International Journal of Pharmaceutics, 41 (1988) 231–236
Elsevier

IJP 01397

Effect of addition of water on the rheological and mechanical properties of microcrystalline celluloses

John N. Staniforth [1], Anand R. Baichwal [1], Jo P. Hart [1] and Paul W.S. Heng [2]

[1] *Particle Engineering Research Group, School of Pharmacy and Pharmacology, University of Bath, Bath (U.K.)* and [2] *National University of Singapore, Singapore (Singapore)*

(Received 8 June 1987)
(Accepted 24 July 1987)

Key words: Microcrystalline cellulose; Wet granulation

Summary

A study was conducted to examine the effect of addition of water on the compactibility of two commercially available microcrystalline celluloses, Avicel PH-101 and Emcocel. The cohesiveness of the two samples when measured by a shear test was found to be different. Addition of water caused an increase in cohesiveness to about 20–30 wt.% for both samples although the change in shear force with water content was different. There was no difference on further increase in amount of water added. These changes in cohesiveness were reflected in the properties of granules formed and the strength of tablets compressed from such granules. For example, while both the microcrystalline cellulose powder samples had identical compressibilities, equivalent amounts of water used for granulation (37 wt.%) formed larger granules with Avicel than Emcocel but the latter formed stronger tablets and the compressibility of these granules was far less than that of the original powder samples. "Normalized work of failure" and "apparent failure viscosity" determinations were carried out to quantify tablet mechanical properties and results suggested that less plastic deformation occurred during compaction of granules in comparison with compaction of powder particles. This indicated that a large proportion of compaction energy was probably utilized in breaking up primary granule structures. Thus they contributed less to increasing contact areas through particle deformation and therefore produced tablets of lower strengths than for powder particles compressed at comparable forces, where relatively more energy was used in causing deformation at particle interfaces.

Introduction

Microcrystalline cellulose (MCC) is by far the most compressible and versatile of tableting excipients and has therefore been used widely in the production of solid dosage forms both by direct compression and following wet granulation. Recently, much interest has been expressed in the moisture uptake and the liquid–solid interactions of starches and celluloses by Zografi et al. (1984) where they have suggested that water sorbed to such materials most likely exists in at least 3 states; tightly bound to anhydroglucose units, less tightly bound, and bulk water. These researchers have also discussed some implications of such behaviour for pharmaceutical systems (Zografi and Kontny, 1986). Since MCC is frequently used in wet granulation which involves a liquid–solid interaction, the aim of the present study was to investigate the effect of addition of water on the properties of two commercially available microcrystalline celluloses which have been found to

Correspondence: J.N. Staniforth, Particle Engineering Research Group, School of Pharmacy and Pharmacology, University of Bath, Bath BA2 7AY, U.K.

have identical physical properties (Pesonen and Paronen, 1986). Avicel PH-101, Lot no. 6547, FMC Corp. Philadelphia, U.S.A. and Emcocel Lot no. 5113 and 5114, manufactured by Finnish Sugar Co. Ltd., Helsinki, Finland for Edward Mendell Co., New York, U.S.A. and Redhill, Surrey, U.K.

Materials and Methods

The experimental study was divided into two parts: (i) a study of the influence of wet granulation on tableting of MCC. (ii) a study of the relationship between cohesiveness of MCC and added water concentration evaluated using a shear test method.

Influence of well granulation

Granulations were prepared using the following formulation: microcrystalline cellulose 2000 g; pre-gelatinized starch (Amigel) 150 g, and water 800 or 1000 ml according to the experiment. Granulation was carried out following pre-mixing of all constituent powders in a high-speed mixer/granulator (type PMAV 25/2G, T.K. Fielder, Chandlers Ford, U.K.). The end-point of the granulation process was monitored utilizing a probe vibration analysis technique described elsewhere (Staniforth et al., 1986). The time required for the end-point in all cases was 2–4 min. Granules thus formed were dried in a fluidized bed drier for approximately 30 min and subsequently characterized by particle size, bulk density, Hausner ratio and angle of response measurements. Granules were sieved through an 800-μm screen, blended in a cube blender for 2 min with magnesium stearate as lubricant and tableted on an instrumented tablet press (Manesty F3) fitted with flat-faced 10.0-mm punches to a compression weight of around 0.360 g. Tablet tensile strength, work of failure and failure viscosity were determined utilizing a tensile tester (JJ T22K, JJ Instruments) as described previously by Patel (1986) and Patel and Staniforth (1987).

