ELSEVIER

International Journal of Pharmaceutics 200 (2000) 67–72

international journal of pharmaceutics

www.elsevier.com/locate/ijpharm

The mechanical properties of compacts of microcrystalline cellulose and silicified microcrystalline cellulose

Stephen Edge [a], D. Fraser Steele [a], Ansong Chen [b], Michael J. Tobyn [a], John N. Staniforth [a,*]

[a] *Pharmaceutical Technology Research Group, Department of Pharmacy and Pharmacology, University of Bath, Bath BA2 7AY, UK*

[b] *Department of Materials Science and Engineering, University of Bath, Bath BA2 7AY, UK*

Received 9 July 1999; received in revised form 19 December 1999; accepted 7 January 2000

Abstract

The mechanical properties of compacts of unlubricated microcrystalline cellulose and silicified microcrystalline cellulose were evaluated using the diametric tensile test. The results suggested that, under comparable testing conditions, compacts of silicified microcrystalline cellulose exhibited greater strength than those of microcrystalline cellulose. In addition to enhanced strength, silicified microcrystalline cellulose compacts exhibited greater stiffness and required considerably more energy for tensile failure to occur. Comparison of the data with that obtained for a dry blend of silicon dioxide/microcrystalline cellulose suggested that the functionality benefits of silicification were not due to a simple composite material model.

Keywords: Silicified microcrystalline cellulose; Mechanical property; Strength

1. Introduction

Microcrystalline cellulose (MCC) is a widely used tableting excipient. In terms of tableting technology, the material is described as a 'filler/binder' in that it is usually added to formulations to enhance compactibility. Recently, a new, modified MCC, silicified microcrystalline cellulose (SMCC), has been developed that is reported to exhibit improved binding functionality in both direct compression and wet granulation (Sherwood and Becker, 1998).

When considering any apparent improved strength benefits of an excipient, it is important to understand the mechanisms of bonding in a compacted material. The reported data for the improved functionality of SMCC was obtained using high-speed tableting. However, these data do not explain the reasons for this improved performance; in particular, whether it is solely a SMCC interparticle interaction or some synergistic effect is occurring in the presence of lubricant.

In terms of materials categorisation, MCC can be considered to be a semicrystalline polymer. It would be expected that the mechanical properties of the polymer would be dominated by the crys-

* Corresponding author. Fax: +44-1225-826-114.
E-mail address: prsjns@bath.ac.uk (J.N. Staniforth)

0378-5173/00/$ - see front matter
PII: S0378-5173(00)00343-4

talline domains. This is particularly true for semicrystalline polymers such as polyethylene. In these types of 'plastic' polymer systems, processing is achieved by thermally induced flow, i.e. heating to the melting point (T_m) of the crystallites; the glass transition (T_g) behaviour is of little importance (in terms of processing). This is in part due to the fact that even though these types of systems can be considered to be random block copolymer chains (crystalline/amorphous), the microscopic structure is essentially isotropic. This is not true for MCC. Indeed, the structure of MCC is complex but it can be considered to consist of particulate aggregates of cellulose (Chatrath, 1992). It is generally accepted that the material contains amorphous and crystalline regions as well as other ordered structures (Doelker et al., 1987). In terms of processing, MCC is treated very differently from other polymer systems in that T_m and T_g are not considered; the material is simply compressed into a desired shape. As it is unlikely that T_m will be reached, it will be the properties of the cellulose structures (as particles and polymers) that will dictate the compression and compaction behaviour of the material. The amorphous regions will be important in terms of chemistry and T_g, especially when processing, storage and testing conditions are considered. It has been reported that silicification of MCC results in no discernible modification of MCC in terms of primary structure (Buckton et al., 1999), as well as particle size and distribution, porosity and crystallinity (Tobyn et al., 1998). These latter three particle characteristics will be crucial factors in MCC compactibility. In order to try to understand the mechanisms by which the functionality of SMCC is enhanced, the materials (MCC and SMCC) were studied as simple powders and compacted in the absence of lubricants at a relatively slow compression rate.

