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Evaluation of the plug formation process of silicified microcrystalline cellulose

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Abstract

To investigate the powder plug formation process of silicified microcrystalline cellulose (SMCC) under compression forces consistent with automatic capsule-filling machines, a single-ended saw-tooth wave was used to make powder plugs with different heights (6, 8, 12 mm), at two different punch speeds (1 and 50 mm/s) on a tablet compaction simulator. SMCC was compared to Starch 1500, anhydrous lactose (direct tableting grade), and microcrystalline cellulose. Heckel analysis showed that 'apparent mean yield pressures' (AMYP) of all tested materials increased with an increase in the plug height and punch speed. AMYP appeared to depend on the material type and punch speed. Not all materials fit the Shaxby–Evans relationship at such low compression forces (less than 250 N). Only SMCC 90, SMCC HD90 and anhydrous lactose data fit the equation at both punch speeds. Due to poor axial load transmission, the *R* values of all tested materials decreased with an increase in the plug height. The experimental data fit the Kawakita equation quite well. Overall, Kawakita's *b* values were inversely related to AMYP values. The maximum breaking force (MBF) of a 12 mm plug formed at a punch speed of 50 mm/s correlated well with the work of compaction, except for SMCC HD90 and SMCC X, which exhibited very high MBF values. This research demonstrated that several grades of SMCC produced plugs having higher MBF than anhydrous lactose and Starch 1500 under similar compression conditions. The apparently higher compactability of these materials at low plug formation forces may be beneficial in developing direct fill formulations for automatic capsule filling machines.

Keywords: Silicified microcrystalline cellulose; Capsule formulation; Capsule filling machine; Simulator; Plug; Compaction

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1. Introduction

Common diluents for capsules include starch and lactose; magnesium and calcium carbonate, calcium phosphate and microcrystalline cellulose (MCC) are also used as fillers (Jones, 1995; Patel and Podczeck, 1996). Forms of these common fillers that have been physically modified to en-

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hance their flowability and compactibility are particularly advantageous in developing direct-fill formulations for automatic capsule filling machines. Examples of such physically modified fillers include pregelatinized starch (e.g. Starch 1500), spray processed a-monohydrate lactose (e.g. Fast-Flo Lactose), directly compressible grades of anhydrous lactose, and unmilled dicalcium phosphate dihydrate (Ditab; Emcompress). The property of compactibility is particularly important when developing direct-fill formulations for machines that function by forming and ejecting compressed powder plugs into capsule shells. Such machines include dosator machines (e.g. Zanasi, MG2) and dosing disc machines (e.g. Hofliger Karg and Bosch GKF models). Dosator machines in particular can benefit from compactible fillers as their presence in the blend can help prevent powder loss from the end of the cylinder during the transfer of plugs from the powder bed to the ejection station and into the shell. In such cases, particularly when formulating for larger dose, poorly compactible drugs, the higher compactibility of MCC may be of particular benefit.

Since its introduction in the 1960s, MCC has been of great benefit to formulation scientists in developing oral solid dosage forms. However, its relatively low bulk density, relatively poor flow characteristics and lubricant sensitivity have been viewed as limitations. Various grades of MCC with different particle size, density and moisture content have been developed in an attempt to address these issues. One alternative approach is silicified microcrystalline cellulose (SMCC), which is manufactured by coprocessing microcrystalline with 2% silicon dioxide, and designed to combine the exceptional compactibility of MCC with enhanced fluidity and density. Sherwood and Becker have compared the direct-compression tableting performance of SMCC 90 with a regular grade of MCC (Avicel PH102) having similar particle size and density. SMCC 90 was ∼10–40% more compactible than the regular MCC in the absence of drug. SMCC 90 also showed a lower lubricant sensitivity, and retained ∼2–3 times the compactibility of the comparable MCC grade in a blending time study (Sherwood and Becker, 1998). An additional report has shown that colloidal silicon dioxide does not affect the dissolution rate of drug formulated with SMCC in capsule formulations when compared with the same drug formulated using a non-silicified grade of MCC (Emcocel 90M) (Guo and Augsburger, 2001). Since SMCC has been reported to have greater compactibility, less lubricant sensitivity, better flowability and higher density than the regular MCC (Edge et al., 2000), SMCC could be a highly suitable alternative excipient for capsule formulations. The present study is part of a larger effort aimed at testing that hypothesis. In this paper, the basic plug formation properties of SMCC are studied and compared with Starch 1500, anhydrous lactose (direct tableting grade) and non-SMCC in direct-fill formulations. Two main particle size grades of MCC are in widespread use, although other grades may be available from various sources. Avicel PH101, Avicel PH103 and Emcocel 50 have a typical particle size of about 50 μm and are representative of the relatively smaller particle size group. Avicel PH102 and Emcocel 90M (both having a typical particle size of about 90 μm) are representative of the relatively larger particle size group. The larger particle size group is often preferred in direct compression tableting and direct-fill encapsulation. The larger particle size favors flow, lower weight variation and reduced adhesion to dosator surfaces (Patel and Podczeck, 1996). Thus, a member of that group, Emcocel 90M, was selected for comparison in this study.

