A Comparative Evaluation of the Mechanical Properties of Various Celluloses[1)]

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The influence of basic properties such as physicochemical or particle properties on the mechanical properties of celluloses with different average degrees of polymerization ($\overline{DP}$), which included powdered α-cellulose and its degradation products as well as commercial microcrystalline celluloses, was investigated. The particle shape approached that of a sphere with a reduction in $\overline{DP}$, causing an increase in flowability and a decrease in the cohesion of cellulose powders. H_{max} and γ in the Leuenberger equation, which were considered to reflect the compactibility and compressibility of powders, respectively, were higher at a lower $\overline{DP}$, suggesting that the particle shape and/or crystallinity of materials affected the bonding properties of a substance in tablet preparation. The mechanical strength was estimated using the crushing test for a granule and the diametral compression test for a tablet. Crushing work, W, increased with a decrease in $\overline{DP}$, which was probably due to a decrease in granule porosity. The compression behavior of granules was estimated by the static method, using the Heckel equation. The compression coefficient, K, in this equation decreased with the crushing work of a granule, thus the reciprocal of K was expected to be a measure of granule strength. The tensile strength of a tablet increased with the crushing work of a granule in the relatively high $\overline{DP}$ region. When the $\overline{DP}$ was low, the crushing work of granule was high and tablet strength tended to reach a maximum.

Key words cellulose; polymerization average degree; compactibility; compressibility; granule crushing test; a tablet tensile strength

Different types of celluloses are widely used as fillers and solid binders together with disintegrates. Microcrystalline cellulose (MCC), which has an average degree of polymerization ($\overline{DP}$) of not more than 350, is particularly useful for direct tableting. Powdered cellulose, newly admitted in JP XIII, is a purified, mechanically disintegrated α-cellulose obtained from a pulp, and its $\overline{DP}$ is between 440 and 2250. In pharmaceutical preparations and their manufacture, it is important to know the influence of the physicochemical and particle properties of celluloses on mechanical properties such as flowability and compressibility of powders, as well as the strength of molded products (granule or tablet), *etc.* However, only a few studies on this subject have been done up until now. Doelker *et al.*[2)] determined the degree of polymerization and crystallinity of 21 celluloses and also investigated the tableting properties of 16 MCCs, as well as their powder characteristics.[3)] Pesonen and Paronen[4–6)] studied the effects of particle and powder properties on the mechanical and dissolution properties of direct compression cellulose tablets and noted that a novel cellulose (agglomerated cellulose) showed the best binding and disintegrating abilities.

The object of this study was to determine the effect of physicochemical and particle properties of celluloses on the mechanical properties of cellulose powders, granules and tablets. Powdered α-cellulose and its degradation products, as well as commercial MCCs, were used as the testing materials. The relationship between the mechanical properties of granules and tablets prepared by the granules was also examined.

Experimental

Materials Powdered α-cellulose (Cel-α, Sigma Chem.) and its degradation products, as well as commercial MCC (Avicel PH-102, Asahi Chem. Ind. and MD-102, Ming Tai Chem.), were used in this study. The degradation was performed as follows. α-cellulose was mixed with 0.5 N HNO_3 in the proportion of 1 : 100 (in weight) and heated at 60 °C (Cel-60), 80 °C (Cel-80), and boiling point (Cel-Boil) for 50 min. Samples were then washed with 0.1% ammonium hydroxide and then with distilled water until they were acid free, after which they were dried at 105 °C. All the samples were stored at a relative humidity (R.H.) of 43% at 25 °C.

Physicochemical and Particle Properties. Degree of Polymerization $\overline{DP}$ This was determined by JP XIII.

Degree of Crystallinity This was determined by X-ray diffraction based on Hermans' theory[7)] using a Rigaku Geiger-Flex diffractometer (Rad IIVC) with Ni-filtered, Cu$K\alpha$ radiation with a voltage of 40 kV, and a current of 20 mA. The scanning rate was 2°/min over a 2θ range of 2—42°.

Water Vapor Sorption Water vapor sorption was measured by the gravimetric method. Cellulose powders dried at 105 °C for 3 h were placed in desiccators at 25 °C, each containing a different saturated solution of salt (LiCl, CH_3COOK, K_2CO_3, NH_4NO_3, KCl), for two weeks. After attaining sorption equilibrium, the samples were weighed and the moisture content at each R.H. was calculated. The amount of water at the apparent BET monolayer was computed.

Specific Surface Area The specific surface area was determined by the BET method from the adsorption of Kr gas at the boiling point of liquid N_2 using an Orr Surface Area Pore Volume Analyzer (Model 2100 D). The apparent water surface area was determined from the moisture sorption data.

True Density True density, ρ, was measured using a helium-air pycnometer (Shimadzu-Micromeritics).