2. Materials and methods

2.1. Materials

Microcrystalline cellulose (Emcocel 90M, MCC90 and Emcocel 50M MCCO50; Penwest Pharmaceuticals Co., NY) and silicified microcrystalline cellulose (based on Emcocel 90M, SMCC90, 2% w/w silicon dioxide content and Emcocel 50M, SMCC50, 2% w/w silicon dioxide content; Penwest Pharmaceuticals Co., NY) were used as supplied. A 'dry' mix consisting of 9.80 g Emcocel 90M and 0.20 g dried colloidal silicon dioxide (15% dispersion w/v Cab-o-Sperse; Cabot Corporation, USA) was prepared by low shear mixing (Turbula). Powders were stored under ambient conditions; the temperature and relative humidity were regularly monitored.

2.2. Preparation of compacts

Compacts were prepared by compacting powders (6 g) in a die (25 mm diameter, heat-treated silver steel) using a load of 100 kN (200 MPa), at a rate of 10 mm/min and a dwell time of 1 min using an Instron 1185 test machine. Compacts were tested on the same day as preparation, typically 3 h after compaction. This allows compaction and testing to be performed under comparable ambient conditions (temperature and relative humidity).

2.3. Testing of compacts

Diametric tensile testing was performed at 5 and 0.05 mm/min using an Instron 1125 test machine. Tensile strength was calculated using the failure load over the diametric area of the compacts (Fell and Newton, 1972). Stress was calculated by dividing the applied load by the compact cross-sectional area (diameter × height). Strain was calculated as a percentage of the deformation divided by the original diameter.

3. Results

There are many variables that need to be considered when comparing experimental data obtained for materials. This is especially true for compacted powders. When pharmaceutical powders are compacted, data such as crushing strength or tensile strength is often reported to describe the integrity of the compact. It is impor-

tant to remember that the compaction and testing conditions will affect the resulting test data of the same material under investigation, which makes comparisons with literature values difficult. In general, there are three main sets of variables that need to be considered when comparing the mechanical properties of compacted powders:

1. compact preparation and testing conditions;
2. powder and compact storage conditions;
3. powder and compact characteristics.

Compaction and testing conditions can be controlled, and it is the interpretation of the 'sample characteristics' that are likely to be the key to understanding the properties of compacted materials. This is a complex subject area and covers: particle size, distribution and shape, chemical composition, surface area, porosity, crystallinity, batch-to-batch variability, etc.

In the case of the present study, the base material in MCC and SMCC is similar in that the cellulose polymers will have comparable characteristics, i.e. molecular weight (M_w) and molecular weight distribution (polydispersity); these two characteristics will affect melt viscosity. As previously stated, it has been reported that there are no significant differences in the particle size and distribution, porosity and crystallinity of the cellulose in MCC90 and SMCC90 (Tobyn et al., 1998). This alleviates some of the problems discussed previously concerning quantifying apparent differences in properties of materials. It has been reported that silicification of MCC results in a marked difference in surface topography and that silicon dioxide appears to be primarily located in the surface of SMCC particles (Edge et al., 1999). This would be expected to have an effect on the compactibility of MCC since surface roughness is reported to influence interfacial adhesion in MCC/MCC laminates (Karehill et al., 1990). In order to evaluate the effect of this apparent surface modification, compacts of MCC and SMCC were prepared and mechanically tested using the diametric tensile test. One important aspect of pharmaceutical mechanical testing is to prepare and test samples using the same protocols. Additionally, it is essential that compacts of comparable density are prepared since porosity (as in relative density) has a marked effect on strength. Indeed, relative density can be a more useful representation of the total stress that a powder bed has experienced during the compaction cycle.

3.1. Determination of suitable compaction and testing protocols

Before the mechanical properties of compacted powders can be compared, it is important that reproducible compaction and testing protocols are used. Not only will this produce reproducible data, but the evaluation of suitable conditions may allow any apparent differences in properties to be magnified. For our powder compaction studies, many compression rates and testing conditions, including the effect of variations in ambient temperature and humidity, were studied until satisfactory protocols were identified.

3.2. Diametric tensile testing

A variety of techniques have been used to investigate the mechanical properties of compacted pharmaceutical powders (Davies and Newton, 1996). The diametric tensile test is an indirect method of determining the tensile strength of homogeneous disk-shaped materials. The test is widely employed for testing the strength of pharmaceutical (Karehill and Nyström, 1990; Elamin et al., 1994) and ceramic (Thoms et al., 1980) compacts. In this test, tensile failure is a result of the application of a compression load normal to the compaction direction. This is in contrast to a 'true' tensile test, where materials are tested in tension and no compression load is applied to the sample in the direction normal to the tensile stress.

