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International Journal of Pharmaceutics 177 (1999) 173–182

international journal of pharmaceutics

Effect of compressional force on the crystallinity of directly compressible cellulose excipients

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Received 2 January 1998; received in revised form 1 July 1998; accepted 14 October 1998

Abstract

The effect of compressional force on the crystallinity of low crystallinity cellulose (LCPC), microcrystalline celluloses (Avicel® PH-101, PH-102 and PH-302 grades) and powdered cellulose (Solka Floc BW-100) has been investigated using an X-ray diffraction method. Microcrystalline and powdered celluloses showed an increase of about 10% in their crystallinities, compared to the values for the corresponding powders, at a compression pressure of 5–10 MPa. The increase in the crystallinity of LCPC was gradual and reached the maximum value of 5% at a compression pressure of 15 MPa. Further increase in compression pressure (to 77 MPa) had no effect on the crystallinity of LCPC, Avicel® PH-101, Avicel® PH-302 and Solka Floc BW-100. Avicel® PH-102, on the other hand, showed a decrease in crystallinity at 15 MPa. Beyond 15 MPa, however, no statistically significant change in the crystallinity of the product was noted.

Keywords: Avicel®; Cellulose excipients; Degree of crystallinity; Direct compression excipients; Low crystallinity cellulose; Solka Floc

1. Introduction

During compression, solid particles rearrange, deform and fragment to form a compact. Several physicomechanical parameters of the material being compressed, such as crystallinity, moisture content, tensile strength, particle size, surface area and density, have been identified that influence the compaction characteristics of solids. Of these, the crystallinity of a material is of fundamental importance because it not only directly influences compactibility but also affects the adsorbtion of water and, hence, flowability.

Currently, microcrystalline cellulose (MCC) and powdered cellulose (PC) are the most commonly and widely used direct compression excipients. There are several different grades of these

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0378-5173/99/$ - see front matter
PII: S0378-5173(98)00340-8

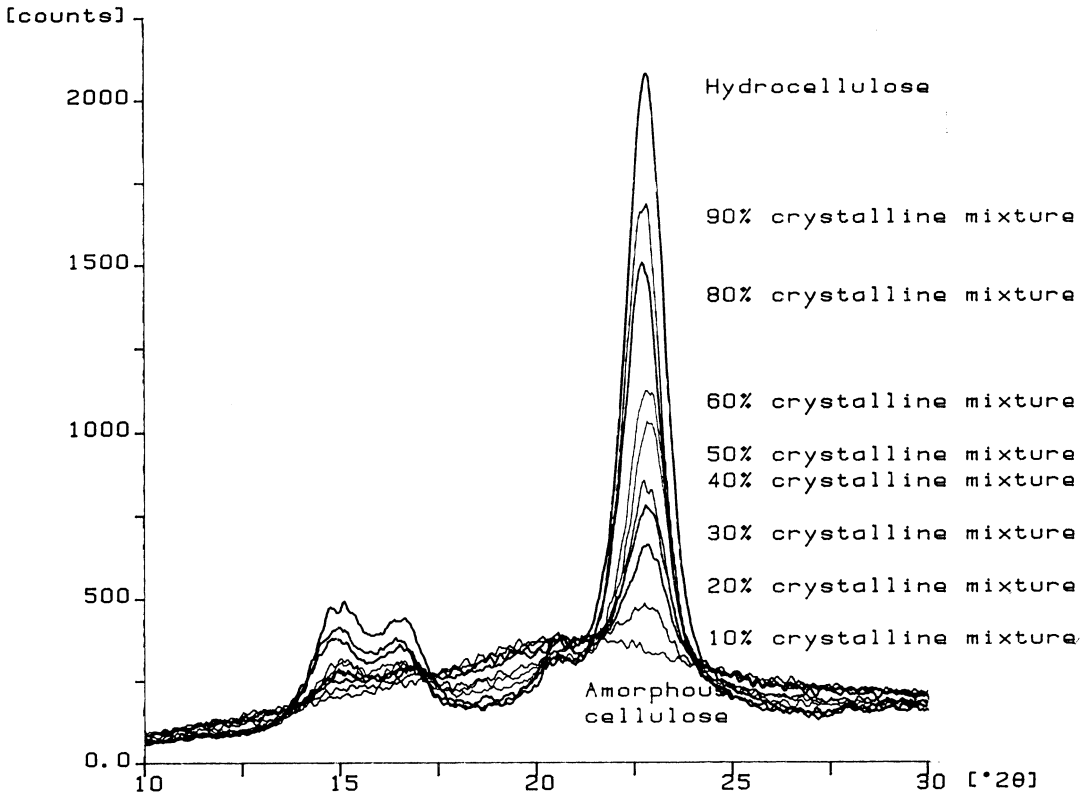

Fig. 1. Powder X-ray diffractograms of blends of hydrocellulose and amorphous cellulose.

materials currently commercially available. Depending on the origin of cellulose source and the processing variables used in their manufacture, the degree of crystallinity of these products varies (Doelker et al., 1987a). Several studies have been reported that describe the effect of the degree of crystallinity of these materials on their tabletting properties. Nakai et al. (1977) reported that low crystallinity cellulose powders produce weaker tablets than higher crystallinity materials. Doelker et al. (1987b), however, found no direct relationship between crystallinity and compression properties, but reported that microcrystalline celluloses, which varied in crystallinity from 53 to 82%, exhibited better compressional properties than microfine powders which had degrees of crystallinity ranging between 26 and 49%. The microfine powders are prepared by mechanical disintegration of α-cellulose.

