Crystallinity index of microcrystalline cellulose particles compressed into tablets

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Abstract

The crystallinity index of compressed microcrystalline cellulose particles has been estimated using ^{13}C CP/MAS NMR and photoacoustic FTIR. The results indicate a slight initial increase in crystallinity followed by a decrease as the compaction pressure increases. The initial increase is explained as a transformation of strained structures in cellulose particles into more ordered forms as a result of the initial compression. At higher compaction pressures the crystallinity begins to decrease. This change in crystallinity seems to be larger on the tablet surface than in the tablet bulk and even larger at the tablet perimeter surface than on the top or bottom surfaces of the tablet. Our explanation for these findings is that these differences reflect different levels of shearing forces acting on different parts of the tablet during compaction.

1. Introduction

Microcrystalline cellulose particles consolidate into strong compacts (stronger compacts than most other substances at equal load) when a bed of particles is subjected to compression forces. Microcrystalline cellulose is therefore used as a tablet excipient by the pharmaceutical industry (Reier and Shangraw, 1966; Sixsmith, 1976; Lamberson and Raynor, 1976; Landín et al., 1993).

The final strength of a tablet is a complex relationship between material properties, volume reduction behavior, dominating bond mechanism and the surface area over which these bonds extend. It is known that during compression the microcrystalline particles exhibit both elastic and plastic deformation (Duberg and Nyström, 1985). Hydrogen bonds and mechanical interlocking are the two dominating factors normally considered in pharmaceutical tablets, whereas solid bridges are assumed to be unlikely (Karehill and Nyström, 1990a,b). The bonding capacity of the microcrystalline cellulose has been explained by the high surface area (Nyström and Karehill, 1986;

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Nyström et al., 1993). However, during compaction the tensile strength evolves differently in the axial as opposed to the radial direction and the compacts become anisotropic. The anisotropy might result in capping tendencies for cellulose at higher compression loads, thereby having a detrimental effect on tablet properties (Wells and Langridge, 1981). Studies of the parameters that affect tablet capping have been reported (Ritter and Sucker, 1980).

The importance of shear forces during compaction has been established and the conclusion drawn that more efficient bonding results if the particles are subjected to shear as well as compressive forces simultaneously. Regions of a compact are weak if they are not subjected to shearing during compression (Train, 1957). A method has been proposed to increase the shear strain in the bulk by using angled punches and rotating the die while pressure is applied, thereby producing a stronger compact (Gregory, 1962).

Cellulose particles subjected to compression forces appear to retain their crystallinity while simultaneously applied shear forces result in a significant decrease in crystallinity (Gravitis et al., 1991). Therefore it may be possible to study the influence of shear forces on the cellulose particles by measuring the crystallinity. The crystallinity of cellulose is also of importance with respect to other physical properties. It has been reported that dry ground cellulose powder with low crystallinity results in tablets of low strength (Nakai et al., 1977). Further it has been demonstrated that the crystallinity of cellulose particles decreases during compression (Hüttenrauch and Keiner, 1976).

The aim of this study was to characterize the change in crystallinity of the tablet bulk and surface layer as a function of compaction pressure. Two different spectroscopic methods; ^{13}C CP/MAS NMR and photoacoustic FTIR, were used to estimate crystallinity. The ^{13}C CP/MAS NMR characterizes a crystallinity index in the tablet bulk while the photoacoustic FTIR is sensitive to the changes induced in the surface layers of the tablets.

A series of cellulose compacts were formed by subjecting them to different pressures (4–1230

MPa) and the tensile strength was estimated both in an axial as well as in a radial direction of the compact. The crystallinity was estimated by NMR on dry compressed cellulose and on wet cellulose from disintegrated tablets. The flat top and perimeter surfaces of the dry tablets were investigated using the FTIR technique.

2. Experimental

2.1. Material

The compacts were made of microcrystalline cellulose, Avicel PH 101, lot 6017, FMC, Ireland.