3.3. Tensile strength

The tensile strength of compacts of SMCC and MCC were determined using the diametric tensile test at 5 mm/min. Eight replicate samples of each excipient were tested. The results are shown in Table 1. It can be seen from Table 1 that, as expected, MCC50 produces stronger compacts than MCC90 (Bolhuis and Chowhan, 1996). Silicification appears to produce compacts of similar

strength, at comparable silicon dioxide contents, for the two typical grades tested. In addition, the apparent strength benefit of silicification appears to be greater for the larger particle-sized MCC90, under these specific conditions, possibly reflecting increased surface coverage of silicon dioxide of the larger particle sized 90 μm grade.

3.4. Toughness

Tensile strength (or crushing strength) is often used to describe the strength of a compact. However, this measurement does not fully reflect inter- and intraparticle cohesion within a compact. The cohesion (integrity or binding capability) in a compact may be further represented by the energy of failure. The energies of failure during diametric tensile testing at 5 mm/min (Table 1) were calculated by integration of the area under the load/deflection curve of the tensile test. The results for MCC90, SMCC90 and a dry blend of MCC90 and silicon dioxide (2% w/w), together with the maximum deflection data, are given in Table 2. It can be seen from Table 2 that silicification produces compacts of greater ductility (deflection under load) than MCC. However, the effect on the energy of failure is even more pronounced, with an increase of over 50% in value (under these conditions). In addition, the tensile strength, energy of failure and ductility of compacts of a dry blend of MCC90 and silicon dioxide (2% w/w) were less than those for pure MCC90.

Table 1
Tensile test data for compacts of MCC, SMCC and a blend of MCC90 and dried colliodal silicon dioxide[a]

Sample	Tensile strength (MPa)	Density (g/cm^3)
MCC50	11.5 ± 0.3	1.45 ± 0.03
SMCC50	13.0 ± 0.3	1.42 ± 0.02
MCC90	10.5 ± 0.2	1.45 ± 0.02
SMCC90	12.7 ± 0.2	1.45 ± 0.02
Blend[b]	9.1 ± 0.2	1.44 ± 0.02

[a] Powder (6 g) compressed using a load of 100 kN at 10 mm/min, with a dwell time of 1 min. Tested at a rate of 5 mm/min. Values after $\pm$ represent the range of measurements ($n = 8$).
[b] MCC90 and dried colloidal silicon dioxide (2% w/w).

Table 2
Mechanical properties of compacts of MCC90, SMCC90 and a blend of MCC90 and dried colliodal silicon dioxide[a]

Sample	Deflection (mm)	Tensile strength (MPa)	E_f (J)
MCC90	0.86 ± 0.01	10.5 ± 0.2	1.6 ± 0.1
SMCC90	1.11 ± 0.02	12.7 ± 0.2	2.6 ± 0.1
Blend[b]	0.70 ± 0.03	9.1 ± 0.2	1.2 ± 0.1

[a] Powder (6 g) compressed using a load of 100 kN at 10 mm/min, with a dwell time of 1 min. Tested at a rate of 5 mm/min. Values after $\pm$ represent the range of measurements ($n = 8$).
[b] MCC90 and dried colloidal silicon dioxide (2% w/w).

3.5. The effect of test rate

The values describing the mechanical properties of materials are usually strain rate dependent, i.e. they vary according to the rate at which the stress is applied to the sample (test rate). This phenomenon has previously been reported for MCC-based tablets (Rees et al., 1970). Our preliminary investigations to determine compaction and testing protocols confirmed this for MCC. In order to understand more fully the effect of test rate on apparent mechanical properties, compacts of MCC and SMCC were tested at the slower rate of 0.05 mm/min. The tensile test data was integrated to calculate the energies of failure, and the results are shown in Table 3. It can be seen from Table 3 that, again, silicified MCCs produce compacts which exhibit greater tensile strength, greater ductility and greater energies of failure than their respective unmodified MCCs, in agreement with the data in Table 2. The values of tensile strength are apparently lower than values obtained at the rate of 5 mm/min, which suggests that, as expected, the apparent mechanical properties of MCCs are strain rate dependent. It is also clear that the strain rate dependence of the mechanical behaviour of MCC has not been changed by the silicification process.