2. Materials and method

2.1. Materials

MCC (Emcocel 90M), SMCC (Prosolv SMCC 50, SMCC 90, SMCC HD90 and an experimental grade of SMCC (SMCC X, which has the similar particle size distribution as SMCC 50, but a higher density) were supplied by Penwest Pharmaceuticals Co (Patterson, NY). Starch 1500 (particle size distribution: 30–150 μm, median diameter 52 μm) (Colorcon, West Point, PA) (Wade and Weller, 1994), anhydrous lactose (particle size distribution: 75 (15–30%), 100 (75–90%) and 150 μm (85–93%)) (direct tableting grade, Quest International, Hoffman Estates, IL) (Wade and Weller, 1994), and magnesium stearate (Mallinckrodt, St. Louis, MO) were also used.

2.2. Compression protocol

Compaction studies were performed using a compaction simulator (Mand Testing Machines Ltd, Stourbridge, UK) located at GlaxoSmithKline Laboratories (King of Prussia, PA), which has been described previously (Cropp et al., 1991). The simulator was equipped with custom-made round, flat-faced, 5.71 mm diameter tooling that was fabricated to match size #1 tamping pins of a piston-tamp type automatic capsule filling machine, in the manner described by Heda et al. (1999). A piezoelectric load cell (Model #9021, Serial #447889, Kistler Instrument Inc, Amherst, NY) was used for the calibration of the upper and lower punch force instrumentation. The output of the force transducers was found to be linear in the 0–1000 N range with a resolution of 0.16 N. The displacement transducers provided a linear response over the entire in-die throw of the punches with a resolution of 3.2 μm.

A single-ended saw-tooth waveform was used to manufacture plugs at constant punch velocities of 1 and 50 mm/s. A punch velocity of 50 mm/s is within the range of tamping-pin or dosator piston speeds in compression for some filling machines. An Hofliger and Karg (H&K) GKF 330 exhibited nearly 100 mm/s (Cropp et al., 1991), which is about three times that recorded for a Zanasi LZ-64 (Mehta and Augsburger, 1981). Plugs with different heights (6, 8 and 12 mm) were made. The die was lubricated with a cotton swab dipped in a saturated solution of magnesium stearate in acetone before it was filled with powder. The compression force was restricted to less than 250 N, as normal capsule filling operations are not expected to exceed that value. The solid fraction within any material was kept constant and fill weight was appropriately adjusted to obtain the plugs of specific heights. The true density of the tested materials was measured by using a multivolume helium pycnometer (Model 1305, Micromeritics, Norcross, GA). The values are 1.55 g/cm^3 for SMCC 50, 1.55 g/cm^3 for SMCC X, 1.54 g/cm^3 for SMCC 90, 1.55 g/cm^3 for SMCC HD90, 1.53 g/cm^3 for Emcocel 90M, 1.47 g/cm^3 for Starch 1500 and 1.55 g/cm^3 for anhydrous lactose. Each set of experiments was repeated three times, and the means are reported.

2.3. Flowability measurement

The minimum orifice diameter of each material was measured by using a Flodex tester (model 211, Hanson Research Corporation, Northridge, CA), and the result is shown in Fig. 1. All tested materials were sieved through #60 screen, and then charged into the apparatus from a hopper

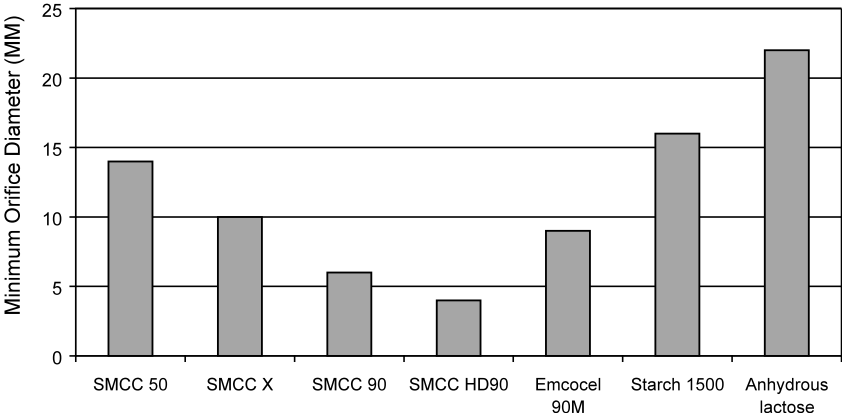

Fig. 1. Minimum orifice diameter of seven tested excipients

with hopper angle of 60° until a powder bed height of 7 cm was reached. The means of three measurements are reported.

