

# Comparative evaluation of powder and tableting properties of low and high degree of polymerization cellulose I and cellulose II excipients

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## Abstract

Low and high degree of polymerization (DP) cellulose II powders have been prepared from Avicel<sup>®</sup> PH-102 and Solka Floc<sup>®</sup> 40NF (low and high DP cellulose I powders, respectively), respectively, by treatment with sodium hydroxide (5N) for 24 h and their powder and tableting properties investigated. Cellulose II powders, compared to the respective cellulose I counterpart, exhibited lower crystallinity, true density, and specific surface area. They were denser and showed higher moisture uptake. The Heckel analyses revealed both low and high DP cellulose II powders to be less ductile than the low DP cellulose I powder and more ductile compared to the high DP cellulose I powder. The crushing strengths of low and high DP cellulose II powders were comparable to that of the high DP cellulose I powder but lower than the low DP cellulose I powder. When compressed to comparable crushing strengths, the low and high DP cellulose II compacts disintegrated faster in comparison to the corresponding cellulose I compacts. Low DP cellulose I and II powders, compared to the high DP cellulose I counterparts were more sensitive to magnesium stearate. Magnesium stearate decreased the disintegration times of low DP cellulose I compacts but had no effect on the low and high DP cellulose II and high DP cellulose I compacts. In conclusion, low and high DP cellulose II powders, despite their different powder properties, show similar tableting properties, leading to the formation of rapidly disintegrating compacts. The low and high DP cellulose I excipients, in contrast, differ in their powder properties as well as tableting characteristics.

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## 1. Introduction

Microcrystalline cellulose (MCC) and powdered cellulose (PC) are currently the most common and widely used direct compression excipients. They are obtained by chemical hydrolysis and mechanical disintegration of cellulose, respectively. Both MCC and PC are currently commercially available in different grades. Studies show that different brands of MCC and PC differ in their physical and mechanical properties and hence their performance as a tablet excipient (Roberts and Rowe, 1987; Parker et al., 1991; Doelker, 1993; Podczek and Révész, 1993). Various factors known to influence the physical and mechanical properties include the origin and nature of the cellulose source, methods of manufacturing, and processing variables employed

during their manufacture (Roberts and Rowe, 1987; Parker et al., 1991; Doelker, 1993; Landin et al., 1993a, 1993b; Podczek and Révész, 1993; Shlieout et al., 2001).

The study of the influence of degree of polymerization (DP) of MCC and PC on their tableting properties continues to be the subject of considerable interest. Shlieout et al. (2001) investigated powder and mechanical properties of MCC having different degrees of polymerization (190–299) and concluded that DP has a major influence on powder properties as well as compactability and compressibility of MCC, making the determination of DP indispensable in order to guarantee reproducibility during tablet production. Dybowski (1997), on the other hand, found no effect of DP on tableting properties of MCC. The changes observed in tableting properties of various MCC with different DPs were attributed to the origin of the cellulose source and the production method used to manufacture MCC. It was emphasized that, for the manufacturer, the DP is a criterion to guide the hydrolysis process and, for the user, it serves as an identification test.

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In this paper, we compare the powder and tableting properties of low and high DP cellulose I and cellulose II-based excipients. Cellulose II powders are a second generation multifunctional direct compression excipient, affording the manufacture of rapidly disintegrating tablets (Kumar et al., 2002; Reus Medina et al., 2004; Reus Medina, 2005; Reus Medina and Kumar, 2006). The low and high DP cellulose II powders, namely UICEL-A/102 and UICEL-S/40—hereinafter referred to as LDPC-II and HDPC-II, respectively, used in this study were prepared from Avicel® PH-102 (low DP cellulose I powder, LDPC-I) and Solka Floc® 40NF (high DP cellulose I powder, HDPC-I), respectively, following the procedure reported earlier (Reus Medina et al., 2004).

## 2. Experimental

### 2.1. Materials

Cotton linter sheets (grade R270) were obtained from Southern Cellulose Products, Inc. (Chattanooga, TN). Avicel® PH-102 (LDPC-I) was received from FMC Corporation (Philadelphia, PA). Solka Floc® 40NF (HDPC-I) was received from Mendell, Penwest Company (Patterson, NY). Magnesium stearate, sodium hydroxide, acetone, ethanol and ethylenediamine were purchased from Fisher Scientific (Fair Lawn, NJ). Copper(II) hydroxide was purchased from Aldrich Chemical Co. (Milwaukee, WI).

### 2.2. Preparation of cellulose II powders

The preparation of LDPC-II from LDPC-I has been previously reported (Reus Medina et al., 2004). HDPC-II was prepared following the same procedure using HDPC-I as the starting material. Briefly, cellulose I powder (LDPC-I or HDPC-I) was soaked in 5N NaOH solution for 24 h. Ethyl alcohol (95%, v/v) was then added. The white powder precipitated was filtered, washed with water until a near neutral pH was obtained, and then air dried until the powder could pass through the mesh of one grid (0.025 in. or 635  $\mu\text{m}$ ) in an oscillated granulator (Erweka AR 400 Apparatebau GmbH, Germany). The sieved material was then dried in an oven at 50–60 °C to the desired moisture content.