2.2. Methods

2.2.1. Powder compression

The cellulose powder was compressed as supplied in a single punch tablet machine (Korsch EK 0, Germany) equipped with 5.47 mm flat faced punches. The powder for each compact was manually poured into the die. The motor of the machine was started when the upper punch was at its highest position and directly after compression the motor (30 rpm) was stopped and the flywheel manually arrested. The maximum value of the upper punch force was registered and the upper punch pressure calculated. No lubrication was used.

After compression the tablets were stored at room temperature (20°C) for more than 48 h; for radial tensile testing in sealed bottles, for axial tensile testing at 40% RH.

2.2.2. Density of compact

The weight and thickness of each compact was measured within a minute after compression. These values and the diameter of the punches (5.47 mm) were used to calculate the tablet density. Results are presented as mean values of ten determinations.

2.2.3. Porosity of compact

The porosity e of the compact was calculated from the equation

$$\epsilon = 1 - \frac{\text{tablet density}}{\text{cellulose particle density}}$$

where the cellulose particle density was assumed to be 1570 kg/m^3 (Ek et al., 1994a).

2.2.4. Compact strength

The compact tensile strength in the axial and radial direction was tested and calculated from reported equations (Nyström et al., 1978).

The radial tensile strength was measured utilizing a diametrical compression test apparatus (Pharma Test PTB 301/501, Tegimenta, Germany). All compacts showed approximately normal tensile failure, i.e. a diametrical fracture between the points of force loading. Results are presented as mean values of six determinations.

The axial tensile strength was measured utilizing an axial tensile test apparatus (M 30 K, Lloyd Instruments, UK) with a straining velocity of 0.3 m/h. Results are presented as mean values of ten determinations.

2.2.5. Disintegration time

The disintegration time in water at 20°C was investigated, in a disintegration tester (Erweka Apparatbau ZT3-2, Germany) in accordance with USP XXI, 1985. The disintegrated cellulose was collected by filtration to about 50% dryness before measurement of the crystallinity index using the NMR equipment.

2.2.6. Spectroscopic measurements

Dry compacts of microcrystalline cellulose were investigated with two different spectroscopic techniques, solid state ^{13}C NMR and photoacoustic FTIR. To avoid sample alteration and preparation error, the diameter of the tablets was made equal to the diameter of the sample rotor used in the NMR measurements. The tablets could therefore be used directly as samples.

NMR equipment. The measurements were performed on a Bruker AMX 300 spectrometer operating at 75.48 MHz. The spinning rate was 5 kHz using a double air bearing probe and ZrO$_2$ rotors. A contact time of 0.8 ms was used with a 2.5 s pulse delay and a 368 ppm sweep width. A total of 3000 transients were acquired for each spectra with 2 K data points and zero-filling to 4 K data points. The chemical shift scale was referenced to the carbonyl peak in external glycine at 176.03 ppm.

NMR spectra. The C4 peak has previously been used to estimate the crystallinity index of microcrystalline cellulose (Ek et al., 1994a,b). A crystallinity index $CrI = a / (a + b)$ was estimated from the NMR spectra by integrating the peaks at 86–93 ppm (a) and 80–86 ppm (b).

IR equipment. The measurements were performed on a Fourier transform infrared spec-

Table 1
Characterising data of compacts of Avicel PH 101

Compaction pressure [a] (MN/m^2)	Porosity [b] (%)	Tablet density (kg/m^3)	Tensile strength		Isotropy ratio [e]	Disintegration time (s)
			radial [c] (MN/m^2)	axial [d] (MN/m^2)		
Powder	79.0	330	–	–	–	–
4	55.2	704	0.31	–	–	1
32	45.5	855	0.78	0.54	0.69	3
56	37.3	985	1.91	–	–	13
62	33.8	1040	2.00	1.02	0.51	9
107	21.7	1230	3.99	–	–	20
125	21.7	1230	4.92	2.18	0.44	28
336	8.9	1430	9.51	4.24	0.44	28
507	7.0	1460	10.6	3.90	0.37	293
801	6.8	1400	10.7	3.65	0.31	248
1230	4.5	1500	11.0	–	–	350

