yield pressure value, P_y, which is the inverse of the slope of the linear portion of the Heckel curve, refers to the pressure at which the material begins to deform plastically. In general, the lower the P_y value,

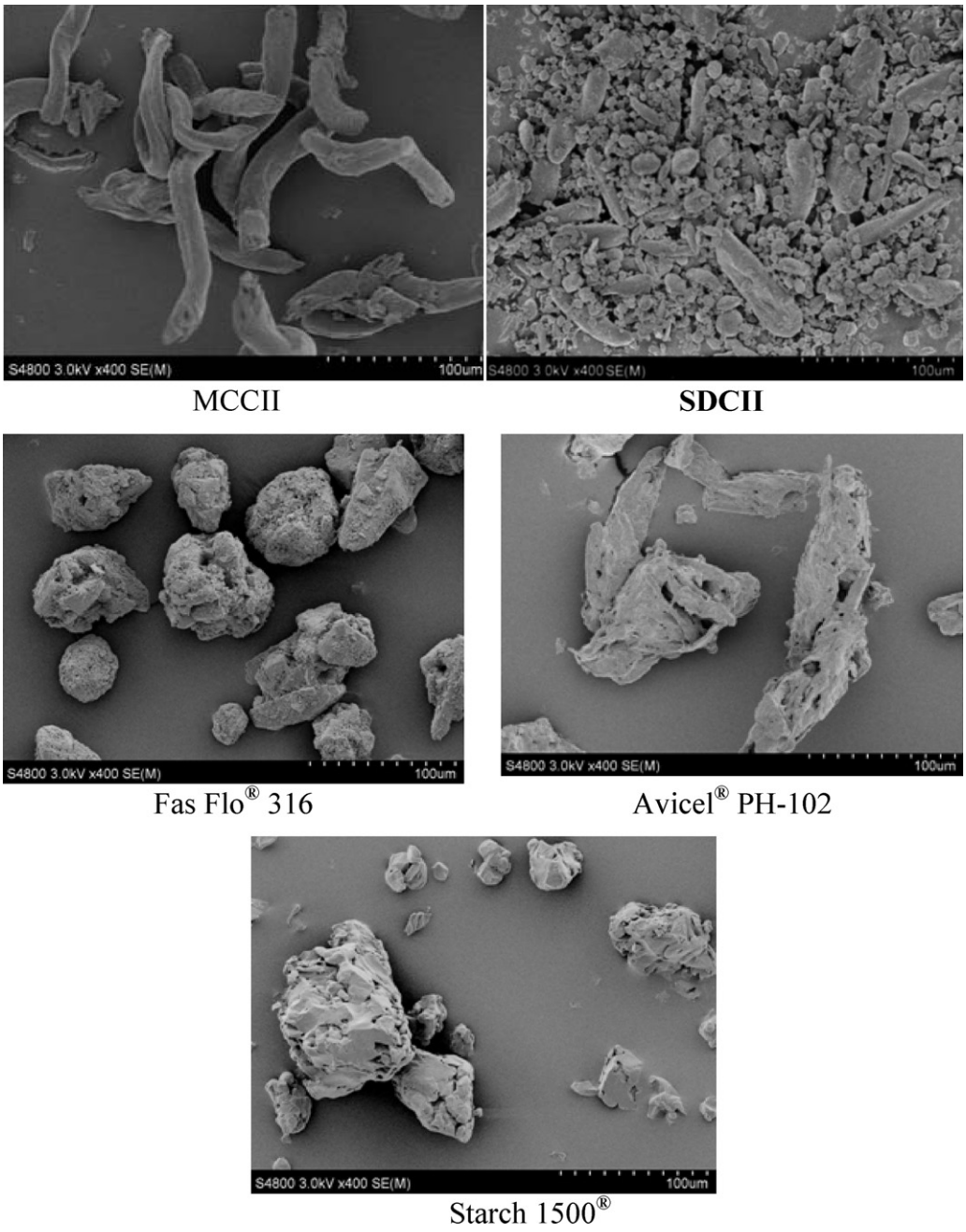

Fig. 2. SEMs of SDCII, MCCII and carbohydrate excipients.