### 2.3. Loss on drying

This test was performed according to the procedure described in the US Pharmacopoeia/National Formulary (USP, 2002) for MCC.

### 2.4. Degree of crystallinity

The degree of crystallinity was determined by powder X-ray diffractometry (XRD). The X-ray diffraction measurements were conducted over a 5–40°  $2\theta$  range on a Siemens Model D5000 diffractometer, equipped with monochromatic Cu K $\alpha$  ( $\alpha_1 = 1.54060 \text{ \AA}$ ,  $\alpha_2 = 1.54438 \text{ \AA}$ ) X-rays. The step width was 0.020°  $2\theta \text{ min}^{-1}$  with a time constant of 0.5 s. The integration

of the crystalline reflections was achieved using the Diffrac<sup>Plus</sup> diffraction software (Eva, Version 2.0, Siemens Energy and Automation, Inc., Madison, WI). The degree of crystallinity of samples was expressed as reported earlier (Kumar et al., 2002). The preparation of cellulose I and cellulose II standards used in the study was achieved following the procedure reported by Patil et al. (1962).

### 2.5. Degree of polymerization (DP)

Degree of polymerization was determined by the viscosity method (ASTM, 1965; Kumar and Kothari, 1999) according the relationship:  $[\eta] = 190 \text{ DP}$ , where 190 is a constant determined by Grobe (1989) for cellulose from a plot between the intrinsic viscosity and degree of polymerization obtained from absolute molecular weight determination methods, and  $[\eta]$  is the intrinsic viscosity of the solution. All experiments were performed at  $25 \pm 0.5 \text{ }^\circ\text{C}$  using an Ostwald capillary viscometer (Size 50) and cupriethylenediamine hydroxide (Cuen) as the solvent. The intrinsic viscosity was calculated by interpolation using the USP table (USP, 2002) that lists the predetermined values of the product of intrinsic viscosity and concentration, ( $[\eta]C$ ), for cellulose samples exhibiting relative viscosity ( $\eta_{\text{rel}}$ ) values between 1.1 and 9.9.  $\eta_{\text{rel}}$  was calculated using the relationship:  $\eta_{\text{rel}} = t/t_0$ , where  $t$  and  $t_0$  are the efflux times for the cellulose solution and Cuen (blank) solvent, respectively.

### 2.6. Scanning electron microscopy

The scanning electron micrographs of the samples were obtained using a Hitachi S-4000 microscope (Hitachi High Technologies America, Inc., Pleasanton, CA). The samples were loaded on aluminum stubs covered with a double-sided tape. They were then coated with a gold/palladium (60/40) mixture for 4 min in an Emitech K550 coater. Images were captured with the IXRF digital capture system (IXRF Systems, Huston, TX).

### 2.7. Specific surface area, densities, Carr index, Hausner ratio, pore volume, and pore diameter

The surface area measurements were performed using a Quantasorb Sorption System (Quantachrome Corp., Boynton Beach, FL). Helium gas was used as the carrier, and nitrogen gas as the adsorbate. A five point Braunaue, Emmett, and Teller (BET) analysis was conducted on all samples, by performing the adsorption and desorption at relative pressures ranging from 0.05 to 0.25. Prior to performing the measurements, all samples were dried at 60 °C under reduced pressure for 24 h. In addition, they were degassed for 12 h at 60 °C under a continuous flow of nitrogen.

Pore volume and pore diameter were calculated at a relative pressure of 0.97 according to the relationship:  $V_{\text{liq}} = [(P_a V_{\text{ads}} V_m)/RT]$ , where  $V_{\text{liq}}$  is the volume of nitrogen adsorbed,  $P_a$  the ambient pressure,  $V_{\text{ads}}$  the volume of nitrogen adsorbed per gram of adsorbent,  $T$  the room temperature in K, and  $V_m$  is the molar volume of nitrogen (34.7  $\text{cm}^3$ ). Assuming

that the cylindrical pores constitute the entire surface, the average pore diameter, ( $d$ , in Å), is given by the equation:  $d = [(4V_{liq} \times 10^4)/S]$ , where  $S$  is the specific surface of the powder and  $V_{liq}$  as defined above.

The true, bulk and tapped densities were determined according to the procedure reported earlier (Kumar et al., 2002). The Carr index (CI) and Hausner ratio ( $H$ ) were determined from bulk and tapped densities according to the following relationships:  $CI = [(\rho_{tap} - \rho_{bulk})/\rho_{tap}] \times 100$  and  $H = \rho_{tap}/\rho_{bulk}$ , where  $\rho_{tap}$  and  $\rho_{bulk}$  are tapped and bulk densities, respectively.