The effect of compressional force on the crystallinity of cellulose excipients has been little studied. Huttenrauch and Keiner (1976) reported that the crystallinity of cellulose decreases during compression. Gravitis et al. (1991) suggested that the decrease in cellulose crystallinity during compression occurs as a result of a simultaneous shearing action. A recent study by Ek et al. (1995), using carbon-13 cross-polarization/magic-angle spinning nuclear magnetic resonance (^{13}C CP/MAS NMR) and photoacoustic Fourier-transform infrared (FTIR) spectroscopies, revealed that the crystallinity of compressed microcrystalline cellulose particles initially slightly increased and then decreased as the compaction pressure was increased. The magnitude of change in the crystall-

inity was the greater on the perimeter surface than on the top or bottom surfaces of the compact, and was greater on the tablet surface than in the tablet bulk. The initial increase in the crystallinity was attributed to an increase in the ordered structure, whereas the different crystallinity index on different portions of the tablets was suggested to be due to different levels of shear forces acting during compaction.

The objective of this study was to investigate the effect of compressional force on the crystallinity of a new directly compressible low crystallinity cellulose (LCPC) (Wei et al., 1996) and commercially available microcrystalline and microfine cellulose excipients using the powder X-ray diffraction technique.

2. Experimental

2.1. Materials

Avicel® PH-101(Lot 1430), Avicel® PH-102 (Lot 2414-1308) and Avicel® PH-302 (Lot Q509C) were received from FMC Corporation (Philadelphia, PA, USA). Solka Floc BW 100 (Lot 8928X) was received from Edward Mendel Co. (Carmel, NY, USA).

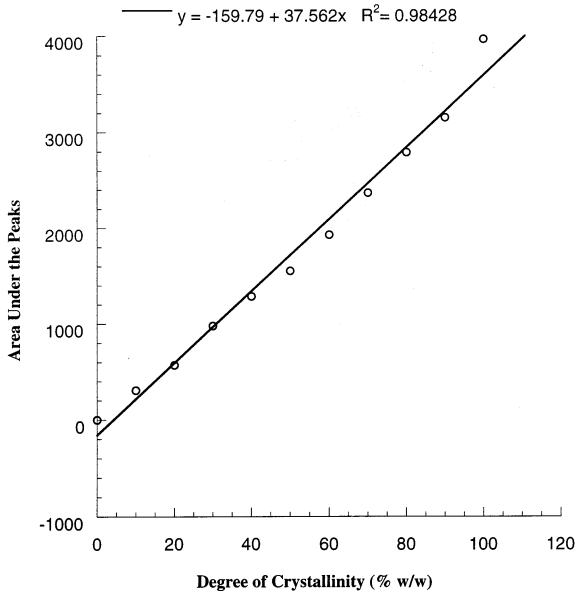

Fig. 2. A plot between area under the peaks and the percentage crystallinity of various blends of hydrocellulose and amorphous cellulose.

LCPC was prepared according to the method of Wei et al. (1996). Briefly, cellulose was reacted with 85% phosphoric acid first at room temperature for 1 h and then at 50°C for 4 h. The resulting translucent, viscous solution was cooled to room temperature and then added to water (about five times the volume of H_3PO_4 used) with constant agitation (700 r.p.m.). The white solid precipitated was filtered and repeatedly washed with water until the pH of the filtrate was neutral. The wet cake was then suspended in acetone, and finally filtered. This process was repeated several times to ensure removal of water from the residue. The acetone-washed powder was dried in air and sieved. The fraction containing particles between 70 and 120 μm in size was collected and used in this study. The commercial cellulose excipients were also sieved, and the fraction that corresponded to the same particle size range as used for LCPC was employed in the study. All fractionated powder samples were equilibrated to about 6% moisture content using appropriate relative humidity chambers.

2.2. Preparation of compacts

Compacts, each weighing 0.5 g, were prepared on a Carver press using a 17-mm die and flat-faced punches at different compression pressures (10–110 MPa), with a dwell time of 30 s.

2.3. Characterization of cellulose excipients

2.3.1. Moisture content

The percentage moisture content in the sample was calculated from the weight loss on heating between 25 and 225°C on a Perkin Elmer series 7 thermal analyzer.

