Drug Development and Industrial Pharmacy, 27(7), 613–621 (2001)

RESEARCH PAPER

Directional Bonding in Compacted Microcrystalline Cellulose

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ABSTRACT

The mechanical properties of compacts of microcrystalline cellulose (MCC) and silicified microcrystalline cellulose (SMCC) were evaluated by tensile testing, diametric compression testing, and compression testing. For tensile and compression testing, cubic specimens were carefully machined from MCC and SMCC compacts, and the tensile and compression strengths were evaluated both normal and parallel to the compaction direction. The cubic tensile strengths were compared to values obtained from the diametric compression test. The results obtained using the diametric compression test suggested compacts of SMCC exhibit greater strength than those of MCC. In addition, the cubes machined from compacts of MCC and SMCC exhibited directional strength; the direction normal to the compaction direction displayed the greater tensile strength; and the parallel direction had greater compression strength. The diametric compression test afforded strength values with reduced spread compared to the values collected from the cubic tensile test, suggesting that the errors involved in collecting diametric compression test data of compacts are less than those for the cubic tensile test. Analysis of the cubes using X-ray diffraction (XRD) suggested that they display directional structural anisotropy, with the direction normal to the compaction direction being more crystalline than the parallel direction. However, it is not clear whether the difference in the directional strength is solely a consequence of the increased crystallinity or a culmination of crystallographic and mechanical keying effects.

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Key Words: *Crystallinity; Directionality; Mechanical strength; Microcrystalline cellulose; Silicified microcrystalline cellulose*

INTRODUCTION

Microcrystalline cellulose (MCC) is used as a filler/binder in the manufacture of pharmaceutical solid dosage tablets. The material has been extensively studied to understand its tableting behavior. For example, the compaction properties of mixtures of MCC with other pharmaceutical materials, such as drugs and other excipients like dicalcium phosphate, have been reported (1–3). However, due to the complexity of tablet formulations, the characteristics of compacted pure MCC and MCC in the presence of lubricants have also been investigated to understand the functionality of the material (4–6).

In tableting technology, MCC is considered to be a plastically deforming excipient. Another description of MCC is as a particulate aggregate of fibrils of a semicrystalline cellulose polymer. The mechanical properties of MCC are more complex than typical fabricated polymer systems in that the samples (compacts) invariably consist of compressed particles. This results in a large interfacial surface area that is responsible for tablet strength (7). This is a crucial characteristic of MCC compacts.

In addition, when considering the potential failure modes of pharmaceutical compacts, it is important to remember that, in general, materials fail under an applied load due to crack propagation. The stress associated with a crack or flaw in a matrix is described as the critical stress intensity factor (8). In contrast to typical polymer systems, pharmaceutical compacts are usually composed of compressed powder. This invariably results in failure by brittle fracture under an applied load, which occurs through the rupture of the interparticle bonding rather than intraparticle failure.

The mechanical strength of polymeric materials is usually determined by the tensile testing of dumbbell-shaped samples. These homogeneous test pieces are typically prepared by molding of the polymer samples. The tensile strength is determined by applying a tensile load to the sample via grips. The plastic flow of ductile materials allows compensation for any misalignment of the sample grips. Pharmaceutical tablets differ from typical polymer systems in that the samples are invariably inhomogeneous noncontinuous matrices of compressed powders. These samples tend to be brittle, making the determination of tensile strength using the conventional mechanical test difficult: Stress concentration occurs in the gripped portion of the sample, and the samples are susceptible to shear stresses that are induced by nonalignment of the test grips. To overcome these difficulties, the mechanical properties of compressed pharmaceutical powders have been determined using flexural tests (9,10) (three- and four-point bending) and the diametric compression test (11). The diametric compression test involves the application of a load normal to the compaction direction. A ''true'' tensile test involves the application of a tensile stress in which no load is applied to the sample normal to the tensile stress.