2.4. Maximum breaking force measurement

The maximum resistance of plugs to breaking in a three-point flexure test, taken as a measure of plug mechanical strength, was determined in the manner described previously (Shah et al., 1986). A vertically mounted motor-driven mechanical slide assembly (Unislide model B4009P20J, Velmex Inc, Bloomfield, NY) was used as the platform to hold the plug. The transducer is a piezoelectric load cell (Kistler model 9712A5, Kistler Instruments). The assembly provided a range of 2000 g with ±1 g resolution. All values reported are the means of three determinations.

2.5. Data manipulation

The compaction profile generated on the compaction simulator was stored on a floppy disc using a digital oscilloscope (Model #440, Nicolet Instrument Corp, Madison WI) and later transferred to a personal computer. Low-pass Fourier transform filtering was performed on the upper and lower force data to maximize the signal to noise ratio using IGOR (WaveMetrics, Lake Osergo, OR).

Many techniques and compaction equations have been utilized to characterize the consolidation behavior of pharmaceutical solids (Celik and Marshall, 1989; Bateman et al., 1989; Cropp et al., 1991). The relationship developed by Heckel to describe the effect of pressure on densification is one of the most widely used such approaches in current literature. That relationship is described in Eq. (1) (Heckel, 1961) as follows:

$$\ln \frac{1}{1-D} = KP + A \tag{1}$$

where D is the ratio of the density of the powder mass at the pressure of P to the true density of the powder mixture (i.e. relative density). K is a material constant, which represents the resistance to volume reduction or the reduction of porosity. The reciprocal of the slope K of the Heckel plot is taken as the mean yield pressure. A is the value of the intercept of the straight line and is a function of the initial bulk volume.

In addition to the Heckel analysis, several other techniques may be used to characterize powder compression. The Kawakita equation (Kawakita and Ludde, 1970/1971) describes the relationship between volume reduction and applied pressure as follows:

$$\frac{P}{C} = \frac{P}{a} + \frac{1}{ab} \tag{2}$$

where P is the applied pressure, V_0 is the initial bulk volume, V is the volume at pressure of P, and a and b are constants characteristic of the powder being compressed. C is the degree of volume reduction, as defined in Eq. (3).

$$C = \frac{V_0 - V}{V_0} \tag{3}$$

Shaxby and Evans developed Eq. (4) (Shaxby and Evans, 1923) that describes how the applied force transfers through a column of powder in a die, such as occurs when powder undergoes compression to form a tablet or a capsule plug.

$$\frac{F_L}{F_U} = \exp\left(-\frac{4HK}{D}\right) \tag{4}$$

F_L is the low punch force, F_U is the upper punch force, H is the height of plug, D is the plug diameter, and K is the material-specific constant.

A method to represent the state of lubrication is the R value, which is the ratio of the peak upper punch force to the peak lower punch force (Nelson et al., 1954) as represented in Eq. (5).

$$R = \frac{\text{Peak } F_L}{\text{Peak } F_U} \tag{5}$$

The value of R indicates how completely the force applied to the upper punch transfers through a column of powder undergoing die compression. Values less than one indicate incomplete force transmission, which is attributed to friction between the confining surface (die wall) and the material undergoing compression.

Table 1
Summary of peak upper/lower punch force, lubrication coefficient and AMYP at punch speed of 1 mm/s