2.3.2. Bulk and tap density

A known quantity of each sample (25 g) was poured through a funnel into a 100-ml tarred graduated cylinder. The cylinder was then lightly tapped twice to collect all the powder sticking on

Table 1
Powder characteristics of LCPC and commercial cellulose excipients

Powder property	LCPC	Solka Floc BW-100	Avicel®		
			PH-101	PH-102	PH-302
True density (g/cm^3)	1.440	1.429	1.577	1.526	1.519
Bulk density (g/cm^3)	0.586	0.268	0.315	0.254	0.413
Tap density (g/cm^3)	0.627	0.389	0.401	0.282	0.497
Crystallinity (%)	44.25	44.68	72.23	84.56	74.28
Porosity (%)	57.32	73.66	75.00	81.93	67.62
Degree of polymerization	31	647	230	215	129
Moisture content (%)	5.824	5.820	5.745	6.011	6.200

the wall at the bottom of the cylinder. The volume was then read off directly from the cylinder and used to calculate the bulk density. For tap density, the cylinder was tapped from a height of 2.5 cm for 50 times on a wooden bench top before a constant reading was obtained.

2.3.3. True density

The true density of powders, dried at room temperature in a vacuum oven under 10 mmHg pressure, was determined using the Quantachrome helium pycnometer. The reference volume and the cell volume were calibrated before each

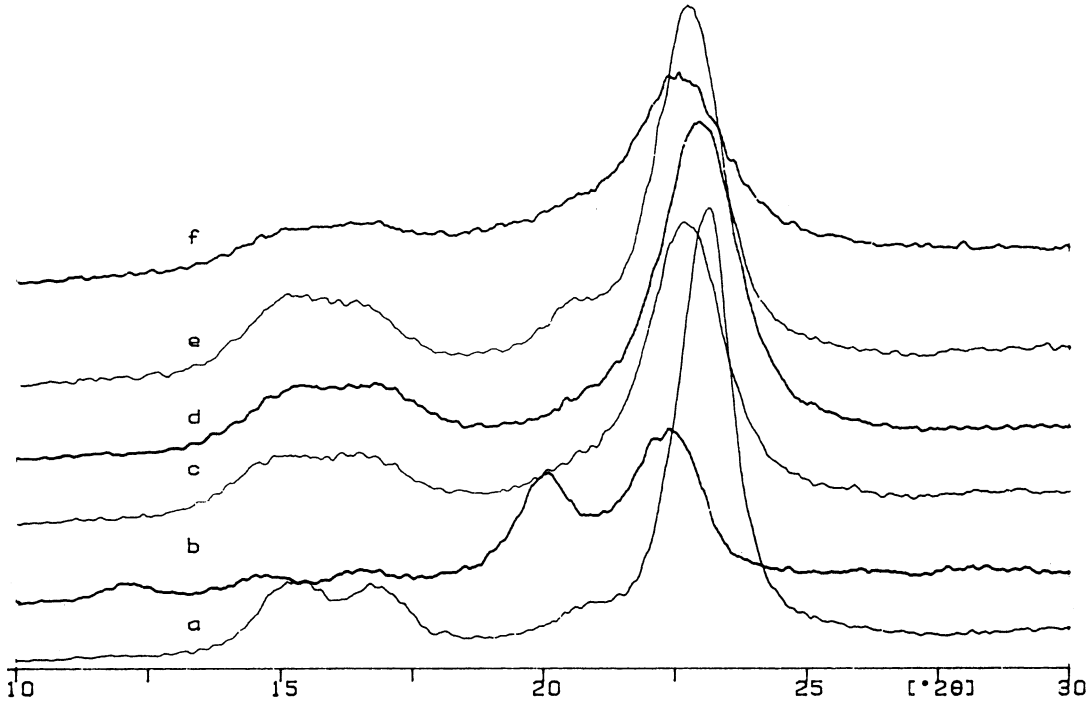

Fig. 3. Powder X-ray diffractograms of (a) hydrocellulose, (b) low crystallinity cellulose (LCPC), (c) Avicel® PH-101, (d) Avicel® PH-102, (e) Avicel® PH-301 and (f) Solka Floc BW-100.

determination using two solid stainless steel spheres having a volume of 2.145 cm^3. The true density was calculated using the equation: $\rho_{true} = W/V_p$, where ρ_{true}, W and V_p are true density, weight of the sample and true volume of powder, respectively.

2.3.4. Porosity

The porosity of the test powders was determined using the equation $\varepsilon = [1 - (\rho_{tap}/\rho_{true})] \times 100$, where ε, ρ_{tap} and ρ_{true} are porosity, tap density and true density of the powder, respectively.

