DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 12(11-13), 2091-2111 (1986)

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

EVALUATION OF A NEW CELLULOSE MATERIAL AS BINDING AGENT FOR DIRECT COMPRESSION OF TABLETS

Timo Pesonen and Petteri Paronen

Department of Pharmaceutical Technology

University of Kuopio, POB 6, SF-70211 Kuopio, Finland

ABSTRACT

The properties of a new microcrystalline cellulose product Emcocel^{R}, was compared with those of fine grade of other commercial microcrystalline cellulose, Avicel^{R} PH 101. The crystal structure of Avicel was noticed to be some more amorphous than that of Emcocel. Both materials were similarly composed of irregularly shaped fibrous cellulose particles. The particle size distribution was clearly larger for Emcocel than for Avicel. Emcocel contained more both very small and very large particles. The loose density was also slightly smaller for Emcocel. There was practically no difference in spesific surface area, water content and effective density of these materials. The behaviour of both microcrystalline cellulose powders during flow and binding processes was similar. Emcocel and Avicel were rather cohesive and only fairly flowing materials. Tablets with very

Copyright © 1986 by Marcel Dekker, Inc.

0363-9045/86/1211-2091$3.50/0

RIGHTSLINK

advantageous strength/pressure profiles were possible to produce using plain materials and also using tablet masses containing high concentrations of acetaminophenone. According to the results of this evaluation the physical and tableting properties of a new microcrystalline cellulose material, Emcocel, resemble very closely those of Avicel PH 101. Thus neither advantage nor disadvantage is derived using Emcocel instead of Avicel PH 101 as a binding component in tablet masses.

INTRODUCTION

Different kind of cellulose materials are widely used as filling and binding agents in direct compression of tablets. Due to the fibrous structure of wood cellulose, there exixts often either flowability or binding difficulties in using cellulose products in tableting. Rather many commercial cellulose products with different particle and tableting properties are available. The differences in particle structures and thus in powder properties of these materials can often be explained by differences in manufacturing processes. Some of the cellulose materials are mechanically aggregated and they often have excellent flow properties but more or less poor binding properties. Microcrystalline cellulose, manufactured by acidic hydrolyse and spray drying processes, is widely used tableting adjuvant and it is proved to be excellent binding agent for tableting (1,2,3). There exists, however, flow difficulties, especially when larger amounts of microcrystalline cellulose are added into the tablet

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

masses (4,5). All the cellulose materials commercially available own thus smaller or greater disadvantages. The continuous development work with cellulose materials is thus motivated.

The aim of this study was to evaluate and compare the physical and binding properties of a new microcrytalline cellulose product, Emcocel^{R} with those of fine grade microcrystalline cellulose, Avicel^{R} PH 101.

MATERIALS AND METHODS

Materials

The test material used was a new form of the microcrystalline cellulose (Emcocel^{R}) manufactured by Finnish Sugar Ltd. (Helsinki, Finland) and marketed by Edward Mendell Co. (New York, USA). The properties of this material were compared with those of fine grade commercial microcrystalline cellulose, Avicel^{R} PH 101 (FMC Corp., Philadelphia, USA).

Crystal structure

The powder x-ray diffractometric EDXD-method was used to evaluate the crystallinity of the cellulose materials. Background index and crystallinity index were used to describe the crystallinity of the materials.

Particle properties

The mean particle size and size distribution of the cellulose materials were evaluated using two methods. Firstly, number size

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

distribution was measured using microscopic method in which Feret's diameter of four hundreds particles is measured. Secondly, volumetric size distribution was measured using electrical sensing zone method (Coulter Counter ZM) in Isoton^{R} II solution and using an orifice tube 280 μm in diameter. Because of the large and rather inconsistent backround signals, only the particles larger than about 6 μm were measured using the last mentioned method.

The mean surface volume diameter, d_{sv}, of four hundreds particles of the cellulose materials based on microcopical evaluation was calculated from the equation (6)

$$d_{sv} = \frac{\sum n_i d_i^3}{\sum n_i d_i^2} \qquad (1)$$

where n_i is the number of particles with diameter d_i. A unit volume of monosized particles with a diameter d_{sv} will have a total surface area identical with the surface of a unit volume of the actual sample having a mean surface-volume diameter d_{sv}.

The specific surface area per unit weight, S_w, for the cellulose powders was determined by using the BET-method from the adsorption of nitrogen gas at the boiling point of liquid nitrogen (Orr Surface Area, Pore Volume Analyzer, Model 2100 E). Six determinations were made.

Particle shapes were studied visually using scanning electron micrographs taken from the powder samples coated with gold using Jeol JFC-1100 sputter coater. Micrographs were taken with

RIGHTSLINK

the Jeol JSM-35 apparatus at an accelerating voltage of 15 kV. The particle shape factor F_s (6)

$$F_s = S_w \cdot \rho_t \cdot d_{sv} \qquad (2)$$

where ρ_t is the effective particle density, was used to obtain numerical value that describes the shape of the cellulose particles. The larger the value of shape factor, the more irregular is the particle shape.

Powder properties

The water content of the materials was determined using a Mettler Drying Unit LP 12, which measured weight loss of a sample with an initial weight of two grams at a temperature of about 115°C for eleven minutes. Three determinations were made.

Loose density was determined by pouring a pre-weighted quantity of about 20 ml of cellulose mass through a funnel in a fine stream into a glass measuring-cylinder with volume of 25 ml. Six determinations were made.