Material type	Plug height (mm)	Peak F_U (N)[a]	Peak F_L (N)[b]	R value	AMYP (MPa)
SMCC 50	6	127.5 (33.1)[c]	88.0 (34.6)	0.69 (0.093)	27.0 (2.02)
	8	101.2 (7.94)	60.6 (4.58)	0.60 (0.089)	29.0 (2.88)
	12	127.0 (1.60)	76.1 (5.2)	0.60 (0.048)	34.7 (0.99)
SMCC X	6	191.7 (43.0)	149.9 (35.9)	0.78 (0.014)	35.1 (1.49)
	8	171.5 (18.6)	120.2 (15.1)	0.70 (0.013)	38.2 (3.83)
	12	217.6 (8.4)	146.1 (9.8)	0.67 (0.026)	48.9 (2.51)
Emcocel 90M	6	149.6 (21.8)	108.2 (12.3)	0.73 (0.028)	38.7 (7.63)
	8	198.1 (20.1)	145.1 (18.8)	0.73 (0.028)	39.7 (0.64)
	12	206.1 (4.2)	130.9 (5.7)	0.63 (0.015)	44.9 (3.38)
SMCC 90	6	196.3 (34.2)	152.5 (31.3)	0.77 (0.039)	35.4 (1.52)
	8	188.8 (20.8)	132.4 (21.5)	0.70 (0.039)	37.1 (3.65)
	12	184.5 (12.5)	110.9 (14.5)	0.60 (0.040)	39.3 (0.87)
SMCC HD90	6	220.7 (40.3)	165.7 (34.6)	0.75 (0.028)	34.4 (4.82)
	8	194.7 (34.9)	139.1 (36.8)	0.71 (0.062)	35.0 (4.67)
	12	213.8 (21.9)	135.1 (15.9)	0.63 (0.042)	38.1 (5.24)
Anhydrous lactose	6	119.6 (30.0)	89.0 (42.1)	0.72 (0.240)	21.7 (3.03)
	8	123.8 (13.6)	69.4 (12.8)	0.56 (0.044)	23.2 (0.61)
	12	122.0 (11.3)	52.6 (8.6)	0.43 (0.038)	24.3 (1.69)
Starch 1500	6	226.5 (16.6)	167.8 (22.0)	0.74 (0.047)	29.1 (0.68)
	8	220.9 (30.9)	155.2 (19.5)	0.71 (0.052)	29.2 (0.21)
	12	198.7 (20.6)	92.6 (74.6)	0.66 (0.055)	32.7 (2.34)

[a] Upper punch force.

[b] Lower punch force.

[c] Numbers in parentheses represent standard deviation; $n = 3$.

3. Result and discussion

As shown in Tables 1 and 2, R values decreased with an increase in plug height for all tested materials. Even though the die was prelubricated with magnesium stearate, the friction at the die wall is still significantly large, leading to reduced axial load transmission. Plugs with greater height exhibit greater force lost in overcoming friction at the die wall (i.e. lower R values) because of their greater contact area with the confining surface. Direct-fill capsule formulations are typically lubricated to facilitate plug ejection. The lubricant also should increase axial load transmission during plug formation. A relatively high axial load transmission indicates the formation of more uniformly compressed plugs which should favor the formation of a stable arch over the open end of the dosator. A stable arch is required to prevent material loss when the dosator is being positioned over the open capsule body (Jolliffe et al., 1980). However, too much lubricant could be a detriment if plugs can prematurely slip from the dosator tube (Tattawasart and Armstrong, 1997), or the plugs become too soft to eject cleanly.

At plug heights of 8 and 12 mm, most R values decreased as speed increased from 1 to 50 mm/s. For the 6 mm plugs, the data were largely mixed, with several R values increasing with punch speed, and others decreasing with punch speed. Since the coefficient of friction between two bodies in motion relative to one another tends to decrease with increased velocity of sliding (Adamson, 1967), it could be expected that R values would generally increase with punch speed. For shorter plugs, where R values are already relatively high, the effect may be less discernable. Other phenomena affected by increasing punch speed, such as decreased time for particle rearrangement and packing, may modify the development of friction at die wall surfaces. Furthermore, such properties as particle size and size distribution, particle shape and texture and deformation properties, which differ among the materials tested, can affect the way materials respond to increased piston speed.

The reciprocal of the slope, K, of the linear portion of the Heckel plot is taken as the mean yield pressure of the material. Since the aim of the present research is to study the compression of excipients in a low force range (less than 250 N), it is more appropriate to consider the reciprocal of K as an apparent mean yield pressure (AMYP) (Heda et al., 1999). At such low compression forces, this value is most likely a measure primarily of resistance to particle rearrangement and packing during plug compression, and undoubtedly includes any frictional resistance to powder bed volume reduction that develops at the die wall.