The important difference between these two techniques for measuring the tensile strength of materials is that, in the diametric compression test, the tensile failure is limited to the stress plain induced by the applied load; the true tensile test produces a tensile failure that reflects the weakest area in the sample. Even though these two tensile tests would be expected to afford different tensile strength values, the true tensile test may afford information concerning the directional strength of compacted pharmaceutical powder via the testing of compressed powder of similar geometry using an apparatus that reduces experimentally induced shear stresses.

The radial and axial tensile strengths of pharmaceutical compacts have been reported (12). However, possible sources of differences in apparent strengths of reported axial and radial tensile strength data of pharmaceutical samples are the presence of shear stresses in the test configuration and differences in the geometries of the test pieces. One way to overcome the problem of test piece geometry is to prepare samples of similar geometry, preferably cubes. The directional tensile strength of cubic tablets of MCC (Avicel PH-101, a 50-μm particle size grade) prepared using a single-punch tablet machine at a relatively small compression load has been previously investigated (13). The study reported that the direction parallel to the compaction direction exhibited significantly greater strength

than the normal direction. However, the samples were tested using a method that did not employ a mechanism to minimize sheer stresses that can be induced during the mounting and testing of the samples. Cubes of compacted MCC have also been previously prepared for tensile testing (using the transverse compression technique); however, no directional strength data were reported (14).

As previously stated, the mechanical properties of polymers are affected by crystallinity. This will be true for the mechanical properties of MCC. If MCC is considered as a homogeneous bulk polymer, then the crystallinity would have a profound effect on strength. However, MCC compacts consist of compressed discrete particles. Our unpublished previous investigations of the failed surfaces of samples (after diametric compression testing) using scanning electron microscopy (SEM) suggested that MCC compacts fail primarily at the particle interfaces rather than within the particles, although some evidence for intraparticle failure was identified. It would be expected that any small changes in the crystallinity of MCC would not affect this interparticle mode of failure. However, mechanical testing involves the application of a load to a material. It will be the way in which a material (of a particular geometry) copes with the applied stress that will affect the apparent strength. It would be expected that the compaction of an anisotropic material (in terms of particle size and particle shape) would result in an anisotropic compact, and that this will affect any apparent mechanical properties.

The relationship among source, compactibility, and crystallinity of MCC powders is complex (15). The apparent crystallinity of MCC depends on the method of determination: both X-ray diffraction (XRD) and infrared spectroscopy have been used to study the crystallinity of MCCs (16,17). Nuclear magnetic resonance spectroscopic and photoacoustic infrared spectroscopic studies of MCC compaction suggest that the axial and radial crystallinity develops differently during MCC compression, with the radial tensile strength always being greater than the axial values (18). In addition, the crystallinity was reported to be lower on the tablet perimeter (far from the compacting surfaces) than the top and bottom flat faces, emphasizing the importance of geometry and compression conditions.

Even though MCC is a highly compactible tableting excipient, manufacturers have continued to try to improve its functionality. Recently, a new modified MCC, silicified microcrystalline cellulose (SMCC), was introduced. This material is reported to exhibit improved compactibility in wet granulation and direct compression tableting (19). Low-speed powder compaction studies also suggested that the material does exhibit improved compactibility compared to unmodified MCC (20). To investigate any anisotropic mechanical properties and the apparent benefits of silicification, cubes were machined from compacts of MCC and SMCC, and the compression and tensile strengths were evaluated in two directions, parallel and normal to the compaction direction. The crystallinity of the cubes was also studied using wide-angle XRD.

EXPERIMENTAL

Materials

MCC (Emcocel 90M, Penwest Pharmaceuticals Co., New York) and SMCC (based on Emcocel 90M, SMCC90, 2% w/w silicon dioxide, Penwest Pharmaceuticals) were used as supplied.

Preparation of Compacts

Compacts were prepared by compacting powders (6 g) in the absence of lubricant in a die (25 mm diameter heat-treated silver steel) using a load of 100 kN at compression and decompression rates of 10 mm/min and a dwell time of 1 min using an Instron 1185. Powders were stored at ambient conditions; the temperature and humidity were monitored during compaction and testing.

