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Comparative evaluations of powder and mechanical properties of low crystallinity celluloses, microcrystalline celluloses, and powdered celluloses

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Abstract

The purpose of this study was to examine and compare the powder and mechanical properties of different batches of low crystallinity powdered cellulose (LCPC-S1 to LCPC-S5) with those of commercial microcrystalline celluloses (MCC) (Avicel PH-101, Avicel PH-102, Avicel PH-103, Avicel PH-301, Avicel PH-302, and Emcocel 90m) and powdered celluloses (PC) (Solka Floc BW-40 and Solka Floc BW-100). Both the LCPC and MCC products were aggregated powders, whereas, the PC materials showed a fibrous structure. The primary particles forming the LCPC aggregates, however, were smaller in size and showed a greater degree of coalescence between boundaries, than those forming the MCC aggregates. The LCPC materials had significantly higher bulk and tap densities and lower porosity values compared with the MCC materials. The yield pressure value calculated from the linear region of the Heckel curve for LCPC varied between 48 and 70 MPa, for Avicel and PC materials between, 80 and 106 MPa, and for Emcocel 90m was 48 MPa. These results suggest that the LCPC products and Emcocel 90m, compared with commercial MCC and PC excipients, undergo plastic deformation at relatively lower compression pressures. The total volume reduction (i.e. compressibility), determined by calculating the area under the Heckel curve (AUHC), however, was comparable for all materials, with the exception of the LCPC-S3, which owing to the low yield pressure value, showed the largest reduction in volume. With the exception of LCPC-S1 and Solka Floc BW-40, all the other materials formed compacts, whose strength ranged from about 522 to 799 MPa^2. The strengths of LCPC-S1 and Solka Floc BW-40 compacts, in contrast, were 214 and 257 MPa^2, respectively. Irrespective of the solid fraction levels, the LCPC compacts, in general, disintegrated much faster than the MCC and PC compacts. In conclusion, the results suggest that the new LCPC materials reported herein have powder properties that are quite different from the MCC and PC materials evaluated, and show clear potential as direct compression excipients.

Keywords: Low crystallinity cellulose; Cellulose excipients; Microcrystalline celluloses; Powdered celluloses; Direct compression excipients

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1. Introduction

Microcrystalline cellulose (MCC) and powdered cellulose (or microfine cellulose) (PC) are commonly and widely used in direct compression formulations as well as in dry granulations prepared by either slugging or roller compaction. MCC is produced by chemical hydrolysis of cellulose using a dilute mineral acid at boiling temperature (Battista and Smith, 1961), whereas, PC is prepared by mechanical disintegration of cellulose. Both MCC and PC are currently commercially available in different grades from various suppliers. Studies show that, depending on the nature and origin of the cellulose source and the processing variables used during their manufacture, different brands of cellulose excipients may differ in physicochemical properties, and hence, their performance as tabletting agents (Doelker et al., 1987b; Landin et al., 1993a,b; Rowe et al., 1994; Podczeck and Revesz, 1993; Pesonen and Paronen, 1986).

Recently, Wei et al., 1996; Banker and Wei, 1995 prepared a new direct compression cellulose excipient, referred to as low crystallinity powdered cellulose (LCPC), by controlled decrystallization and depolymerization of cellulose with phosphoric acid. Preliminary studies have shown that, this material is superior to Avicel PH-101 in its tabletting properties (Banker and Wei, 1995). More recently, Kumar and Kothari, 1999 investigated the effect of compressional force on the crystallinity of LCPC and various commercial MCC and PC excipients. They found that the degree of crystallinity of all materials increased at low compression pressures (5–15 MPa). The magnitude of increase in the crystallinity of LCPC, however, was lower and gradual compared with that of MCC and PC products.

In this paper, we report a comparative evaluation of powder and mechanical properties of different batches of LCPC and the most commonly and widely used commercial MCC; (Avicel PH-101, Avicel PH-102, Avicel PH-103, Avicel PH-301, Avicel PH-302, and Emcocel 90m) and PC (Solka Floc BW-40 and Solka Floc BW-100). The goal was to investigate the physicochemical properties of LCPC on its performance as a tabletting excipient, and to compare these relationships with other direct compression excipients.

2. Materials and methods

2.1. Materials

The various raw materials used for the preparation of LCPC included cotton linter sheet (Grade R270, Southern cellulose Products, Inc, Chattanooga, TN), phosphoric acid (85% w/w, Food grade, Lot No. TO 8450-061794, Monsanto Pharmaceutical Ingredients, St. Louis, MO), and acetone USP/NF (Lot no. 970721, Van Waters and Rogers Inc, Summit, IL). The MCC products previously identified were obtained from two sources: the Avicel® PH types from FMC Corporation (Philadelphia, PA) and Emcocel® type 90M from Penwest Company (Patterson, NY). The powdered celluloses, Solka Floc® BW 40 and Solka Floc® BW 100, were obtained from Penwest Company, Patterson NY. All other chemicals used were either Analytical or ACS grade and purchased from either Aldrich Chemical Co (Milwaukee, WI) or Fisher Scientific (Fair Lawn, NJ).