Relation between cohesiveness of MCC and added water concentration

Cohesiveness of cellulose samples mixed with different amounts of water in a cube blender for 5 min was determined by a shear test based on the sandwich viscometer method. The sandwich viscometer consisted of a Perspex box of dimensions 292 × 152 × 38 mm. This shear cell was filled reproducibly with 610 g of the test powder and packed in an identical fashion each time. A centre Perspex plate with carborundum paper on either side formed the "moving member" and was sheared at a constant rate through the packed powder in the viscometer using a JJ tensile tester (Fig. 1). Peak shear force was measured and plotted against the amount of water added.

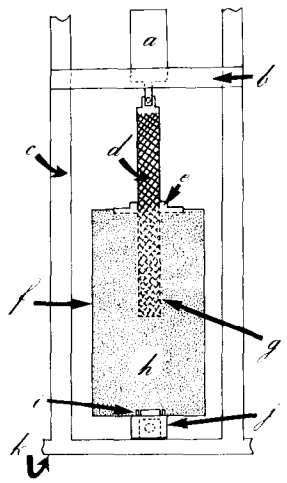

Fig. 1. Sandwich rheometer (scale ca. 1:4); a, load cell; b, upper moving crosshead; c, drive screw; d, carborundum paper; e, upper locating guide; f, shear cell; g, moving member; h, powder packed to uniform porosity; i, lower locating guide; j, connection of sandwich rheometer shear cell to lower stationary crosshead; k, tensile tester.

Results and Discussion

Results obtained using the sandwich viscometer demonstrated initial differences in the cohesiveness of the two MCC samples which were evident up to 20–30% w/w of added water (Fig. 2). At 20–30% w/w and higher concentrations of added water there were no differences in the cohesiveness of either material. Avicel (MCC-I) was more cohesive than Emcocel (MCC-II) initially but the latter demonstrated a more rapid change in cohesiveness with addition of water up to 20–30%

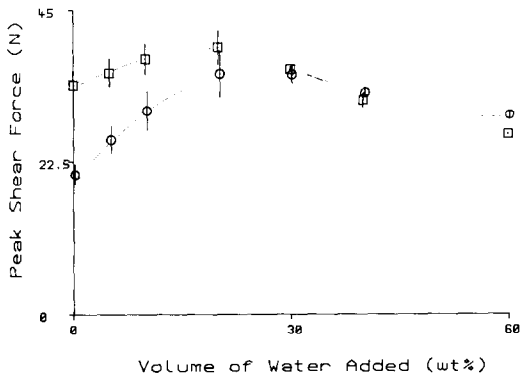

Fig. 2. Relationship between peak shear force and volume of water added for MCC samples; (□———□), MCC-I; (○———○), MCC-II, evaluated using the shear test method. Vertical lines indicate ± S.E.M.

w/w. These results agree with those presented by some other researchers (Khan and Pilpel, 1986) who measured the tensile strengths of samples of microcrystalline cellulose (Avicel PH101) containing up to 15 wt.% of added moisture and concluded that moisture caused increases in the range of interparticle forces. Khan and Pilpel (1986) found that the first 3 wt.% of moisture was strongly bound to particles whereas at higher levels, moisture appeared to form pendular bonds on the MCC surface. The initial increase in cohesiveness with added water up to 20–30% w/w could be due to such pendular bonds on the surfaces of the cellulose samples whereas at higher levels (greater than 20–30% w/w), the volume of free water was sufficient to completely separate particles by a continuous liquid film which increased fluidity and reduced cohesiveness. The rheological differences between the two MCC samples described above (Fig. 2) were reflected in the properties of wet granules formed in a high speed mixer/granulator and the physicomechanical properties of tablets formed from such granules.

Table 1 shows that granules formed using identical volumes of water as granulating fluid (800 ml, corresponding to about 37% w/w) were larger in size for MCC-I than those formed with MCC-II which could be due to the fact that MCC-I had shown greater cohesiveness than MCC-II (Fig. 2) and addition amounts of moisture produced stronger pendular bonds resulting in larger MCC-I granules. Other micromeritic data shown in Table 1 for MCC-I and MCC-II granules with 37% w/w water as granulating fluid were in agreement with the relative size differences between the two sets of granules.

Results shown in Table 1 confirmed that minimum variations existed in the properties of granules formed from two different batches of MCC-II on addition of 37% of water as granulating fluid. When the amount of granulating fluid was increased to 1000 ml (corresponding to 46.5% w/w) of water, granules similar to those formed with MCC-I granulated with 37% w/w water were obtained and corresponding data for these are also presented in Table 1.