Particle Size Distribution and Average Particle Diameter Using a series of sieves with different sized openings (210, 149, 105, 75, 45 μm), the size distribution of particles less than 210 μm in diameter was examined. From log-probability plots of cumulative frequency in percent against size, the average particle diameter, d_p, was determined.

Particle Shape The particle shape index, ψ, was determined using an image analyzer (Luzex-FS, Nireco), by dividing the actual projected area of a particle, A, by the area of a circle whose circumference was equivalent to the perimeter of the projected image, PM, as shown by Eq. 1:

$$\psi = 4\pi A/PM^2 \quad (1)$$

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Powder Properties and Strength of Tablets Prepared by Powder Compression Tapping Test: A 25 ml glass cylinder was filled with testing material which had passed through a sieve (710 μm in opening size). From the bulk volume, V_0, and weight, W, of a powder sample, the bulk (loose) density, ρ_b, was calculated. The cylinder was then tapped mechanically with a Tap denser (Seishin Enterprise). The volume of powder at 500 taps was used to obtain the tapping density ρ_t. The Hausner ratio, ρ_t/ρ_b, was taken as a measure of powder flowability.

Variation in powder volume, V, with the number of taps, N, was often expressed by the Kawakita equation for tapping [8]:

$$C=abN/(1+bN) \tag{2}$$

where C is the volume reduction given by $(V_0-V)/V_0$, and a and b are the constants related to powder flowability. From the linear relationship between N/C and N, the constants were determined.

Cohesive Property of Powder Cohesion was found by the method of Carr.[9]

Compactibility and Compressibility Each cellulose powder was compressed using a universal tester (Shimadzu Autograph AG 5000E) with a 16 mm flat-faced punch at 25, 50, 100, and 150 MPa . Variation in porosity, ε, with applied stress, P, was then examined.

Brinell hardness testing was carried out for the assesment of tablet strength. A steel sphere (2.5 mm in diameter) attached to the testing apparatus (Grano, Okada Seiko) was pushed at 1 mm/min into the upper surface of the tablet up to a force of 9.8 N. The diameter of the indentation, d, on the tablet was measured with an image analyzer. Brinell hardness, H, was determined by the following equation, derived geometrically:

$$H=2F/\{\pi D(D-\sqrt{D^2-d^2})\} \tag{3}$$

where F is the indentation force applied, and D the diameter of the sphere. Compressibility, γ, and compactibility of materials, H_{max} in Leuenberger's equation[10] were computed based on the porosity variation with compression stress and Brinell hardness:

$$H=H_{max}[1-\exp\{-\gamma P(1-\varepsilon)\}] \tag{4}$$

A nonlinear regression analysis program (Systat, Apple) was used for all data compilation.

Granule Properties and Strength of Tablets Prepared by Granule Compression

Granulation Each powder was kneaded with 100—200 ml water per 100 g powder, and the moist mass was forced by hand through a 1.00 mm screen, dried at 105 °C for 3 h, and the sieved through two screens to obtain granules 0.71 to 1.00 mm in size. Granules were stored at a R.H. of 43% at 25 °C.

Granule Porosity Granule porosity, ε_g, was obtained from the following equations:

$$\varepsilon_g=1-(W_g/V_g\cdot\rho) \tag{5}$$

$$V_g=(\pi/6)\cdot d_g^3 \tag{6}$$

where W_g is the mean weight of a granule determined by an electric balance ($n=20$). V_g is the mean volume of a granule which was calculated by the mean granule diameter, d_g, measured by an image analyzer (Luzex-FS, Nireco).

Granule Crushing Test Granule resistance to fracture was measured by placing a granule between a plate and a miniature press attached to the particle hardness tester (Grano, Okada Seiko). The change in load induced by the displacement of the miniature press was recorded. The test was conducted until displacement was 100 μm. The area under the load-displacement curve represented the work done on the granule during crushing. Twenty granules of each material were tested.

Granule Compression Test Granules, 0.5 g, were compressed using a universal tester (Shimadzu Autograph AG-5000) with a 16 mm flat-faced punch at 1 mm/min. The compression force applied was set at 50 kg for observation of the relationship between compression stress and powder volume using the Heckel equation:

$$-\ln\varepsilon=KP+A \tag{7}$$

where ε is the porosity of the powder compact at pressure P, and K and A are constants.

Strength of Tablets Prepared by Granule Compression For this determination, tablets compressed at 500 kg were used in the diametral compression test. The tensile strength of a tablet, T_t, was found as follows:

$$T_t=2w/\pi D_t L \tag{8}$$

where w is the maximum load, D_t, the tablet diameter and L, the tablet thickness. The mean of 5 tablets was determined.

Porosity of Tablet The Porosity of tablet, ε_t, was obtained from the following equation:

$$\varepsilon_t=1-(4W_t/\rho\cdot D_t\cdot L) \tag{9}$$

where W_t, D_t and L are the weight, diameter and thickness of a tablet, respectively.