2.2. Methods

2.2.1. Preparation of LCPC

Two small (500 g) and three larger (3 kg) scale batches of LCPC were prepared from cotton linters and phosphoric acid (85% w/w) according to the procedure reported previously (Wei et al., 1996; Kumar and Kothari, 1999). The purified wet product obtained by this method was passed through an oscillating mill (Erweka AR 400, Heusenstamm, Ottostr, Germany), equipped with a 40 in. screen, and then dried at 30 °C in a convection oven for 4 h. The dried powder was fractionated on a Cenco-Meinzer sieve shaker (Central Scientific Co, Chicago, IL) for 1 h. The fraction that passed through a 140 mesh screen and retained on a 200 mesh screen, corresponding to an average particle size of about 90 μm, was collected and used in this study.

Commercial cellulose excipients were also fractionated and the fraction that contained the same particle size range was used.

2.2.2. Powder characterization

Morphological studies were performed by scanning electron microscopy (SEM) using a Hitachi S-4000 microscope. Photographs were taken using Polaroid films.

True density (ρ_{true}), bulk density (ρ_{bulk}), tap density (ρ_{tap}), porosity (ε), moisture content, degree of crystallinity, and degree of polymerization (DP) were determined as reported previously (Kumar et al., 2001; Kumar and Kothari 1999; Kothari, 1998).

The Hausner ratio was calculated from a ratio of tap density to bulk density.

2.2.3. Moisture sorption

Desiccators with relativity humidities of 6.4, 11.3, 21.6, 32.8, 38.2, 57.5, 68.9, 74.2, 84.3, and 93.7% were prepared using saturated aqueous solutions of LiBr, LiCl, CH_3COOK, $MgCl_2$, NaI, NaBr, KI, $NaNO_3$, KCl, and KNO_3, respectively, (Nyqvist, 1983). The cellulose samples were dried in a vacuum oven at 40 °C and at a reduced pressure of 10 μm Hg for 24 h prior to starting the moisture uptake studies. Approximately, 0.5–1.0 g of dried sample was accurately weighed and placed in various controlled relative humidity chambers maintained at 25 °C. The weight of the samples was periodically monitored until a constant weight was obtained. Typically, the samples used in this study required 10–14 days to reach equilibrium moisture content.

2.2.4. Mechanical characterization

Compacts, each weighing about 500 mg, were prepared on a Carver press over a compression force ranging from 330 to 4000 lbs, corresponding to the compression pressures of 8–106 MPa, respectively, using a 13 mm diameter die and flat-faced punches and a dwell time of 30 s. The Heckel plots were constructed by plotting the natural log of the inverse of the compact porosities (calculated from: $\varepsilon = (1 - \rho_{app}/\rho_{true})$, where ε is the porosity of the compacts, ρ_{app} is the apparent density of the compact and ρ_{true} is the true density of the particles) against the respective compression pressures. The regression analysis was performed on the linear portion of the curve. The slope values obtained were converted to yield pressures (P_y) using the relationship: $P_y = 1/\text{slope}$. The areas under the Heckel curves (AUHC) were calculated by the trapezoidal method and used as a measure of the extent of volume reduction that the material had undergone over the entire compression pressure range.

The tensile strength of the compacts was determined using the Qtest I™ (MTS, Cary, NC) universal tester and the crosshead speed (i.e. rate of load application) of 11 lbs/s, according to the method developed by Ramsey (1996). The peak load required to cause diametrical splitting of the tablet was then used to calculate the tensile strength according to the equation $\sigma_o = 2P/\pi Dt$, where σ_o is the maximum radial tensile strength, P is the applied load, D is the diameter of the compact, and t is the compact thickness (Fell and Newton, 1970). The tensile strength values were then plotted against the respective compression pressures. The area under the tensile strength versus compression pressure curve was calculated by the trapezoidal method, and used to express the compactibility of the material as has been reported by Habib et al., 1996. Tensile strength measurements were made on ten compacts prepared at each compression pressure between 8 and 107 MPa. Thus, the compactibility value reported is an average of areas of ten tensile strength versus compression pressure curves.

2.2.5. Disintegration studies

The disintegration test was performed in water at 37 °C using an Erweka GmbH apparatus (type 712, Erweka, Offenbach, Germany). The disintegration times reported are averages of six determinations.

3. Results and discussion

3.1. Characterization of powder properties

Table 1 lists the powder characteristics of various LCPC, MCC, and PC materials used in this study. The SEM photographs of these materials are shown in Fig. 1.

3.1.1. Morphology

All batches of LCPC and various MCC products used in the study consisted of aggregated powders (Fig. 1). The primary particles forming the LCPC aggregates, however, were smaller in size and showed a high degree of coalescence between boundaries compared with those forming the MCC aggregates. Further, the LCPC aggregates showed more smooth surfaces and were more densely packed than the MCC products. Among the LCPC products, LCPC-S1 showed the highest degree of coalescence between boundaries of the primary particles. Solka Floc BW-40 and Solka Floc BW-100, in contrast, are fibrous materials.

