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Effect of country of origin on the properties of microcrystalline cellulose

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Summary

The characteristics of four brands of microcrystalline cellulose manufactured in Finland, India, Ireland and Japan have been determined; all four were nominally similar to Avicel PH 101. There were significant differences in lignin content, hemicellulose sugars content and composition, presence or absence of cellulose II, enthalpy of immersion, particle size and flow properties. Crystallinity correlated with water-cellulose interaction, and particle size with flow properties.

Introduction

In recent years, a considerable number of microcrystalline celluloses have been marketed by various companies. Differences between them as regards the possible wood used as raw material and the manufacturing processes by which they are obtained would suggest that their properties may also differ significantly. Comparative studies of specific properties have supported this hypothesis (Bolhuis and Lerk, 1973; Doelker et al., 1987a; Roberts and Rowe, 1987; Parker et al., 1988).

In an accompanying paper (Landín et al., 1993) we investigated the source (raw material or manufacturing process) of differences in chemical composition, crystal structure, interaction with water and particulate properties of three batches of microcrystalline cellulose produced by a single manufacturer. In this article we compare four brands of microcrystalline cellulose, all similar to Avicel PH 101, that were produced by different manufacturers in Finland, India, Ireland and Japan.

Materials and Methods

The four brands of microcrystalline cellulose studied were as follows: Emcocel (Edward Mendell, Finland), MCC from India (Steetley

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Berk, U.K), Avicel PH 101 (FMC, Ireland) and Unimac MG 100 (Unitika Rayon, Japan).

Chemical analysis

Determination of lignin

Lignin was assayed by the methods of Morrison (1972) and Jaegher et al. (1985). The α-cellulose fraction was dissolved in 5 ml of 25% acetyl bromide in glacial acetic acid, and then heated for 30 min at 70°C in a thermoblock. After cooling, 5 ml of 2 N NaOH solution was added. The mixture was centrifuged at 4000 rpm for 10 min, the pellet was discarded and 0.5 ml of hydroxylamine was added to the supernatant. Lignin was determined by reading the absorbance of the final solution at 280 nm (lignin at 10 μg/ml gives an absorbance of about 0.24).

Determination of hemicelluloses

Cellulose samples were hydrolyzed with 2.0 M trifluoroacetic acid (TFA) for 1 h at 121°C. The sugars released were derivatized to alditol acetates (Albersheim et al., 1967), which were determined in a Hewlett Packard Model 5890-II gas-liquid chromatograph equipped with a column sp 2330, 30 m.

Analysis of total sugar content

Cellulose samples were hydrolyzed with 72% H_2SO_4 for 3 h at room temperature. After addition of 5.5 ml of water the mixture was heated for 2.5 h at 100°C, neutralized with $Ba(OH)_2$, brought to pH 5.5 and dried. Sugars released were analyzed as described previously.

Crystal structure

Powder X-ray diffraction

Measurements were carried out at room temperature, on a Siemens X-ray diffractometer D5000 using monochromatic CuKα radiation and a scanning rate of 0.25° 2θ/min over the range 4–50° 2θ. Samples for analysis were prepared by pressing the powder into the cavity of a sample holder and smoothing with a glass slide.

The crystallinity index of each sample was calculated by two methods. Method 1 was implemented using a computer program to draw the demarcation line between the surface of the crystalline reflections and the diffuse halo of the amorphous regions (Doelker et al., 1987b). Method 2 used intensity measurements at 22.6 and 19.0° 2θ according to Nelson and O'Connor (1964) as used by Chatrath et al. (1991)

Infrared spectroscopy

Infrared spectra were obtained with a Cignus 100, Mattson spectrophotometer by use of the potassium bromide pellet technique. The spectra was produced over the range 400–4000 cm^{-1}.

The crystallinity index was calculated using the method of Nelson and O'Connor (1964) from measurements at wavenumbers 1317 and 2900 cm^{-1}.

Raman spectroscopy

The Raman spectra were recorded on a Omars 89 Raman system using the 5145 Å line of a coherent radiation Argon Ion Laser for excitation.

True density determination

The true particle densities (δ_t) of the microcrystalline cellulose powders were determined using a helium-air pycnometer (Quantacrome Mod. PY2).

Measurements were carried out at least three times for each sample.