the higher the ductility of the material. In the present study, Avicel® PH-102 (~73 MPa) and Starch 1500® (~73 MPa) had the lowest values; whereas, Fast Flo® 316 had the highest P_y value (~167 MPa). SDCII and MCCII presented the intermediate P_y values (~116 and 122 MPa, respectively). These results are in good agreement with the values reported in the literature [Avicel® PH-102: 77.3 MPa (Mitrevej, Faroongsarng, & Sinchaipanid, 1996) and 70.8 MPa (Reus, 2005); Starch 1500®: 72 MPa (Martinez-Pacheco, Gomez Amoza, & Vil-Jato, 1987); Fast Flo® 316: 152 MPa (Martinez-Pacheco et al., 1987); MCCII prepared from Avicel® PH-102 and cotton linter: 125.6 and 103.1 MPa, respectively (Reus, 2005)]. Both Avicel® PH-102 and Starch 1500® are known to deform by a plastic mechanism (David & Augsburger, 1977; Van Veen, Bolhuis, Wu, Zuurman, & Frijlink, 2005), while Fast Flo® 316 is recognized as a brittle material (Vromans, Bolhuis, Lerk, Van de Biggelaar, & Bosch, 1987). Thus, from the P_y values, SDCII is less ductile than Avicel® PH-102 and Starch 1500®, but is comparable in its ductility to MCCII. Based on the area under the Heckel curve, the overall compressibility of the materials followed the order: MCCII ≥ Avicel® PH-102 > SDCII ≥ starch 1500® > Fast Flo® 316.

The D_0, D_a and D_b parameters, calculated from the Heckel plots, represent initial packing of the material upon die filling, total packing at low pressures, and the degree of powder bed arrangement due to fragmentation at low pressures, respectively. The D_0 values follow the same trend than the bulk density values suggest that Starch 1500® and Fast Flo® 316 have the highest densification at zero pressure, MCCII and Avicel® PH-102 the lowest and SDCII an intermediate value. The rank order of materials with respect to the D_a parameter was as follows: MCCII > SDCII > Fast Flo® 316 > Avicel® PH-102 > Starch 1500®, suggesting a decreasing tendency to fragmentation and, consequently, densification at lower pressures. The D_b values followed the same trend, except for