The effective density of the materials, ρ_t, was determined with an air comparison pycnometer (Beckman model 930) using helium as an inert gas. Five measurements were made.

Flow properties

Flowability was, firstly, determined by a tapping density treatment using a modified Neumann apparatus (7,8). Behaviour of

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

the masses in the tapping procedure was compared using the numerical constants obtained from the Kawakita's equation. The glass cylinder with volume of 25 ml was filled with the material studied. After observing the weight and loose volume (V_0) the cylinder was mechanically tapped by a specially cut cam rotated by Erweka AR 400 motor. Six measurements were taken.

Values for volume of the powder column (V) after different number of taps (N) and loose volume of the powder column (V_0) were used to calculate the degree of volume reduction,

$$C = \frac{V_0 - V}{V} \qquad (3)$$

The Kawakita's equation for the densification of powder solids is (9,10)

$$\frac{N}{C} = \frac{1}{a} N + \frac{1}{ab} \qquad (4)$$

where a and b are constants; a describes the degree of volume reduction at the limit of tapping and is called compactability; 1/b is considered to be the constant related to cohesion and is called cohesiveness. To obtain numerical values for constants a and 1/b, C was evaluated first; and graphs of N/C vs N were plotted. The constants of linear equation were calculated separately for all six measurements using tapping numbers below 30 and 13 observation points according to the method of least square. Compactability, a, and cohesiveness, 1/b, were obtained from the slope 1/a and the intercept 1/(ab).

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

The flowability of the cellulose materials was, secondly, studied by means of the weight variation of compressed tablets. Magnesium stearate, 0.5 m/m %, was added manually using cards among cellulose particles before tabletting. The tablets, 13 mm in diameter and about 330 mg average weight, were compressed at the speed of 35 tabl/min using Korsch EK-0 single punch tablet press. The total weight of the mass tabletted was 250 g and one hundred tablets were weighted separately and the variation in weight (relative standard deviation) was determined.

Binding properties

The ability of cellulose materials to form strong tablets was tested by tabletting the materials at different compressional forces using an instrumented Korsch EK-0 single punch machine and evaluating the mechanical strength of the tablets. The tablets, 13 mm in diameter and 300 mg average weight, were compressed at compressional forces about 2, 5, 8, 12 and 22 kN using the speed of 35 tabl/min. The mechanical strength of the tablets was evaluated 24 hours after tabletting with the diametrial breaking strength test (Schleuniger ZE) as a mean of ten measurements. Friability was tested using Roche Friabilator (Erweka). Three times six tablets were weighted before and after the treatment of 100 revolutions. The results were presented as a share of weight loss from the initial weight in per cents.

The binding capacity of the materials studied was evaluated by tabletting the materials with different amounts of acetamino-

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

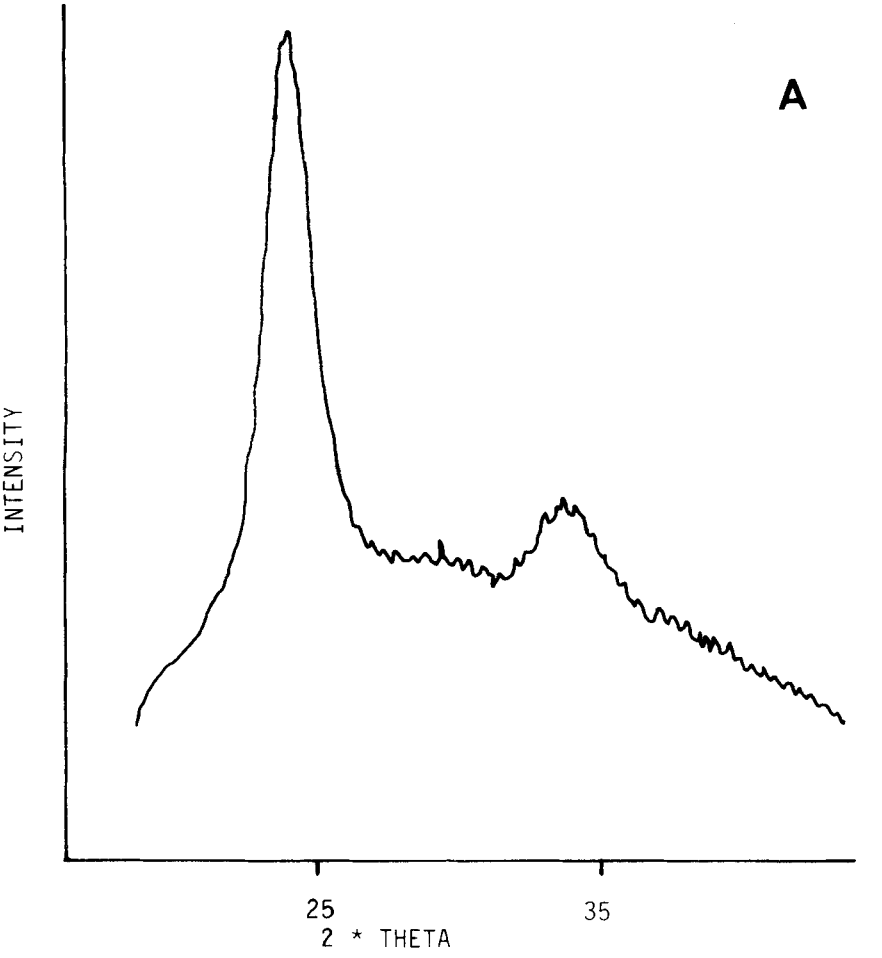

FIGURE 1

X-ray diffractograms for Emcocel (A) and Avicel PH 101 (B).

phenone. The tablet masses contained 10, 30, 50, 70 and 90 m/m % of acetaminophenone. The tablets, 13 mm in diameter and 300 mg average weights, were compressed at the constant force of 8 kN. The success of tableting was followed and the breaking strength of six tablets was measured (Schleuniger 2 E) 24 hours after tableting.