Powder properties

Particle size analysis

Particle size distributions were recorded using a Coulter LS 100 Laser Diffraction Particle Size Analyser in triplicate for each variety. The results are expressed in terms of mean surface diameter (d_s).

The mean surface volume diameter (d_{sv}) was calculated from the following equation (Allen, 1978):

$$d_{sv} = \sum n_i d_i^3 / \sum n_i d_i^2$$

where n_i is the number of particles with diameter d_i from number size distributions.

TABLE 1

Characteristics of the batches of microcrystalline cellulose; mean values (standard deviations)

Property	Origin			
	Ireland	Finland	Japan	India
Lignin (%)	0.66	0.70	0.35	0.95
	(0.05)	(0.09)	(0.07)	(0.14)
Hemicelluloses (TFA)				
Xylose	0.35	0.32	0.17	0.62
	(0.04)	(0.06)	(0.05)	(0.08)
Manose	0.20	0.12	0.12	0.10
	(0.01)	(0.02)	(0.02)	(0.01)
Glucose	1.52	1.68	2.09	1.48
	(0.10)	(0.25)	(0.36)	(0.06)
Total sugars (H_2SO_4)				
Fucose	0.6	–	–	–
Arabinose	0.7	1.4	14.0	0.6
Xylose	5.4	3.9	3.9	6.0
Manose	5.7	7.1	3.8	4.6
Galactose	–	1.7	–	–
Glucose	87.6	86.0	78.2	88.4
α (%) (Method 1)				
X-ray diffraction	62.9	64.3	62.1	61.2
α (%) (Method 2)				
X-ray diffraction	84.2	86.2	83.5	81.7
$\alpha_{1371}/\alpha_{2900}$				
IR spectroscopy	50.6	58.3	51.6	50.8
True density	1.563	1.543	1.532	1.539
	(0.022)	(0.017)	(0.014)	(0.011)
Laser light scattering				
d_s (μm)	47.27	57.58	39.87	22.42
Surface area (m^2/g)	1.153	0.982	1.128	1.582
	(0.109)	(0.036)	(0.021)	(0.068)
Equilibrium moisture (%)				
(65% RH)	7.54	6.73	7.15	6.94
E_0 (−J/g)	54.24	47.32	48.32	53.24
Compressibility (%)	39.17	36.11	42.02	48.45
Flowability index	41.00	50.00	45.00	36.50
Classification	not good	not good	not good	bad
Floodability index	73.00	78.90	71.50	85.00
Classification	fairly bad	fairly bad	fairly bad	very high
Mean yield pressure (MPa)	48.68 (1.68)	41.96 (1.50)	43.26 (1.51)	47.02 (0.85)
at moisture content (%)	5.46	4.20	4.61	4.56
Mean yield pressure (MPa)	75.06 (5.43)	68.97 (0.83)	74.30 (2.06)	71.80 (1.98)
at moisture content (%)	4.03	3.76	3.72	3.73

The particle shape factor F_s was evaluated as follows (Allen, 1978):

$$F_s = S_w \delta_t d_{sv}$$

where S_w is the specific surface area determined using nitrogen adsorption.

Scanning electron microscopy (SEM)

Samples of each powder were prepared and examined using a ISI 60 scanning electron microscope. Samples to be studied were mounted on double sided tape on aluminum stubs and coated with gold under vacuum.

Equilibrium moisture

Samples of 15 g of each excipient were stored in hermetic glass bottles containing sulfuric acid solutions for maintaining 20, 40, 60, 80 and 100% RH. After equilibration the moisture content the samples were determined using a Shimadzu thermobalance to measure weight loss by 2 g sample after 11 min at a temperature of about 115°C (Pesonen and Paronen, 1986).

Nitrogen adsorption

The specific surface area of each excipient sample was determined in a Micromeritics ASAP 2000 apparatus. Samples were first degassed by heating under vacuum for 24 h at 70°C and a pressure of 10^{-3} mmHg. Nitrogen adsorption took place at 77 K and relative pressures from 0.01 to 0.98. The specific surface area (s_w) of the samples was estimated from

$$s_w(\mathrm{m}^2/\mathrm{g}) = 4.37 V_m(\mathrm{cm}^3/\mathrm{g})$$

where V_m is the volume of nitrogen necessary to form a monolayer which can be calculated from the BET equation (Stanley-Wood et al., 1990).

