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RESEARCH PAPER

Compaction Properties of Microcrystalline Cellulose Using Tableting Indices

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ABSTRACT

The compaction properties of microcrystalline cellulose (MCC) from 6 different sources were investigated and compared using tableting indices. The 50-μm and 100-μm grades were studied in order to determine lot-to-lot variability within a source, variability between sources, and the influence of storage conditions on the compaction properties of MCC. Two lots of each grade of MCC were obtained from each source and tested as received. It was found that the Avicel and Emcocel products demonstrated the most similarities based on tableting indices. Significant lot-to-lot differences in the tableting indices were observed for Fibrocel, Omnicel, and Spectrum MCC products. The brittle fracture index was low for all products tested and not significant. Storage of compacts at elevated humidity conditions prior to determining the tableting indices decreased the magnitude of the tensile strength, dynamic indentation hardness, and bonding index. Particle size analysis revealed differences between the labeled mean particle size and the experimentally determined value for some of the MCC grades and sources investigated. The percent weight gain of MCC powder at 18 hr was less than 0.6% at 30% relative humidity, and ranged from about 0.75% to 1.46% at 51% and 75% relative humidities. The x-ray diffraction patterns were similar for the MCC grades and sources investigated. MCC products from different sources are not directly substitutable based on the differences in physicomechanical properties observed for the tableting indices.

INTRODUCTION

Microcrystalline cellulose (MCC) is one of the most widely used tableting excipients in pharmaceutical manufacturing today. It is available in various particle size distributions and used in wet granulation and direct compression processes. In most tablet formulations, microcrystalline cellulose comprises a significant proportion by weight of the total composition. MCC powders consolidate to form compacts primarily through plastic deformation, and the compacts also demonstrate some elasticity with time dependent behavior (1). The physicomechanical properties of MCC are influenced by chemical composition, degree of polymerization, degree of crystallinity, moisture content, particle size, and particle shape (2). Doelker found that no correlation could be observed between degree of polymerization and mechanical properties due to the random orientation of the crystallites of MCC products investigated. In contrast, he observed a relationship between the degree of crystallinity and plasticity for MCC studied from different sources (2). The chemical, physical, and mechanical properties of microcrystalline cellulose have been thoroughly investigated by numerous authors (3–8). It is this database from which comparisons can be made between the various grades of MCC and between the different sources supplying MCC. However, the database does not include compaction properties derived from tableting indices for the most recently introduced MCC products now available to the pharmaceutical industry.

In the present study, lot-to-lot variation and source-to-source variation in compaction properties for two grades of MCC products were investigated using tableting indices. The particle size distribution and x-ray diffraction patterns also were investigated. In addition, the influence of humidity levels during storage of the MCC compacts on the tableting indices and the percent weight gain of MCC as a function of storage conditions were studied.

MATERIALS AND METHODS

Table 1 lists the sources for the MCC products investigated in this study. Two lots of MCC were obtained from each of 6 manufacturers. The materials were used as received from the source. The true densities of the powders were determined using a helium pycnometer (Model 1330, Micromeritics Instrument Corp., Norcross, GA). Two mean particle sizes of MCC were evaluated, 50 μm microns and 100 μm. The products having a mean particle diameter of 50 μm were Avicel PH-101, Emcocel 50 M, Fibrocel RI 20-50, Omnicel PH-101, Spectrum CE112, and Tabulose 101. The products having a mean particle diameter of 100 μm were Avicel PH-102, Omnicel PH-102, and Tabulose 102. Emcocel 90 M and Fibrocel RI 20-90 were included in this comparison since they have a mean particle diameter of 90 μm and are often compared to MCC products having mean particle diameters of 100 μm. An

Table 1

List of Microcrystalline Cellulose Manufacturers, Products, and Lot Numbers Used in This Investigation

FMC Corporation Philadelphia, PA		Mendell Corporation Patterson, NY		Resources Industry, Inc. Lafayette, IN	
Avicel PH-101	Avicel PH-101	Emcocel 50 M	Emcocel 90 M	Fibrocel RI 20-50	Fibrocel RI 20-90
1401	2432	9B5A1X	9B5G1X	D52355	1031F
1517	2516	9B5A3X	9B5B2X	L101855	1102D
Pharmaceutical Ingredients Ltd. Belle Mead, NJ		**Spectrum Corporation New Brunswick, NJ**		**Blanver Farmoquimica Ltda. Cotia, Brazil**	
Omnicel PH-101	Omnicel PH-102	CE112		Tabulose 101	Tabulose 102
10106043194	10207047094	KJ379		10001/95	11039/95
10106044794	10297071495	JL272		10004/95	11049/95

MCC grade with a mean particle diameter of 100 μm was not available from Spectrum Corp.