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

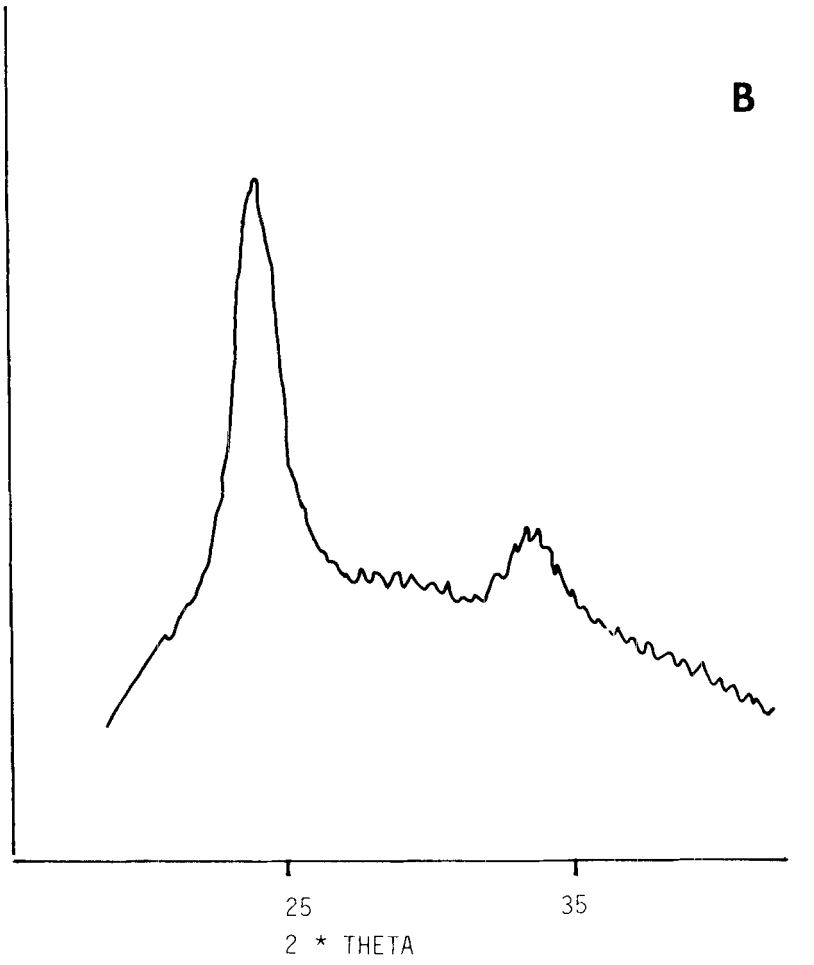

FIGURE 1 CONTINUED.

RESULTS AND DISCUSSION

Crystal structure

The x-ray diffractograms for the microcrystalline cellulose powders are in Fig. 1. According to the background index the relative amount of the amorphous phase in powders was 52.7 % for Avicel and 41.8 % for Emcocel. The crystallinity index describes

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

Table 1. Particle properties of Emcocel and Avicel PH 101

	Emcocel	Avicel PH 101
Numerical mean particle size (μm)	11.7	12.5
Volumetric mean particle size (μm)	22.2	13.4
Surface-volume diameter (μm)	35.8	41.3
Specific surface area (m^2/g)	1.27	1.26
Shape factor (-)	68.8	79.7

the ratio of the volume of the crystalline phase to the total sample volume. This value was 62.7 % for Avicel and 66.9 % for Emcocel. Thus these parameters point out that Avicel has some more amorphous structure than Emcocel. Both materials are, however, greatly amorphous or more specifically, microcrystalline.

Particle and powder properties

The values for mean particle size based on numerical distribution data in Table 1 show no significant difference between the materials. On the other hand the detailed numerical size distribution data in Fig. 2 show that Emcocel contains more very small particles than Avicel. It has been pointed out that volumetric size distribution data correlate better than numeric size distribution data with the actual flow and bulk properties of the powdered solid materials (11). According to volumetric size distri-