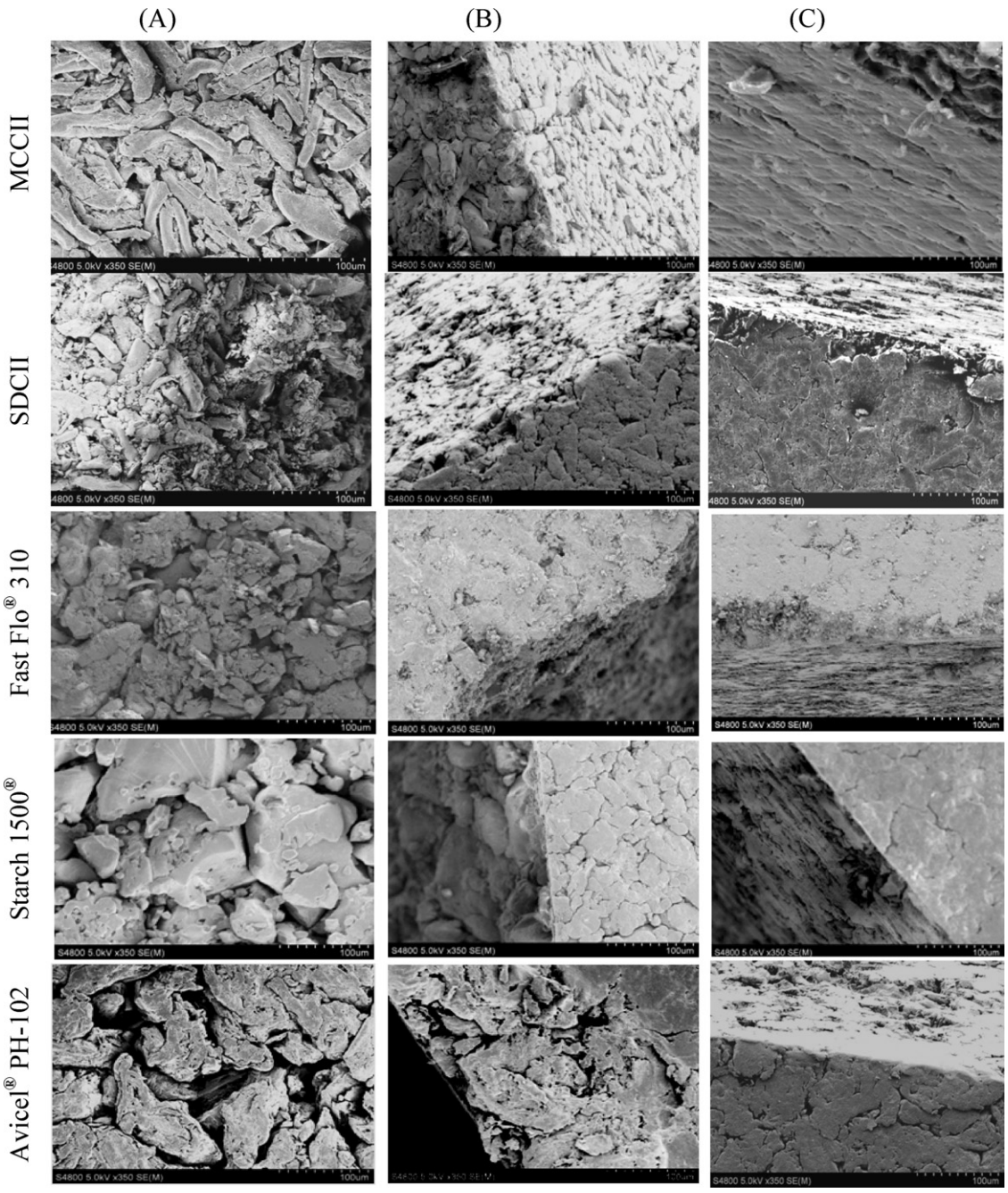

Fig. 3. Cross-section images of SDCII, MCCII and carbohydrate excipient compacts made at (A) 10 MPa, (B) 120 MPa, and (C) 260 MPa compression pressures.

that Avicel® PH-102 showed a higher degree of powder bed rearrangement than Fast Flo® 316. This was attributed to the highly crystalline aggregated structure and ductile nature of the former; Fast Flo® 316, in contrast, deformed by a brittle mechanism.

The cross-section views of tablets of SDCII, MCCII and commercial excipients made at 10, 120 and 260 MPa compression pressures are shown in Fig. 3. At 10 MPa, particle fragmentation is evident only for MCCII, SDCII and Fast Flo® 316, causing their compacts to have a significantly reduced void volume compared to compacts of Starch 1500® and Avicel® PH-102. At higher applied pressures (120 and 260 MPa), all compacts showed increased powder bed densification. The particle morphology in the case of SDCII and MCCII tablets appears similar. At 10 MPa, the surface of tablets of MCCII, Starch 1500® and Avicel® PH-102 look less packed compared to those of the SDCII and Fast Flo® 316 and Starch 1500® compacts. It should be emphasized that MCCII and Avicel® PH-102 were the two materials with the highest powder porosity and hence showed the highest compressibility.