The dynamic indentation hardness (*P*), tensile strength (*TS*), bonding index (*BI*), and brittle fracture index (*BFI*) were determined for each lot of MCC. Square compacts of the powders were prepared using a Carver 25-ton laboratory press (Fred Carver Company, Menomonee Falls, WI) equipped with a load cell and LCD display (ISI, Inc., Round Rock, TX) to monitor the applied compression force. The compacts were made using a die measuring 0.75 in. on a side. A split-die was used that allowed for triaxial decompression. A steel cap was placed between the upper punch and the load cell to concentrate the compressive force at the center of the powder bed. Some compacts were prepared with a stress-concentrating hole using an upper punch with a spring-loaded retractable pin. The maximum compression load was held constant for 30 sec for all compacts. Groups of 3 square compacts from each lot of material were made and then stored for 18 hr at 30%, 51%, or 75% relative humidity at 23°C. All compacts were made at a solid fraction of 0.65. The solid fraction of the compacts was determined from the apparent density divided by the true density. The apparent density was obtained from the ratio of the weight to the volume of the compact which was determined using a digital micrometer.

The tensile strength of compacts with (TS_0) and without (*TS*) a stress concentrator was measured with a Instron Universal Tester (Model 4201, Instron Corp., Boston, MA) and has been previously discussed (9). The rate of load application was chosen so that a time constant of 10 sec was obtained between the maximum force and $1/e$ times the maximum force. The *BFI* was calculated by the equation:

$$BFI = (TS/TS_0 - 1)/2 \tag{1}$$

The dynamic indentation hardness was determined using a pendulum impact apparatus and has been previously described (13). The chordal radius of the contact area produced by a spherical indenter was measured using an optical microscope (Zeiss Corp., Germany) with a stage-mounted digital micrometer. The inbound velocity (V_1), rebound velocity (V_r), and the chordal radius were used to calculate *P* by the following equation:

$$P = (4mgrh_r/\pi a^4)[(h_i/h_r) - 3/8] \tag{2}$$

where m is the mass of the indenter, g is the gravitational constant, r is the radius of the indenter, a is the chordal radius of the dent, h_i is the initial height of the indenter, and h_r is the rebound height of the indenter. The *BI* was calculated by the following equation:

$$BI = TS/P \tag{3}$$

Particle size analysis was determined by laser diffraction (Model SALD-1100, Shimadzu Scientific Instruments, Columbia, MD). Each sample of MCC was added to purified water and dispersed using a magnetic stirring bar prior to the particle size measurement. Moisture sorption of MCC was determined by monitoring the weight gain of preweighed MCC samples stored at room temperature in humidity chambers controlled at 30%, 51%, and 75% relative humidities for 18 hr. X-ray diffraction was determined using a Philips vertical scanning diffractometer (Type 42273, Philips Electronic Instruments, Mount Vernon, NY). Statistical comparisons were made using one-way analysis of variance (ANOVA) to evaluate differences. Results were judged to be significant based upon the 95% probability values ($p < 0.05$).

RESULTS AND DISCUSSION

Comparison of Different Types and Sources of MCC

The particle size distribution results determined for each of the products investigated are shown in Table 2. Descriptive particle diameters were extrapolated from plots of cumulative percent frequency versus particle diameter plots at the 10% cumulative percent undersize (M10), 50% cumulative percent undersize (M50), and 90% cumulative percent undersize (M90). It was found that the mean particle size for the 50-μm grades of Avicel PH-101, Emcocel 50M, and Omnicel PH-101 was 49.4, 53.1, and 48.7 μm, respectively. The M10 and M90 particle diameters were useful in comparing particle size distributions. Tabulose 101 had a mean particle size of 61.7 μm which was significantly greater than the labeled value of 50 μm. Fibrocel RI 20-50 and Spectrum CE112 had mean particle sizes of 44.3 and 40.5 μm, respectively, which were significantly less than the labeled value. In addition to the mean particle diameter, the particle size distribution was important to compare. The geometric standard deviation (GAD) was obtained by plotting the logarithm of the particle size against the cumulative percent frequency on a probability scale, and the results are shown in Table 2. The results indicated that Omnicel PH-101 and Spectrum CE112 had GSD values of 1.27 and 1.34, respectively. Avicel PH-101 and Tabulose 101 each had the same