Results and Discussion

Physicochemical and Particle Properties These properties are listed in Table 1. There was marked variation in the $\overline{DP}$ of the materials. $\overline{DP}$ decreased with temperature in the treatment of α-cellulose, and crystallinity increased with decreased $\overline{DP}$, indicating that hydrolysis occured in amorphous regions in cellulose.

Apparent water surface areas were quite large compared to the Kr surface area, suggesting that water molecules penetrated into the amorphous regions of cellulose. A good correlation between S_{H_2O}/S_{Kr} and crystallinity supported the above postulation. α-cellulose was quite fibrous, and the particle index, ψ, increased with a reduction in $\overline{DP}$.

Mechanical Properties of Powders The Hausner ratio, constants a and b in the Kawakita tapping equation, cohesion, H_{max} and γ in the Leuenberger equation of six cellulose powders are listed in Table 2. The Hausner ratio and constant a, regarded as flowability, decreased with a decrease in $\overline{DP}$, which was attributed to an increase in the particle shape index. Spherical particles are considered to easily change their locations.

Table 1. Physicochemical and Particle Properties of Six Celluloses

Sample	$\overline{DP}$	Degree of crystallinity (%)	BET surface area			True density ρ (g/cm^3)	Average particle diameter d_p (μm)	Particle shape index ψ
			S_{H_2O} (m^2/g)[a]	S_{Kr} (m^2/g)[b]	S_{H_2O}/S_{Kr}			
Cel-α	754	27	159	1.00	159	1.48	97.0	0.126
Cel-60	421	34	154	1.07	144	1.47	97.5	0.171
Cel-80	234	40	151	1.10	137	1.51	114.0	0.259
Cel-Boil	127	57	136	1.30	105	1.55	128.0	0.642
PH-102	219	65	137	1.34	102	1.53	98.0	0.421
MD-102	208	58	—	1.33	—	1.55	88.2	0.407

a) Water vapor sorption. b) Adsorption of Kr gas.

Table 2. Mechanical Properties of Six Cellulose Powders

Sample	Hausner ratio	Kawakita equation		Cohesion (%)	Leuenberger equation	
		a	$1/b$		H_{max} (MPa)	$\gamma \times 10^2$ (MPa^{-1})
Cel-α	2.17	0.550	13.7	15.8	96.2	0.65
Cel-60	2.01	0.514	13.9	14.6	100.6	0.45
Cel-80	1.64	0.396	11.1	15.7	115.5	0.73
Cel-Boil	1.23	0.191	11.5	12.8	144.8	2.21
PH-102	1.40	0.284	8.2	7.16	151.7	1.46
MD-102	1.52	0.340	10.3	8.15	150.1	1.40

Table 3. Mechanical properties of Cellulose Granules and Tablets

Sample	Porosity of granule ε_g	Crushing work of granule $W \times 10^5$ (J)	Compression coefficient in Heckel Eq. $K \times 10^2$ (MPa^{-1})	Reciprocal of compression coefficient in Heckel Eq. $1/K$ (MPa)	Porosity of tablet ε_t	Tensile strength of tablet prepared by compression of cellulose granules T_t (MPa)[b]
Cel-α	0.861	0.66 (0.17)[a]	9.14	10.9	0.329	0.44
Cel-60	0.876	0.68 (0.28)	8.97	11.1	0.316	0.58
Cel-80	0.834	1.16 (0.69)	7.99	12.5	0.308	1.07
Cel-Boil	0.662	6.35 (2.03)	6.21	16.1	0.300	1.40
PH-102	0.704	4.66 (1.51)	5.98	16.7	0.310	1.36

a) Standard deviations ($n=20$) are in parentheses. *b*) Values are means of 5 tablets.