Preparation of Cubes

Cubes ($8.45\,\text{mm} \pm 0.1\,\text{mm}$) were machined from the central part of the MCC and SMCC compacts using a milling machine. Compacts were milled using a slow speed; the size of the cutting volume was reduced as the required compact dimensions were approached when the time between each cut was lengthened to reduce any heating effects. All of the samples were examined visually to detect any macroscopic cracks. None were detected in any of the samples, and all the samples survived the machining stage apparently intact.

Tensile Testing of Compacts and Cubic Specimens

Diametric compression testing and cubic tensile testing were performed using an Instron 1125 using a crosshead speed of 1 mm/min. The tensile strength was calculated from the failure load (21). The tensile stresses were derived from the applied load divided by the original cross-sectional area of the corresponding cubic specimens. The deflection in compression and elongation in tension were monitored and were used to generate stress/strain data for the respective tests. The elastic (Young's) modulus is defined as the ratio of the stress to the strain data and can be represented by the slope of the stress/strain data (22). The greater the slope, the greater the apparent modulus.

$$E = \frac{\sigma}{\varepsilon}$$

where E is the elastic (Young's) modulus, σ is the stress, and ε is the strain.

The specially designed tensile test apparatus is shown diagrammatically in Fig. 1. The sample cubes were glued (Araldite^{TM} epoxy resin, Ciba-Geigy, Stafford, UK) into aluminum mounts. To reduce the possibility of inducing shear stresses, $9 \times 9 \times 0.5$ mm recesses were machined into the center of the aluminum mounts. The aluminum mounts, with the specimen glued in between, were carefully screwed into the steel mounts. The top mount was fixed into the load cell. The bottom mount was attached to the test machine via a chain mechanism to reduce pretest loading from the specimen gripping procedure. The samples were tensile tested by increasing the load on the steel chain. Three specimens were fabricated and tested for each testing procedure. All samples failed within the gauge length of the cubes; no samples failed in the glue/sample region.

Compression Testing of Cubic Specimens

Compression testing was performed using an Instron 1125 using a crosshead speed of 0.05 mm/min. The compressive stresses were derived from the applied load divided by the original cross-sectional area of the corresponding cubic specimens. The deflection in compression and elongation in tension were monitored and used to generate stress/strain data for the respective tests.

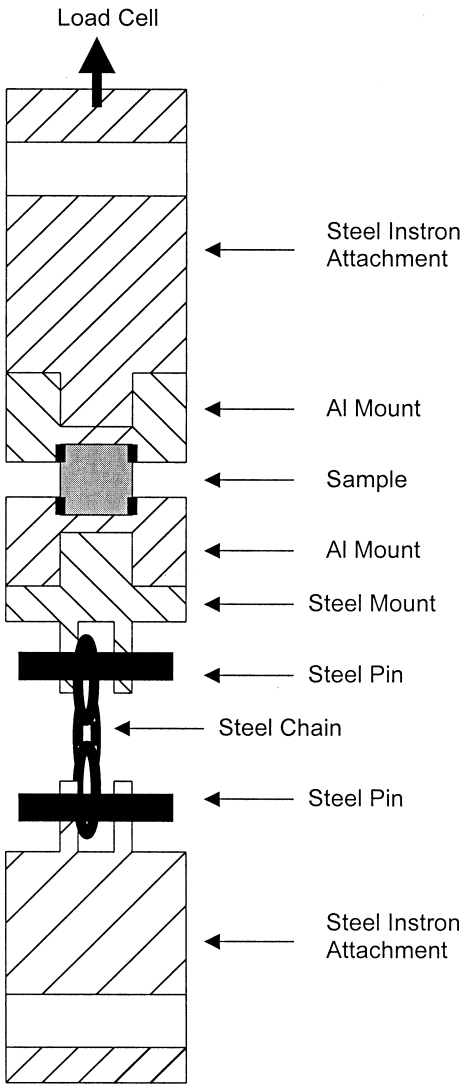

Figure 1. Representation of cubic tensile test apparatus.

X-ray Diffraction

Spectra were obtained using an X-ray powder diffraction system (Phillips X-ray analytical, Cambridge, UK). Each sample was analyzed by a single 2θ sweep at a rate of 0.02 degrees 2θ, step time 13 s.

