Drug Development and Industrial Pharmacy, 22(12), 1253-1257 (1996)

Microcrystalline Cellulose: Investigation of Porous Structure of Avicel 102 from Mercury Porosimeter Measurements

O. Zouai, C. Thomas, and Y. Pourcelot-Roubeau

Pharmaceutics and Industrial Pharmacotechnic Laboratory, Faculty of Pharmacy, Burgundy University, Dijon, France

ABSTRACT

To complete study on rheological and mechanical behavior of cellulose, the authors investigated the porous structure of a microcrystalline cellulose: Avicel 102. The research required the raw material itself and two size fractions of the single sample. With them, compacts were obtained. The aim of the work was to evaluate the correlation between particle size, porous structure of powders, and porous network of compacts and the tensile strength of the corresponding compacts. With the method used, an important interparticulate porosity of Avicel 102 was observed. Overall porosity increased when particle size increased on account of the particulate rearrangement. Porous networks of compacts obtained at low pressure presented a smaller overall porosity compared to powders. Higher values were observed when particle size increased, and consequently, the tensile strength of porous network of compacts decreased.

INTRODUCTION

In earlier publications concerning microcrystalline cellulose, we had insisted on the importance of packing properties and on its influence on compacting behavior. We had considered Avicel 102 as a good excipient for flowing and tableting properties because of its low Hausner ratio, large range of particle size, and plastically deformed particles (1,2).

In this present work, we investigate the "highly porous nature of Avicel 102" (3) to bring supplementary information. In fact, pore volume and porogram are other parameters that must be measured and controlled in compaction of powders (4) because, in many types of powder processing, the voids between the powder particles undergo considerably more changes that the particles themselves (5). Having studied some physical properties of Avicel 102 at the particulate and bulk levels, we want, now, to characterize the porosity of the mass and also to evaluate, for Avicel 102, the correlation between particle size, porosity of powders, and the tensile strength of compacts.

For this investigation we conducted porosimetric studies of Avicel 102, two particle sieve fractions of Avicel 102, and a porous network of compacts obtained at low applied pressure.

MATERIAL AND METHODS

The samples of microcrystalline cellulose used were:

- Avicel 102, Ph. Eur. FMC Corporation represented in France by Seppic Paris, lot 7213
- Two particle sieve fractions of a single batch of Avicel 102: smaller than 160 μm and in the range 160–315 μm

Obtaining Powders

A single batch of Avicel 102 was homogenized in a mixer, Erweka KB 15, for 10 min at 58 revolutions a minute. One part was used without any treatment for porosimetric study and tableting. The other part was sieved for 10 min, to maximal speed, with a tamisor, Erweka VT, to obtain two size fractions from the single batch: a < 160-μm fraction and a 160- to 315-μm fraction.

Compaction and Characterization of Tablets

Tablets of the different samples of Avicel 102 were prepared by direct compression, in an automatic way on a tableting machine, Erweka EKO. All fabrications used: 12 mm diameter flat-faced punches; an unlubricated die with a depth of 10 mm; constant superior punch deplacement selected to obtain, with a low applied pressure, compacts of adequate strength without subjecting the compacts to excessive stresses (9). This need for basic information led to our present investigation.

The mean diameter and thickness of 10 tablets were calculated using a micrometer with an accuracy of 0.01 mm.

The tensile strength of 10 tablets was measured with Erweka TBT/S Apparatus.

The mean tensile failure force P was used to calculate the radial tensile strength σ_x by the equation (7,8):

$$\sigma_x = \frac{2P}{\pi Dt}$$

where σ_x is the tensile stress megapascals, P the applied load (newtons), and D the diameter and the thickness of the tablets (millimeters).

These operations were conducted at ambient conditions (50% RH).

Study of the Porous Structure (Powders and Network of Compacts

This was achieved through the method of mercury intrusion (4,6).

Experiments were conducted using a Micromeritics Mercury Penetration Porosimeter, model 9300, which covers a pressure field from 6.9 to 2.10^5 KPa, corresponding to pore size from 360 to 0.006 μm.

We undertook the measurements on each samples tested under the following operating conditions:

- Test powder sample of 250 mg (± 10%)
- Special 5-cc penetrometer for borosilicate glass powder equiped with a 1.131 cc capillary
- Test solid sample of 365 mg (± 10%) (one tablet)
- 3-cc penetrometer for borosilicate glass solid equiped with 0.412 cc capillary
- Mercury contact angle measuring 130°
- Superficial tension of mercury measuring 484 dyn/cm
- Informatic program 9310 arranged with 44 couples applied pressure penetrated volume to estimate the overall porosity and pore size distribution

Three repetitive analyses were made with all samples. Excellent reproducibility was achieved in all cases, and results given are the average of the three obtained values on the same subsample.