### 2.8. Water uptake

The equilibrium moisture curves were obtained with a Symmetrical Vapor Sorption Analyzer SGA-100 (VTI Corporation, Hialeah, FL). Prior to performing the measurements, all samples were dried at 60 °C under reduced pressure for 24 h.

### 2.9. Preparation of tablets

Tablets, each weighing about 500 mg, were prepared on a Carver hydraulic press (Fred S. Carver Inc., Summit, NJ) at 105 MPa using a 13-mm diameter die and flat-face punches and a dwell time of 30 s. For the Heckel analysis, the pressure range employed was from 10 to 150 MPa.

### 2.10. Heckel analysis, crushing strength, and tensile strength

The Heckel analysis was conducted in the same manner as described earlier (Kumar et al., 2002). Briefly, tablets, each weighing 500 mg, were compressed at different pressures (10–147 MPa) using a 13 mm tooling set. The Heckel plots were constructed by plotting the natural log of the inverse of the compact porosity against the respective compression pressures. Regression analysis was performed on the linear portion of the curve, and the slope value obtained was converted to mean deformation pressure ( $P_y$ ) using the relationship:  $P_y = 1/\text{slope}$ . The compact porosity ( $\epsilon$ ) was calculated using the relationship:  $\epsilon = (1 - \rho_{app}/\rho_{true})$ , where  $\rho_{app}$  is the apparent density of the compact and  $\rho_{true}$  is the true density of the particles. The apparent density ( $\rho_{app}$ ) of the compact was calculated from the ratio of the tablet mass to the volume of the compact. The latter, at a given pressure, was calculated according to the equation:  $v = \pi r^2 h$ , where  $v$  is the volume,  $r$  the radius, and  $h$  is the thickness of the compact. The tablet thickness is expressed as averages of five measurements, made after about 48 h of tablet production, and at five different points between the two surfaces of the tablet.

Crushing strengths were determined using a Dr. SCHLEUNIGER® Phramatron tablet hardness tester (Schleuniger Model 8, Manchester, NH). The tensile strength of the compacts was determined using the Qtest I™ universal tester (MTS, Cary, NC) and the crosshead speed (i.e., the rate of load application) of 0.03 mm/s. 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  $\sigma_o$  is the maximum radial tensile strength,  $P$  the applied load,

$D$  the diameter of the compact, and  $t$  is the compact thickness (Fell and Newton, 1970; Majuru and Wurster, 1997). Multiple compacts of each material were used for tensile strength determinations.

### 2.11. Lubricant sensitivity ratio

Magnesium stearate was used as the lubricant at a concentration of 0.5%. The cellulose powder and magnesium stearate were mixed using a V-blender for 5 or 30 min. Tablets, each measuring 13 mm in diameter and weighing 500 mg, were prepared using a compression pressure of 105 MPa. The lubricant sensitivity was expressed as the lubricant sensitivity ratio (LSR):  $LSR = (S_0 - S_{lub})/S_0$ , where  $S_0$  and  $S_{lub}$  are the crushing strengths of tablets prepared without and with lubricant, respectively.

### 2.12. Disintegration studies

The disintegration test was performed according to the US Pharmacopoeia/National Formulary disintegration method (USP, 2002) in water at 37 °C using an Erweka GmbH apparatus (type 712, Erweka, Offenbach, Germany).

## 3. Results and discussion

### 3.1. Powder properties

The selected powder properties of HDPC-II and HDPC-I, along with those of LDPC-II and LDPC-I recently reported by us (Reus Medina et al., 2004), are presented in Table 1. The powder X-ray diffraction patterns of these materials are compared in Fig. 1, while the scanning electron micrographs are reproduced in Fig. 2. LDPC-II and LDPC-I have been previously identified to contain the cellulose II and cellulose I lattices, respectively (Reus Medina et al., 2004). As can be seen in Fig. 1, the X-ray diffraction pattern of HDPC-II is similar to that of LDPC-II, indicating that HDPC-II also possesses the cellulose II lattice. HDPC-I, in contrast, displays the peaks pattern that is characteristics of the cellulose I polymorphic form present in LDPC-I, native cellulose, and acid-catalyzed hydrolysis products of cellulose (Kothari, 1998).

HDPC-II, compared to HDPC-I, shows higher bulk and tap densities, lower porosity, and lower crystallinity. Similar obser-

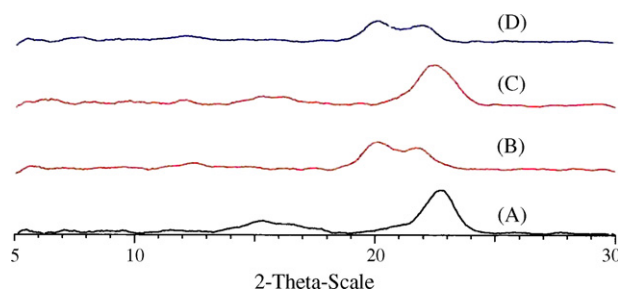


Fig. 1. Powder X-ray diffractograms of (A) LDPC-I, (B) LDPC-II, (C) HDPC-I, and (D) HDPC-II.