Pore size distributions were calculated from the nitrogen adsorption isotherms by the BJH method (Stanley-Wood, 1983).

Immersion calorimetry

Immersion calorimetry was carried out on prepared microcrystalline cellulose samples using a Tronac model 458 Solution Calorimeter described previously (Parker and Rowe, 1991)

Samples of microcrystalline cellulose of differing moisture contents were prepared by storage over saturated salt solutions or in glass desiccator jars.

Measurements were carried out in duplicate for each level of moisture, and graphs of enthalpy of immersion against moisture content of sample could then be plotted.

These curves were characterized by the value of the enthalpy of immersion for 12% humidity (E_{12}) and by the value estimated by extrapolation for the dry powder (E_0) (Parker, 1989).

Flow properties

Bulk density determination

A Hosokawa powder tester was used to measure the tapped density as particles in a powder were rearranged, packed and compacted at 50 taps/min for periods of time up to 20 min.

After determination of the tapped bulk density values, the results could be used to calculate the indices of flowability and floodability and the compressibility (Thomsom, 1984).

Compression properties

The compression properties of the cellulose materials were tested by preparing 200 mg tablets 9 mm in diameter in a single punch machine equipped with transducers (Martínez-Pacheco et al., 1988). Tablets were compressed to 25% of initial volume at a rate of 41 tablets/min. Powders were stored under two different moisture conditions (ambient and after storage in an oven 48 h at 50°C).

Mean yield pressures underload were determined using Heckel plots of the data from compression force-displacement cycles (Humbert-Droz et al., 1982).

Results and Discussion

Table 1 lists the results of the analyses performed on the microcrystalline celluloses studied.

Chemical composition varied considerably as regards both lignin content and the total and relative quantities of hemicellulose sugars, suggesting that different woods were used as raw materials. More specifically, the mannose/xylose ratios suggest, according to the criteria of Baehr et al. (1991) that the Indian and Japanese brands were derived from hardwood, and the Irish and Finish brands from softwood. The striking differences in non-cellulose content, are suggestive of manufacturing processes of significantly different intensities, ranging from the Indian brand, with highest lignin and hemicellulose sugar contents, to the Japanese brand with the lowest.

For all four brands, X-ray diffractograms obtained to analyse their crystal structures (Fig. 1) show the peaks at 15, 16 and 22.6° 2θ that are characteristic of cellulose I. The Japanese brand also has peaks at 12 and 20° 2θ that are characteristic of cellulose II (Atalla, 1976).

Raman spectra of the Japanese brand and Avicel PH 101 show appreciable differences. Some changes occur in the regions about 1100, 900 and below 600 cm^{-1} that confirm the presence of a significant proportion of cellulose II (Fig. 2) (Atalla, 1976; Chatrath et al., 1991). Since native cellulose is cellulose I, the cellulose II content corroborates the above conclusion that it was the Japanese brand that had undergone the most vigorous manufacturing process.

The two measures of crystallinity based on X-ray diffraction data both pointed to the Finnish brand as the most crystalline, as did the measure based on IR spectroscopy although with the latter interbrand differences were more pronounced. The spectroscopic method was the more suitable for these microcrystalline celluloses, since it takes into account the contribution of cellulose II (Nelson and O'Connor, 1964), which was present only in the Japanese brand. The true density data show the relative insensitivity of this parameter to differences in crystallinity.

The mean cumulative particle size distribution curves obtained by laser scattering (Fig. 3) show marked differences between the brands studied, as do the mean surface diameters (Table 1); the small particle size of the Indian brand is particularly striking. These differences, together with