Table 2

Particle Size Results of Microcrystalline Cellulose Products

	Lot Number	M10	M50	M90	Geometric Standard Deviation
50-μm grade					
Avicel PH-101	1401	17.7	49.4	101.8	1.19
Emcocel 50M	9B5A1X	18.0	53.1	105.6	1.24
Omnicel PH-101	10106044794	15.0	48.7	100.5	1.27
Fibrocel RI 20-50	D52355	16.4	44.3	96.5	1.23
Tabulose 101	10001/95	24.8	61.7	110.2	1.18
Spectrum CE112	KJ379	11.5	40.5	102.2	1.33
100-μm grade					
Avicel PH-102	2432	31.8	78.2	143.6	1.22
Emcocel 90M	9B5B2X	34.1	88.6	156.0	1.35
Omnicel PH-102	10207047094	48.7	14.9	201.4	1.23
Fibrocel RI 20-90	1031F	43.4	90.0	172.1	1.19
Tabulose 102	11039/95	44.3	94.8	182.0	1.20

GSD value of 1.19. A distribution in which the GSD is equal to 1 is monodisperse, and as the GSD deviates from 1, the distribution becomes more polydisperse. Therefore, the distributions found between the different sources of the 50-μm grade were variable. Similar results are presented in Table 2 for the 100-μm grade of MCC. In this case, the mean particle diameter for Tabulose 102 was 95.8 μm, which was close to the labeled mean particle size. Likewise, Emcocel 90M and Fibrocel RI 20-90 had a mean particle diameter of 88.6 and 90.0 μm, which compared favorably to their labeled value of 90 μm. The mean particle diameter for Avicel PH-102 was lower than expected at 78.2 μm, and for Omnicel PH-102, it was higher than expected at 114.9 μm. The GSD was similar for each of the 100-μm grades of MCC investigated and ranged between 1.19 and 1.25. This indicated that the powder particles comprising the 100-μm grade had similar degrees of polydispersity.

Grades of MCC are typically classified by the mean particle diameter, and for some of the newer MCC products, by moisture level. The compaction properties of two commonly used grades of MCC were investigated in this study using tableting indices, and were the 50-μm and 100-μm mean particle diameter grades. The results obtained at 23°C and 30% relative humidity for *TS*, *P*, *BI*, and *BFI* for the 50-μm grade of MCC are shown in Table 3. The results indicate that the lot-to-lot differences within a source for *TS*, *P*, and *BI* were not significant for Avicel PH-101, Emcocel 90M, and Tabulose 101. This demonstrates good uniformity between lots among these sources. The results for Fibrocel RI 20-50 showed significant differences between the two lots investigated of 41% for *TS* and 23% for *BI*. Similar magnitudes of lot-to-lot differences were found for Omnicel PH-101 and Spectrum CE112. This demonstrates poor uniformity between lots. Precision is a measure of the agreement among values between groups of data, and can be quantitated by comparing the magnitude of the standard deviation in relation to that of the mean. The precision was less than 6% for the *TS* measurements, and less than 10% for the *P* measurements and *BI* values for all sources. The magnitude of the *BFI* was variable for each lot-to-lot comparison made, but for all sources, the low magnitude of the *BFI* indicated that the 50-μm grade of MCC was able to relieve stresses significantly such that brittle fracture was not significant. The two lots of Emcocel 50M had the best precision for the *BFI* values of 27% and 20%, whereas the precision of Tabulose 101 (lot 10004/95) was 111%, Fibrocel RI 20-50 (lot 052355) was 100%, and Spectrum CE112 (lot KJ379) was 277%. The poor precision for these products came from the measured values of TS_0, and this indicated that there are significant differences between lots within a source in how the MCC relieves stresses created from the stress-concentrating hole in the center of the compact.