Granulation is often recommended (Carstensen, 1980) as a method for increasing the flowability and compactibility of powder mixtures. Results obtained in this study for the two microcrystalline celluloses suggested that improved flowability and

TABLE 1

Micrometric properties of granules formed with different amounts of water in two types of MCC

Formulation	Poured bulk density (P) (kg dmE-3)	Tapped bulk density (T) (no. of taps)			Hausner ratio (T/P)	Angle of repose (deg.)	Carr's index $(T-P)/T \times 100$	Geom. Mean Diam. (μm)	Geometric S.D. (σ_g)
		100	500	1000					
MCC I (lot 6547; 800 ml water)	0.58	0.64	0.67	0.68	1.172	29.25	14.71	501	1.778
MCC II (Lot 5113; 1000 ml water)	0.64	0.67	0.69	0.70	1.094	33.69	8.57	355	1.779
MCC II (Lot 5114; 800 ml water)	0.45	0.51	0.54	0.55	1.222	39.58	18.18	150	1.664
MCC II (Lot 5113; 800 ml water)	0.53	0.61	0.65	0.66	1.245	35.15	19.70	119	2.068

MCC I = Avicel PH101; MCC II = Emcocel.

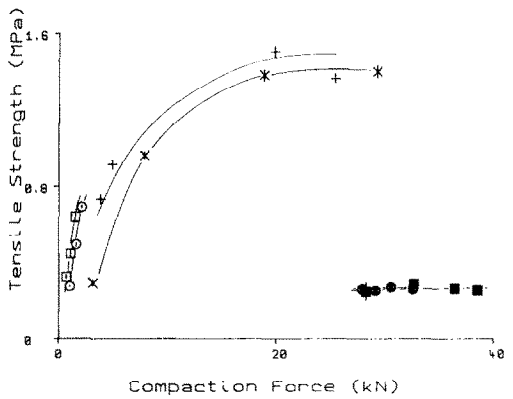

Fig. 3. Relationship between tensile strength of tablets and compaction force for microcrystalline cellulose powder samples; (□———□), MCC-I; (○———○), MCC-II and granules made with 37 wt.% added water; (+———+), MCC-II (Lot no. 5114); (×———×), MCC-II (Lot no. 5113); (■———■), MCC-I and granules made with 46.5 wt.%; (●———●) MCC-II. Vertical lines indicate ± S.E.M.

increased compactibility were mutually exclusive. There was a dramatic decrease in the compactibility of both MCC samples when granulated, as shown by their tensile strength/compression force profiles (Fig. 3).

On compression, MCC-I tablets with 37% w/w added water and MCC-II with 46.5% added water formed the weakest tablets despite the fact that these formulations formed the largest granules (Fig. 2). MCC-II granulations with 37% w/w added water formed compacts with intermediate strengths while ungranulated microcrystalline cellulose powders (both MCC-I and MCC-II) formed the strongest tablets. There were no differences in the tensile strengths of non-granulated MCC-II or MCC-I tablets confirming earlier work by Pesonen and Paronen (1986). Further, the two batches of MCC-II granulated with 37% w/w added water showed no differences in the tensile strengths of compressed tablets, again confirming minimum batch variations in this product (Fig. 3).

The results clearly demonstrated that the strength of interparticle bonding was greatest for the powder samples of microcrystalline cellulose probably due to the higher degree of plastic deformation taking place during tablet compaction and consequently, allowing particles to establish areas of intimate contact over which strong attractive electrostatic forces develop thus resulting in strong interparticle bonding. With the granules, most of the compression force was utilized in breaking up the primary granule structure and hence did not establish areas of intimate contact to provide strong bonds between the cellulose particles.

This hypothesis appeared to be supported by observation of scanning electron photomicrographs (Figs. 4–6). As shown in Fig. 4 MCC-II powder is fibrous in nature and on compression could establish areas of intimate contact and form strong bonds. On granulation with 800 ml of water (corresponding to 37% w/w), most of the cellulose particles were converted to granules (Fig. 5) and the granules did not appear to be strong which could be the reason for the intermediate strength of tablets made from these granules (Fig. 3). Increasing the amount of water used as granulating fluid to 1000 ml (corresponding to 46.5% w/w) formed extremely dense granules and there was no evidence of any ungranulated cellulose particles (Fig. 6). Therefore these granules formed the weakest tablets (Fig. 3) since all the compaction energy was probably utilized in breaking up the granule structure rather than providing areas of intimate contact to form strong bonds.