3.1.2. Degree of crystallinity

As has been reported previously (Kumar and Kothari, 1999), the diffraction patterns of LCPC show peaks due to both cellulose I (14, 16, 22° 2θ) and cellulose II (12, 20 and 22° 2θ) polymorphs, whereas MCC and PC display peaks that are characteristics of the cellulose I polymorph. The proportion of cellulose I in the product has recently been shown to decrease with increasing agitation rate during the precipitation step (Kumar et al., 2001). As noted in Table 1, the degrees of crystallinity of the LCPC products prepared on a small scale (LCPC-S1 and LCPC-S3) were 39 and 43%, whereas those prepared on a larger scale (LCPC-S2, LCPC-S4, and LCPC-S5) showed values ranging between 43 and 54%. Although,

Table 1
Powder characteristics of low crystallinity cellulose, MCC and powdered cellulose

Material	Moisture %, w/w ($n=3$)	Crystallinity % ($n=3$)	DP	Density (g/cc)			Hausner ratio	Porosity (%)
				True ($n=3$)	Bulk ($n=6$)	Tap ($n=6$)		
LCPC-S1[a]	5.50 (0.14)	39.23 (0.24)	36	1.480 (0.008)	0.695 (0.021)	0.768 (0.018)	1.10	48.08
LCPC-S2[b]	5.00 (0.02)	42.94 (1.58)	23	1.460 (0.006)	0.605 (0.008)	0.720 (0.009)	1.19	50.68
LCPC-S3[a]	6.23 (0.14)	43.25 (0.84)	31	1.430 (0.005)	0.453 (0.018)	0.548 (0.005)	1.20	61.86
LCPC-S4[b,c]	4.12 (0.23)	45.27 (1.03)	37	1.440 (0.006)	0.586 (0.007)	0.615 (0.001)	1.05	57.32
LCPC-S5[b]	6.50 (0.05)	54.06 (0.45)	41	1.447 (0.004)	0.605 (0.009)	0.722 (0.018)	1.19	50.00
Avicel® PH-101[c]	5.20 (0.09)	72.23 (2.67)[d]	207	1.577 (0.005)	0.315 (0.014)	0.410 (0.010)	1.30	74.08
Avicel® PH-102[c]	2.08 (0.08)	84.51 (2.75)[e]	194	1.526 (0.008)	0.254 (0.003)	0.276 (0.001)	1.09	81.93
Avicel® PH-103	2.71 (0.09)	71.57 (2.45)[d]	225	1.490 (0.027)	0.254 (0.003)	0.268 (0.007)	1.06	82.00
Avicel® PH-302[c]	3.47 (0.03)	74.38 (1.27)[f]	122	1.519 (0.004)	0.413 (0.005)	0.492 (0.006)	1.19	67.62
Emcocel® 90 m	4.56 (0.38)	74.29 (7.09)[g]	222	1.462 (0.015)	0.270 (0.004)	0.337 (0.005)	1.25	76.92
Solka Floc® BW 40	5.18 (0.14)	72.70 (3.45)	758	1.483 (0.033)	0.141 (0.003)	0.261 (0.004)	1.85	82.40
Solka Floc® BW 100[c]	5.72 (0.43)	44.68 (0.02)[h]	667	1.429 (0.018)	0.268 (0.013)	0.376 (0.012)	1.40	73.66

[a] Prepared using 500 g of cotton linter and 5 l of H_3PO_4.
[b] Prepared using 3 kg of cotton linter and 30 l of H_3PO_4.
[c] Taken from Kumar and Kothari (1999).
[d] Literature value 61.8–82% (Doelker, 1993; Doelker et al., 1987a; Sottys et al., 1984; Rowe et al., 1994).
[e] Literature value 62.4–80.1 (Doelker, 1993; Sottys et al., 1984; Rowe et al., 1994).
[f] Literature value 63.5–73.8% (Rowe et al., 1994; Sottys et al., 1984).
[g] Literature value 64.4 (Rowe et al., 1994).
[h] Literature value 49% (Doelker et al., 1987a)
Numbers in parenthesis represent the standard deviations of n determinations.