The results obtained at 23°C and 30% relative humidity for the 100-μm grade of MCC are shown in Table 4. The lot-to-lot differences detected within a

Table 3

Compaction Properties Determined at 23°C and 30% Relative Humidity for MCC Products Having a Mean Particle Diameter of 50 μm. Mean and Standard Deviation (in parentheses)

Product	Lot Number	*TS* (N/cm²)	*BFI*	*P* (*k*N/cm²)	*BI* (× 10⁻²)
Avicel PH-101	1401	197.1	0.034	8.980	2.2
		(4.71)	(0.029)	(0.728)	(0.2)
	1517	202.4	0.081	8.983	2.3
		(4.74)	(0.022)	(0.422)	(0.1)
Emcocel 50M	9B5A1X	201.8	0.054	8.206	2.5
		(6.95)	(0.015)	(0.463)	(0.1)
	9B5A3X	214.9	0.118	9.145	2.4
		(6.46)	(0.024)	(0.655)	(0.2)
Fibrocel RI 20-50	D52355	131.0	0.012	7.890	1.7
		(6.99)	(0.012)	(0.227)	(0.1)
	L101855	184.7	-0.005	8.683	2.1
		(2.45)	(0.014)	(0.699)	(0.2)
Tabulose 101	10001/95	149.0	0.044	7.565	2.0
		(3.86)	(0.011)	(0.268)	(0.1)
	10004/95	141.2	0.027	7.973	1.8
		(2.65)	(0.030)	(0.632)	(0.1)
Omnicel PH-101	10106043194	151.6	0.027	8.279	1.8
		(1.40)	(0.011)	(0.214)	(0.0)
	10106044794	181.3	0.117	8.115	2.2
		(5.05)	(0.020)	(0.290)	(0.1)
Spectrum CE112	KJ379	121.8	0.018	8.235	1.5
		(6.78)	(0.050)	(0.717)	(0.1)
	JL272	154.9	0.019	7.965	1.9
		(4.19)	(0.013)	(0.261)	(0.1)

source for *TS*, *P*, and *BI* were not significant for Avicel PH-102 and Emcocel 90M. Again, this demonstrated good uniformity between lots from these two MCC sources. Emcocel 90M demonstrated the highest values for *TS* and *BI*, followed by Avicel PH-102. Fibrocel RI 20-90 displayed significant lot-to-lot differences of 35% for *TS* and 15% for *BI*, whereas only a 2% difference between lots was found for *P*. Similar results were observed for Tabulose 102. Omnicel PH-102 displayed significant lot-to-lot differences of 33% for *TS*, 14% for *P*, and 20% for *BI*. This demonstrated poor uniformity between lots for the other sources investigated. The precision in the data for *TS, P,* and *BI* was good and similar to that found for the 50-μm grade. Likewise, the magnitude of the *BFI* was small and variable for each lot-to-lot comparison made for all sources, but for each lot, the low magnitude of the *BFI* indicated that the 100-μm grade of MCC was able to relieve stresses sufficiently such that brittle fracture was not significant. The best precision in the *BFI* data for the two lots was observed for Emcocel 90M (18% and 21%) and Avicel PH-102 (38% and 21%). The precision was not as good for Fibrocel RI 20-90 (100% and 61%), Tabulose 102 (17% and 95%), and Omnicel PH-102 (50% and 100%). A similar argument can be made that the poor precision originated from the measured values of TS_0, and the lot-to-lot reproducibility was best for Avicel PH-102 and Emcocel 90M.

Doelker (2) stated that Avicel products have been compared to other direct compression tableting excipients, and that with the introduction of new MCC products from other sources, it is imperative to evaluate their basic mechanical properties because these properties can cause differences in tableting. The basic mechanical properties including hardness, degree of polymerization, crystallinity, and moisture content of Avicel products compared favorably to Emcocel products (2). The mechanical properties including tableting indices of Fibrocel RI, Tabulose, Omnicel, and Spectrum products have not been previously reported in the literature. The

Table 4

Compaction Properties Determined at 23°C and 30% Relative Humidity for MCC Products Having a Mean Particle Diameter of 100 μm. Mean and Standard Deviation (in parentheses)