Scanning Electron Microscopy

SEM was performed after gold coating (Edwards Sputter Coater, UK) using a Jeol 6310 (Jeol Instruments, Tokyo, Japan) system.

RESULTS AND DISCUSSION

Particles of MCC consist of nonhomogeneous fibrils or small agglomerates of a semicrystalline polymer (23). The compression of MCC would therefore be expected to produce anisotropic compacts. Machined cubes of MCC and SMCC were tested normal and parallel to the compaction direction. The directions of analysis are represented in Fig. 2. The data obtained from the cubic tensile test were compared to tensile strengths obtained from the diametric compression test.

Tensile Testing

The tensile strengths of MCC and SMCC obtained using the cubic tensile test and the diametric compression test are presented in Table 1. Tensile strengths obtained using the diametric compression test for compacts of SMCC and MCC were typical for these compaction and testing protocols (20). Samples were tested on the same day to reduce effects of aging and conditions on the apparent strength.

It can be seen from Table 1 that cubes and compacts of MCC and SMCC appear to exhibit similar mechanical behavior, although the strength of SMCC appears to be greater than that of MCC in both directions. The sets of data were subjected to the Student t test. The normal direction data were compared to the parallel data for each material. These comparisons had a significance of $P < .05$. The diametric compression test data between MCC and SMCC also had a significance of $P < .05$. However, when the normal direction data of MCC and SMCC and the parallel data of MCC and SMCC are compared, values of $P > .05$ were obtained. These observations suggest that the direction normal to the compaction direction appears to exhibit greater tensile strength than the parallel direction in the cubic tensile test, and compacts of SMCC exhibit greater tensile strength than those of MCC when evaluated using the diametric compression test. This is in contrast to a previous study of the directional tensile strength of cubic MCC tablets, which reported that the parallel direction exhibited the greatest strength (13).

The stress/strain data obtained from the tensile testing of cubes of MCC and SMCC are shown in Fig. 3. It can be seen from Fig. 3 that, again, MCC and SMCC cubes display similar mechanical behavior in terms of different stress/strain levels in the different directions. The elastic modulus is comparable for each material in the same direction; however, the direction normal to the compaction direction displays a greater elastic modulus than the parallel direction, which is represented by the increased slope of the stress/strain data for the normal direction samples.

The diametric compression test data, in Table 1, appear to give more reproducible strength values than the cubic tensile test. This probably reflects the cumulative errors associated with the two testing procedures and the differences in fracture areas; the diametric compression test restricts failure to the load line between the platens, whereas the cubic tensile test can result in failure sites within the entire gauge section of the specimen. In all cases, the samples failed in the central portions of the cubes. Invariably, the parallel direction gave a relatively even fracture surface in the center of the

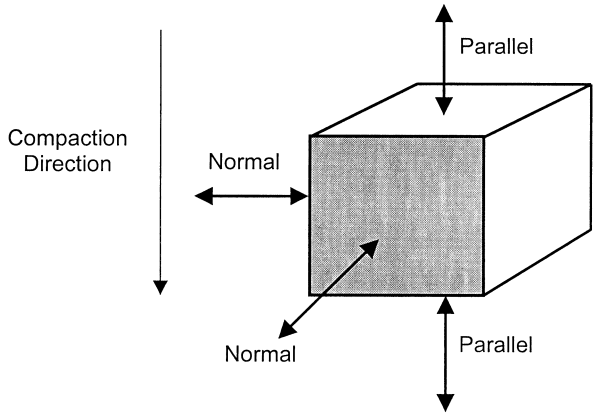

Figure 2. Representation of mechanical testing directions.