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

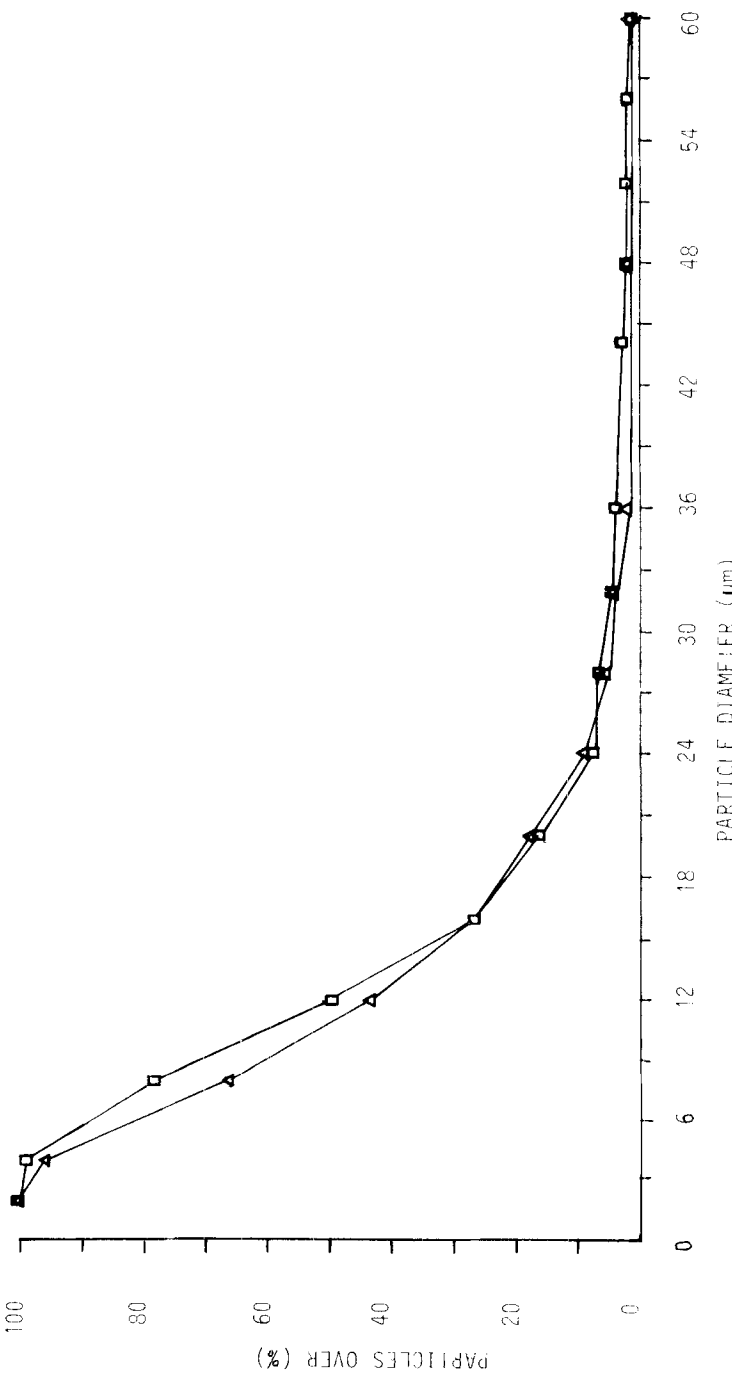

FIGURE 2

Microscopically measured cumulative particle size distribution for Emcocel (Δ) and for Avicel PH 101 (□).

RIGHTSLINK

bution obtained by measuring only the particles larger than about 6 μm, the mean particle size of Emcocel is clearly larger than that of Avicel (Table 1).

Thus Emcocel contains numerically small but volumetrically large fraction of rather large cellulose particles and aggregates (Fig. 3). According to both numeric and volumetric size distributions Emcocel owns some larger particle size distribution and thus contains more very small and very large particles than Avicel.

The mean surface volume diameter was practically same for Emcocel and Avicel (Table 1). Thus the apparent surface of unit volume of particles was about the same. The surface volume diameter takes into account only the outer surfaces of the particles. The specific surface area measured using gas adsorption technique measures the total free surface of the powders. Thus also the walls of the pores inside particles are taken into account. Emcocel and Avicel was noticed to have same specific surface area (Table 1). Thus according the surface volume diameter and specific surface area these two materials are composed of the very similar, equally porous particles.

The shape factor values in Table 1 and scanning electron micrographs in Fig. 4 confirm the similarity of the particles in these powders. The shape factor values were very far from the value six, which is the theoretical value for spherical particles. This points out that the particle shape of the microcrystalline cellulose powders is very irregular and non-