Table 1  
Powder properties of cellulose I and cellulose II excipients

	LDPC-II	HDPC-II	LDPC-I	HDPC-I
Moisture content (%)	3.72 (0.29)	1.03 (0.03)	2.14 (0.1)	4.63 (0.15)
True density, $\rho_{\text{true}}$ (g/ml)	1.533 (0.002)	1.527 (0.004)	1.550 (0.013)	1.557 (0.032)
Bulk density, $\rho_{\text{bulk}}$ (g/ml)	0.429 (0.006)	0.204 (0.019)	0.332 (0.009)	0.141 (0.003)
Tapped density, $\rho_{\text{tap}}$ (g/ml)	0.538 (0.002)	0.361 (0.014)	0.403 (0.003)	0.261 (0.004)
Hausner ratio	1.18 <sup>a</sup>	1.77	1.27 <sup>a</sup>	1.85
Carr index (%)	15.29 <sup>a</sup>	43.49	21.37 <sup>a</sup>	45.98
Porosity (%)	65	76	74	83
Degree of crystallinity (%)	68.2 (3.5)	55.6 (2.1)	79.8 (4.6)	66.4 (2.9)
Degree of polymerization (DP) <sup>b</sup>	187 (178, 195)	738 (726, 749)	211 (220, 201)	750 (745, 754)

<sup>a</sup> Taken from Reus Medina et al. (2004).

<sup>b</sup>  $n=2$  (values are given in the parentheses).

vations were made for LDPC-II, compared to LDPC-I (Reus Medina et al., 2004; Reus Medina, 2005). Among cellulose II powders, LDPC-II is denser and less porous. It also shows better flow compared to HDPC-II. These differences are attributed to their different morphologies and DPs. HDPC-II is fibrous (Fig. 2D) and has an average DP value of 738. LDPC-II, in contrast, is composed of aggregated fibers (Fig. 2B) and its DP corresponds to about 187. The similar morphology and DP of HDPC-II and HDPC-I lend further support to the earlier observation (Reus Medina et al., 2004) that the method used for preparing cellulose powders has no effect on these properties.

LDPC-II and HDPC-II are less crystalline and show lower true densities compared to the respective starting material (LDPC-I and HDPC-I, respectively) (Table 1).

The flow behavior of powders can be assessed using Hausner ratio ( $H$ ) and Carr index (CI) values. Well (1988) reported that a Hausner ratio of less than 1.2 is indicative of good flowability,

while a value of 1.5 or higher suggests a poor flow display by the material. The CI values of 5–10, 12–16, 18–21, and 23–28 have been used to represent excellent, good, fair, and poor flow properties, respectively (Carr, 1965). The lower CI and  $H$  values obtained for HDPC-II and LDPC-II, compared to the respective starting material (LDPC-I and HDPC-I, respectively), indicate that the LDPC-II powders, in general, show better flow than the cellulose I counterpart. Among cellulose II powders, LDPC-II shows better flow than HDPC-II. The higher CI and  $H$  values obtained for HDPC-II and HDPC-I, compared to the values for LDPC-II and LDPC-I, are attributed to their fibrous structures, which facilitate entanglement and, consequently, impede flow.

The BET-N<sub>2</sub> specific surface area, pore volume, and pore diameter results are presented in Table 2. The specific surface area of HDPC-II was ~60% of that observed for HDPC-I. The corresponding value for LDPC-II, in contrast, was ~33% of that of LDPC-I. Among cellulose II powders, HDPC-II had a higher