Table 1

Comparison of the Tensile Strengths of Cubes and Compacts of Silicified Microcrystalline Cellulose (SMCC) and Microcrystalline Cellulose (MCC)

		Tensile Strength (MPa)	
Sample	Test	Parallel	Normal
SMCC	Tensile	4.7, 4.7, 4.1	11.2, 10.4, 8.8
SMCC	Diametric tensile	—	10.5, 10.4, 10.4
MCC	Tensile	3.9, 3.6, 3.9	9.6, 7.5, 9.1
MCC	Diametric tensile	—	8.3, 8.3, 8.5

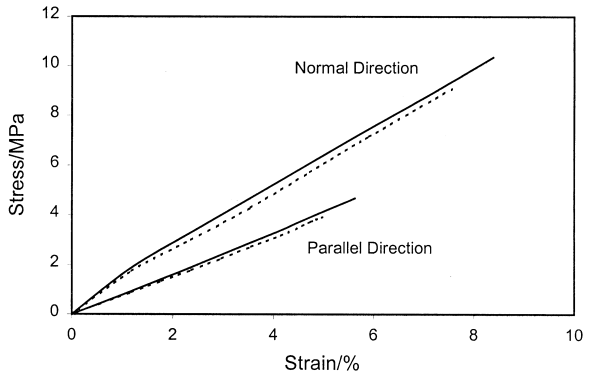

Figure 3. Stress/strain curves from the cubic tensile test for MCC (broken line) and SMCC (solid line) tested normal and parallel to the compaction direction.

cubes; the normal direction samples showed a rougher fracture surface. There was no evidence for failure in the glue or glue/sample interface using this procedure. Our previous experimental design did produce such failures, presumably due to nonalignment of the grips, which resulted in shear stresses applied onto the samples. These observations also suggest that the apparent reproducibility of the failure modes of the cubic samples is not an artifact of the machining process.

Compression Testing

To evaluate further the mechanical properties of MCCs, the compression strength was studied in the directions normal and parallel to the compaction direction. Cubes of MCC and SMCC were compression tested at 0.05 mm/min. The resulting load/deflection data were converted into stress/strain data. The stress/strain data for the compression testing of cubes of MCC and SMCC are shown in Fig. 4. It can be seen from Fig. 4 that all the materials behave similarly in that the direction parallel to the compaction load exhibits greater compression strength than the normal direction. The actual compression strengths were not calculated from these experiments.

Fracture Surfaces

The failed samples were studied visually and by SEM to assess any differences in failure modes. In the cubic tensile test, the failed surfaces obtained from cubes tested normal to the compaction direc-

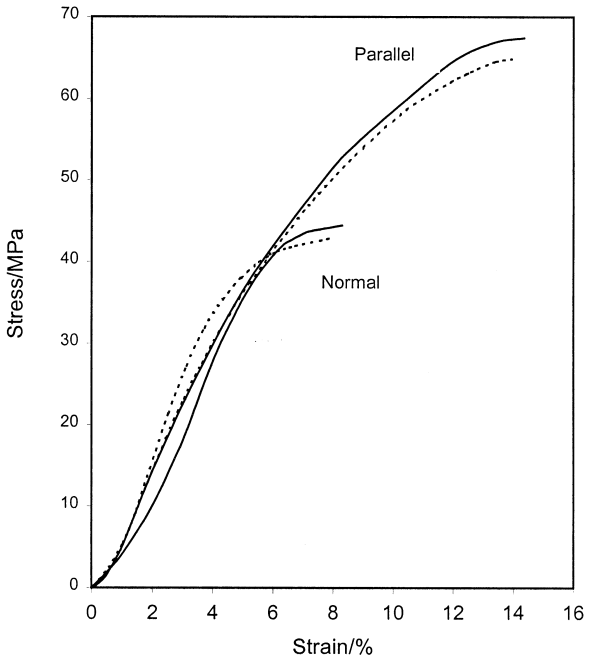

Figure 4. Stress/strain curves from the compression test of cubes of MCC (broken line) and SMCC (solid line) tested normal and parallel to the compaction direction.

tion were rougher in appearance than those tested parallel to the compaction direction. Typical low magnification scanning electron micrographs of fracture surfaces from samples tensile tested in the normal direction and parallel direction are shown in Figs. 5 and 6, respectively. Again, these suggest that the fracture modes in the two directions are different.