2.3.5. X-ray measurements

The X-ray diffraction measurements on powders and compacts of the cellulose excipients were conducted on a Philips PW 1710 powder X-ray diffractometer using monochromatic CuKα radiation and a scanning rate of 3°2θ/min over the range of 10–30°2θ. A sample holder in which the 17-mm diameter tablet could be directly placed was custom-made and used for the compacts. For powder samples, the standard Philips sample holder was used. Hydrocellulose, prepared from a reaction between cotton linter and 2 N HCl at a boiling temperature for 30 min (Battista and Smith, 1961), was used as the 100% crystalline reference. The integration of the crystalline reflections was achieved using APD Phillips software version 2.01. The crystallinity of the samples was determined by integration of the peaks due to crystalline reflections, and expressed as the percentage ratio of the integrated intensities of the sample to that of hydrocellulose.

To validate the use of hydrocellulose as the 100% crystalline reference, a series of blends of hydrocellulose and amorphous cellulose (prepared from hydrocellulose by ball-milling) were prepared and their crystallinities were determined. The diffractograms and the plot depicting a linear relationship between areas under the peaks and the theoretical crystallinity values of various blends are presented in Fig. 1 and Fig. 2, respectively.

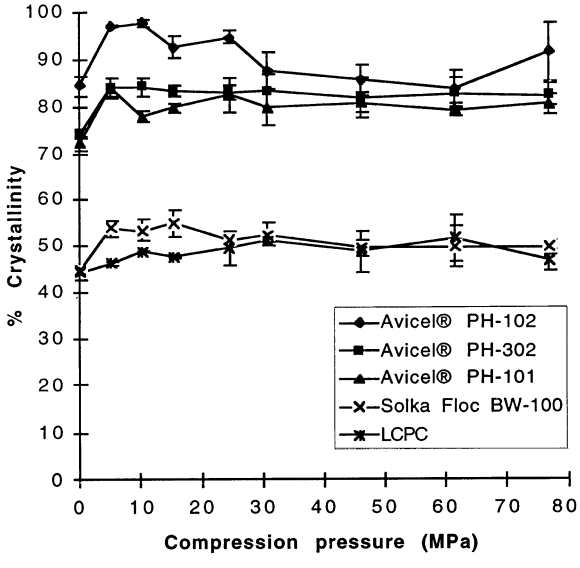

Fig. 4. Effect of compressional force on the crystallinity of low crystallinity cellulose (LCPC) and commercial cellulose excipients. Each value is an average of two measurements. The vertical line at each compression pressure represents the range of the two values.

3. Results and discussion

3.1. Characteristics of powders

The selected powder properties of LCPC, Avicel® PH-101, Avicel® PH-102, Avicel® PH-103, and Solka Floc BW-100 are presented in Table 1. Of these materials, LCPC exhibited the lowest porosity and, consequently, the highest bulk and tap densities. The smaller true densities obtained for LCPC and Solka Floc BW-100 compared to those for the three grades of Avicel® are consistent with their low crystallinity values, as has been suggested by Huttenrauch and Keiner (1988).

The powder X-ray diffraction patterns of LCPC, hydrocellulose, Avicel® PH-101, Avicel® PH-102, Avicel® PH-103 and Solka Floc BW-100 are shown in Fig. 3. As is obvious, except for LCPC, all materials exhibited similar diffraction patterns. Depending on the source and chemical