At high pressures, MCCII undergo fragmentation to produce fibers of sizes comparable to that present in SDCII. In the case of Fast Flo® 316 compacts, the surface shows the presence of fine particles and the interior of the tablet appeared stratified, conforming to the literature report that the material undergoes fragmentation during consolidation (Vromans & Lerk, 1988). The coalescence of particle boundaries observed in the case of Starch 1500® and Avicel® PH-102 compacts is attributed to their ability to deform plastically during consolidation (Nicklasson, Johansson, & Alderborn, 1999). However, at 120 MPa, Avicel® PH-102 compacts were less densely packed than Starch 1500®. At 260 MPa, the core and outer surfaces of Avicel® PH-102 and Starch 1500® compacts appear similar.

Table 1
Powder properties.

Sample		MCCII	SDCII[d]	Avicel® PH-102	Starch 1500®	Fast Flo® 316
Geometric mean diameter[a] (μm ± SE[b])	N.A.	89.9 ± 5.0	52.5 ± 3.0	70.9 ± 7.0	47.2 ± 2.9	83.2 ± 7.2
Loss on drying (% ± SD[c])	$n = 3$	3.6 ± 0.4	2.8 ± 0.7	3.7 ± 0.3	9.2 ± 0.0	1.0 ± 0.2
Degree of crystallinity (%)	$n = 3$	68.0 ± 1.4	61.5 ± 1.2	72.1 ± 2.6	7.5 ± 1.2	87.0 ± 1.5
True density (g/cc)	$n = 3$	1.538 ± 0.025	1.554 ± 0.006	1.551 ± 0.003	1.500 ± 0.003	1.554 ± 0.003
Bulk density (g/cc)	$n = 5$	0.38 ± 0.03	0.55 ± 0.00	0.37 ± 0.00	0.61 ± 0.02	0.59 ± 0.01
Tapped density (g/cc)	$n = 5$	0.54 ± 0.06	0.81 ± 0.00	0.48 ± 0.00	0.78 ± 0.01	0.71 ± 0.00
Powder porosity (%)	$n = 1$	75.5	64.4	76.2	59.1	62.3
Flow rate (g/min)	$n = 3$	1.33 ± 0.22	5.2 ± 0.63	4.51 ± 0.21	2.36 ± 0.09	1.92 ± 0.29
P_y[e]	$n = 1$	122.0	116.3	73.5	73.0	166.7
D_0[f]	$n = 1$	0.24	0.36	0.24	0.41	0.38
D_a[g]	$n = 1$	0.80	0.71	0.57	0.51	0.65
D_b[h]	$n = 1$	0.56	0.36	0.34	0.10	0.27
AUHC[i]	$n = 1$	625.1	526.3	596.5	514.1	420.9
R^2	$n = 1$	0.9850	0.9990	0.9963	0.9979	0.9922
Disintegration time (s)	$n = 5$	129.5 ± 3.7	70.3 ± 2.5	>5 h	2056 ± 48.2	296 ± 25.1

[a] Determined from the cumulative frequency versus particle size plot constructed using log-normal scales.
[b] Standard error.
[c] Standard deviation.
[d] Prepared in 1 kg batch.
[e] Yield pressure.
[f] Initial rearrangement as a result of die filling.
[g] Total powder packing at low pressures.
[h] Particle rearrangement/fragmentation at early compression stages.
[i] Area under the Heckel curve.

Fig. 4 shows the relationship between crushing strength and compression pressure. SDCII formed compacts that were stronger than Starch 1500® compacts, which in turn, were stronger compared to those made from Fast Flo® 316. The magnitude of difference in crushing strength of SDCII and Starch 1500® or Fast Flo® 316 compacts appears to increase with an increase in applied force. The comparable tensile strength for SDCII and MCCII suggests that spray drying did not affect the compaction property of the cellulose II powders, irrespective of modifications in morphology and powder properties caused by spray drying.