Product	Lot Number	*TS* (N/cm^2)	*BFI*	*P* (kN/cm^2)	*BI* ($\times 10^{-2}$)
Avicel PH-102	2432	172.2	0.045	7.854	2.2
		(1.58)	(0.017)	(0.345)	(0.1)
	2516	165.7	0.037	7.770	2.1
		(2.15)	(0.008)	(0.369)	(0.1)
Emcocel 90M	9B5G1X	211.4	0.140	8.864	2.4
		(4.39)	(0.025)	(0.266)	(0.1)
	9B5B2X	200.7	0.115	8.283	2.4
		(2.91)	(0.024)	(0.326)	(0.1)
Fibrocel RI 20-90	1031F	107.3	0.010	8.423	1.3
		(1.29)	(0.011)	(0.287)	(0.0)
	1102D	137.9	0.031	8.668	2.0
		(5.00)	(0.019)	(0.616)	(0.1)
Tabulose 102	11039/95	159.8	0.054	7.565	2.0
		(6.26)	(0.009)	(0.365)	(0.1)
	11049/95	141.0	0.028)	8.101	1.7
		(3.09)	(0.23)	(0.234)	(0.1)
Omnicel PH-102	10207047094	155.7	0.069	7.646	2.0
		(6.63)	(0.031)	(0.239)	(0.1)
	10297071495	141.1	0.016	8.730	1.6
		(3.48)	(0.031)	(0.188)	(0.1)

Avicel and Emcocel products for both grades investigated were the most similar in magnitude for the parameters measured. Fibrocel RI 20-90 gave the lowest value of *TS* (107.3 N/cm^2) and the lowest value of *BI* (0.013). Omnicel PH-102 also had a low *BI* value, (0.016). The results comparing sources and lots within a source illustrate the importance of determining the basic compaction properties when substituting MCC from one source with MCC with a second source. The data indicated that the Avicel products and Emcocel products will be the most likely to be directly substituted for each other, whereas formulation modifications will probably be necessary when substituting the Fibrocel RI, Tabulose, Omnicel, or Spectrum products for either Avicel or Emcocel products. Doelker et al. (1) reported similar results when comparing mechanical and tableting properties between Avicel PH-101 and Emcocel 50M, and between Avicel PH-102 and Emcocel 90M.

Influence of Storage Conditions

An important parameter influencing the mechanical properties of MCC is moisture. Storage at elevated humidity conditions will adversely effect the compaction properties of MCC because of the lubricating action of the water which facilitates the slippage and flow of individual microcrystals of MCC (6). The results presented in Figs. 1 and 2 demonstrate the influence of storing the compacts at 30%, 51%, or 75% relative humidity on *TS*. The magnitude of *TS* decreased as the humidity was increased for all 50-μm, grades of MCC shown in Fig. 1. The precision of the measurements at 51% and 75% relative humidities was similar to those previously described at 30% relative humidity. Similar trends were observed in Fig. 2 for the 100-μm grades of MCC. The rate of decrease of *TS* as a function of humidity level was less for the 50-μm grades of MCC than for the 100-μm grades of MCC. All of the MCC products investigated demonstrated similar decreases in *TS* as the humidity was increased.

P is the resistance of a material to plastic deformation. The results presented in Fig. 3 reveal that *P* decreased as the humidity was increased for the 50-μm grade. It can be seen that *P* for Avicel PH-101 and Tabulose 101 remained constant at 50% relative humidity, and then decreased at 75% relative humidity. The other 50-μm grades of MCC products showed a more linear and rapid decrease in *P* as the humidity was in-

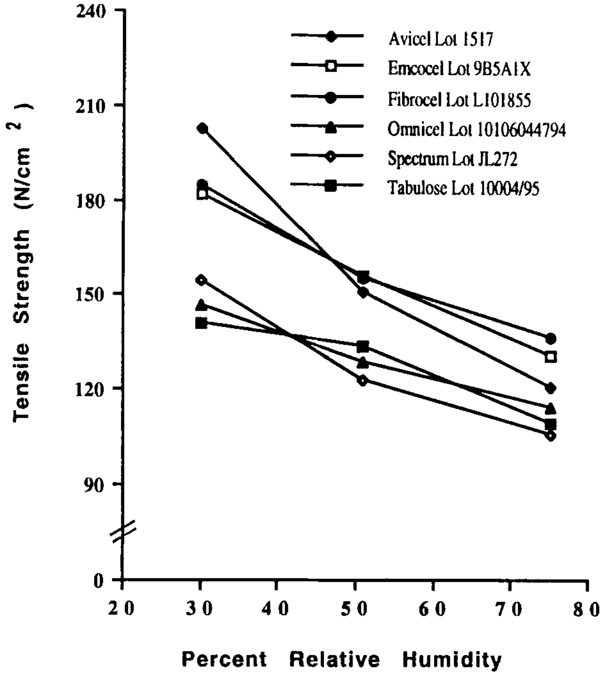

Figure 1. Influence of humidity on the tensile strength of MCC products having a mean particle size of 50 μm.