[a] Maximum upper punch pressure, average of more than 10 compacts.
[b] $\epsilon = 1 -$ (tablet density/cellulose particle density).
[c] Microcrystalline cellulose compressed as supplied, compacts stored more than 48 h in sealed bottles.
[d] Microcrystalline cellulose compressed as supplied, compacts stored more than 48 h in air, 20°C 40% RH.
[e] Ratio between axial and radial tensile strength.

trometer (Perkin Elmer 2000), equipped with a photoacoustic detector (MTEC 200, MTECH Photoacoustics, USA). The measurements were performed with a helium filled sample chamber, accumulation of 32 scans and a resolution of 8 cm^{-1} in the range of 4000 cm^{-1} to 400 cm^{-1}. The mirror velocity (optical path difference velocity) was 0.05 cm/s. The measuring depth was calculated from the expression $L = (D/pf)^{1/2}$ was found to be around 20 μm, the thermal diffusivity (D) is defined by $D = k/rC$ and the modulation frequency (f) by $f = wv$, at a given wavenumber w and optical path difference velocity v. The values of thermal conductivity $(k = 0.26$ W/mK), density $(r = 1570$ kg/m^3) and specific heat $(C = 1.25$ kWs/kgK) were taken from information on cotton cellulose (Temming and Grunert, 1973).

IR spectra. A crystallinity index was defined as $CrI = a/b$ where the absorption was estimated at $a = 1372$ cm^{-1} and $b = 2900$ cm^{-1}. As base for the band at 2900 cm^{-1} the height of the adjacent shoulder near 3000 cm^{-1} was chosen. For the band at 1372 cm^{-1} a base line was drawn between the maximum at approximately 1290 and 1410 cm^{-1} (Nelson and O'Connor, 1964).

3. Results

Results from the compaction of microcrystalline cellulose are summarized in Table 1 and Fig. 1. The tablet strength and density increases and the porosity and isotropy decreases during consolidation of microcrystalline cellulose into tablets. When the compaction pressure reaches 200-300 MPa the decrease in tablet porosity levels off corresponding to a tablet density around 1400-1500 kg/m^3. This is close to the density of the microcrystalline cellulose particle which has been reported to be 1570 kg/m^3 (Ek et al., 1994a). The porosity of the final tablets after deloading and expansion were in the order of 5-10%. The tablet strength increases as long as the particles consolidate into a compact of higher density, but when the final density level is reached the tensile strength also levels off. The isotropy ratio decreases as the compaction pressures increase since the axial strength decreases whereas the radial strength is constant or even shows a slight increase.

The crystallinities of the cellulose particles, estimated with ^{13}C CP/MAS NMR and photoacoustic FTIR, are summarized in Table 2 and Fig. 2. The crystallinity index for a dry compacts estimated by the FTIR technique are of the order of 0.26-0.42 while the corresponding ^{13}C CP/MAS NMR values are about 0.49-0.54. The crystallinity index of wet cellulose particles from disintegrated compacts is in the range of 0.57-0.59. When the wet cellulose particles were redried at 23°C, 50% RH the crystallinity index decreased to 0.54-0.56. That is, the redried parti-

Table 2
Crystallinity index of cellulose (Avicel PH 101) compressed into tablets characterized with ^{13}C CP/MAS NMR and photoacustic FTIR