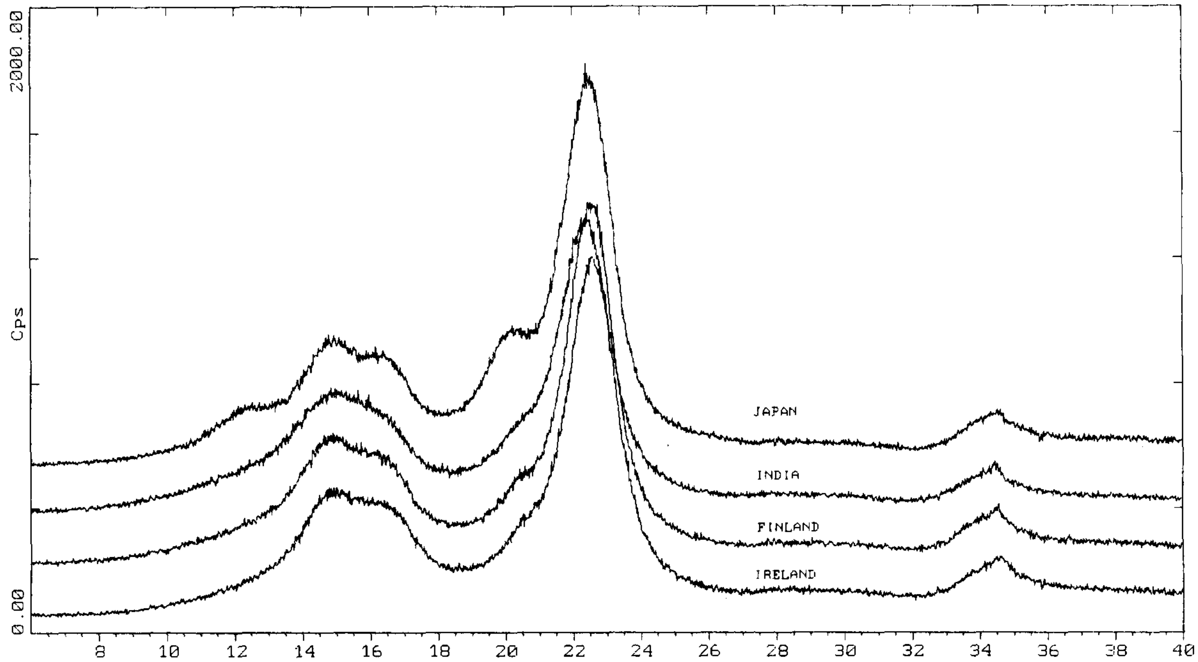

Fig. 1. X-ray diffraction scans. Abscissa: ° 2θ.