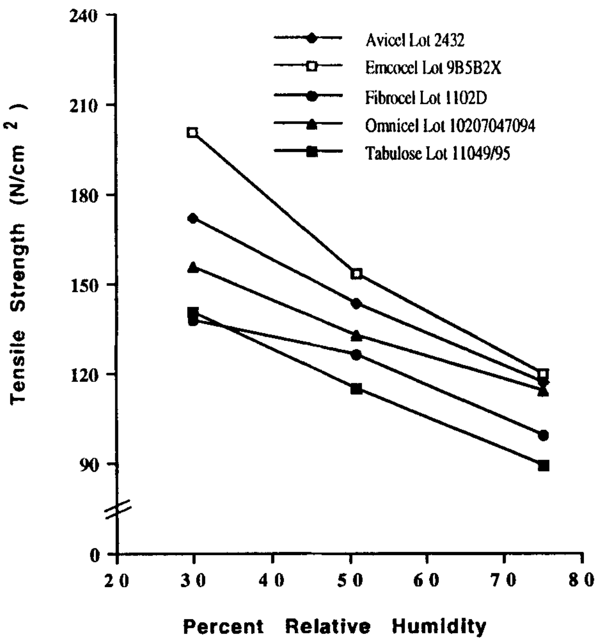

Figure 2. Change in tensile strength as a function of storage conditions for MCC products having a mean particle size of 100 μm.

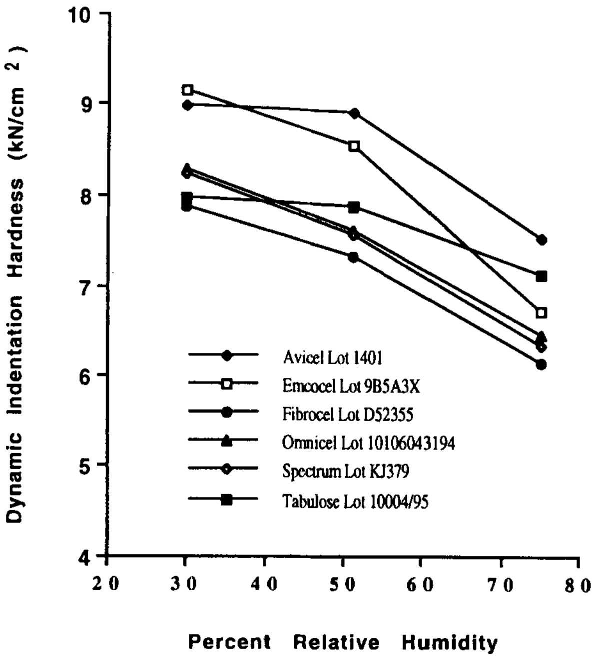

Figure 3. Relationship between dynamic indentation hardness and humidity level for MCC compacts stored for 18 hr at 23°C and 31%, 50%, or 75% relative humidity.

creased. Avicel PH-101 and Emcocel 50M had comparable magnitudes of *P* at 30% and 51% relative humidities, and greater than the other MCC products tested. The Fibrocel, Omnicel, and Spectrum products had similar magnitudes and slopes for *P* at each storage condition. Similar results were found for the 100-μm grade. This indicated that the ability of MCC to resist plastic deformation depends on the source of the material and the humidity of the environment.

The bonding index estimates the areas of true contact formed during compression that will remain following decompression. Hiestand stated that the dwell time of the indenter on the compact will be less than a millisecond when *P* is determined using the dynamic pendulum impact apparatus. The *BI* determined from the dynamic measurement of *P* has been called the worst-case bonding index since the viscoelastic decay of the stress during the time the indenter is in contact with the compact is minimal (10). The results for *BI* as a function of storage conditions are presented in Table 5. Both of the Avicel and Omnicel grades showed a decrease in *BI* between the 30% and 51% relative humidity conditions, and then the *BI* remained constant between the 51% and 75% relative humidity conditions. Both Tabulose grades showed small changes in *BI* as the humidity was in-

Table 5

Influence of Storage Conditions on BFI and BI for the 50-μm and 100-μm Grades of MCC. Mean and Standard Deviation (in parentheses)