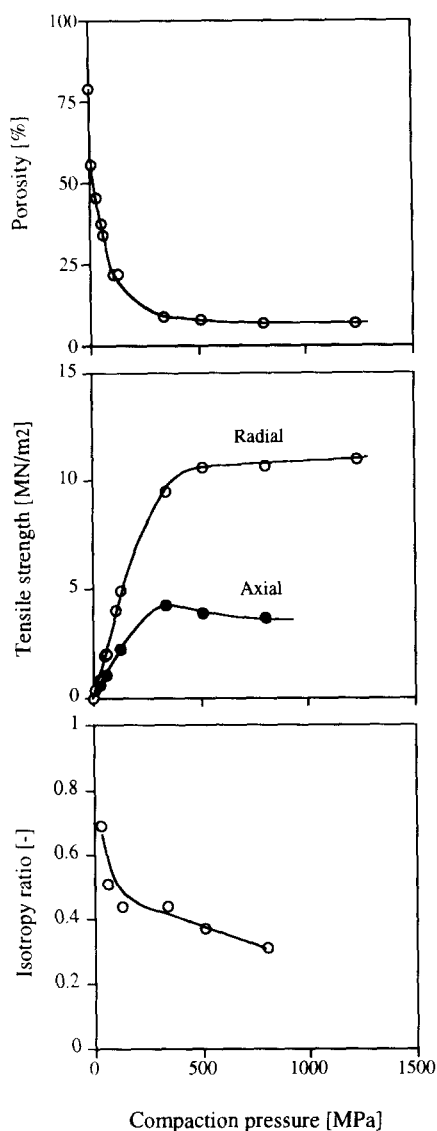| Compaction pressure (MN/m^2)	NMR on cellulose particles			FTIR on tablet surface	
	compact	wet	redried [a]	top/bottom	perimeter
Powder	0.51	0.59	0.55	0.38	0.38
4	0.51	0.58	0.55	0.37	–
32	0.52	0.58	0.55	0.40	0.37
56	0.54	0.58	0.54	0.42	0.38
63	0.50	0.58	0.54	0.40	0.40
107	0.50	0.58	0.54	0.38	0.37
125	0.51	0.58	0.55	0.37	0.35
336	0.48	0.56	0.54	0.35	0.29
507	0.48	0.57	0.55	0.35	0.30
801	0.49	0.57	0.54	0.33	0.28
1230	0.49	0.57	0.52	0.32	0.26

[a] Redried at 23°C, 50% RH.

Fig. 1. Porosity, radial and axial tensile strength and isotropy of the tablets obtained by compacting of microcrystalline cellulose particles (Avicel PH 101) into 100 mg tablets in an single punch tablet machine. No lubrication was used.

niques. The crystallinity index for dry compacts shows an initial plateau or a slight increase followed by a decline as the porosity decreases. The crystallinity on the surface of the compact is lower on the perimeter surface than on flat face surfaces of the tablets. It also appears that the changes in crystallinity is higher on the surfaces (photoacoustic FTIR method) than in the bulk of the tablet (^{13}C CP/MAS NMR method). Wet cellulose particles from disintegrated compacts, exhibited a slight reduction of the crystallinity index with increasing density.

4. Discussion

It is known that different spectroscopic methods and evaluation techniques result in different levels of the crystallinity index (Jeffries et al., 1969). One example is the crystallinity index for microcrystalline cellulose which was found to be between 60–80% by X-ray methods and between 50–60% using transmission IR spectroscopy (Landín et al., 1993). In our study the absolute value of the initial crystallinity detected on cellulose powder by NMR and IR was 0.51 and 0.38 respectively (see Table 2). However, changes in the crystallinity index as determined from IR experiments on cellulose I and cellulose II have been reported to be of the same order as those determined by X-ray methods (Nelson and O'Connor, 1964).

We have in this work used the photoacustic IR technique. The absorption wavelengths are the same in as in other IR techniques (Vidrine, 1980; Griffiths and de Haseth, 1986), but errors due to sample preparation are eliminated. The compacts were too opaque for direct use in transmission IR. Another reason for using the photoacustic IR technique is that the technique can be used for the evaluation of surface composition of solid samples. However, care should be taken since the evaluation of the spectra of opaque compacts and powders may be complicated by scattering effects due to varying particle or pore size causing non-linear effects in the recorded spectra (Russell, 1982).

cles obtained a value between the dry compressed and the wet disintegrated cellulose particle and did not decrease to the original value measured in dry compacts.

There is considerable agreement between the results obtained from the two spectroscopic tech-

Although photoacustic IR is a well suited method for surface layer studies, there appears to be no investigations of the crystallinity of cellulose reported in the literature using the photoacoustic IR technique.

4.1. Influence of drying rate on the crystallinity of the cellulose particles

During manufacturing of microcrystalline cellulose a final drying is rapidly carried out in a spraydrier (Ek et al., 1994a) and a crystallinity index of 0.51 (NMR) is obtained. If these particles are wetted the crystallinity index increases to 0.59 (NMR). When redried at 23°C, 50% RH the value decreases to 0.55 (NMR). Even the drying conditions seem to be important for the properties of the microcrystalline cellulose.