An examination of Tables 1 and 2 reveals that AMYP tends to increase as punch speed changes from 1 to 50 mm/s. An increase in AMYP with speed was also reported by Heda et al. (1999) who suggested that the resistance of the bed to compression increases at higher speed because there is less time available for particle rearrangement and repacking. AMYP also tends to increase as piston height increases, reflecting the compression of greater masses and the greater plug contact area with the die wall at which friction must be overcome. When the punch speed increased from 1 to 50 mm/s, the AMYP of all tested materials increased, but to different degrees. Any reduction in die wall friction that may occur at higher punch speed, as suggested by the R values, appears to be largely overwhelmed by the increased resistance to

Table 2
Summary of peak upper/lower punch force, lubrication coefficient and AMYP at punch speed of 50 mm/s

Material	Plug height (mm)	Peak F_U (N)[a]	Peak F_L (N)[b]	R value	AMYP (MPa)
SMCC 50	6	171.6 (26.6)[c]	121.4 (15.9)	0.71 (0.051)	42.9 (1.41)
	8	107.9 (7.1)	58.9 (3.0)	0.55 (0.067)	46.0 (2.84)
	12	159.9 (18.7)	76.9 (19.2)	0.48 (0.113)	47.5 (5.62)
SMCC X	6	223.1 (6.8)	175.5 (3.5)	0.79 (0.010)	48.8 (3.19)
	8	202.0 (20.5)	131.1 (19.1)	0.65 (0.037)	49.9 (3.70)
	12	262.0 (13.5)	138.2 (18.6)	0.53 (0.046)	63.6 (0.85)
Emcocel 90M	6	222.2 (16.5)	162.6 (13.5)	0.73 (0.014)	44.5 (0.60)
	8	221.6 (21.3)	147.9 (19.0)	0.67 (0.038)	47.1 (1.63)
	12	233.1 (24.9)	117.5 (13.8)	0.50 (0.025)	47.3 (0.91)
SMCC 90	6	211.9 (25.8)	159.2 (31.1)	0.75 (0.054)	35.6 (0.64)
	8	222.3 (4.9)	154.0 (6.8)	0.69 (0.032)	40.8 (1.24)
	12	221.6 (24.6)	109.5 (11.9)	0.49 (0.014)	43.0 (1.75)
SMCC HD90	6	235.2 (19.8)	181.0 (12.2)	0.77 (0.014)	50.8 (2.25)
	8	250.0 (7.2)	166.5 (16.7)	0.67 (0.048)	51.4 (0.76)
	12	258.2 (19.1)	133.6 (7.3)	0.52 (0.012)	51.8 (1.16)
Anhydrous lactose	6	138.2 (21.4)	92.4 (22.8)	0.66 (0.078)	28.7 (3.04)
	8	160.1 (11.5)	93.4 (3.8)	0.58 (0.032)	30.9 (0.24)
	12	151.4 (8.8)	71.0 (5.3)	0.47 (0.031)	31.0 (1.94)
Starch 1500	6	161.1 (2.6)	150.8 (6.9)	0.94 (0.039)	39.2 (1.62)
	8	196.2 (17.1)	126.5 (49.0)	0.63 (0.207)	44.2 (2.73)
	12	209.0 (5.5)	127.7 (16.6)	0.61 (0.064)	50.3 (0.88)

[a] Upper punch force.

[b] Lower punch force.

[c] Numbers in parentheses represent standard deviation; $n = 3$.

Table 3
Kawakita constant *a* and *b* at plug height of 6 mm

Material	Punch speed (mm/s)	*a*	*b* (MPa^{-1})
Starch 1500	1	0.30 (0.029)[a]	7.80 (5.86)
Anhydrous lactose	1	0.39 (0.009)	4.57 (2.36)
SMCC 50	1	0.40 (0.004)	1.61 (0.50)
SMCC X	1	0.35 (0.014)	1.99 (0.80)
Emcocel 90M	1	0.36 (0.030)	1.61 (0.93)
SMCC 90	1	0.51 (0.010)	0.39 (0.09)
SMCC HD90	1	0.41 (0.012)	0.70 (0.10)
Starch 1500	50	0.40 (0.006)	2.40 (0.34)
Anhydrous lactose	50	0.40 (0.004)	2.73 (0.25)
SMCC 50	50	0.48 (0.008)	0.62 (0.16)
SMCC X	50	0.43 (0.001)	0.76 (0.04)
Emcocel 90M	50	0.56 (0.002)	0.26 (0.02)
SMCC 90	50	0.52 (0.008)	0.35 (0.06)
SMCC HD90	50	0.49 (0.009)	0.40 (0.02)

[a] Numbers in parentheses represent standard deviation; $n=3$.

compression that develops in the powder bed. MCC and SMCC exhibited a higher percentage increase in AMYP with punch speed than anhydrous lactose.

The Kawakita equation describes the relationship between the applied pressure and volume reduction. In the case of piston compression, the constant *a* is said to be equal to the initial porosity and the constant *b* is considered to be related to the forces that resist compression (Kawakita and Ludde, 1970/1971). The experimental data in Table 3, Table 4, and Table 5 reveal that, regardless of punch speed or plug height, the values of *a* are somewhat consistent for given materials. Ideally, there should be no differences in initial porosity for a given material. Any differences actually found are likely attributable to experimental technique, owing to the difficulty in filling powders having a range of flow properties into small-diameter die cavities. Most discrepancies are noticeable for the 12 mm plugs which were the most difficult to fill uniformly.