	BFI			*BI* (× 10^{-2})		
	30%	51%	75%	30%	51%	75%
50-μm grade						
Avicel PH-101 #1517	0.081	0.057	0.016	2.2	1.7	1.6
	(0.022)	(0.029)	(0.010)	(0.2)	(0.0)	(0.1)
Emcocel 50M #9B5A1X	0.054	0.066	0.077	2.5	2.1	2.1
	(0.015)	(0.023)	(0.012)	(0.1)	(0.1)	(0.1)
Fibrocel RI 20-50 #D52355	0.012	0.023	0.055	1.7	1.7	1.8
	(0.012)	(0.034)	(0.029)	(0.1)	(0.1)	(0.1
Omnicel PH-101 #10106044794	0.027	0.065	0.041	2.2	1.8	1.9
	(0.011)	(0.019)	(0.031)	(0.1)	(0.1)	(0.1)
Spectrum CE112 #JL272	0.019	0.035	0.047	1.9	1.6	1.4
	(0.013)	(0.018)	(0.022)	(0.1)	(0.2)	(0.1)
Tabulose 101 #10004/95	0.027	0.034	0.021	1.9	1.7	1.5
	(0.030)	(0.006)	(0.022)	(0.1)	(0.1)	(0.1)
100-μm grade						
Avicel PH-102 #2432	0.045	0.046	-0.010	2.2	1.7	1.7
	(0.017)	(0.004)	(0.009)	(0.1)	(0.0)	(0.2)
Emcocel 90M #9B5G1X	0.140	0.054	0.061	2.4	2.1	2.1
	(0.025)	(0.006)	(0.029)	(0.1)	(0.1)	(0.1)
Fibrocel RI 20-90 #1102D	0.031	0.068	0.029	2.0	1.5	1.7
	(0.019)	(0.019)	(0.054)	(0.1)	(0.1)	(0.1)
Omnicel PH-102 #10207047094	0.069	0.032	0.023	2.0	1.8	2.0
	(0.031)	(0.029)	(0.008)	(0.1)	(0.1)	(0.1)
Tabulose 102 #11039/95	0.028	0.009	0.019	2.0	1.8	1.7
	(0.023)	(0.018)	(0.003)	(0.1)	(0.2)	(0.1)

creased. The *BI* for the 50-μm grade of Fibrocel was not significantly influenced by humidity, and the 100-μm grade of Fibrocel showed a slight increase in *BI* as the humidity was increased.

The results shown in Table 5 also show the influence of humidity on *BI* for both grades of MCC investigated. The *BFI* determined for the 50-μm grade increased slightly as the humidity was increased, but due to the large standard deviations associated with the measurements of TS_0, the changes in *BFI* were not significant. Similar results were found for the 100-μm grade of MCC. According to Eq. (1), the *BFI* compares the ratio of *TS* to TS_0, which is then normalized to fall between 0 and 1. Upon exposure to elevated humidity conditions, TS_0 decreased at a faster rate than *TS* as the humidity was increased. This resulted in the slight increase in *BFI* over the range of humidities investigated. The presence of the stress concentrating hole in the MCC compact in combination with the moisture sorption resulting from storage at elevated humidity conditions caused this difference between TS_0 and *TS*. MCC is a plastic material and is able to adequately relieve stresses such that the *BFI* is not of concern for any of the storage conditions tested.

Malamataris et al. (7) investigated the influence of moisture on the mechanical properties of MCC and found similar results. Bolhuis et al. (11) found that MCC was the most moisture sensitive among the common direct compression excipients tested at both 50% and 85% relative humidities. The amount of water sorbed caused by storage at elevated humidity conditions is directly related to the reduction in crushing strength of MCC compacts (11). Doelker (2) stated that moisture-mediated changes in MCC tablets are an important problem even though conflicting results have been reported. Therefore, it is necessary to quantitate these effects so that a rational decision can be made regarding which experiments will be needed to justify substituting one MCC product for another.