4.2. Crystallinity increase at low compaction pressures

The results indicate a slight increase in crystallinity at low compaction pressures and a subsequent decrease in crystallinity as the pressure increases. The initial increase may be explained as reordering of the cellulose particles by releasing some of the stresses and irregularities built into the material during the spray drying manufacturing operation. It is known that rapid drying,

e.g. spray drying (Hüttenrauch, 1983; Sebhatu et al., 1994) and dry grinding (Hermans and Weidinger, 1946; Elamin et al., 1994) produces a material with a fraction of amorphous substance which is unstable and tends to slowly convert back into the crystalline form (Byrn, 1982). The slight increase in crystallinity can not be traced in wet cellulose particles which have been obtained by disintegrating tablets in water. Since water is a strong swelling media for cellulose, it seems likely that in the wet particles the cellulose has released the drying stresses induced during spraydrying.

4.3. Crystallinity decrease at higher compaction pressures

In general, the crystallinity of cellulose particles tends to decrease during compression. The decrease in crystallinity may be explained by structural irregularities introduced in the crystal lattice by shearing and stressing of the cellulose particles (Gravitis et al., 1991). In an effort to study these latter mechanisms, the thermo-introduced irreversible transformation of the polymorphs cellulose I_a to cellulose I_b (Debzi et al., 1991; Lennholm et al., 1994) was investigated. However, the data obtained gave no further guidance concerning the understanding of the generated results. An alternative explanation may be partial melting in hot spot areas (Hanus and
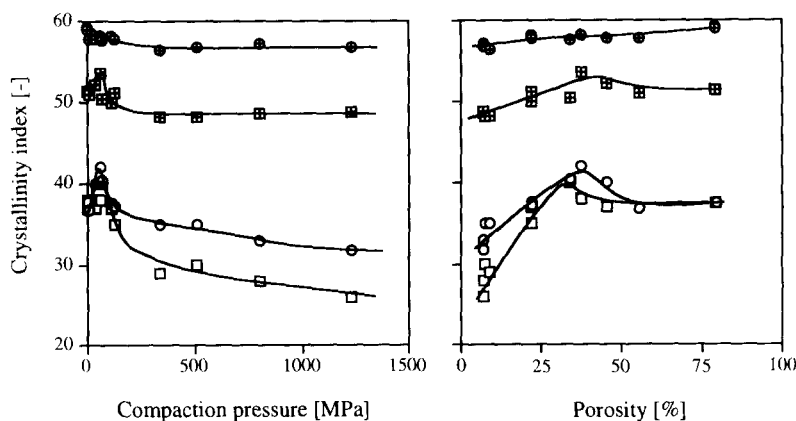

Fig. 2. Crystallinity index versus compaction pressure and tablet porosity of microcrystalline cellulose compacts. From the top, the marks and curves refer to: (⊕) wet disintegrated cellulose particles (NMR); (⊞) dry cellulose particles in compacts (NMR); (○) dry cellulose particles on the flat tablet surface (photoacoustic IR); (□) dry cellulose particles on the tablet perimeter surface.

King, 1968; Rankell and Higuchi, 1968; Nordin et al., 1974).

The change in crystallinity seems to be greater on the tablet surface as determined by the photoacoustic IR method, than in the tablet bulk, shown by the NMR method. Furthermore, it appears that the crystallinity decrease is more pronounced at the tablet perimeter surface than on the top or bottom of the tablet, Table 2. However care should be taken when evaluating small changes in IR spectra due to complications deriving from scattering by the particulate material.

Our explanation is that the variations in crystallinity reflect different levels of shearing forces acting on different parts of the tablet during compaction. The shearing forces are greatest during the compression/decompression phase when the highest pressures are applied, i.e. when the upper punch is at its lowest position during the compression cycle, but there is also an additional shearing force acting on the perimeter surfaces when the tablet is ejected. Although this shear force is lower, the total shear work is substantial since the distance over which this force acts is substantial.