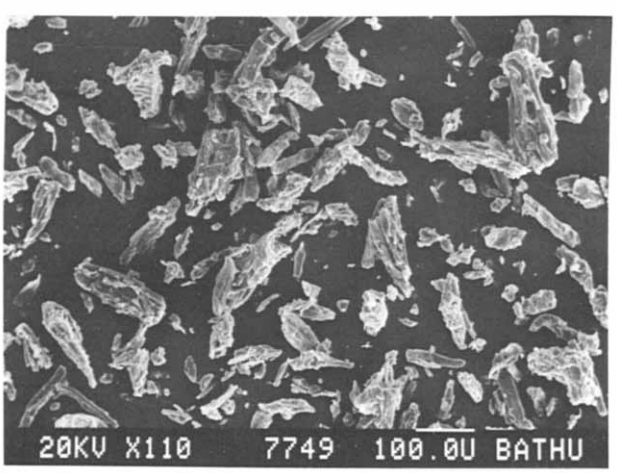

Fig. 4. Scanning electron micrograph of MCC-II (Emcocel) powder. ×70.

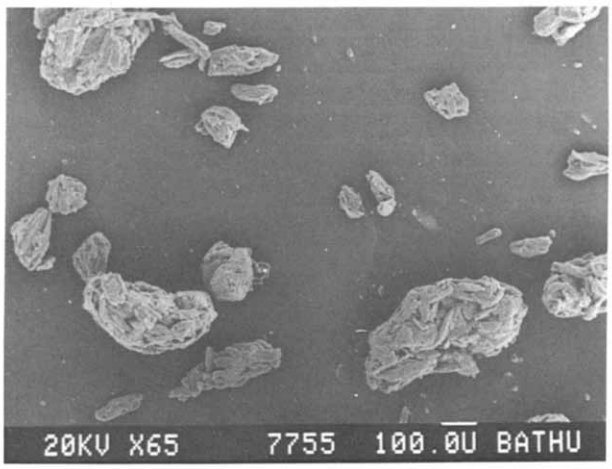

Fig. 5. Scanning electron micrograph of MCC-II granulated with 37wt.% (800 ml) water as granulating fluid. ×40.

By continuously monitoring the force applied to break the tablet and the distance moved by the platen, another parameter called the "normalized work of failure" (NWF) which can be related to the toughness of tablets was calculated according to Rees and Rue (1978). Data trends for NWF values (Fig. 7) were in agreement with tablet tensile strength values (Fig. 3) and revealed that the non-granulated cellulose samples formed the toughest tablets which progressively decreased in toughness as shown by a decrease in NWF values

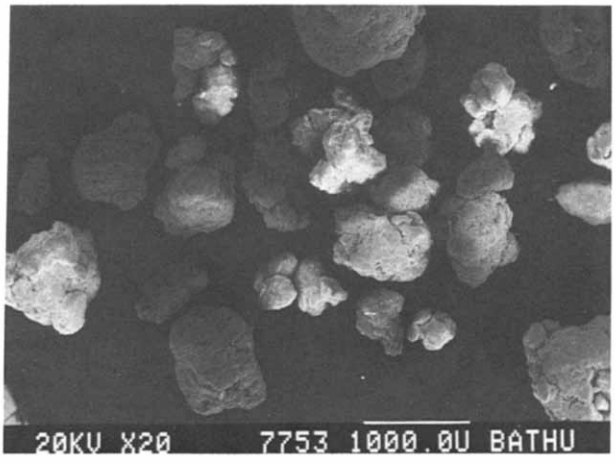

Fig. 6. Scanning electron micrograph of MCC-II granulated with 46.5 wt.% (1000 ml) water as granulating fluid. ×13.

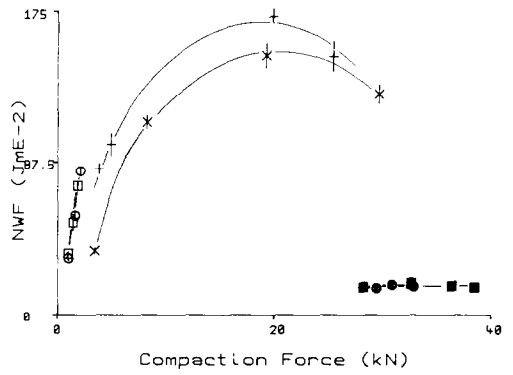

Fig. 7. Relationship between NWF and compaction force for MCC powder samples. (□———□), MCC-I; (○———○), MCC-II and granules made with 37 wt.% added water; (+———+), MCC-II (Lot no. 5114); (×———×), MCC-II (Lot no. 5113); (■———■), MCC-I and granules made with 46.5 wt.%; (●———●), MCC-II. Vertical lines indicate ± S.E.M.

with increasing amounts of water utilized as granulating fluid. It has been demonstrated elsewhere (Patel, 1986) that NWF determinations allow quantitative differences in plasticity of some excipients to be distinguished. The results from this study (Fig. 7) agree well with such earlier observations where the non-granulated cellulose showed a higher degree of plasticity and resulted in stronger tablets being formed.