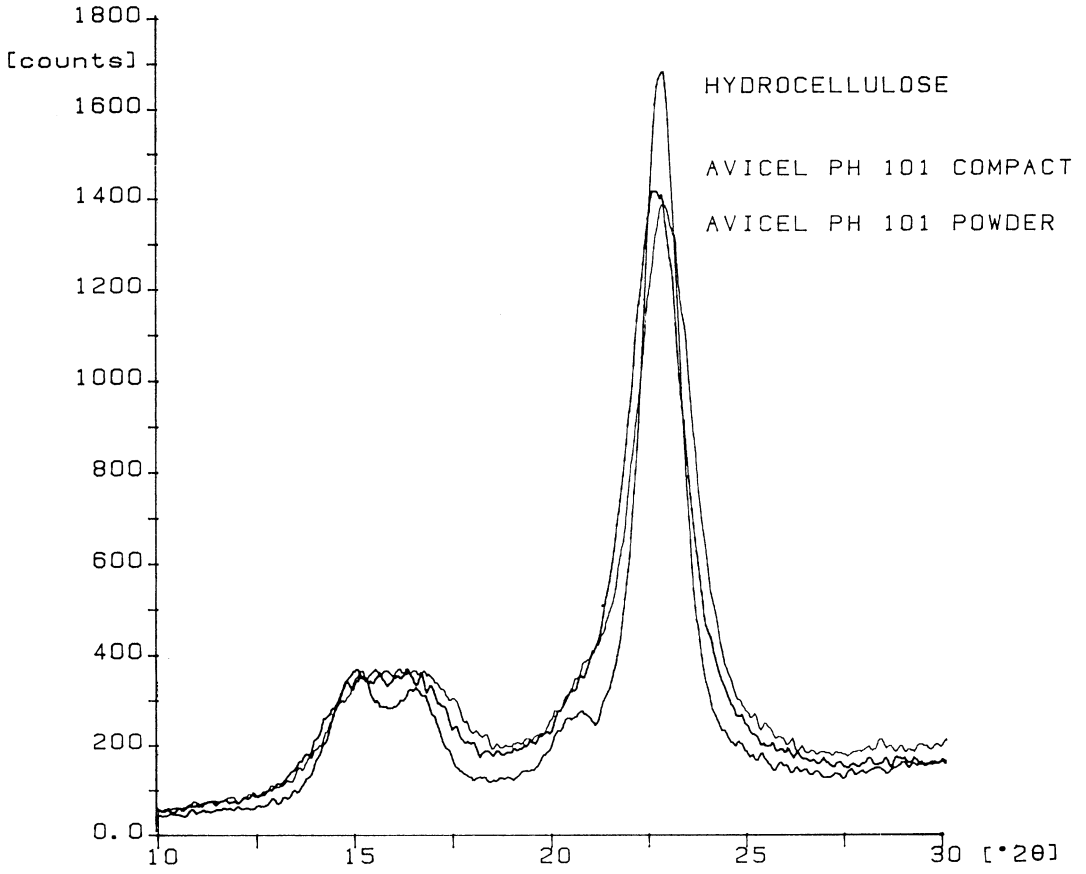

Fig. 5. X-ray diffractograms of hydrocellulose, Avicel® PH-101 powder and Avicel® PH-101 compact that showed the maximum crystallinity increase.

treatment, cellulose is capable of existing in different crystal forms (Isogai, 1994). Cellulose I, which is represented by the native cellulose, typically shows peaks at 15, 16 and 23°2θ due to 1$\bar{1}$0, 110 and 002 reflections, respectively (Isogai, 1994). A shoulder at 20°2θ due to 012 reflection has also been noted in certain cellulose materials (Rowland and Roberts, 1974). Mercerized and regenerated celluloses are examples of cellulose II type and typically exhibit peaks at about 12, 20 and 22°2θ due to 1$\bar{1}$0, 110 and 002 reflections, respectively (Isogai, 1994). The diffraction patterns shown in Fig. 3 for various cellulose excipients used in the study clearly suggest that hydrocellulose, the three grades of Avicel® and Solka Floc BW-100 all belong to the same crystalline lattice as that of cellulose I, whereas LCPC is predominantly cellulose II in structure. The weak crystalline peaks at about 14 and 17°2θ in the diffractogram of LCPC are indicative of the presence of a small percentage of cellulose I in the sample. The regeneration of cellulose II from phosphoric acid solution has been previously reported by Whitmore and Atalla (1985). It must be noted that, except for severely ball-milled cellulose, which recrystallizes in a cellulose II lattice, mechanical decrystallization of cellulose typically does not cause lattice transformation (Nakai et al., 1977).