Consolidation of tablets due to shear forces has also been shown by compressing lead shot. The high shear forces at the tablet surfaces resulted in rewelding and high bonding strength between the particles, especially on the perimeter surface. In the inner region of the tablets there was no substantial increase in bonding strength (Train and Hersey, 1960). It has been concluded that shear forces have an essential influence on the tablet strength which would explain density variations in tablets (Train, 1957).

5. Conclusions

^{13}C CP/MAS NMR and photoacustic FTIR are two spectroscopic methods which offer the possibility of studying crystallinity in the tablet bulk and at the tablet surface respectively. From our study on the compression of cellulose particles, it appears that the changes in crystallinity at the tablet surface differs from the changes in crystallinity in the inner region of the tablet.

References

Byrn, S.R., Solid State Chemistry of Drugs, Academic press, London, 1982, p. 10.

Debzi, E.M., Chanzy, H., Sugiyama, J., Tekely, P. and Excoffier, G., The Iα I transformation of highly crystalline cellulose by annealing in various mediums. Macromolecules, 24 (1991) 6816–6822.

Duberg, M. and Nyström, C., Studies on direct compression of tablets XII. The consolidation and bonding properties of some pharmaceutical compounds and their mixtures with Avicel 105. Int. J. Pharm. Tech. Prod. Mfr., 6(2) (1985) 17–25.

Ek, R., Alderborn, G. and Nyström, C., Particle analysis of microcrystalline cellulose: Differentiation between Individual particles and their agglomerates. Int. J. Pharm., 111 (1994a) 43–50.

Ek, R., Lennholm, H., Davidson, R., Nyström, C. and Ragnarsson, G. Pore swelling in porous cellulose beads made of cellulose fibre and fibre fragments. Int. J. Pharm., In press. (1994b).

Elamin, A.A., Ahlneck, C., Alderborn, G. and Nyström, C., Increased metastable solubility of milled griseofulvin depending on the formation of a disordered surface structure. Int. J. Pharm., 111 (1994) 159–170.

Gravitis, J., Kokorevics, A., Teeäär, R., Zharov, A. and Lippmaa, E., Structural changes of wood and its components initiated by the simultaneous action of shear deformation and high pressure. J. Pulp Paper Sci., 17 (1991) J 119–J123.

Gregory, H.R., In Rottenburg, P.A. (Ed.), Proceedings of Symposium on the Handling of Solids, Inst. Chem. Engrs., 1962, p 7.

Griffiths, P.R. and de Haseth, J.A., Fourier transform infrared spectrometry. In Elving, P.J., Winefordner, J.D. and Kolthoff, I.M. (Eds.), Chemical Analysis, John Wiley and Sons, New York, 1986, pp. 312.

Hanus, E.J. and King, L.D., Thermodynamic effects in the compression of solids. J. Pharm. Sci., 57 (1968) 677–684.

Hermans, P.H. and Weidinger, A., On recrystallization of amorphous cellulose. J. Am. Chem. Soc., 68 (1946) 2547–2552.

Hüttenrauch, R. and Keiner, I., Einfluß des preßdrucks auf den ordnungsgrad von cellulosepulvern. Pharmazie, 31 (1976) 490–491.

Hüttenrauch, R., Modification of starting materials to improve tabletting properties. *Pharm. Ind.*, 45 (1983) 435–440.

Jeffries, R., Jones, D.M., Roberts, J.G., Selby, K., Simmens, S.C. and Warwicker, J.O., Current ideas on the structure of cotton. *Cellulose Chem. Technol.*, 3 (1969) 255–274.

Karehill, P.G. and Nyström, C., Studies on direct compression of tablets XXI. The importance of surface roughness for the compactability of some directly compressible materials with different bonding and volume reduction properties. *Int J. Pharm.*, 64 (1990a) 35–43.

Karehill, P.G. and Nyström, C., Studies on direct compression of tablets XXIII. Investigation of bonding mechanisms of some directly compressed materials by strength characterization in media of different dielectric constant (relative permittivity). *Int, J. Pharm.*, 61 (1990b) 251–260.