The results presented in Table 6 indicate that the percent weight gain of the 50- and 100-μm grades of MCC were influenced by the level of humidity during

Table 6

Percent Weight Gain of MCC at Various Storage Conditions for 18 hr

	Percent Relative Humidity		
	30%	51%	75%
50-μm grade			
Avicel PH-101 #1401	0.516	0.775	1.23
Emcocel 50M #9B5A1X	0.549	0.843	1.42
Fibrocel RI 20-50 #D52355	0.582	0.841	1.36
Omnicel PH-101 10106043194	0.514	0.836	1.27
Spectrum CE112 #KJ379	0.483	0.878	1.29
Tabulose 101 #10001/95	0.555	0.778	1.23
100-μm grade			
Avicel PH-102 #2432	0.546	0.841	1.24
Emcocel 90M #9B5B2X	0.452	0.742	1.29
Fibrocel RI 20-90 #1031F	0.483	0.874	1.35
Omnicel PH-102 #10207047094	0.643	0.846	1.36
Tabulose 102 #11039/95	0.515	0.867	1.32

storage. The percent weight gain for the 50-μm grade ranged from 0.45% to 0.64% when stored at 30% relative humidity, 0.78% to 0.88% when stored at 51% relative humidity, and from 1.23% to 1.42% when stored at 75% relative humidity for 18 hr. Similar results were obtained for the 100-μm grade. The results indicated that each of the MCC grades and sources investigated had similar propensities to sorb water when exposed to the various humidity conditions. Even though the percent weight gain was less than 1.5% for all samples, the amount was still significant enough to influence the physicomechanical properties of the compacts as indicated from the results obtained for the bonding indices.

A powder x-ray diffraction pattern for Avicel PH-101 is shown in Fig. 4. Similar x-ray diffraction patterns were obtained for other samples investigated. Suzuki et al. (12) reported powder x-ray diffraction patterns for Avicel PH-101 that compared favorably to those obtained in this investigation. The results indicated comparable levels of crystallinity for each grade and source of MCC investigated. The results from the powder x-ray diffraction study support the results found from the moisture sorption study, since similar magnitudes of crystallinity will have similar sorption characteristics when exposed to elevated humidity levels.

In conclusion, this study found that appropriately designed studies must be performed before interchangeably substituting MCC from different sources based on results obtained for the tableting indices. The Avicel and Emcocel products demonstrated the most similarities in *TS*, *P*, and *BI*. The lot-to-lot variability was the lowest

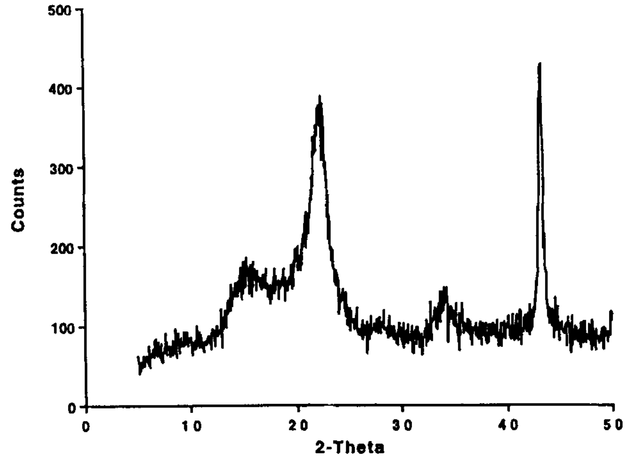

Figure 4. Powder x-ray diffraction pattern obtained for Avicel PH-101.

for Avicel and Emcocel. On the other hand, significant differences in mechanical properties between lots within a source were observed for Fibrocel, Omnicel, and Spectrum products. The *BFI* for all MCC grades investigated was less than 0.2, indicating that this parameter was insignificant (19). Particle size analysis revealed differences between some of the labeled mean particle diameters and the experimentally determined mean particle sizes. The x-ray diffraction patterns were similar for all MCC grades and sources investigated. In addition, storing at elevated humidity conditions will effect the physicomechanical properties of MCC, and the extent of this influence depends on the source of the MCC product. Water sorption acts to increase slippage and flow of particles of MCC, thereby causing a decrease in *TS*, *P*, and *BI*. *P* measured for the Avicel and Tabulose grades was not influenced by storing the compacts at 51% relative humidity but decreased when stored at 75% relative humidity. The weight of MCC powder stored at elevated humidity conditions for 18 hr was found to increase due to sorption of water during storage for all grades and sources investigated. Even though the percent weight gain and x-ray diffraction patterns were comparable, the observed differences in the physicomechanical properties between the 2 grades and 6 sources studied illustrate the importance of completely characterizing and evaluating each MCC product prior to use in a tablet formulation. The tablet formulation may have to be further optimized due to differences in the compaction properties of MCC powder obtained from different sources.

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