If the Kawakita constant *b* is related to the forces resisting compression, its value must be reflective of the interparticle friction and cohesion that resist repacking and densification and of the frictional resistance that develops at the die wall during compression. Therefore, *b* should provide the same general information as AMYP. However, it is important to recognize that *b* and AMYP should be inversely related. Eq. (2) can be rearranged as follows:

$$b = \frac{C}{P}\left(\frac{1}{a-C}\right) \tag{6}$$

Eq. (6) indicates that *b* is inversely related to *P* and will have units of (pressure)$^{-1}$. Moreover, it is apparent that the greater the pressure required to cause a given increase in the relative volume reduction, *C*, the smaller will be *b*. Indeed, overall, *b* values were inversely related to AMYP values. When punch speed was increased from 1 to 50 mm/s, all Kawakita *b* values decreased, indicating greater resistance to compression. The

Table 4
Kawakita constant *a* and *b* at plug height of 8 mm

Material type	Punch speed (mm/s)	*a*	*b* (MPa^{-1})
Starch 1500	1	0.27 (0.01)[a]	7.29 (1.11)
Anhydrous lactose	1	0.29 (0.01)	5.35 (1.86)
SMCC 50	1	0.33 (0.01)	1.92 (0.16)
SMCC X	1	0.37 (0.01)	0.82 (0.22)
Emcocel 90M	1	0.66 (0.18)	0.16 (0.06)
SMCC 90	1	0.51 (0.01)	0.26 (0.04)
SMCC HD90	1	0.45 (0.01)	0.33 (0.06)
Starch 1500	50	0.32 (0.01)	2.92 (0.39)
Anhydrous lactose	50	0.35 (0.01)	1.57 (0.23)
SMCC 50	50	0.37 (0.01)	1.33 (0.19)
SMCC X	50	0.41 (0.01)	0.50 (0.06)
Emcocel 90M	50	0.54 (0.02)	0.19 (0.03)
SMCC 90	50	0.70 (0.03)	0.11 (0.01)
SMCC HD90	50	0.49 (0.04)	0.21 (0.04)

[a] Numbers in parentheses represent standard deviation; $n=3$.

Table 5
Kawakita constant *a* and *b* at plug height of 12 mm

Material type	Punch speed (mm/s)	*a*	*b* (MPa^{-1})
Starch 1500	1	0.22 (0.00)[a]	2.50 (0.68)
Anhydrous lactose	1	0.30 (0.01)	1.33 (0.26)
SMCC X	1	0.39 (0.04)	0.21 (0.02)
SMCC 50	1	0.47 (0.11)	0.28 (0.10)
Emcocel 90M	1	0.75 (0.12)	0.07 (0.02)
SMCC 90	1	0.71 (0.02)	0.09 (0.01)
SMCC HD90	1	0.79 (0.07)	0.07 (0.00)
Starch 1500	50	0.27 (0.00)	1.26 (0.09)
Anhydrous lactose	50	0.32 (0.01)	0.69 (0.04)
SMCC 50	50	0.38 (0.02)	0.37 (0.08)
SMCC X	50	0.42 (0.01)	0.17 (0.01)
Emcocel 90M	50	0.54 (0.04)	0.11 (0.02)
SMCC 90	50	0.60 (0.04)	0.10 (0.01)
SMCC HD90	50	0.56 (0.05)	0.10 (0.02)

[a] Numbers in parentheses represent standard deviation; $n=3$.

rank ordering among plug lengths appeared to be largely retained, but not that of the materials, except that Starch 1500 and anhydrous lactose consistently exhibited the highest *b* values. Generally, Starch 1500 and anhydrous lactose exhibited substantially higher *b* values and lower AYMP values than the other materials tested, regardless of plug height or punch speed.

At the 50 mm/s punch speed, SMCC HD90, SMCC 90, SMCC X, anhydrous lactose and Emcocel 90M seem to obey the Shaxby–Evans relationship, as may be seen in Fig. 3. At the 1 mm/s punch speed, only SMCC HD90, SMCC90 and anhydrous lactose data are fit by the Shaxby–Evans equation (Fig. 4). The Starch 1500 data did not fit the Shaxby–Evans equation at either punch speed. This result differs from that of Heda et al. (1999) in that at the punch speed of 10 mm/s, Avicel 102, anhydrous lactose and Starch 1500 fit Shaxby–Evans equation very well. Since the compression force employed in the present study (~ 250 N) is much lower than that used by Heda et al. (~ 500 N), the current data may have been more sensitive to small variations in the initial bulk density of powders as filled into the die.