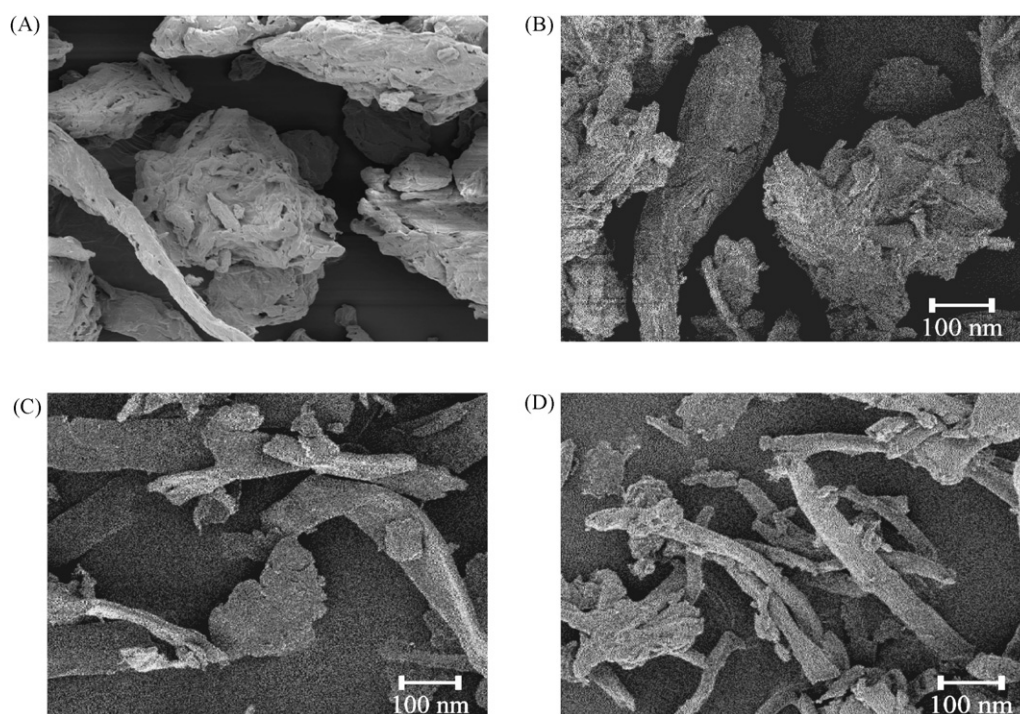


Fig. 2. Scanning electron micrographs (500 $\times$ ) of (A) LDPC-I, (B) LDPC-II, (C) HDPC-I, and (D) HDPC-II.

Table 2  
Specific surface area, pore volume, and pore diameter of cellulose I and II excipients

	Specific surface area (m <sup>2</sup> /g) <sup>a</sup>	Pore volume (cm <sup>3</sup> /g) <sup>a</sup>	Average pore diameter (Å) <sup>a,b</sup>
LDPC-II	0.474 (0.008)	0.0006 (0.0001)	51.42 (4.68)
LDPC-I	1.453 (0.013)	0.0027 (0.0001)	73.93 (0.99)
HDPC-II	0.895 (0.032)	0.0012 (0.0001)	54.07 (3.47)
HDPC-I	1.467 (0.032)	0.0023 (0.0001)	62.99 (3.17)

<sup>a</sup>  $n = 3$ . Standard deviations are given in parentheses.

<sup>b</sup> Pore diameter =  $(4 \times V_{liq} \times 10^4) / SSA$ .

specific surface area than that of LDPC-II. The pore volume of HDPC-II, compared to LDPC-II, was also higher. Both HDPC-II and LDPC-II powders, compared to the respective cellulose I powder, showed a decrease in pore volume; in the case of HDPC-II, the pore volume decreased to nearly half of that determined for HDPC-I. For LDPC-II, the decrease in pore volume was about 4.5 times. The smaller surface areas seen for cellulose II powders (LDPC-II and HDPC-II), compared to the specific surface areas of cellulose I powders (LDPC-I and HDPC-I), are attributed to their lower porosity, lower pore volume and lower pore diameter values, which, in turn, could be due to the more extensive hydrogen bonding network known to exist in cellulose II (Krassig, 1996).

The moisture sorption isotherms of HDPC-II and LDPC-II, and their starting materials, are compared in Fig. 3. Cellulose II powders (i.e., HDPC-II and LDPC-II), in general, showed higher water uptake than the respective cellulose I powders (i.e., HDPC-I and LDPC-I). Both LDPC-II and HDPC-II show comparable affinity toward moisture below 60% relative humidity. Above 60% relative humidity, however, HDPC-II begins to show higher

Table 3  
Water vapor content sorbed on cellulose I and II excipients

	Moles of water vapor sorbed by various celluloses		Accessible specific surface area to water (m <sup>2</sup> /g)
	Theoretical <sup>a</sup>	Experimental	
LDPC-I	0.0013	0.0019	142.40
HDPC-I	0.0021	0.0022	168.54
LDPC-II	0.0022	0.0027	201.63
HDPC-II	0.0028	0.0026	199.09

<sup>a</sup> Calculated assuming 1:1 (mol/mol) interaction between water and anhydroglucose repeat unit in the amorphous regions as follows:  $\{[1 \text{ g}/162 \text{ g mol}^{-1}] \times \{1 - (\% \text{ degree of crystallinity}/100)\}$ , where 162 is the molecular weight of the repeat anhydroglucose unit.

water uptake compared to LDPC-II and, above 80% relative humidity, the moisture uptake exceeds by about 5%. LDPC-I and HDPC-I, in contrast, showed no significant difference in their water uptake over the whole relative humidity range used. The rank order of materials with respect to their affinity for moisture is: HDPC-II  $\geq$  LDPC-II > HDPC-I > LDPC-I. The higher water uptake by HDPC-II compared to HDPC-I, and by LDPC-II in comparison with LDPC-I, is attributed to their lower degree of crystallinity, i.e., greater disorder (amorphous) regions. Amorphous regions lack hydrogen bonding and, hence, serve as potential sites for interaction with water molecules. Table 3 lists the number of moles of water calculated from the water vapor sorption data, assuming each repeat unit in the amorphous regions binds to one water molecule, and experimentally observed per gram of various celluloses evaluated. Also, included in the table is the specific surface area of cellulose accessible to water, calculated using the BET method and water sorption isotherms. There exists a reasonably good agreement