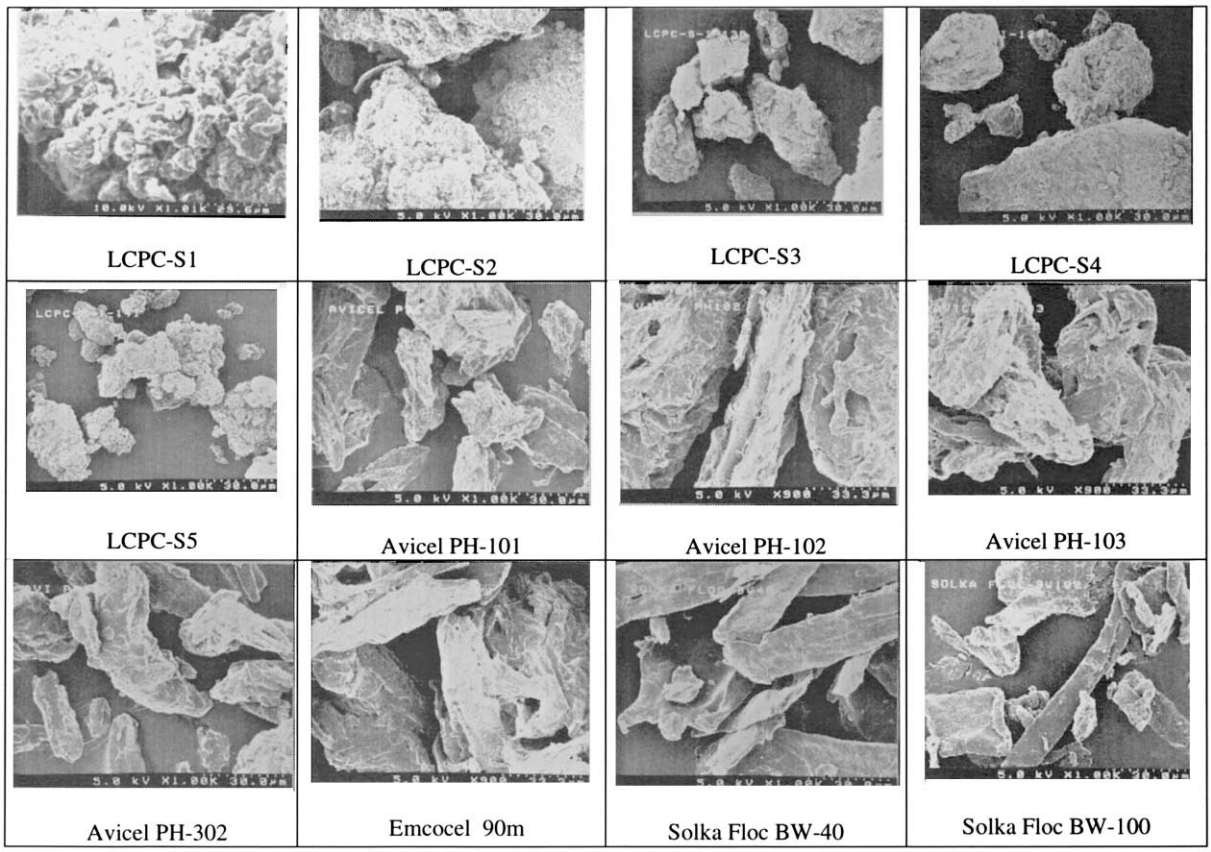

Fig. 1. SEM of LCPC, MCC, and PC materials.

LCPC-S2 and LCPC-S3 had the same crystallinity values, the relatively higher values obtained for LCPC-S4 and LCPC-S5 suggest that the agitation rate (700 rpm) employed during the precipitation step was not adequate to prevent the cellulose chains from aligning themselves, hence increasing the crystallization of these cellulose materials.

The degree of crystallinity of the MCC products varied from 70 to 85%. In the literature, the crystallinity values for some of these materials have been reported to range between 61.8 and 82% (Rowe et al., 1994; Doelker, 1993; Doelker et al., 1987a; Sottys et al., 1984). The differences among the literature values for the crystallinity of MCC, and also between the literature values and those reported in this study, can be attributed to the different data manipulations used in evaluating the degree of crystallinity as well as the batch-to-batch variability among the products themselves.

The degrees of crystallinity of Solka Floc BW-40 and Solka Floc BW-100 were 73 and 45%, respectively. As supplied, these materials have an average particle size of 60 and 40 μm, respectively. Thus, the greater extent of mechanical disintegration to produce the smaller particles of Solka Floc® BW 100 may account for its lower crystallinity compared with that of Solka Floc® BW 40. The crystallinity values for several other brands of PC have been reported to be between 30 and 60% (Doelker et al., 1987a).

3.1.3. Degree of polymerization

The DP of the LCPC products, as determined by the viscosity method, ranged from 23 to 40, whereas MCC products (Avicels and Emcocel)

showed values between 122 and 225. Solka Floc BW-45 and BW-100, in contrast, had DP values of 758 and 667, respectively. This difference in the DP of LCPC, MCC, and PC products can be attributed to the different methods employed in their manufacture. As noted above, LCPC is prepared by reacting cellulose with phosphoric acid. In the process, cellulose initially swells and subsequently dissolves in the acid, causing complete destruction of the cellulose crystallinity. The latter makes all the anhydroglucose ether linkages in the cellulose chains accessible for hydrolysis, and consequently, the preparation of low DP products. In the case of MCC, which is produced from a reaction between cellulose and a dilute mineral acid, no specific decrystallization step is involved. Therefore, only amorphous regions of the starting cellulose material are hydrolyzed, producing highly crystalline level-off DP products. In general, MCC products prepared from native cellulose fibers show a DP value between 113 and 300, whereas, those produced from regenerated celluloses have a DP value ranging from 25 to 60 (Battista and Smith, 1961; Doelker et al., 1987a). Powdered celluloses, in contrast, are produced by mechanical disintegration of cellulose and typically show DP values in the range between 517 and 784 (Doelker et al., 1987a).