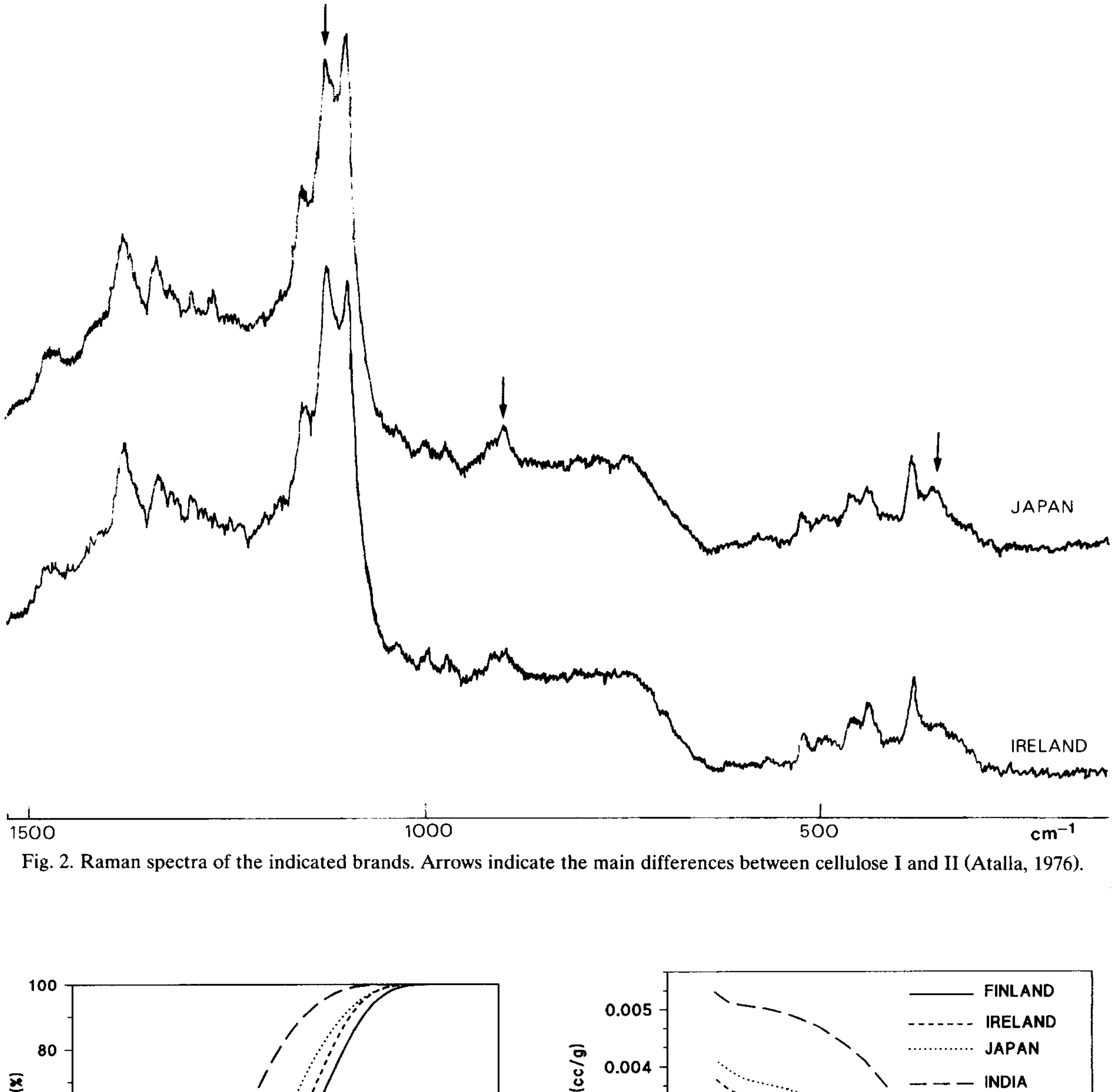

Fig. 2. Raman spectra of the indicated brands. Arrows indicate the main differences between cellulose I and II (Atalla, 1976).

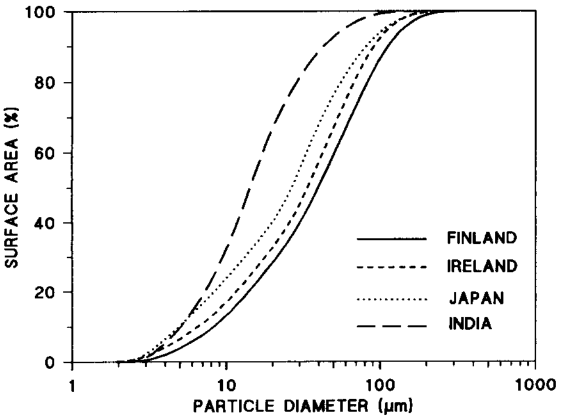

Fig. 3. Particle size distributions determined by laser light scattering.

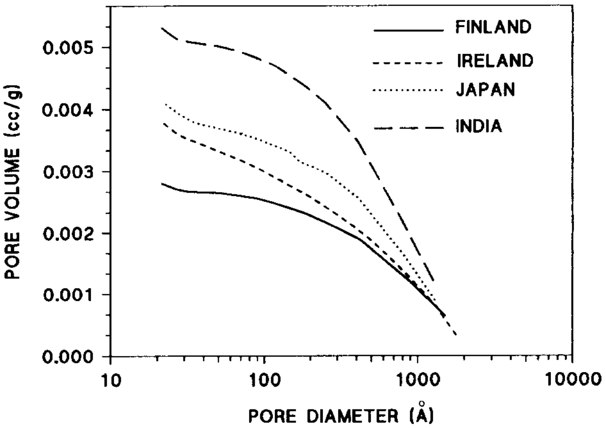

Fig. 4. Pore size distribution calculated from nitrogen adsorption isotherms by the BJH method.