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

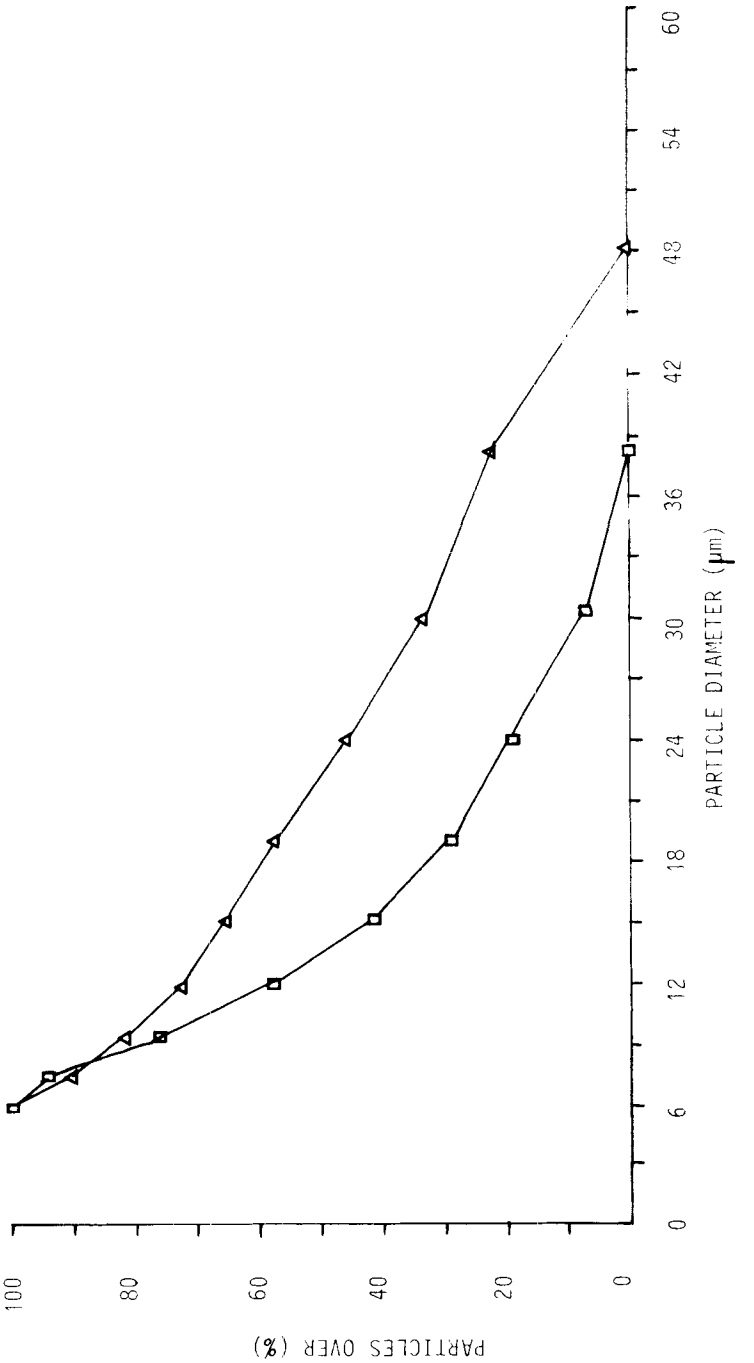

FIGURE 3

Cumulative volumetric particle size distribution for Emcocel (Δ) and for Avicel PH 101 (□) measured using Coulter Counter-method.

RIGHTSLINK

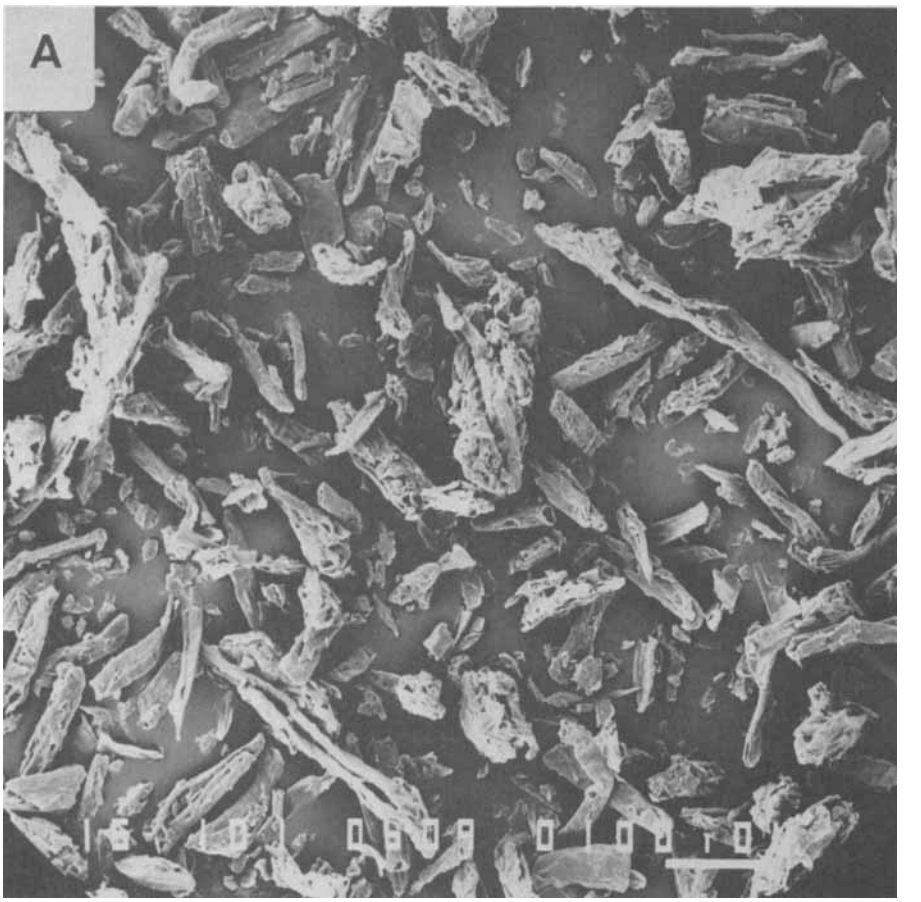

FIGURE 4

Scanning electron micrographs for Emcocal (A) and Avicel PH 101 (B) powders. Bar = 100 μm

spherical. Emcocel and Avicel contain numerous small, relatively regular particles among the fibrous-shaped large particles. There seems to exist also some partially aggregated irregular particles in these powders.