3.1.4. Densities and porosity

The true density of the LCPC products, compared with that of the Avicel products, was lower, ranging between 1.440 and 1.480 g/ml (vs. 1.490–1.577 g/ml for MCC). Emcocel 90m had a true density value of 1.462 g/ml. Among LCPC products, LCPC-S1 had the highest true density value (1.480 g/ml). This is attributed to increased coalescence of LCPC-S1 particles (Fig. 1), causing a decrease in the surface volume and consequently, an increase in the true density value.

The bulk and tap densities of LCPC products were higher than that of MCC or PC. This is attributed to their low porosity values, ranging from about 45 to 60% versus between 68 and 82% obtained for MCC and PC. The bulk density gives an estimate of the ability of a material to flow from a hopper into the die cavity of a rotary compression machine, whereas, the tap density is a measure of how well a powder can be packed in a confined space on repeated tapping. In general, the higher the bulk and tap densities, the better the potential for a material to flow and to rearrange under compression. The Hausner ratio, which is the quotient of tap and bulk densities, has also been used to predict the flowability of a material (Wells, 1988). According to Wells, a value of less than 1.20 indicates good flowability of a material, whereas, a value of 1.5 or higher suggests the material will have poor flow properties. In this study, with the exception of Avicel PH-101, Emcocel 90m, and Solka Floc BW grade products, all the materials studied showed the Hausner ratio values equal to or below 1.20, suggesting that these materials possess good flowability. Since all materials evaluated, had the same average particle size, these results further suggest that factors other than particle size, such as moisture content and particle irregularity, which can cause bridging and lump formation during actual production operations, would contribute to the flow properties of these materials.

The bulk and tap density values calculated for the MCC materials in this study are comparable to those reported in the literature (Siaan et al., 1997, 1998). PCs are known to flow poorly and are seldom used alone in a direct compression formulation (Podczeck and Revesz, 1993; Bolhuis, 1996). Different tap density values seen for various cellulose excipients in this study are primarily due to the differences in their intra-particle porosity and particle shape, which can affect the slippage of the particles over one another and into the voids within the powder bed.

3.1.5. Moisture content

The moisture content of the LCPC products varied between 4.12 and 6.50%, whereas, commercial MCC products had a moisture content value between 2.08 and 4.58%. Solka Floc BW-40 and Solka Floc BW-100, in contrast, contained 5.18 and 5.72% moisture contents, respectively. Several investigators have observed a direct relationship between moisture content and degree of crystallinity of cellulose excipients. In this study, however, no such relationship between the two variables was noted (Fig. 2). The results obtained,

however, do show that, at ambient temperature, cellulose excipients with a degree of crystallinity of 55% or less, in general, show a high moisture content than those having a crystallinity value above 70%. This is because the lower the degree of crystallinity the larger the number of free hydroxyl groups available for interaction with water molecules. The variability seen in the moisture content values among the various low or high crystallinity cellulose products suggest that not only the degree of crystallinity, but also the accessibility of the adsorption sites to water molecules, determines the final moisture content value of the cellulose excipients.

3.1.6. Moisture uptake studies

Fig. 3 shows the moisture sorption isotherms for the selected LCPC (LCPC-S1, LCPC-S4, LCPC-S5) and MCC (Avicel PH-102, and Avicel PH-302) products. The crystallinity of these materials covers the range between 39 and 74%, whereas, the porosity value varied from 48 to 82% (Table 1). As can be seen in Fig. 3, all of the materials show Type II isotherms. Compared with the LCPC products, Avicel® PH-102 and Avicel® PH-302 showed a much sharper inflection point, at 30 and 11% relative vapor pressures, respectively. The isotherms for the LCPC materials are relatively smoother throughout the entire relative vapor pressure region. Zeronian et al. (1983) reported that a correlation exists between the amorphous content of cellulose and the number of molecules of water adsorbed per anhydroglucose unit when a monomolecular layer of water was formed on the samples (W_m). However, in this study, no correlation between these two parameters was observed. The similarity seen in the moisture sorption behavior of the materials used in this study may be attributed to a net balance between the crystallinity and porosity (surface area) of these two materials. The moisture sorption isotherm for Avicel® PH-102 is in good agreement with that reported in the *Handbook of Pharmaceutical Excipients* (Mathur, 1986).