The maximum breaking force (MBF) of 12 mm plugs made at the 50 mm/s punch speed was measured and compared with the work done in forming the plugs. Of all materials tested, Starch 1500 and anhydrous lactose exhibited the lowest values of MBF, which were unmeasurable for Starch 1500 and 0.16 N for anhydrous lactose. This observation parallels the rank order of the compactability of MCC, Starch 1500, and lactose in tableting (Doelker, 1993). Starch 1500 and anhydrous lactose also exhibited the lowest values

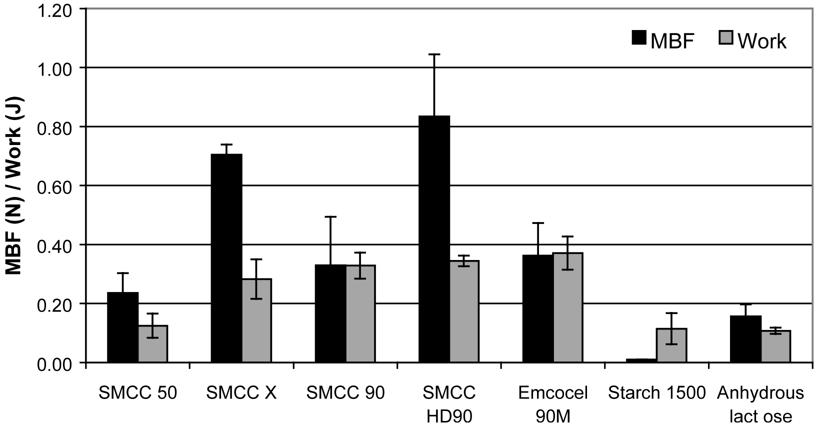

Fig. 2. Compaction work and MBF at punch speed of 50 mm/s and plug height of 12 mm.

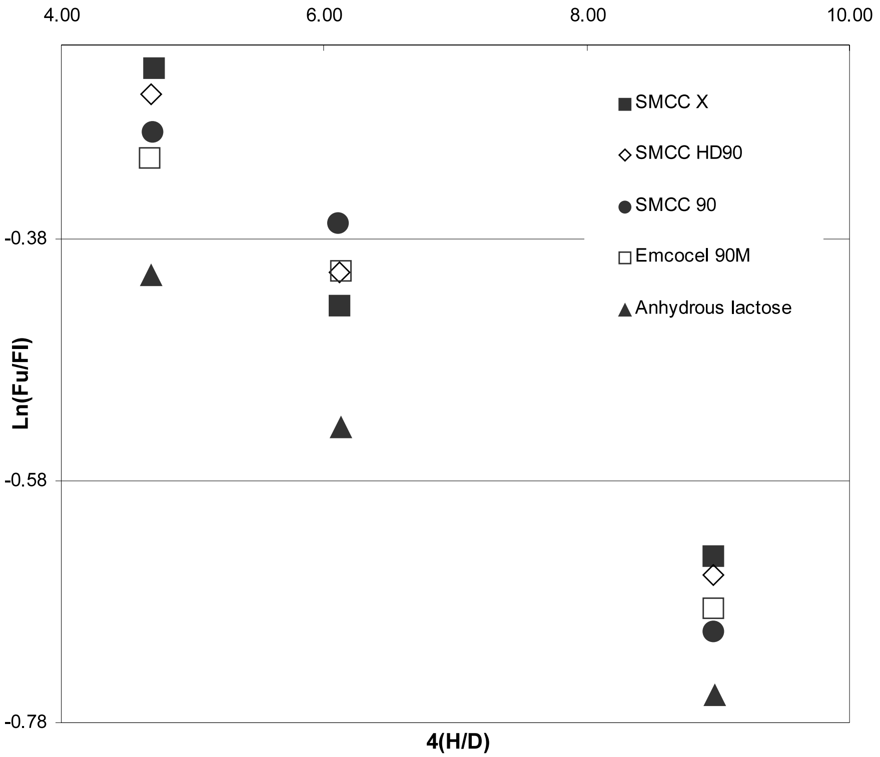

Fig. 3. Shaxby–Evans plot at punch speed of 50 mm/s.

of work done in compaction (Fig. 2). These results suggest that SMCC and MCC could achieve the same ‘low’ compaction of Starch 1500 and anhydrous lactose with lower compression force and work input.