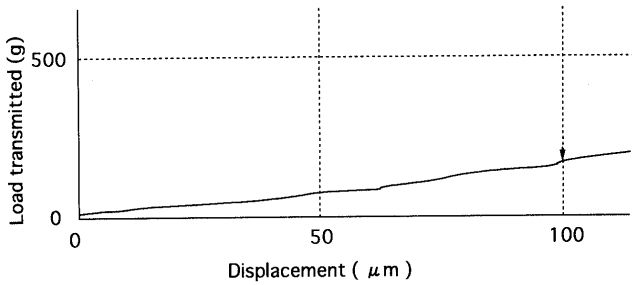

Fig. 1. An Example of Granule Compression Curve

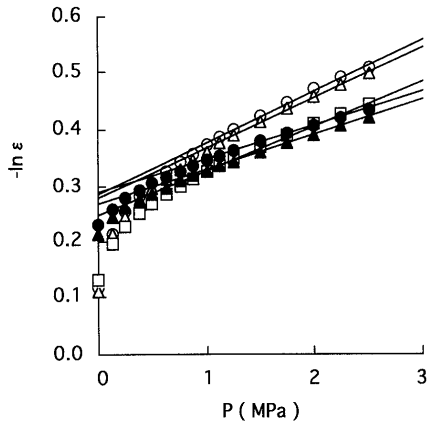

Fig. 2. Heckel Plots for Various Celluloses

Cel-α (○), powdered α-cellulose; Cel-60 (△), α-cellulose treated with 0.5 N HNO_3 at 60 °C for 50 min; Cel-80 (□), α-cellulose treated with 0.5 N HNO_3 at 80 °C for 50 min; Cel-Boil (▲), α-cellulose treated with 0.5 N HNO_3 at boiling point for 50 min; PH-102 (●), MCC Avicel PH-102.

The reciprocal of b of the Kawakita tapping equation is regarded to be a parameter related powder cohesion.[8] Particle shape approached that of a sphere with the progress of degradation, causing a decrease in cohesion, which made it difficult to agglomerate powder particles.

Compactibility and compressibility: The compressibility of a powder was usually determined based on a change in the volume or porosity of the powder bed with applied pressure. Various compression equations have been proposed and an attempt has been made to relate parameters in the equations to the properties of a compact mass such as tablet strength. The compactibility or strength of a compressed tablet was usually measured by the diametral compression test. However, this method would not apply to tablets prepared from α-cellulose powder or products degradated at a low temperature because complicated fracture of tablets occured during the test. The Brinell hardness test was then performed on tablets compressed at various stress values, and H_{max} and γ in the Leuenberger equation were determined (Table 2). Both parameters were higher at a lower $\overline{DP}$. H_{max} and γ are considered to reflect the compactibility and compressibility of powders, respectively. Leuenberger[11] classified the bonding properties of powders according to these parameters. Table 2 indicates that the binding force between particles in compression tends to increase with an increase in crystallinity and the shape index.

Mechanical Properties of Granules Crushing Work of Granules: Figure 1 shows the relationship between the load transmitted and the displacement of a granule during crushing. From this relationship, the energy required to compress a granule vertically until the displacement of 100 μm can be calculated. Table 3 shows granule porosity, ε_g, and crushing work, W, for cellulose granules. W increased with a decrease in granule porosity.

Application of the Heckel Equation: Heckel plots were made using data obtained from the granule compression measurement. In Table 3 the compression coefficient, K, in the Heckel equation, calculated from the slope of the linear portion in Fig. 2, was shown together with the

reciprocal of K. $1/K$ increased with crushing work, W. This indicated that $1/K$ was considered to be related to granule resistance to deformation, and is thus expected to be a measure of granule strength.

Relationship between Granule Strength and Tablet Strength In Table 3, the tensile strength of a tablet, T_t, prepared by the compression of granules was also shown. The tensile strength of a tablet increased with the crushing work of a granule. However, when the crushing work increased above a certain level, T_t seemed to reach a maximum. When the granule strength was small, granules appeared to be easily crushed by compression. Tablet strength then depends on granule strength. When granule strength was large, it was supposed that fracture of the granules would occur incompletely and effective intergranular contact would be diminished, causing a reduction in tablet strength.[12] Taking into account the above two tendencies, the effect of granule strength on tablet strength should be discussed.

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References

1) This work was presented at the 116th Annual Meeting of the Pharmaceutical Society of Japan, Kanazawa, March 1996, Part 4, p. 62.
2) Doelker E., Gurny R., Schurz J., Janosi A., Matin N., *Powder Technol.*, **52**, 207—213 (1987).
3) Doelker E., Mordier D., Iten H., Humbert-Droz P., *Drug. Dev. Ind. Pharm.*, **13**, 1847—1875 (1987).
4) Pesonen T., Paronen P., *Drug. Dev. Ind. Pharm.*, **12**, 2091—2111 (1986).
5) Pesonen T., Paronen P., *Drug. Dev. Ind. Pharm.*, **16**, 31—54 (1990).
6) Pesonen T., Paronen P., Ilkka J., *Drug. Dev. Ind. Pharm.*, **18**, 159—173 (1992).
7) Hermans P. H., Weidinger A., *J. Appl. Phys.*, **19**, 491—506 (1948).
8) Yamashiro M., Yuasa Y., Kawakita K., *Powder Technol.*, **34**, 225—231 (1983).
9) Carr R. L., *Chem. Eng.*, **72**, 163—168 (1965).
10) Leuenberger H., *Int. J. Pharmaceut.*, **12**, 41—55 (1982).
11) Jetzer W., Leuenberger H., Sucker H., *Pharm. Technol.*, **7**, 33—39 (1983).
12) Horisawa E., Komura A., Danjo K., Otsuka A., *Chem. Pharm. Bull.*, **43**, 2261—2263 (1995).