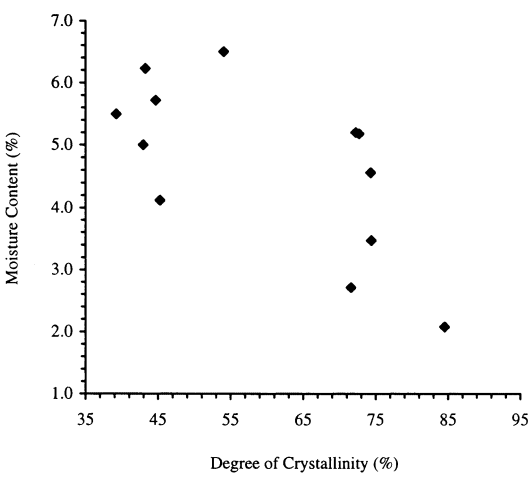

Fig. 2. Correlation between moisture content and percent crystallinity.

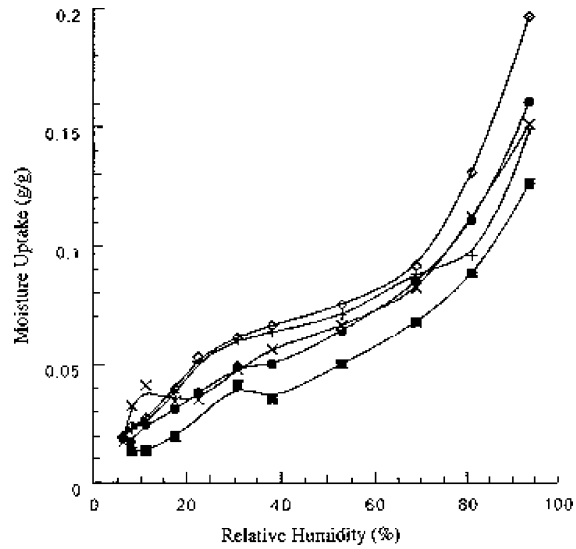

Fig. 3. Moisture sorption isotherms of LCPC-S1 (◇), LCPC-S4 (+), LCPC-S5 (●), Avicel PH-102 (■), and Avicel PH-302 (×).

3.2. Mechanical properties

The Heckel plots for different batches of LCPC and different grades of MCC, and PC excipients are shown in Fig. 4 and Fig. 5. Table 2 lists the compression pressure range over which the regression analysis was performed, the regression analysis results, and the yield pressure (P_y) values were calculated using the relationship 1/slope. As noted in Table 2, for all products, the range of compres-

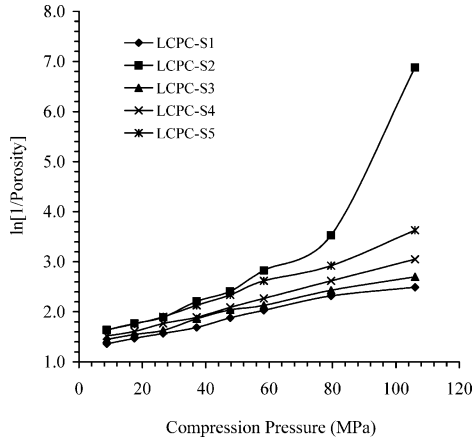

Fig. 4. Heckel plots for LCPC excipients.

sion force over which the ln(1/porosity) function showed a linear relationship varied from material to material. A careful examination of the Heckel plots shows that the MCC and PC products, compared with the LCPC products, displayed two linear regions interrupted by a short plateau (Avicel PH-102, Avicel PH-103, and Avicel PH-302) or identified by a change in the slope of the line (Avicel PH-101, Emcocel 90m, Solka Floc BW-40 and Solka Floc BW-100). This difference in the Heckel profiles of LCPC and MCC or PC products could be due to difference in the polymorphic forms of the cellulose present in these materials. As has been reported earlier (Kumar and Kothari, 1999), the crystalline component of LCPC predominantly contains the cellulose II lattice; cellulose I is present only in small amounts. The proportion of cellulose I in the product has recently been shown to decrease with increasing agitation rate employed during the regeneration step from its solution in phosphoric acid (Kumar et al., 2001). Commercial MCC and PC products used in the study, in contrast, contain the cellulose I polymorph. The cellulose chains are arranged in parallel in cellulose I, whereas, an anti-parallel arrangement exists in cellulose II (Krassig, 1993). Compared with cellulose I, cellulose II is widely believed to be more stable and has a lower energy due to the extra hydrogen bonds between the chains.

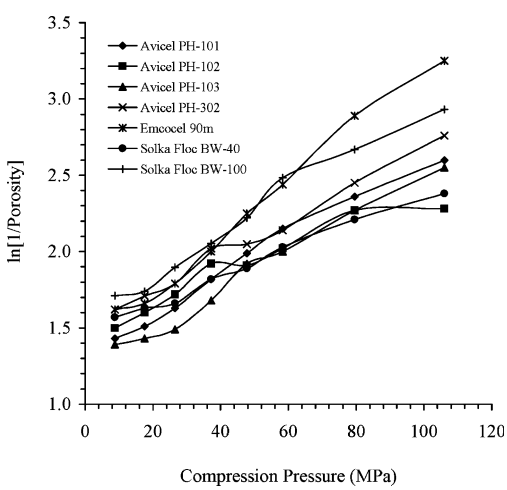

Fig. 5. Heckel plots for MCC and PC excipients.