RESULTS AND DISCUSSION

Quantitative results of the porosimetric study are listed in Table 1. Cumulative pore size distributions are shown Fig. 1 and Fig. 2. Incremental pore volumes are shown Fig. 3 and Fig. 4.

From the data in Table 1, we can state that:

1. Total mercury intrusion for Avicel 102 (single sample) and the < 160-μm fraction are quiet similar, showing averages of 1.83 and 1.77 cc/g. For the 160- to 315-μm fraction, mercury total intrusion is higher, with an average of 2.40 cc/g. Concerning the porous network of compacts, we can present same remark, with a yet smaller overall porosity: 0.79.0.83, and 1.00 cc/g.

Table 1

Quantitative Results of Porosimetric Study of Powders and Porous Network Compacts

	Powders			Porous Network of Compacts		
Particle size of raw material (μm)	Bulk	160–315 μm	<160 μm	Bulk	160–315μm	<160 μm
Mercury total intrusion volume (cc/g)	1.8317	2.4050	1.772	0.7888	1.0020	0.8294
Median pore diameter volume (μm)	27.5609	62.9881	23.1764	7.788	10.2418	8.6720
Bulk density (g/cc)	0.3539	0.3060	0.3839	0.6868	0.5994	0.6527

2. Median pore diameter of the 160- to 315-μm fraction is also higher: 62.99 μm for only 27.56 and 23.17 μm for bulk Avicel 102 and for <160-μm fraction. These results agree with Hausner (5), who explains that, when a powder mass consists of fine particles, pores between particles will be also fine. If the powder mass consists of coarse particles, voids between particles will be coarse. At one and the same time, for a powder mass consisting of a combination of fine and coarse particles, voids between coarse particles are filled with fines. The difference will be in a more complex shape of the pores. As Hausner, we can then assume that pore size is a function of particles size and shape. Variations observed with the porous network of compacts show the same trend, with smaller values.

Referring to Fig. 1, we see that the three cumulative curves present quiet similar profiles. If we refer to the works of Le Thiesse (10), we observe that the overall porosity of Avicel 102 is essentially interparticulate (pore diameters between 10 and 100 μm). Profiles are separated because of different median pore diameters. Avicel 102 profile being between the two others but near to <160-μm fraction than the 160- to 315-μm fraction.

If we refer to Fig. 2 when powders are submitted to compaction, because applied pressure is low, we can observe that at the beginning of the compaction, it is Avicel 102 and the <160-μm fraction that are first compacted, and the curves are confounded.

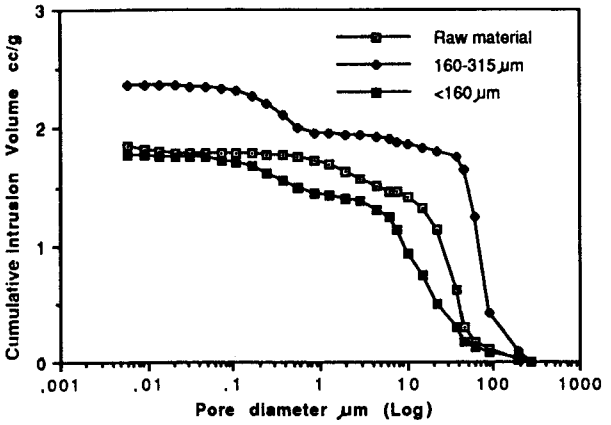

Figure 1. Cumulative intrusion volume (cc/g) for powders.

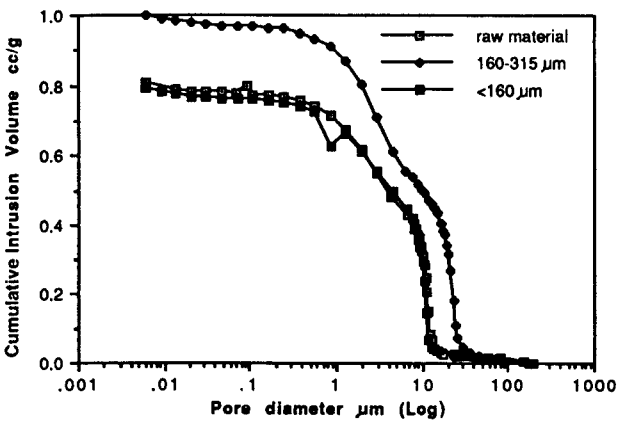

Figure 2. Cumulative intrusion volume (cc/g) for compacts.