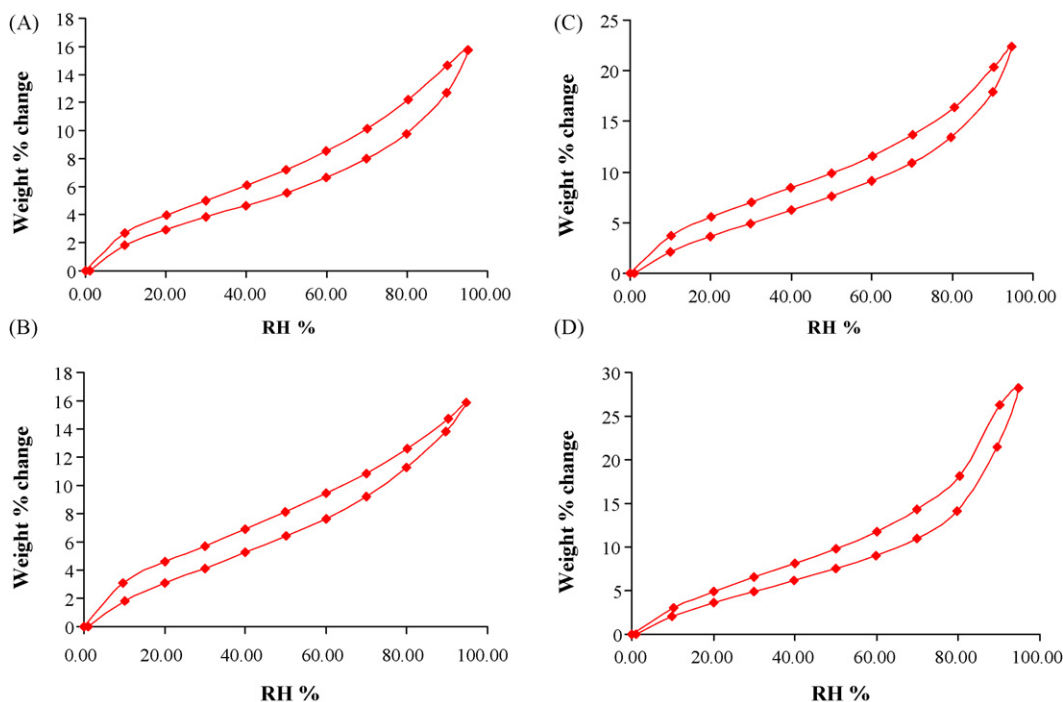


Fig. 3. Water sorption isotherms of (A) LDPC-I, (B) HDPC-I, (C) LDPC-II and (D) HDPC-II. The lower curve represents sorption and the upper curve desorption.

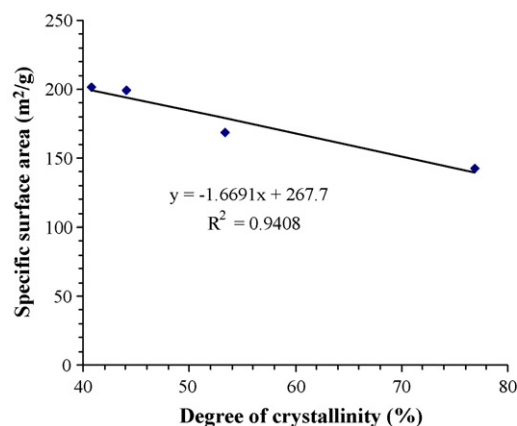


Fig. 4. Relationship between degree of crystallinity and specific surface area.

between the experimentally observed and calculated number of moles of sorbed water. It is also interesting to note in Fig. 4 that the hysteresis loops are narrower for LDPC-I and HDPC-I than for LDPC-II and HDPC-II. This suggests that water vapor in cellulose II products is more tightly held. Since the preparation of cellulose II from cellulose I results in more disordered regions, which could be randomly distributed, it is plausible that the sorption of moisture leads to a small but significant conformational change, owing to the plasticization effect of water, causing some amorphous regions to be surrounded by the crystalline regions such so that the sorbed water is prevented from desorption. Another factor that could contribute to the observed difference in the hysteresis loops is the close packing and inter-chain bonding of the crystalline lattice structure in cellulose II that makes sorbed water to exist more as a tightly bound structure than as a loosely bonded form. Shlieout et al. (2001) and Zografis et al. (1984) made similar observations for cellulose I powders with different degrees of polymerization or degrees of crystallinity.

Fig. 4 shows that specific surface area accessible for interaction with water, calculated from water sorption data, and degree of crystallinity follows a linear relationship.

### 3.2. Tableting properties

The crushing strengths of low and high DP cellulose I and cellulose II compacts are compared in Fig. 5. The results show the low and high DP cellulose II powders to be less compactable than the low DP cellulose I powder but comparable to the high DP cellulose I powder. There was no significant difference in crushing strengths of low and high DP cellulose II compacts.