The yield pressure values calculated using the compression pressure range given in Table 2 clearly show that with the exception of Emcocel® 90M, all of the MCC and powdered celluloses undergo permanent deformation at higher compression pressures, compared with the LCPC products. These results suggest that LCPC is more ductile than the Avicel products. The literature yield pressure values for Avicel® PH-101 and Avicel® PH-102 range between 37 and 101.11 MPa (Doelker et al. 1987b; Podczeck and Revesz, 1993; Mondedero Perales et al., 1994). PC obtained from different sources, in contrast, has been reported to exhibit a value of between 87 and 125 MPa (Podczeck and Revesz, 1993). This discrepancy between literature values is due to difference in methods (i.e. 'out of die' vs. the 'in die' methods) used to determine the porosity values and/or from differences in the choice of the boundary values limiting the linear segment of the Heckel profiles. The different yield pressure values obtained for LCPC is attributed to minor changes in reaction conditions during their manufacture, leading to different powder characteristics, as noted in Table 1. The lower yield pressure values obtained for LCPC and Emcocel 90m compared with those of Avicel and PC could be due to their low degree of crystallinity.

With the exception of LCPC-S3, LCPC-S5, and Emcocel 90m, all materials evaluated showed an AUHC value between 191 and 227 MPa. The

Table 2
Mechanical properties of LCPC and Avicel products

Product	Heckel analysis				AUHC (MPa)	AUTSC (MPa)^2
	Compression pressure range (MPa)[a]	R^2	Slope	Yield pressure, P_y (MPa)		
LCPC-S1	27–80	0.9972	0.144	69.44	191.26	521.70
LCPC-S2	8–80	0.9908	0.0143	69.93	205.13	214.02
LCPC-S3	27–80	0.9917	0.0304	32.36	310.94	798.55
LCPC-S4	37–106	0.9994	0.0167	59.88	219.48	544.45
LCPC-S5	16–80	0.9934	0.0208	48.08	248.41	542.29
Avicel PH-101	48–106	0.9913	0.0102	98.03	201.22	833.13
Avicel PH-102	48–80	0.9990	0.0114	87.72	193.37	807.97
Avicel PH-103	58–106	0.9971	0.0115	86.96	191.57	788.37
Avicel PH-302	48–106	0.9950	0.0125	80.00	210.37	565.33
Emcocel 90m	37–80	0.9986	0.0207	48.31	233.35	781.63
Solka Floc BW 40	37–80	0.9902	0.0095	105.26	191.98	257.39
Solka Floc BW 100	58–107	0.9987	0.0094	106.38	227.25	585.79

[a] Used in regression analysis to calculate yield pressures.

corresponding values for LCPC-S3, LCPC-S5, and Emcocel 90m were 311, 248, and 233 MPa, respectively. The relatively higher AUHC values for these materials are due to their lower yield pressure values, meaning that they show a greater degree of plastic deformation and consequently, a larger reduction in volume.

The relationship between tensile strengths of LCPC, MCC, and PC compacts and the respective compression pressure is shown in Fig. 6 and Fig. 7. With the exception of LCPC-S2 and Avicel PH-102, all the other materials showed a linear increase in mean tensile strengths over the whole compression pressures range used in this study. LCPC-S2 and Avicel PH-102, in contrast, exhibited the linear relationship only up to 80 MPa. The AUTSC data presented in Table 2 indicate that LCPC-S3, Avicel PH-101, Avicel PH-102, Avicel PH-103, and Emcocel 90m all formed the strongest compacts. The compactability of LCPC-S1, LCPC-S4, and LCPC-S5, in contrast, were similar to that Avicel PH-302 or Solka Floc BW-100 and LCPC-S2 and Solka Floc BW-40 formed the weakest compacts. A multiple regression analysis using DP, moisture content, crystallinity, and porosity (in different combinations) as independent variables and AUTSC as a dependent variable was performed, but no correlation was obtained between the variables and AUTSC, further indicating that the compactibility is a complex property.

3.3. Disintegration properties

The disintegration times and tensile strengths of the selected LCPC (LCPC-S2, LCPC-S4, and

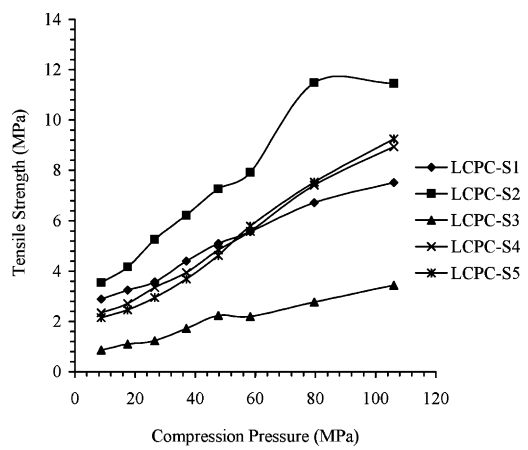

Fig. 6. Effect of compression pressure on the tensile strength of LCPC compacts.