Another parameter described by Patel and Staniforth (1987) and termed "apparent failure viscosity" (AFV) was plotted against top punch force (Fig. 8). Apparent failure viscosity was obtained by treating the tablets as non-Newtonian plastic solids and was calculated by dividing the tensile strengths of tablets by the tablet strain rate. Essentially, AFV uses the time component of tablet loading as a multiplier and was therefore found to have a similar sensitivity to changes in excipient plasticity as NWF measurements although it is shear rate-based rather than shear strain-based. As illustrated in Fig. 8, AFV gave a similar ranking of the MCC samples as the NWF profiles (Fig. 7). Since AFV is a measure of the resistance to deformation offered by the tablet when subjected to diametral loading, its value will be large when the resistance to flow is high and this situation arises as a result of formation of a large number of high

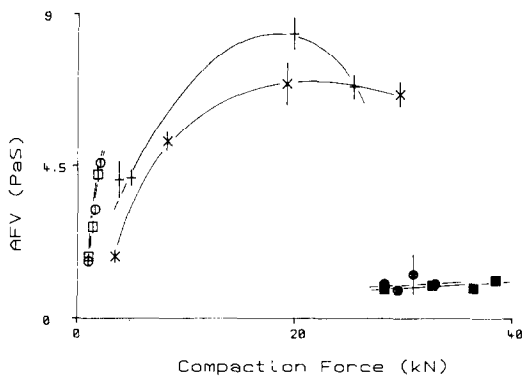

Fig. 8. Relationship between apparent failure viscosity and compaction force for MCC powder samples. (□———□), MCC-I; (○———○), MCC-II and granules made with 37 wt.% added water; (+———+), MCC-II (Lot no. 5114); (×———×), MCC-II (Lot no. 5113); (■———■), MCC-I and granules made with 46.5 wt.%; (●———●), MCC-II. Vertical lines indicate + S.E.M.

strength interparticle bonds. These conditions predominate when plastic deformation of the Non-granulated cellulose particles occurred on compaction.

In conclusion, the results suggest that MCC powder possesses a similar high plasticity for both Avicel and Emcocel samples whereas granulating with water may cause differing degrees of loss of compactibility. This appears to be due to differences in moisture uptake of the two samples.

Acknowledgements

The authors wish to thank Dr. D. Jordan and Mr. P. Flanders of Hoechst (U.K.) Ltd., Milton Keynes, U.K. for help in preparing granules using the high speed mixer/granulator.

References

Carstensen, J.T. (Ed.), *Solid Pharmaceutics: Mechanical Properties and Rate Phenomena*, Academic, New York, 1980, p. 135.

Khan, F. and Pilpel, N., The effect of particle size and moisture on the tensile strength of microcrystalline cellulose powder. *Powder Technol.*, 48 (1986) 145–150.

Patel, C.I., *Design and Characterization of Direct Compression Excipients*, Ph.D. Thesis, University of Bath, Bath, 1986.

Patel, C.I. and Staniforth, J.N., Determination of apparent failure viscosity of tablets. *J. Pharm. Pharmacol.*, in press.

Pesonen, T. and Paronen, P., Evaluation of a new cellulose material as binding agent for direct compression of tablets. *5th Pharmaceutical Technology Conference*, Harrogate, 1986.

Rees, J.E. and Rue, P.J., Work required to cause failure of tablets in diametral compression. *Drug. Dev. Ind. Pharm.*, 4 (1978) 131–156.

Staniforth, J.N., Walker, S. and Flanders, P., Granulation monitoring in a high speed mixer/processor using a probe vibration analysis technique. *Int. J. Pharm.*, 31 (1986) 277–280.

Zografi, G., Kontny, M.J., Yang, A.Y.S. and Brenner, G.S., Surface area and water vapor sorption of microcrystalline cellulose. *Int. J. Pharm.*, 18 (1984) 99–116.

Zografi, G. and Kontny, M.J., The interactions of water with cellulose- and starch-derived pharmaceutical excipients. *Pharm. Res.*, 3 (1986) 187–194.