There were distinct cracks in the samples tested normal to the compaction direction (Fig. 5). These cracks were normal to the compaction direction. No similar cracks were identified in the samples tested parallel to the compaction direction (Fig. 6). The topographies of the parallel direction fracture surfaces were relatively smoother in appearance and appeared to consist of flattened discrete MCC particles. Analysis of the cubes from compression testing (micrographs not shown) using SEM suggested that cracks were more pronounced in the cubes tested normal to the compaction direction (weakest compression, greatest tensile strength): The cracks were normal to the compaction direction. The presence of these cracks normal to the compaction direction is similar to that observed for the failed surfaces of the cubic tensile test. Compression testing of

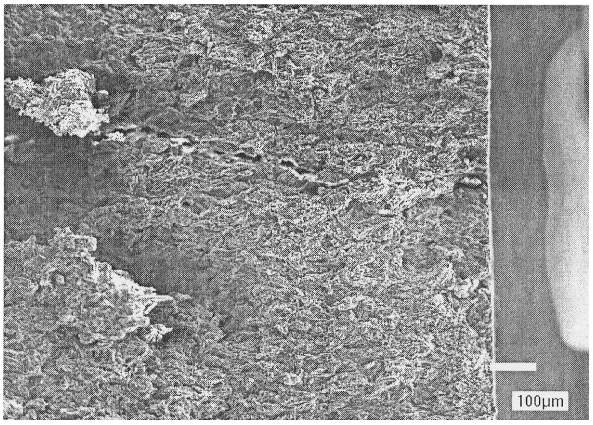

Figure 5. SEM image of fracture surface from cubic tensile test for SMCC tested normal (↔) to compaction direction (×100).

Figure 6. SEM image of fracture surface from cubic tensile test for MCC tested parallel (↕) to compaction direction (×100).

samples parallel to the compaction direction also resulted in cracks that were mainly normal to the compaction direction.

Obviously, the presence of decompression (post-compaction) cracks would reduce the parallel strength of MCC compacts. However, it is difficult to study the internal morphology of compacts. To try to resolve this issue, the fracture surfaces of the samples from the diametric compression test were studied using SEM. This suggested that microcracks, normal to the compaction direction, may be present in the compacts. This suggests that the presence of decompression microcracks may affect the parallel tensile strength. The compression test data suggest that the normal direction exhibits the lowest compression strength, which together with the tensile test observations, indicates the presence of weaker bonding in the parallel direction. Examination of the surfaces from the tensile test at higher magnifications showed that some intraparticle fracturing may have occurred in the normal direction, which suggests that mechanical keying may be an important factor for the strength of compacts in the normal direction.

The mechanical testing of cubes of MCC and SMCC has suggested that compacts of MCCs exhibit directional strength. The tensile strengths, as determined using the diametric compression test, suggest that compacts of SMCC exhibit greater tensile strength than those of MCC. In addition, tablets and compacts of SMCC are reported to exhibit enhanced tensile strength compared to compacts of MCC (19,20). However, the reasons for these observations are unclear.

Possible reasons for any apparent differences in the tensile strengths of compacted powders are particle size distribution and crystallinity effects. It has previously been reported that MCC and SMCC exhibit comparable crystallinity and particle size distributions, as well as similar porosities and macroscopic structures (24). To investigate the possibility that orientation of the crystallinity of the powders was occurring during compaction, the faces of the cubes were studied using XRD.

X-ray Diffraction

Examination of the XRD patterns of MCC and SMCC powders suggested that, as previously demonstrated, there were no significant differences in crystallinity between the two materials (24). X-ray diffraction patterns obtained in the normal and parallel directions from the cubes are shown in Figs. 7 and 8. It can be seen from Figs. 7 and 8 that the data obtained from each direction for MCC and SMCC were similar, suggesting that orientation, in terms of crystallinity, is not significantly affected by the presence of silicon dioxide (in SMCC) during compaction. This is in agreement with previous studies into the crystallinity of MCC and SMCC powders (24). In addition, there appear to be changes in ratios of the diffraction lines at 20.5° 2θ and 22.5° 2θ.