It was reported that there are no significant differences in the particle size and distribution, porosity and crystallinity of the cellulose in Emcocel 90M and SMCC 90, except the surface topography (Tobyn et al., 1998). Silicification changes the surface topography of MCC as the silicon dioxide appears to be primarily located in the surface of SMCC particles (Edge et al., 2000). Additionally, the surface roughness is reported to influence interfacial adhesion in MCC/MCC laminates (Karehill et al., 1990). Based on such observations, Edge et al. suggest that such surface effects could be the reason for the higher compactability of SMCC in tableting. Under different compression conditions, SMCC compacts always showed higher tensile strength than MCC. Examination of the failure surfaces using scanning electron microscopy revealed that failure primarily occurred at the interparticle interfaces (Edge et al., 2000). This result indicated that the strength enhancement of SMCC might be a consequence of an interfacial interaction rather than a modification of bulk MCC properties, but to what extent such a phenomenon may contribute to plug MBF is not known.

It is well documented that SMCC 90 compacts show higher tensile strength than Emcocel 90M at the same compression condition. However, from Fig. 2, it was noticed that SMCC 90 did not show higher MBF than Emcocel 90M. In the present study, the compression force (~ 250 N) is very low compared to typical tableting (~ 10–20 KN). Any possible plastic deformation during plug formation is likely to be extremely limited.

The MBF correlated well with the work of compaction, except for SMCC HD90 and SMCC X, which exhibited disproportionately high

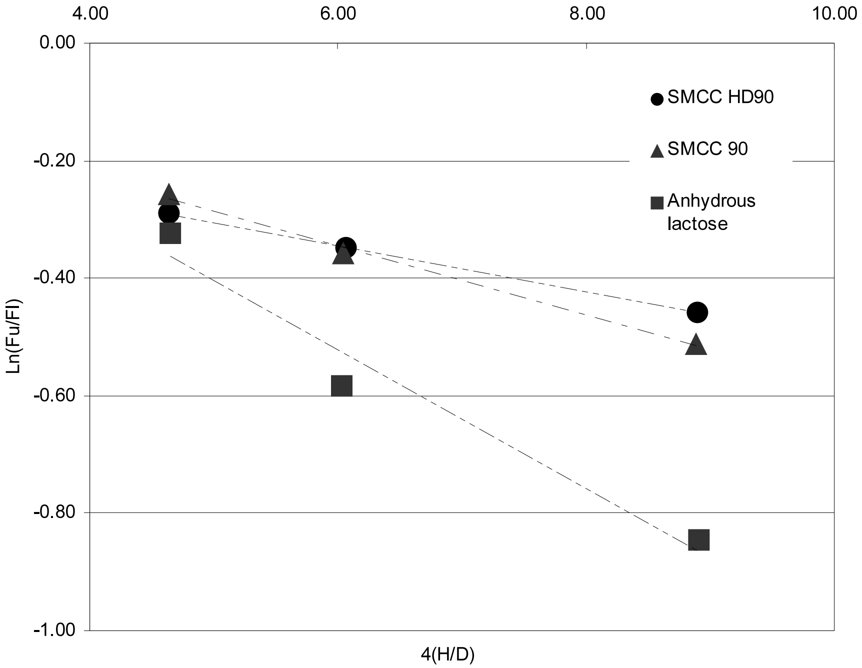

Fig. 4. Shaxby–Evans plot at punch speed of 1 mm/s.

MBFs. Plugs with higher MBF (Fig. 2) are expected to transfer to capsule shells with reduced powder loss, thereby improving weight variation and content uniformity. Except for their densities, SMCC HD90 and SMCC X have physical properties similar to SMCC 90 and SMCC 50, respectively. The apparently greater compactability of SMCC HD90 and SMCC X may be related to their higher densities and the formation of lower porosity plugs, but further studies will be required to fully explain this observation.

4. Conclusion

An investigation of the compression physics of SMCC under low compression force offered some interesting insight into the plug formation process of SMCC compared with other commonly used materials in capsule formulation. Even at low compression force, SMCC and MCC can be distinguished from Starch 1500 and anhydrous lactose by their compression properties. From Heckel analysis, the AMYPs were found to be dependent on both the punch speed and material type; SMCC and MCC materials exhibited higher values of AMYP than Starch 1500 and anhydrous lactose. These conclusions were supported by the Kawakita analysis. Additionally, at the low compression forces studied, there was evidence that the materials loading and packing in the die cavity may play an important role in the compression process. This research also demonstrated that several grades of SMCC produced plugs having higher MBF than anhydrous lactose and Starch 1500 under similar compression conditions. The apparently higher compactibility of these materials at low plug formation forces may be beneficial in developing direct-fill formulations for automatic capsule filling machines.

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