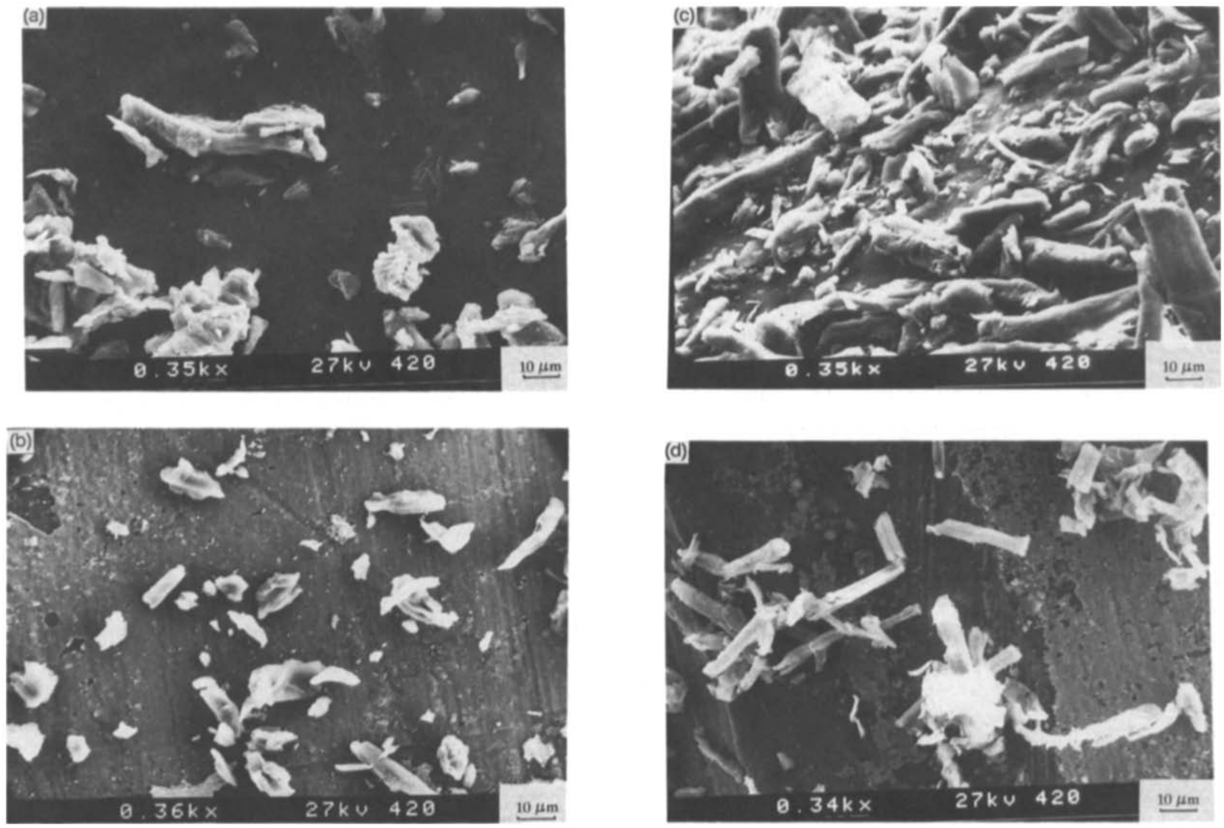

Fig. 5. Microphotographs of samples of the four batches of microcystalline cellulose studied. (a) Ireland; (b) Finland; (c) Japan; (d) India.

similarly marked differences in intraparticular porosity (Fig. 4), explain the variability of specific surface area (Table 1). Photomicrographs show the particles of all four brands to have the typical morphology of microcrystalline cellulose, and corroborate the smaller particle size of the Indian brand (Fig. 5).

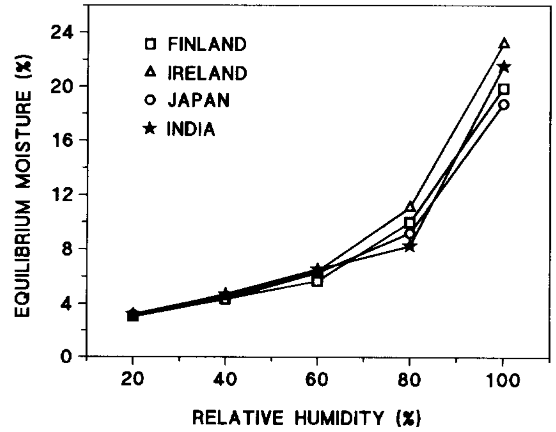

Fig. 6. Equilibrium moisture-humidity curves.