Lamberson, R.L. and Raynor, G.E., Tableting properties of microcrystalline cellulose. *Mfg. Chem. Aerosol News*, 47 (June) (1976) 55–61.

Landín, M., Martínez-Pacheco, R., Gómez-Amoz, J.L., Souto, C., Concheiro, A. and Rowe, R.C., Effect of country of orgin on the properties of microcrystalline cellulose. *Int. J. Pharm.*, 91 (1993) 123–131.

Lennholm, H., Larsson, T. and Iversen, T., Determination of and cellulose I_a and I_b in lignocellulosic materials. *Carbohydr. Res.*, 261 (1994) 119–131.

Nakai, Y., Fukuoka, E., Nakajima, S., and Hasegawa, J., Crystallinity and physical characteristics of microcrystalline cellulose. *Chem. Pharm. Bull.*, 25 (1977) 96–101.

Nelson, M.L. and O'Connor, R.T., Relation of certain infrared bands to cellulose crystallinity and crystal lattice type. Part I. Spectra of lattice types I, II, III and of amorphous cellulose. Part II. A new infrared ratio for estimation of crystallinity in celluloses I and II. *J. Appl. Polymer Sci.*, 8 (1964) 1311–1341.

Nordin, S.B., Nyrén, J.O. and Back, E.L., An indication of molten cellulose produced in laser beam. *Textile Res. J.*, 48 (1974) 152–154.

Nyström, C., Malmqvist, K., Mazur, J., Alex, W. and Hölzer, A.W., Measurement of axial and radial tensile strength of tablets and their relation to capping. *Acta Pharm. Suec.*, 15 (1978) 226–232.

Nyström, C. and Karehill, P.G., Studies on direct compression of Tablets XVI. The use of surface area measurements for evaluation of bonding surface area in compressed powders. *Powder Technol.*, 47 (1986) 201–209.

Nyström, C., Alderborn, G., Duberg, M. and Karehill, P.G., Bonding surface area and bonding mechanism-two important factors for the understanding of powder compactability. *Drug Dev. Ind. Pharm.*, 19 (1993) 2143–2196.

Rankell, A.S. and Higuchi, T., Physics of tablet compression XV. Thermodynamic and kinetic aspects of adhesion under pressure. *J. Pharm. Sci.*, 57 (1968) 574–577.

Reier, G.E. and Shangraw, R.F., Microcrystalline cellulose in tableting. *J. Pharm. Sci.*, 55 (1966) 510–514.

Ritter, A. and Sucker, H.B., Studies of variables that affect tablet capping. *Pharm. Technol. Int.*, 3(3) (1980) 24–54.

Russell, J.D., Infrared Spectroscopy of inorganic compounds. In Willis, H.A., Van der Maas, J.H. and Miller, R.G.J. (Eds), *Laboratory Methods in Vibrational Spectroscopy*, John Wiley and sons, New York, 1982, Chapter 18.

Sebhatu, T., Angberg, M. and Ahlneck, C., Assessment of the degree of disorder in crystalline solids by isothermal microcalorimetry, *Int. J. Pharm.*, 104 (1994) 135–144.

Sixsmith, D., Microcrystalline cellulose as a tablet excipient. *Mfg. Chem. Aerosol News*, 47 (Aug) (1976) 27–28.

Temming, H. and Grunert, H., *Temming-linters. Technical information on cotton cellulose*, Peter Temming AG, Glückstadt, 1973.

Train, D. and Hersey, J.A., Some fundamental studies in the cold compaction of plastically deforming solids. *Powder Metallurgy*, 6 (1960) 20–35.

Train, D., Transmission of forces through a powder mass during the process of pelleting. *Trans. Inst. Chem. Eng.*, 35 (1957) 258–266.

Vidrine, D.W., Photoacoustic fourier transform infrared spectroscopy of solid samples. *Appl. Spectrosc.*, 34 (1980) 314–319.

Wells, J.I. and Langridge, J.R., Dicalcium phosphate dihydrate microcrystalline cellulose systems in direct compression tableting. *Int.J. Pharm. Tech. and Prod. Mfr.*, 2(2) (1981) 1–8.