The values of water content and effective density for Emcocel resembled nearly those for Avicel (Table 2). The loose

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

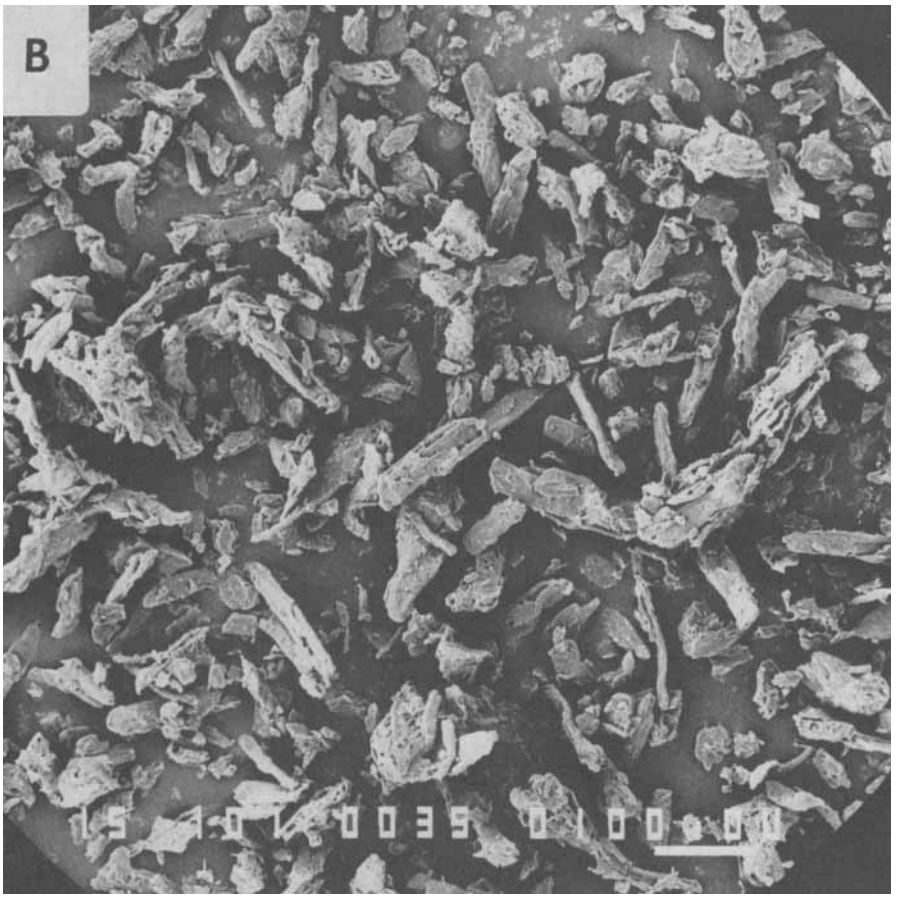

FIGURE 4 CONTINUED.

density was slightly smaller for Emcocel than for Avicel. This may be due to the some wider particle size distribution of Emcocel than that of Avicel.

Flow properties

The parameter values obtained from the Kawakita's plots (Fig. 5) point out that both cellulose materials densified similarly

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

Table 2. Powder and flow properties of Emcocel and Avicel PH 101

	Emcocel	Avicel PH 101
Water content (%)	4.6	4.9
Loose density (g/ml)	0.232	0.262
Effective density (g/ml)	1.521	1.521
Compactibility (%)	31.8	29.2
Cohesiveness (-)	7.3	7.5
Weight variation of tablets (%)	1.08	0.78

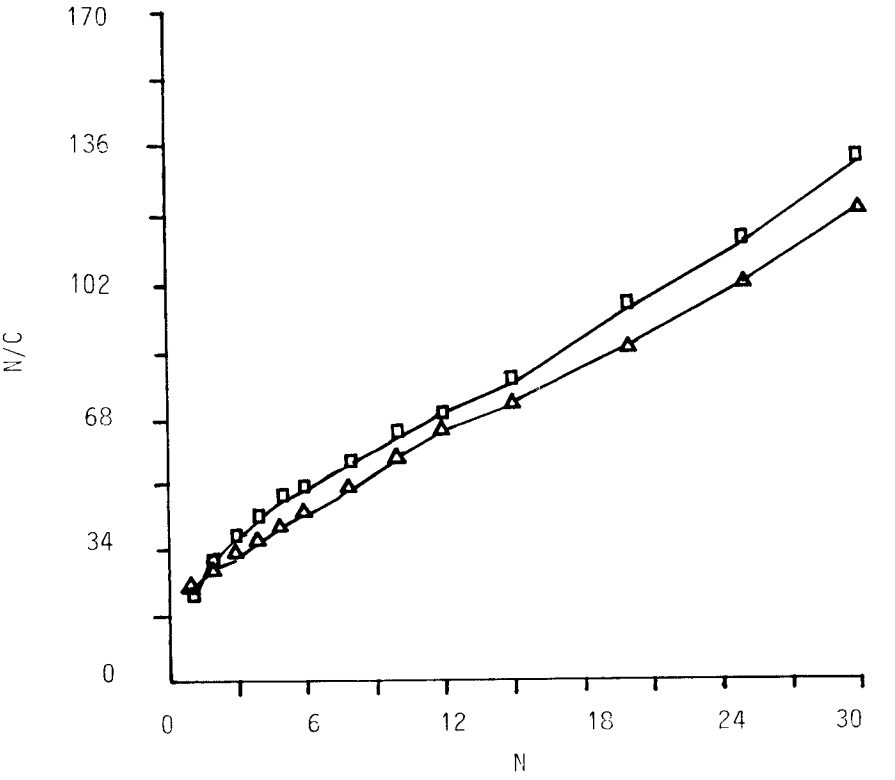

FIGURE 5

Kawakita's plot for Emcocel (△) and for Avicel PH 101 (□) powders.