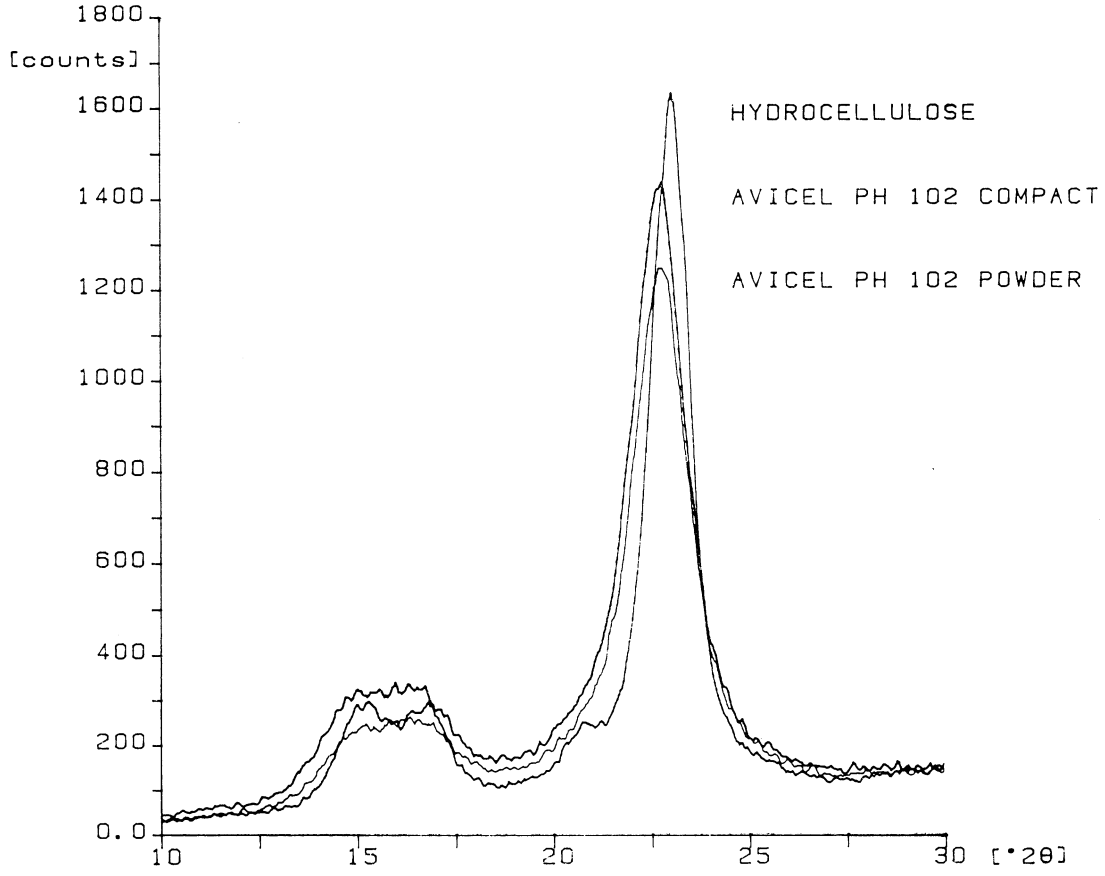

Fig. 6. X-ray diffractograms of hydrocellulose, Avicel® PH-102 powder and Avicel® PH-102 compact that showed the maximum crystallinity increase.

3.2. Effect of compression pressure on the crystallinity of cellulose excipients in intact compacts

The change in the crystallinities of cellulose excipients as a function of compression pressure is shown in Fig. 4. In Figs. 5–9 the X-ray patterns of hydrocellulose and cellulose excipient in powder and compact forms are compared.

As has been reported for Avicel® PH-101 by Ek et al. (1995) using ^{13}C CP/MAS NMR and photoacoustic FTIR, all materials used in the present study showed an increase in crystallinity at low compression pressure. The magnitude of the increase in crystallinity, however, was about 10% for the commercial cellulose excipients and about 5% for LCPC, compared to the values for the corresponding powder forms. Avicel® PH-101, Avicel® PH-302 and Solka Floc BW-100 exhibited this increase in crystallinity at 5 MPa (ANOVA: $F = 4.9897$, $p < 0.01$; $F = 3.7585$, $p < 0.05$; and $F = 3.4127$, $p < 0.04$, respectively), whereas in the case of Avicel® PH-102 the maximum increase in the crystallinity occurred at 10 MPa (ANOVA: $F = 5.8661$, $p < 0.01$). In the case of LCPC, the increase in crystallinity was gradual, reaching the maximum value at a compression pressure of 15 MPa. The occurrence of maximum increase in crystallinity for the three grades of Avicel® and Solka Floc BW-100 at a relatively low compres-