Equilibrium moisture curves obtained to investigate the characteristics of water-cellulose interaction (of major importance in many applications of microcrystalline cellulose) showed only small differences (Fig. 6). This probably explains why there was no significant correlation between equilibrium moisture content and crystallinity, as there was in our study of three batches of Emcocel which differed much more widely in equilibrium

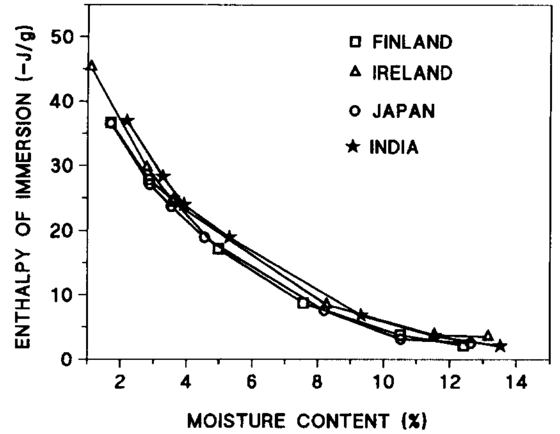

Fig. 7. Dependence of enthalpy of immersion on moisture content.

moisture content (Landín et al., 1992). Even so, the material with the lowest equilibrium moisture content at 65% relative humidity was the most crystalline brand.

The enthalpy of immersion data show greater differences among the four brands (Fig. 7). For the three brands with no cellulose II, there was close correlation between enthalpy of immersion at zero moisture content (calculated by extrapolation) and crystallinity as measured by IR spectroscopy, very similar to that obtained in the accompanying article using three batches of Emcocel (Landín et al., 1993). As expected the Japanese brand deviated considerably from this relationship (Fig. 8). The enthalpy of immersion of microcrystalline cellulose, due to interaction between water and -OH groups on the cellulose backbone, is the sum of a major contribution from the amorphous component of the cellulose and a minor contribution from the outer region of the crystalline component. Correlation between enthalpy of immersion and crystallinity is therefore to be expected if there is only one crystalline species (celulose I) present. This will not be the case if cellulose II is also present.

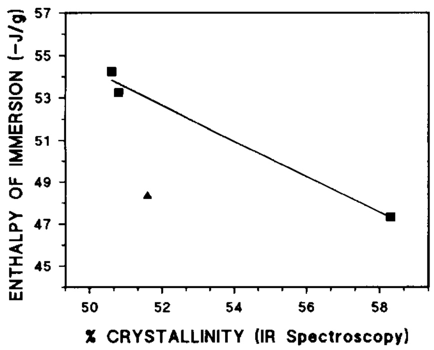

Fig. 8. Dependence of enthalpy of immersion on crystallinity (IR spectroscopy) ((▲) Japanese sample).

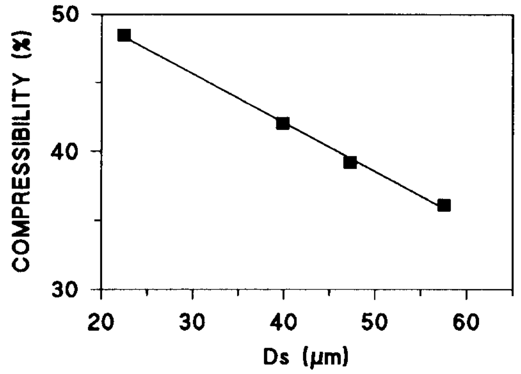

Fig. 9. Dependence of compressibility on mean particle size.

The four brands differed significantly in compressibility (Table 1). In view of the close correlation between compressibility and mean surface diameter (Fig. 9), these differences are attributed to the variation in particle size. The importance of particle size for flow properties is corroborated by the fact that Carr's classification scheme (Carr, 1965) assigns the Indian brand (which has the smallest particles) to a poorer flowability class than the other brands.

Unlike flow properties, mean yield pressure did not vary significantly with particle size, possibly because the dominant densification mechanism for microcrystalline cellulose is particle deformation. For each individual brand, mean yield pressure did depend heavily on moisture content (Table 1).

Conclusions

In conclusion, the above findings show that the brands studied differ significantly in chemical composition, crystal structure and particle size.

All these differences are potentially relevant to use, as is illustrated by the heavy dependence of flow properties on particle size and may explain the differences seen in their rheological behaviour (Rowe and Sadeghnejad, 1989).

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