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

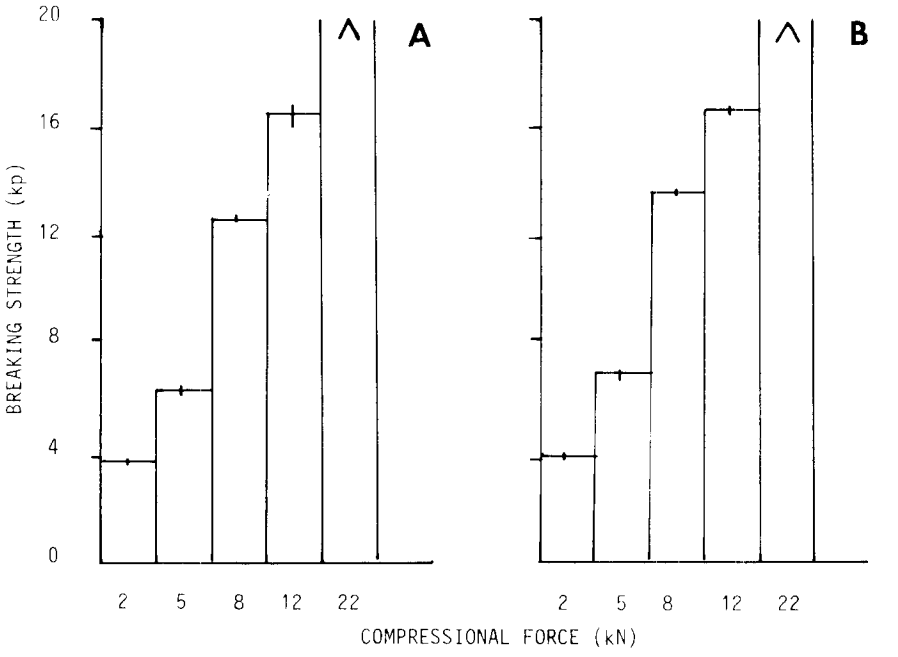

FIGURE 6

Breaking strength of tablets as a function of compressional force for Emcocel (A) and Avicel PH 101 (B).

(compactibility values in Table 2) and attained the final packing state at the same densification rate (cohesiveness values in Table 2). Thus the behaviour of Emcocel and Avicel was nearly similar during tapping treatment. According to the published results the compactability and cohesiveness values obtained indicate fair flowability and moderate cohesiveness for Emcocel and Avicel (10,11). The values of these parameters based on tapping test depend, however, on the method used (7). Thus the weight variation obtained during the proper tableting process may indicate better the actual flowability of powders. The weight variation

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

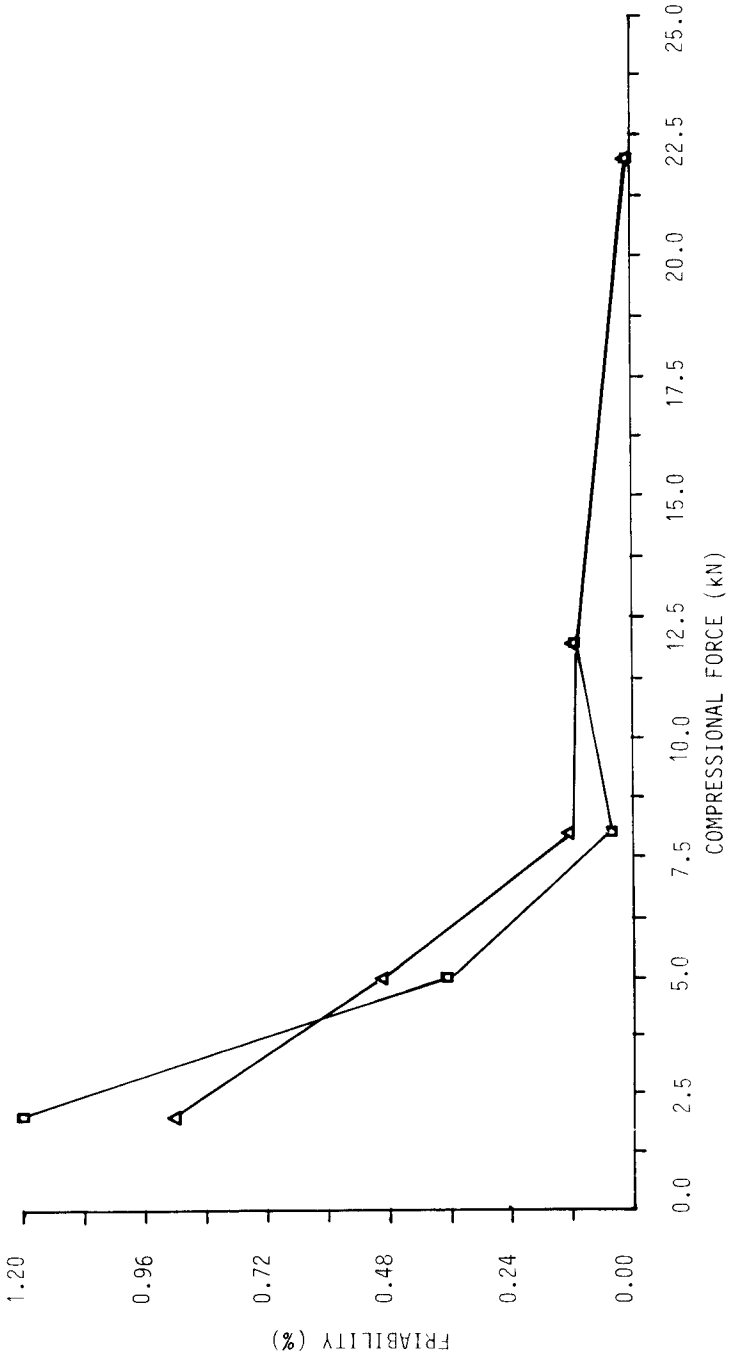

FIGURE 7

Friability of tablets as function of compressional force for Emcocel (△) and Avicel PH 101 (□).