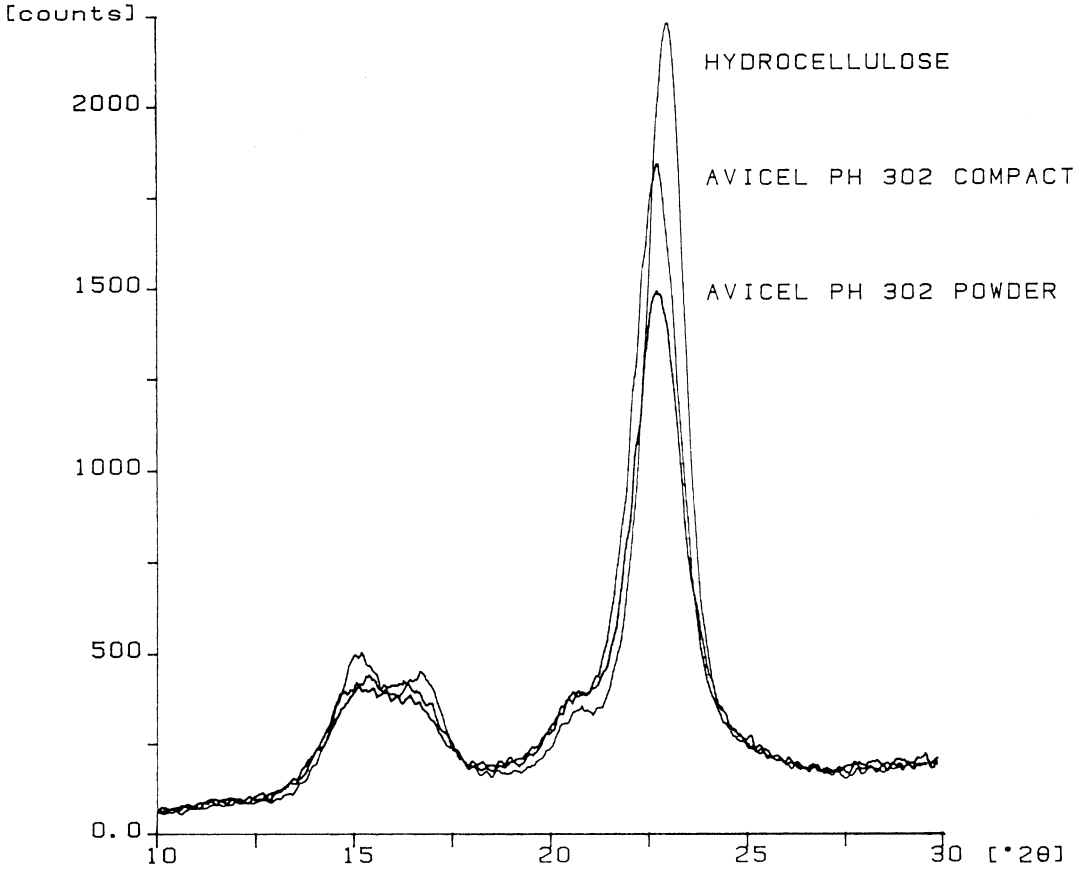

Fig. 7. X-ray diffractograms of hydrocellulose, Avicel® PH-302 powder and Avicel® PH-302 compact that showed the maximum crystallinity increase.

sion pressure compared to that for LCPC can be attributed to the difference in their methods of preparation and, consequently, different distribution and arrangement of crystallite and amorphous regions in the structure. All three grades of Avicel® are produced by hydrolysis of purified α-cellulose with mineral acids until the level-off degree of polymerization is obtained. They are highly aggregated, crystalline powders. Solka Floc BW-100, on the contrary, is prepared by either wet or dry milling of the purified α-cellulose. This results in partial amorphization and limited depolymerization of cellulose. In both cases, however, the cellulose chains are still oriented and, hence, facilitate an increase in crystallinity at a low compression pressure. LCPC, being recrystallized from a completely amorphous state in solution, probably possesses more randomly distributed crystalline and amorphous regions, and hence shows a gradual increase in crystallinity with an increase in compression pressure to 15 MPa.

Further increase in compression pressure (to 77 MPa) produced no statistically significant effect on the crystallinity of LCPC and commercial cellulose products except for Avicel® PH-102, in which the crystallinity decreased by about 5% at 15 MPa. Beyond 15 MPa, however, no further statistically significant change in the crystallinity was noted.

Ek et al. (1995), using ^{13}C CP/MAS NMR, reported a 5% increase in the crystallinity of

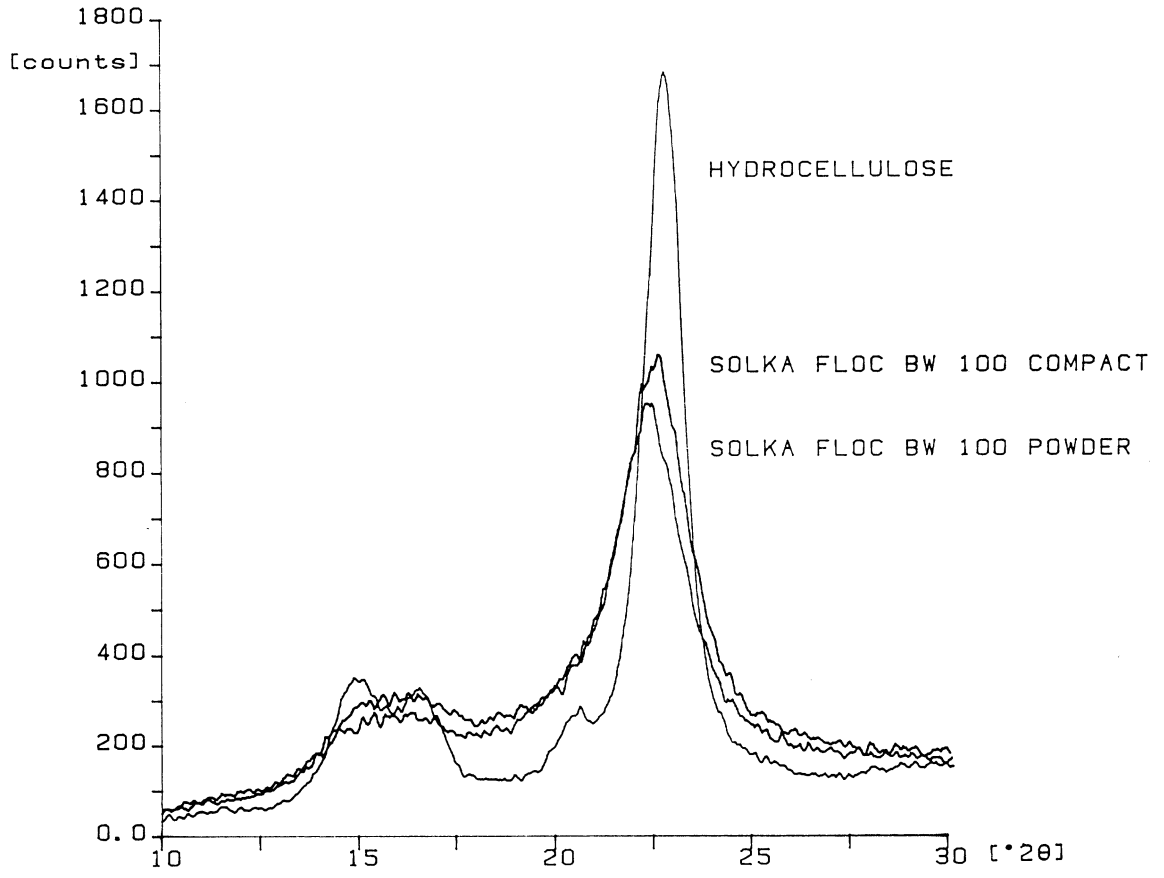

Fig. 8. X-ray diffractograms of hydrocellulose, Solka Floc BW-100 powder and Solka Floc BW-100 compact that showed the maximum crystallinity increase.