To assess the effect of a poorly compressible substance on the compactibility of SDCII and other materials, compacts containing different weight ratios of the test material and acetaminophen were prepared and their crushing strength was determined. The results are presented in Fig. 5. The crushing strength values of SDCII-acetaminophen compacts were comparable to those of Avicel® PH-102. In case of MCCII and Starch 1500®, the increase in crushing strength was insignificant until the level of the excipient in the compact exceeded 25%. Fast Flo® 316, in contrast, did not show any increase in crushing strength with increasing its weight percentage level in the compact. These results clearly suggest that SDCII and Avicel® PH-102 serve as the most effective binders and offer potential to produce tablets for use with poorly compressible drugs by direct compression. MCCII, in contrast, is effective only when used in amounts higher than 50%. Thus, despite the fact that MCCII showed the highest compressibility among the materials (Table 1), but presented a low dilution potential for acetaminophen. Also, the fibrous character of MCCII and the rod elongated shape of acetaminophen (Billon, Bataille, Maury, Terol, & Jacob, 1999) might have prevented the formation of contact points needed for the formation of strong compacts.

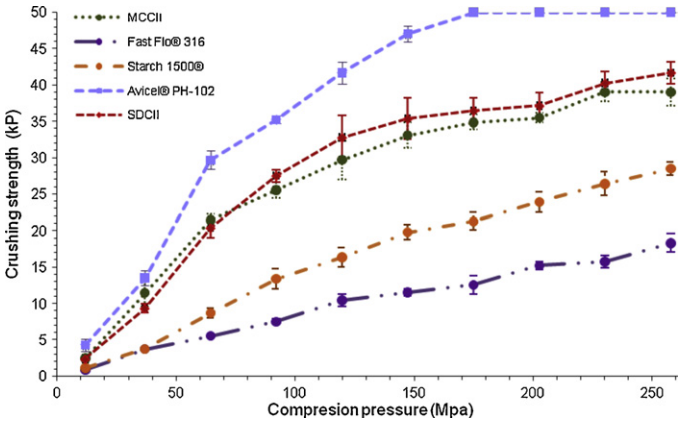

Fig. 4. Crushing strength of SDCII, MCCII and carbohydrate excipient compacts.

3.3. Compact friability and lubricant sensitivity

Tablets, prepared using 60, 120, and 200 MPa compression pressures, were tested for friability. Fig. 6 showed that all tablets made of Avicel® PH-102, MCCII, and SDCII had <1% friability. In case of Starch 1500®, only tablets that were made at 120 and 200 MPa passed the test. For Fast Flo® 316 tablets, irrespective of the pressure applied had friability values >1%. These results correlate well with the crushing strength results shown in Fig. 5.

The lubricant sensitivity was tested with magnesium stearate at 0.5%, 1.0% and 2.0% (w/w) concentrations. Magnesium stearate

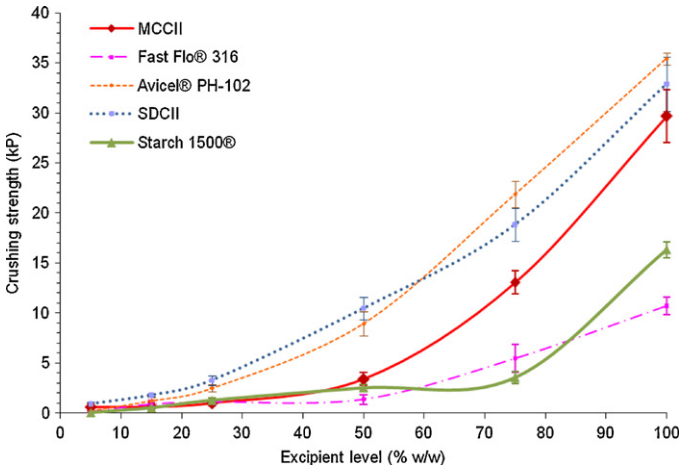

Fig. 5. Crushing strength of SDCII, MCCII and carbohydrate excipient compacts containing different amounts of acetaminophen.