It is not clear whether the reduced strength of the parallel direction is a consequence of reduced crystallinity or changes in the crystalline orientation. The

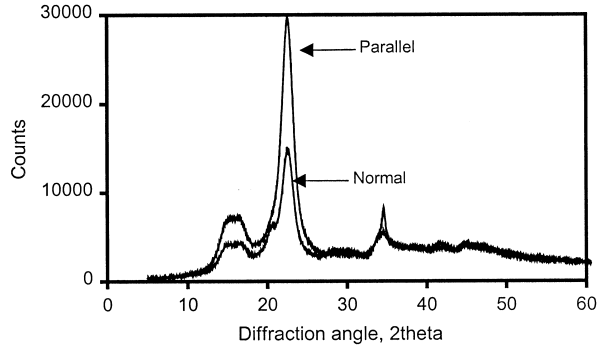

Figure 7. XRD patterns of SMCC machined cube.

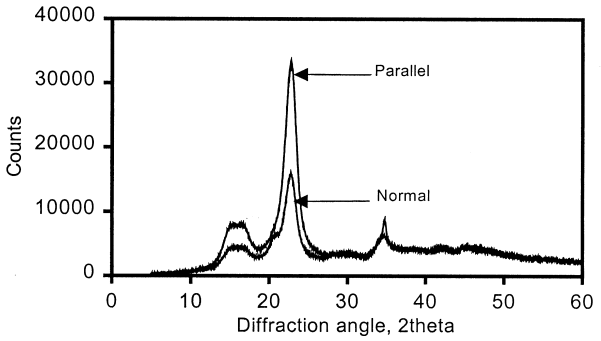

Figure 8. XRD patterns of MCC machined cube.

compacts exhibit anisotropic structure (in terms of amorphous/crystalline regions) and anisotropic crystallinity in terms of apparent polymorph (cellulose II 110 plane exhibits a diffraction angle at 19.8° 2θ) (25) or crystal plane orientation ratio. This suggests that the cellulose polymorphs (if cellulose II is present) are not randomly distributed in MCC, or there is some further reordering of the cellulose on compaction. If MCC and SMCC compacts were continuous matrices, then the apparent orientation of the cellulose crystallinity would be expected to result in anisotropic mechanical properties since the elastic properties of polymer crystals are reported to exhibit directional modulus (22, p. 273). However, compacted powders are more complex in that they are noncontinuous. Therefore, any direct relationship between degree of crystallinity and apparent strength is difficult to identify. However, it would be expected that, if the interparticle bonding is sufficiently strong, a direction that exhibits greater apparent crystallinity would be expected to show greater stiffness when a load is applied as described in Fig. 4.

CONCLUSIONS

Overall, these results suggest that compression of MCC and SMCC produces anisotropic compacts in terms of strength and crystallinity. Testing of compacted MCC and SMCC using the diametric compression test suggest that SMCC compacts exhibit greater strength than those of MCC. In terms of the "true" tensile test, the directions normal to the compaction direction appear to exhibit the greatest strength for MCC and SMCC, which is in contrast to a previous study that reported that the parallel direction was stronger (13). This may reflect the speed of compression or the MCC grade used. However, the larger particle size grade in the present study would be expected to orientate during compression so that the parallel direction exhibited the lower strength. The tensile strength data obtained from mechanical testing appear to be more reproducible for the diametric compression test than for the cubic tensile test. This probably represents the errors involved in these mechanical testing procedures; the cubic tensile test involves gluing and mounting of the specimen. In terms of compact crystallinity, it would be expected that, for this system, the crystallinity (crystal structure and degree) would be unaffected as long as dissolution and/or chemical modification of the crystalline regions did not occur during the silicification process.

The present data suggest that this is the case, and that the apparent differences in strength between MCC and SMCC are not due to any significant changes in bulk directional crystallinity. However, the large apparent difference in directional strength in both MCC and SMCC compacts may be a consequence of the anisotropic structure of the compacts, which includes crystallographic, mechanical keying, and possible decompression cracking effects.

ACKNOWLEDGMENT

We thank Penwest Pharmaceuticals Company for financial support (S. E., D. F. S.) and the provision of MCC and SMCC. We also thank a referee for useful comments.

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