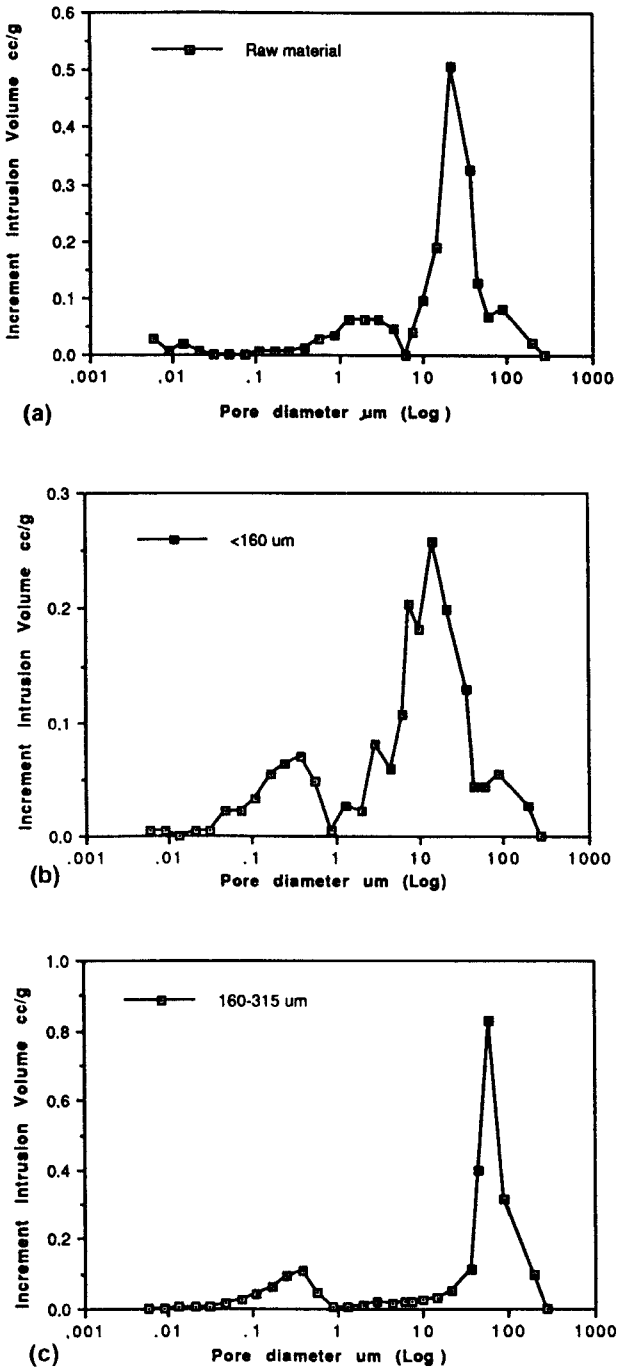

Figure 3. Incremental intrusion volume (cc/g) for powders.

As shown in Fig. 3 (incremental intrusion volume), for Avicel 102 raw material, there is no mercury intrusion for diameters between 0.01 and 1 µm. We can think as Hausner, that voids between coarse particles (160- to 315-µm fraction) are filled with fine particles (< 160-µm fraction), Avicel 102 being a combination of the two fractions.

Referring to Fig. 4, for the three porous networks, interparticulate porosity is situated at the 10-µm pore