The Heckel plots for all the materials studied are presented in Fig. 6 and the Heckel parameters are shown in Table 4. A comparison of the yield pressure values suggests the low and high DP cellulose II powders to be less ductile than the low DP cellulose I powder but comparable or slightly more ductile than the high DP cellulose I powder. The comparable yield pressure values of the low and high DP cellulose II powders suggest that they consolidate into a compact by the same mechanism. This may offer an advantage from the manufacturing standpoint, in that, it does not matter if the cellulose II powder is prepared from

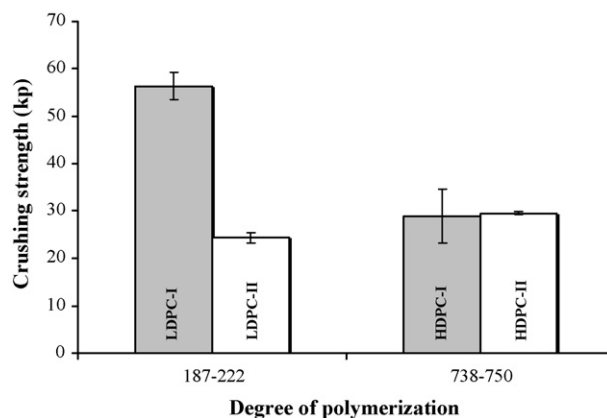


Fig. 5. Crushing strength of low and high DP cellulose I and II tablets.

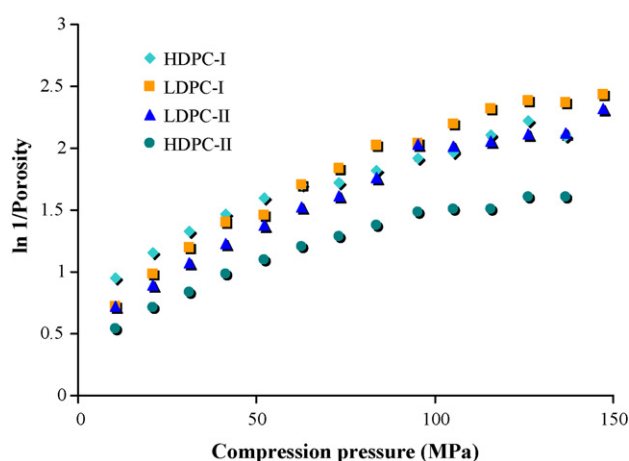


Fig. 6. Heckel plots for the low and high DP cellulose I and II tablets.

the low or high DP cellulose I source, its mechanical properties will not be affected.

The tensile strength values for the low and high DP cellulose I and cellulose II compacts are included in Table 4. The results show the low and high DP cellulose II powders to be comparable in their compactability. Their tensile strength values are comparable to that of the high DP cellulose I compact but significantly lower compared to that of the low DP cellulose I compacts. The difference in compactability of low and high DP cellulose I powders is probably due to the difference in their DP and/or particle morphology. Since the low and high DP cellulose II powders have DP and particle morphology similar to the respective cellulose I counterpart, the lower compactability observed for the low

Table 4  
Heckel parameters and tensile strengths of cellulose I and II compacts

	Heckel parameter		Tensile strength (MPa) <sup>a</sup>
	$P_y$ (MPa)	$R^2$	
LDPC-II	97.1	0.9951	3.08 (0.16)
LDPC-I	69.4	0.9920	9.77 (0.31)
HDPC-II	101.0	0.9927	4.51 (0.17)
HDPC-I	120.5	0.9817	3.85 (0.19)

<sup>a</sup> Number in parentheses are standard deviation;  $n = 3$ .

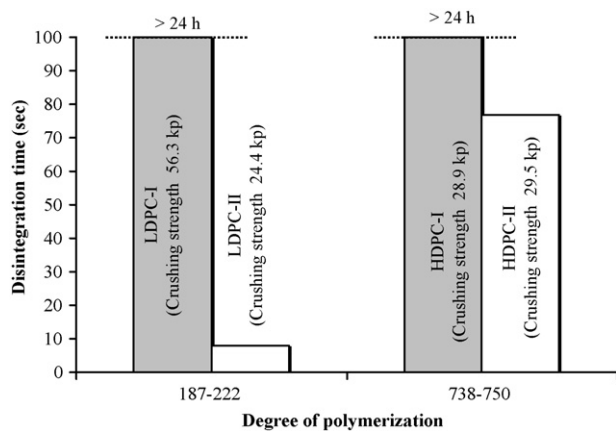


Fig. 7. Disintegration times of low and high DP cellulose I and cellulose II tablets made at 105 MPa compression pressure.