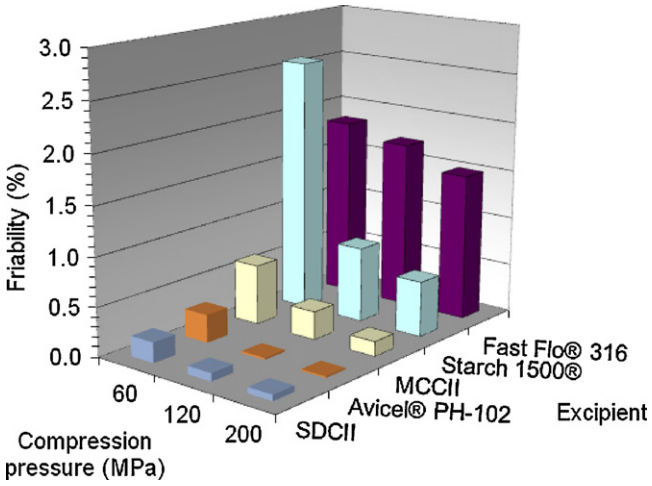

Fig. 6. Friability of SDCII, MCCII and carbohydrate excipient compacts.

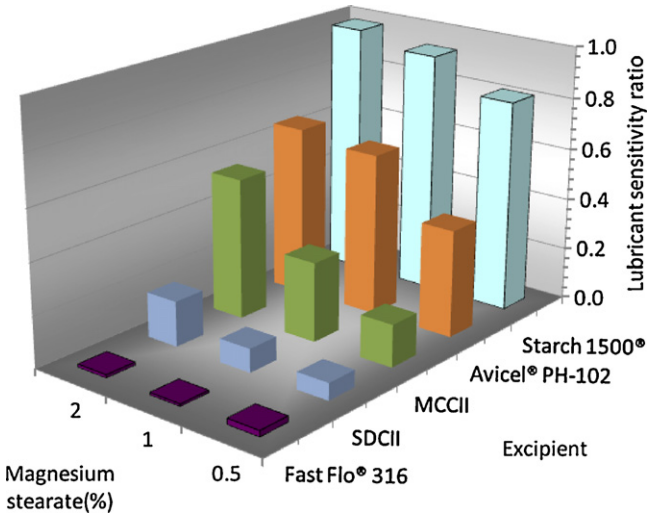

Fig. 7. Sensitivity of SDCII, MCCII and carbohydrate excipient compacts to magnesium stearate.

is commonly used in tablet formulations to reduce friction between materials and machine tooling. The results presented in Fig. 7 showed the following rank order of materials in terms of their sensitivity towards magnesium stearate: Starch 1500® > Avicel® PH-102 > MCCII > SDCII > Fast Flo® 316. These results suggest that plastically deforming materials are more sensitive to magnesium stearate than brittle materials. Thus, for brittle materials, such as Fast Flo® 316, the negative effect of magnesium stearate on crushing strength is negligible since new surfaces, free of magnesium stearate, are constantly being formed during compaction. It has been reported that magnesium stearate covers the surface of the particles and thereby, restricts the contact between particles rendering compacts of low strength. Thus, the lubricant film covering the particle surface is not complete especially for highly irregular and poorly flowing powders/particles, in which the lubricant is trapped in the particle cavities (Bolhuis & Zuurman, 1995; Vromans & Lerk, 1988).

The disintegration profiles of compacts made at 10–260 MPa compression pressures are illustrated in Table 1. As is evident, SDCII compacts, showed the fastest disintegration followed by MCCII < Fast Flo® 316 < Starch 1500® < Avicel® PH-102.

4. Conclusions

The above result shows that spray drying improved the functional properties of MCCII. Unprocessed cellulose II (MCCII) or spray-dried cellulose II (SDCII) had a better disintegrant ability, but lower compactibility than microcrystalline cellulose I (Avicel® PH-102). However, when mixed and compressed with acetaminophen, SDCII was as compactable as Avicel® PH-102. Further, MCCII has a comparable compressibility to that of Avicel® PH-102. The spray-dried powder (SDCII) was found to be less friable, less sensitive to magnesium stearate, and possessed better acetaminophen loading capacity than MCCII and comparable to that of Avicel® PH-102.

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