3.6. Effective stiffness

The slopes of the load/deflection and stress/strain curves can give an indication of the resis-

Table 3
Mechanical properties of compacts of MCC and SMCC[a]

Sample	Test rate (mm/min)	Deflection (mm)	Tensile strength (MPa)	E_f (J)	Density (g/cm^3)
MCC90	5	0.88 ± 0.02	10.3 ± 0.2	1.7 ± 0.1	1.45 ± 0.01
MCC90	0.05	0.73 ± 0.02	8.9 ± 0.3	1.2 ± 0.2	1.44 ± 0.01
SMCC90	5	1.13 ± 0.03	12.7 ± 0.3	2.6 ± 0.1	1.44 ± 0.01
SMCC90	0.05	0.96 ± 0.04	11.1 ± 0.4	2.0 ± 0.2	1.45 ± 0.01

[a] Powder (6 g) compressed using a load of 100 kN at 10 mm/min, with a dwell time of 1 min. Tested at a rate of 5 and 0.05 mm/min. Values after $\pm$ represent the range of measurements ($n = 4$).

tance of a material to deformation, i.e. the effective stiffness or stiffness. The data (load/deflection), for compacts of SMCC90 and MCC90 that were subjected to diametric tensile testing (at 0.05 and 5 mm/min), were converted to stress/strain curves. A typical set of stress/strain curves is shown in Fig. 1. The data in Fig. 1 suggest that silicification produces a material which, when compacted, exhibits a slightly greater stiffness normal to the compaction direction when tested at the slow test rate of 0.05 mm/min. Testing at 5 mm/min resulted in similar load/deflection and stress/strain curves for both sets of materials. All the samples tested exhibited this mechanical behaviour. In addition, the similarity in stiffness of the different materials suggests the presence of similar bonding mechanisms (under these conditions).

3.7. Reinforcement mechanisms

Simple compaction and testing of powders of SMCC and MCC has suggested that SMCC exhibits enhanced tensile strength compared with MCC. If SMCC was a simple composite of MCC and silicon dioxide then, under comparable testing conditions, its maximum strength (in tension and compression) can be very roughly approximated to:

$$\sigma_{\text{composite}} = \sigma_{\text{MCC}} v_{\text{MCC}} + \sigma_{\text{SD}} v_{\text{SD}}$$

where σ is the strength and v the volume fraction.

The tensile test data for SMCC, MCC and a blend of MCC and silicon dioxide suggest that the strength of compacts of SMCC is greater than would be expected for a simple composite, given that compacted silicon dioxide is a very brittle material. However, the preparation and testing of a homogeneous blend that contains silicon dioxide particles of similar size to those in SMCC would address this hypothesis. This probably reflects the method of silicification in that the size and distribution of silicon dioxide aggregates and the MCC/silicon dioxide interfacial adhesion determines the compactibility of SMCC. The strength enhancement in SMCC compacts may be as a consequence of mechanical reinforcement.

4. Conclusions

The compaction of MCC and SMCC at a relatively slow compression rate results in compacts of comparable relative density, suggesting that the two materials exhibit comparable compression behaviour. The tensile strength (diametric tensile test) of compacts of SMCC was found to be greater than that of the respective MCC, the

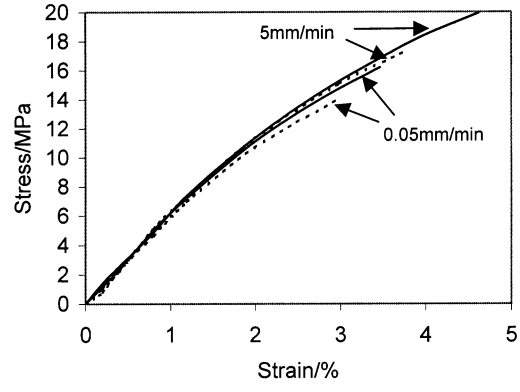

Fig. 1. Stresss/strain data of compacts of MCC90 (– – –) and SMCC90 (——) from the tensile test experiments of Table 3. Tested at 5 and 0.05 mm/min.