Avicel® PH-101, compared to that of the powdered form, at 56 MPa. Between 56 MPa and 1230 MPa, the crystallinity of the compacts decreased by 9%, about 4% lower than that of the powdered form. These results, however, can not be compared with the present findings because no data are available on the moisture content of the material and dwell time used during compression. The different amounts of moisture content are known to plasticize cellulose to different degrees and, consequently, alter its mechanical properties (Khan et al., 1988)

In conclusion, the results showed (1) that the crystallinity of cellulose excipients increases at low compression pressures, and (2) that the magnitude of changes depends on the compression pressure applied and the ability of the cellulose crystallites to reorient themselves under compressional force. LCPC being less influenced by the compression pressure may have attractive features as a direct compression tablet excipient. Further research to investigate how low crystallinity cellulose serves as a potential disintegrant in conjunction with its binding properties and how this property of maintaining its crystallinity under compressional force may give it a distinct advantage over the other types of excipients is in progress.

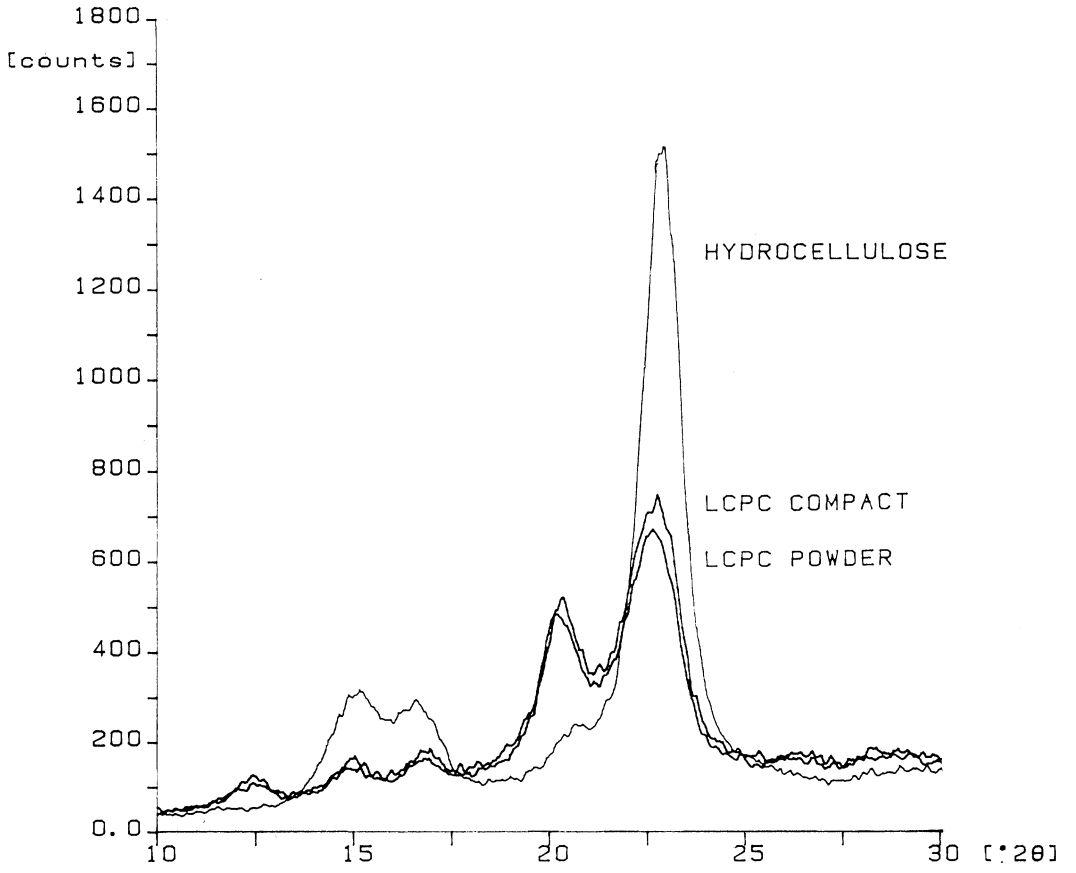

Fig. 9. X-ray diffractograms of hydrocellulose, LCPC powder and LCPC compact that showed the maximum crystallinity increase.

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