RIGHTSLINK

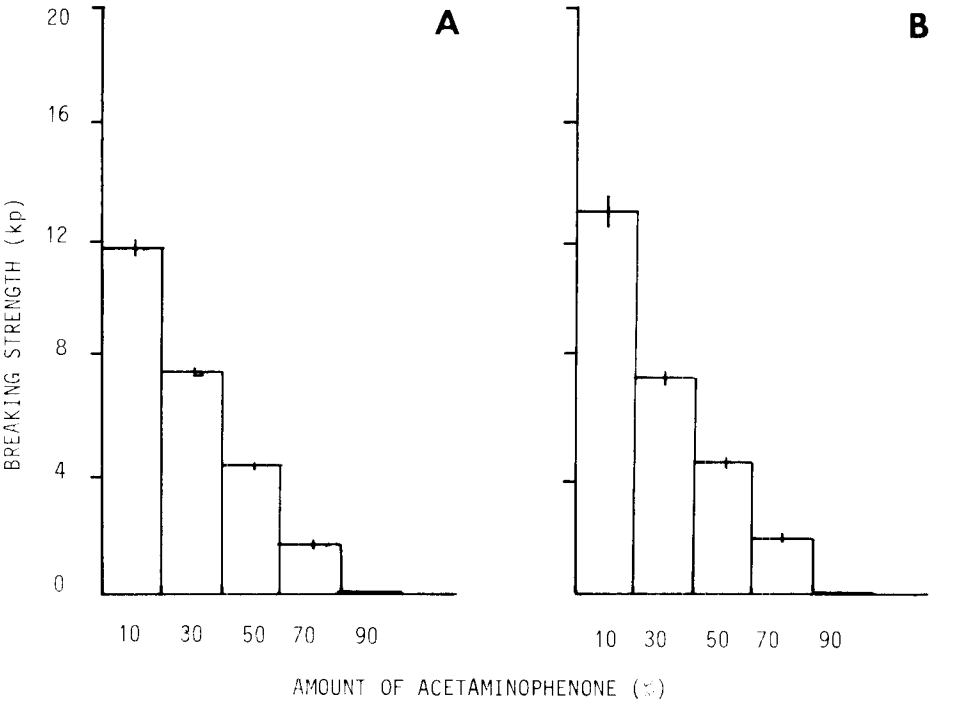

FIGURE 8

Breaking strength of tablets contained different amounts of acetaminophenone for Emcocel (A) and Avicel PH 101 (B). Tablets were compressed at compressional force of 8 kN.

results in Table 2 point out that it is well possible to produce tablets within the weight variation limits of the official demands using both cellulose materials tested. The weight variation was trivially larger for tablets containing plain Emcocel than for tablets containing plain Avicel.

Binding properties

Strong tablets were possible to produce at very low compressional forces for both materials studied Fig 6 and 7. Between

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

Emcocel and Avicel there was no remarkable difference in tablet breaking strength or triability. Emcocel and Avicel have also similar ability to bind acitaminophenone into tablets. Both of these materials were able to bind acetaminophenone up to 70 % and still produce tablets which were strong enough to be handled (Fig. 8).

CONCLUSION

According to the results of this study the physical and binding properties of Emcocel are nearly similar to those of Avicel PH 101. Both of these powders are only moderately flowing materials with a very good ability to form firm tablets. Thus in the pharmaceutical point of view there is neither advantage nor disadvantage to use Emcocel instead of Avicel PH 101 in tablet masses.

REFERENCES

1. Lerk, C.F., Bolhuis, G.K. and DeBoer, Pharm. Weekblad. 109, 945 (1974)
2. Schwartz, B. and Bareitz, J.F., Drug Cosmet. Ind. 118, 60 (1976)
3. Sixsmith, D., J. Pharm. Pharmacol. 29, 82 (1977)
4. Rudnic, E.M., Chilamkurti, R. and Rhodes, C.T., Drug Dev. Ind. Pharm. 6, 279 (1980)
5. Paronen, P., Xylan as a direct compression adjuvant for tablets, Dissertation, University of Kuopio, Kuopio 1983
6. Allen, T., Particle size measurements, Chapman and Hall Ltd., London 1978

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK

7. Neumann, B.S., in Advances in Pharmaceutical Sciences, Vol. 2, p. 181, Bean, H.S., Beckett, A.H., Carless, J.E. (eds), Academic Press, London (1976)
8. Juslin, M., Kahela, P., Paronen, P., Turakka, L., Acta Pharm. Fenn. 90, 83 (1981)
9. Kawakita, K., Lüdde, K.H., Powder Technol. 4, 61 (1970/71)
10. Yamashiro, M., Yuasa, Y., Kawakita, K., Powder Technol. 34, 225 (1983)
11. Carstensen, J.T., Solid Pharmaceutics: Mechanical Properties and Rate Phenomena, Academic Press, New York (1980)

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/22/12
For personal use only.

RIGHTSLINK