apparent enhancement being greater for the larger 90 μm particle-sized grade. The effect on compact toughness was even more pronounced, the energies of failure being significantly greater for compacts of SMCC. Again, the effect was greater for the larger particle-sized 90 μm grade. These apparent differences in mechanical strength cannot be satisfactorily explained in terms of modifications of the particle size, porosity or crystallinity of SMCC. Our examination of the failure surfaces using scanning electron microscopy suggested that when compacts of MCC fail during testing, the failure primarily occurs at the interparticle interfaces. The mechanical data together with the comparable densification characteristics of MCC and SMCC suggest that this apparent strength enhancement may be a consequence of an interfacial interaction rather than modification of bulk MCC properties. These data are in agreement for data reported for lubricated SMCC and MCC tablets in that silicification of MCC appears to produce materials with greater binding capability. In the test rate regimes used, it has also been shown that the higher the rate, the higher the apparent strength.

Acknowledgements

We thank Penwest Pharmaceuticals Co. for financial support (S.E.) and the provision of MCC and SMCC.

References

Bolhuis, G.K., Chowhan, Z.K., 1996. Materials for direct compression. In: Alderborn, G., Nyström, C. (Eds.), Pharmaceutical Powder Compaction Technology. Marcel Dekker, New York, pp. 419–500.

Buckton, G., Yonemochi, E., Yoon, W.L., Moffat, A.C., 1999. Water sorption and near IR spectroscopy to study the differences between microcrystalline cellulose and silicified microcrystalline cellulose before and after wet granulation. Int. J. Pharm. 181, 41–47.

Chatrath, M., 1992. The effect of wet granulation on the physico-mechanical characteristics of microcrystalline cellulose. PhD Thesis. University of Bath.

Davies, P.N., Newton, J.M., 1996. Mechanical strength. In: Alderborn, G., Nyström, C. (Eds.), Pharmaceutical Powder Compaction Technology. Marcel Dekker, New York, pp. 165–191.

Doelker, E., Gurny, R., Schurz, J., Jánosi, A., Matin, N., 1987. Degrees of crystallinity and polymerisation of modified cellulose powders for direct tableting. Powder Technol. 52, 207–213.

Edge, S., Potter, U.J., Chen, A., Steele, D.F., Tobyn, M.J., Staniforth, J.N., 1999. The location of silicon dioxide in silicified microcrystalline cellulose. Pharm. Pharmacol. Commun. 5, 371–376.

Elamin, A.A., Alderborn, G., Ahlneck, C., 1994. The effect of pre-compaction processing and storage conditions on powder and compaction properties of some crystalline materials. Int. J. Pharm. 108, 213–224.

Fell, J.T., Newton, J.M., 1972. Determination of tablet strength by diametrical compression test. J. Pharm. Sci. 59, 688–691.

Karehill, P.G., Nyström, C., 1990. Studies on direct compression of tablets. XXII. Investigation of strength increase upon aging and bonding mechanisms for some plastically deforming materials. Int. J. Pharm. 64, 27–34.

Karehill, P.G., Glazer, M., Nyström, C., 1990. Studies on direct compression of tablets. XXIII. The importance of surface roughness for the compactibility of some directly compressible materials with different bonding and volume reduction properties. Int. J. Pharm. 64, 35–43.

Rees, J.E., Hersey, J.A., Cole, E.T., 1970. The effect of rate on the strength of tablets. J. Pharm. Pharmacol. 22 (Suppl.), 64S–69S.

Sherwood, B.E., Becker, J.W., 1998. A new class of high functionality excipients: silicified microcrystalline cellulose. Pharm. Technol. 22, 78–88.

Thoms, M.B., Doremus, R.H., Jarcho, M., Salsbury, R.L., 1980. Dense hydroxyapatite: fatigue and fracture strength after various treatments, from diametral tests. J. Mater. Sci. 15, 891–894.

Tobyn, M.J., McCarthy, G.P., Staniforth, J.N., Edge, S., 1998. Physicochemical comparison between microcrystalline cellulose and silicified microcrystalline cellulose. Int. J. Pharm. 169, 183–194.