DP cellulose II powder, compared to the cellulose I counterpart, could be due to the anti-parallel cellulose chains arrangement (Krassig, 1996), leading to greater hydrogen bonding network and thereby limiting chains mobility during compression. No significant difference in the compactability of high DP cellulose II and I powders suggest that the DP and/or particle morphology, not the polymorphic form, could be the determining factor(s).

The disintegration times of the low and high DP cellulose I (LDPC-I and HDPC-I) and cellulose II (LDPC-II and HDPC-II) tablets, along with their crushing strengths, are depicted in Fig. 7. As can be seen, cellulose II compacts disintegrated significantly faster compared to the cellulose I compacts. Among the cellulose II powders, the low DP cellulose II is superior in its disintegration property. The slower disintegration of the high DP cellulose II powder could be due to increased fibers entanglement during consolidation. Table 5 lists the disintegration times of the low and high DP compacts compressed to comparable crushing strengths. The results suggest that the faster disintegration property observed for the cellulose II powders with respect to the cellulose I powders could be intrinsic to the cellulose II lattice present in these materials.

The lubricant sensitivity study results presented in Fig. 8 show that the low DP cellulose II powder is more sensitive to magnesium stearate than the rest of the materials tested following 5 or 30 min of mixing. The high DP cellulose II powder, in contrast, showed comparable sensitivity to magnesium stearate with respect to its cellulose I counterpart, but significantly less compared to low DP cellulose II. A likely reason for the higher

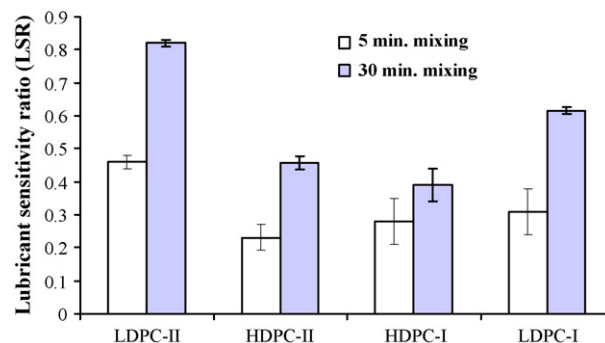


Fig. 8. Lubricant sensitivity ratio of low and high DP cellulose I and cellulose II powders.

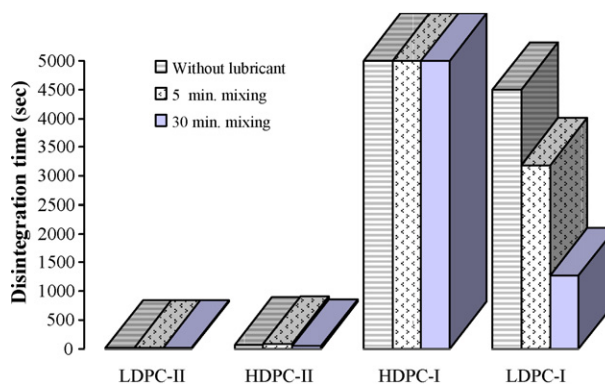


Fig. 9. Effect of lubricant on the disintegration time of cellulose I and cellulose II tablets.

lubricant sensitivity of the low DP cellulose II powder, versus the cellulose I powder, to magnesium stearate could be its higher bulk density, leading to a more efficient mixing and, consequently, coating of particles. No significant difference seen in lubricant sensitivity of the low and high DP cellulose I and II powder is attributed to their fibrous structure, which restricts flow and as a result hampers mixing with magnesium stearate particles. Thus, low DP celluloses, irrespective of their polymorphic form, appear to be more sensitive to magnesium stearate.

The effect of mixing time of magnesium stearate on the disintegration times of low DP and high DP cellulose I and II compacts is shown in Fig. 9. Except for the LDPC-I compacts, which showed a decrease in disintegration time with an increase in mixing time, there was no effect of magnesium stearate on the disintegration times of any of the compacts.

#### 4. Conclusions

Despite their different powder properties, the low and high DP cellulose II, prepared from Avicel<sup>®</sup> PH-102 (LDPC-I) and Solka Floc<sup>®</sup> 40NF (HDPC-I), respectively, show comparable compression and compaction properties. The rapid disintegration of their compacts, irrespective of the compression pressure being used, suggests that both low and high DP materials could be used to manufacture rapidly disintegrating tablets. The low and high DP cellulose I powders, in contrast, show different powder and tableting properties.

Table 5  
Disintegration times and crushing strengths of cellulose I and II compacts

	Crushing strength (kp)	Disintegration time
LDPC-II <sup>a,b</sup>	22.0 (1.0)	12.7 s (3.4)
LDPC-I <sup>c,b</sup>	25.1 (0.8)	56.4 s (18.4)
HDPC-II <sup>a,d</sup>	28.9 (1.3)	60.2 s (9.2)
HDPC-I <sup>a,d</sup>	26.7 (0.8)	>210 min

<sup>a</sup> 105 MPa.

<sup>b</sup> *n* = 20.

<sup>c</sup> 52 MPa.

<sup>d</sup> *n* = 6.



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