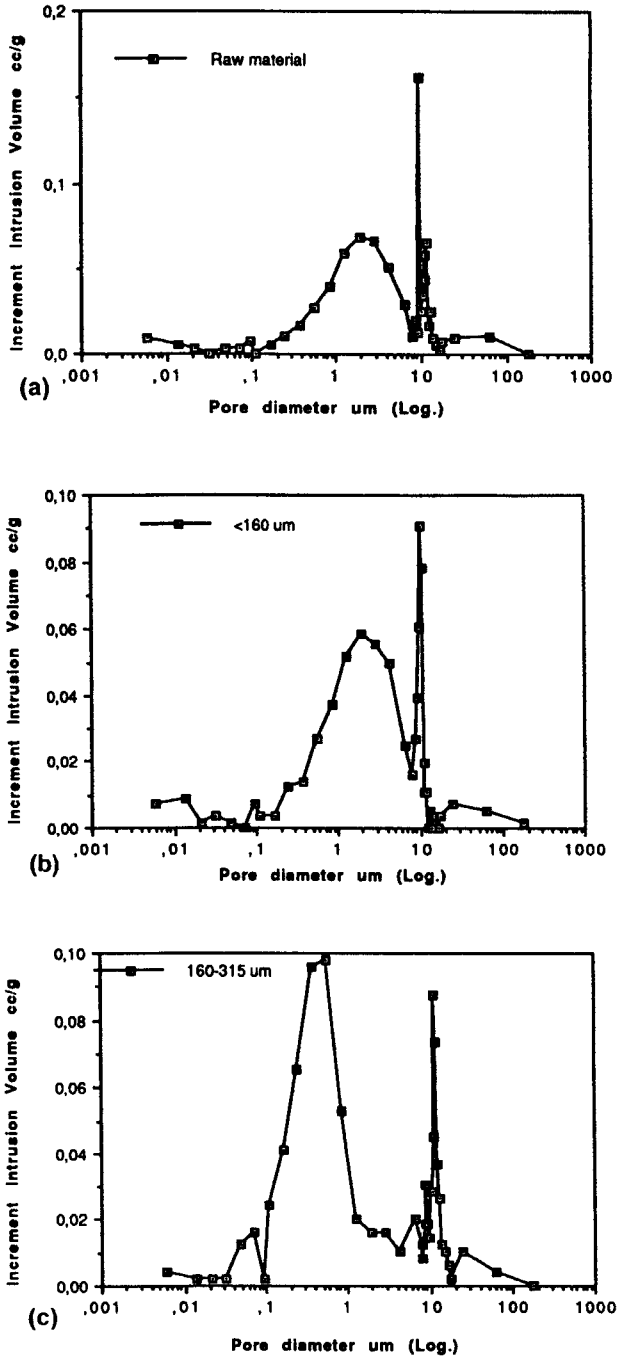

Figure 4. Incremental intrusion volume (cc/g) compacts.

Table 2

Quantitative Results of Characterization of Tablets

	Particle Size of Raw Material		
	Bulk	160-315 μm	<160 μm
Mass (g)	0.367 ± 0.018	0.325 ± 0.016	0.367 ± 0.018
Diameter (mm)	12.1 ± 0.01	12.13 ± 0.01	12.09 ± 0.01
Thickness (mm)	5.04 ± 0.01	5.03 ± 0.00	5.04 ± 0.01
Crushing strength (newton)	24.7 ± 4	14.7 ± 4	24.7 ± 3
Tensile strength (MPa)	0.257	0.151	0.258

diameter with different level pics. Intraparticulate porosity is transfered toward smaller pore diameters for the 160- to 315-μm fraction: 0.1 to 1 μm for it; while we read 1 to 10 μm for the Avicel 102 and the <160-μm fraction.

From the data in the Table 2, we can state that results indicate a much smaller tensile strength for tablets manufactured from the 160- to 315-μm fraction with 0.151 MPa instead of 0.257 and 0.258 MPa for Avicel 102 and the <160-μm fraction. That is in correlation with a higher porosity.

CONCLUSION

We have, in an earlier paper, described some physical characterization, packing characteristics, and tableting behavior applied to Avicel 102 compared with four other commercial celluloses (1,2). We investigated, in the present work, the porous structure of Avicel 102, two particle size fractions of the single sample, and a porous network of compacts (integral and incremental porograms).

We have tried to evaluate (qualitatively and quantitatively) the correlation between porosity, particle size, and tensile strength of compacts. With the method used, an important interparticulate porosity is observed with similar porosimetric profile, for all different particle size fractions. The results of the porosimetric study made it possible to explain the correlation between particle size and porosimetry. Indeed, we find that the integral and incremental programs are quite the same for bulk Avicel 102 and the fine particle size fraction (<160 μm), the 160- to 315-μm fraction presents differences for total mercury intrusion volume and for median pore diameter. They increase when particle size increases. In this case cumulative pore volume presents a profile transfered towards higher pore diameters.

The results of tablets characterization show, for a low applied pressure, a correlation between particle size, porosity, and tensile strength. Tensile strength of compacts decreases when particle size and porosity increase.

REFERENCES

1. C. Thomas, A. M. Mottot, and Y. Pourcelot-Roubeau, in *6th Interantional Conference on Pharmaceutical Technology*, APGI, Paris, Vol. 1, pp. 231–240.
2. C. Thomas and Y. Pourcelot, Drug Dev. Ind. Pharm., 19(15), 1947–1964 (1993).
3. K. Marshall and D. Sixsmith, Drug Dev. Commun., 1(1), 51–71 (1974–1975).
4. H. M. Rootare and R. G. Graig, Powder Technol., 9, 199–211 (1974).
5. H. H. Hausner, Powder Technol., 30, 3–8 (1981).
6. D. Faudot, Petrol Techn., 273, 19–30 (1980).
7. J. T. Fell and J. H. Newton, J. Pharm. Pharmcol., 20, 657–658 (1968).
8. J. T. Fell and J. H. Newton, J. Pharm. Sci., 59(5), 688–691 (1970).
9. P. J. Dees and J. Polderman, Powder Technol., 29, 187–197 (1981).
10. J. C. Le Thiesse, 2ème Journée Scientifique Préformulation du Médicament et Développement Galénique, Faculté de Pharmacie, Dijon, 1989, pp. 43–89.