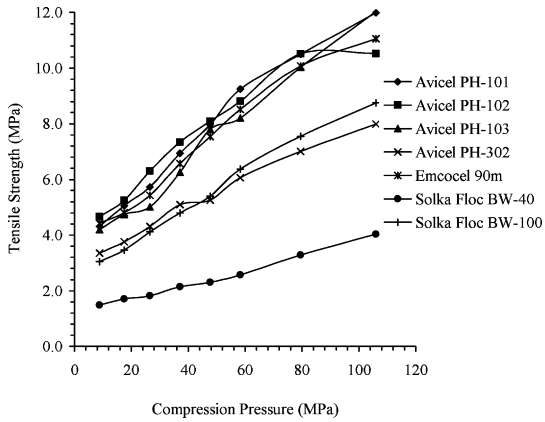

Fig. 7. Effect of compression pressure on the tensile strength of MCC and PC compacts.

LCPC-S5), MCC (Avicel PH-102, Avicel PH-103, and Avicel PH-302), and PC (Solka Floc BW-100) compacts, made to solid fraction levels of 0.80, 0.85, and 0.90, are presented in Table 3. Only LCPC and Avicel PH-302 compacts disintegrated at the three solid fraction levels. Compacts of both Avicel PH-101 and Avicel PH-102 disintegrated only at the lowest solid fraction of 0.80. At the intermediate and the highest solid fraction levels, compacts of both of these materials did not disintegrate at all during the test period. Compacts made from Solka Floc BW-100 at the three different solid fraction levels, by contrast, swelled and softened but remained intact during the test period.

The disintegration times and tensile strengths of compacts of the three LCPC products and Avicel PH-302, presented in Table 3, increased with increasing solid fraction levels. Compared with the compacts of Avicel PH-302, LCPC compacts disintegrated rapidly at the three solid fraction levels investigated. Since, the tensile strength values obtained for all the LCPC compacts, except for those made from LCPC-S2 at solid fraction levels of 0.85 and 0.90, were comparable to the values obtained for the Avicel compacts, it appears that the difference seen in the disintegration times for LCPC and Avicel compacts could be due to difference in the degree of crystallinity of the two materials as well as the ease of accessibility for water molecules to enter and interact with free hydroxyl groups. The disintegration times for compacts of MCC and PC from different vendors have been recently reported by Podczeck and Revesz, 1993. Although, the solid fraction levels of the tablets were not reported, the disintegration times for MCC tablets ranged from 196 to 2412 s, whereas, tablets made from PC had a disintegration time of greater than 14 400 s.

4. Conclusions

The powder and mechanical properties of different batches of LCPC were examined and compared with those of commercial MCC and PC excipients. The results show that LCPC powders are low crystallinity, low DP, and less porous products. Although, no definite relationship was observed between crystallinity and true density or moisture content of the various materials, the

Table 3
Tensile strength (TS) and disintegration times (DT) of LCPC and Avicel compacts at different solid fractions (SF)

Product	SF = 0.80		SF = 0.85		SF = 0.90	
	TS (N)	DT (s)	TS (N)	DT (s)	TS (N)	DT (s)
LCPC-S2	109.05	7 (1)	149.75	9 (1)	221.63	14 (2)
LCPC-S4	308.60	14 (1)	447.30	35 (1)	524.26	91 (8)
LCPC-S5	266.77	9 (1)	411.49	14 (1)	504.49	83 (12)
Avicel PH-102	412.41	2254 (528)	–	>21 600	–	>21 600
Avicel PH-103	424.48	5941 (2451)	–	>21 600	–	>21 600
Avicel PH-302	258.84	24 (7)	346.87	99 (37)	471.76	1439 (784)
Solka Floc BW 100	–	>21 600	–	>21 600	–	>21 600

LCPC products, in general, tend to pick up higher moisture content at a given vapor pressure compared with high crystallinity MCC and PC products. The yield pressure (P_y) values, calculated from the linear region of the Heckel curves, varied between about 48 and 70 MPa for the LCPC products. These values are significantly lower than was exhibited by the Avicel (80–98 MPa) and PC products (106 MPa). The P_y value for Emcocel 90m was 48 MPa. These results suggest that LCPC products and Emcocel 90m, compared with Avicel PH types and Solka Floc excipients, undergo plastic deformation at relatively lower compression pressures. The overall compressibility, determined by calculating the AUHC, was found to be the same for all materials except for the LCPC-S3, which, owing to the low yield pressure value, showed the largest volume reduction. The tablet strengths (compactability) of LCPC, MCC, and Solka Floc BW-100 products varied between about 522 and 798 MPa[2]. The compacts of LCPC at solid fraction levels of 0.80, 0.85, and 0.90 disintegrated much more rapidly compared with selected MCC and PC compacts used in the disintegration test. In conclusion, the results show that LCPC has clear potential as a unique direct compression excipient.

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