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Rheological characterization of microcrystalline cellulose and silicified microcrystalline cellulose wet masses using a mixer torque rheometer

Pirjo Luukkonen [a,*], Torben Schæfer [b], Leena Hellén [c], Anne Mari Juppo [d], Jouko Yliruusi [a]

[a] *Pharmaceutical Technology Division, Department of Pharmacy, University of Helsinki, P.O. Box 56, Helsinki, FIN-00014, Finland*
[b] *The Royal Danish School of Pharmacy, Denmark*
[c] *Orion Pharma R&D, Finland*
[d] *AstraZeneca R&D Mölndal, Pharmaceutical Technology Solids, Sweden*

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Abstract

The rheological properties of silicified microcrystalline cellulose (Prosolv 50) were compared with those of standard grades of microcrystalline cellulose (Emcocel 50 and Avicel PH 101). Cellulose samples were analyzed using nitrogen adsorption together with particle size, flowability, density and swelling volume studies. The rheological behaviour of the wet powder masses was studied as a function of mixing time using a mixer torque rheometer (MTR). Silicified microcrystalline cellulose exhibited improved flow characteristics and increased specific surface area compared to standard microcrystalline cellulose grades. Although the silicification process affected the swelling properties and, furthermore, the mixing kinetics of microcrystalline cellulose, the source of the microcrystalline cellulose had a stronger influence than silicification on the liquid requirement at peak torque. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Mixer torque rheometer; Microcrystalline cellulose; Silicified microcrystalline cellulose; Mixing kinetics

1. Introduction

Silicified microcrystalline cellulose (SMCC) is a combination of co-processed microcrystalline cellulose (MCC) and colloidal silicon dioxide. Edge et al. (1998) found that silicon dioxide is primarily located on the surface of SMCC, and in some cases, silicon dioxide was also detected in the internal regions of some particles. Silicified microcrystalline cellulose provides better compactability and material flow properties than regular microcrystalline cellulose (Sherwood et al., 1996). SMCC has also been claimed to be more resistant

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* Corresponding author. Fax: +358-9-70859144.
E-mail address: pirjo.luukkonen@helsinki.fi (P. Luukkonen)

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to wet granulation than conventional MCC grades, since SMCC maintains compaction properties after wetting and drying. Staniforth and Chatrath (1996) suggested that the reduced bonding capacity of MCC was the result of the reversible formation of intra- and interfiber hydrogen bonds. Buckton et al. (1998) found in a NIR spectroscopy study that MCC, SMCC and wet granulated SMCC had essentially identical spectra, so there was no fundamental difference in the physical form of the cellulose in MCC and SMCC. Wet granulated MCC, on the other hand, showed differences indicating a minor change in internal hydrogen bonding. Tobyn et al. (1998) compared the physicochemical properties of MCC and SMCC using several different methods. They concluded that the silicification process produces a material which is chemically and physically very similar to standard MCC.

Several authors have studied the differences between regular microcrystalline cellulose grades, Avicel PH 101 and Emcocel (Staniforth et al., 1988; Raines, 1990; Newton et al., 1992; Landín et al., 1993a,b; Kleinebudde, 1997). A major cause of intermanufacturer variability among microcrystalline celluloses are the variability of the source of pulp and of the manufacturing process (Landín et al., 1993a,b). Penwest Pharmaceuticals changed the manufacturer and the source of pulp of the microcrystalline cellulose in 1990 (personal communication), so most of these previous studies were conducted with an Emcocel grade which is not equivalent to the currently used Emcocel 50.

It has been shown that the rheological properties of wet masses can be successfully monitored by a mixer torque rheometer (Parker et al., 1990; Rowe and Parker, 1994; Chatlapalli and Rohera, 1998). Several authors have compared the rheological properties of different MCC grades (Rowe and Sadeghnejad, 1987; Parker and Rowe, 1991; Hancock et al., 1992), but the rheological properties of silicified microcrystalline cellulose have not been studied previously. The amount of water added at the maximum torque should be comparable with that found for the optimum production of pellets during spheronisation (Miyake et al., 1973; Rowe and Sadeghnejad, 1987). In extrusion–spheronisation experiments with water-soluble excipients the window of critical liquid requirement was slightly higher for the SMCC grade than for the MCC grade (Luukkonen et al., 1998).

The aim of this study was to investigate the rheological properties of silicified microcrystalline cellulose wet masses in comparison to the standard grades of MCC using a mixer torque rheometer and to correlate these with the physical properties of the materials.

2. Materials and methods

2.1. Materials

Microcrystalline cellulose (MCC) was obtained from two sources, Avicel PH 101 (6616C) from FMC (Co. Cork, Ireland) and Emcocel 50 (5S7547) and silicified microcrystalline cellulose (SMCC) Prosolv 50 (K5S6005) from Penwest Pharmaceuticals (Nastola, Finland). Silicified microcrystalline cellulose has a 2% w/w silicon dioxide concentration.

2.2. Particle size

The particle size distribution was studied using a Malvern 2600c (Malvern Instruments, England) equipped with dry powder feeder. The mean and median particle size data are the mean of three determinations.

2.3. Specific surface area

The specific surface area of each sample was determined in a Coulter SA 3100 apparatus (Coulter, Miami, FL). The samples were first degassed under vacuum at 40°C for 24 h. The pore volume size distributions were calculated from the nitrogen adsorption isotherms by the BJH model (Barrett et al., 1951). The specific surface area was tested in triplicate.

2.4. Flowability

The flowability was determined by an automatic flowability recorder (constructed at Orion

Corporation, Finland, i.e. non-commercial equipment). The angle of repose was determined by measuring the angle of the powder pile. Flowability was tested from six powder samples and the data were analyzed with the *t*-test.

2.5. Density

The poured and tapped densities of the materials were determined according to test of apparent volume (Ph. Eur. 2nd Ed.). True density measurements were made using a helium pycnometer (type Accupyc 1330, Micromeritics, Dunstable, UK). The density values are the mean of three determinations.

2.6. Swelling volume

The swelling volume was determined using a method described by Podczeck and Révész (1993). 500 ± 0.5 mg of each material were placed in a 20 ml graduated test tubes with 10.0 ml of distilled water. The solids were suspended by vigorous shaking and allowed to settle down until the volume was constant. The swelling volume was noted and the relative increase on swelling calculated on the basis of the poured bulk volume. The experiments were carried out in triplicate.

2.7. Wet massing studies

The rheological profiles of the wet masses were monitored using a mixer torque rheometer (Model MTR, Caleva, Dorset, England) similar to that described by Parker et al. (1990) and Rowe (1995). Fifteen grams of dry powder was mixed in the rheometer for 3 min to obtain the baseline response. Water (0.8–1.5 ml g^{-1}) was added in a single addition and the mixture was wet massed at 52 rpm for 12 min. The mixer torque rheometer measured two different torque parameters, the amplitude of the oscillations (torque range) and the mean torque increase from the baseline (mean torque). The mean torque describes the mean resistance of the mass to mixing and the torque range reflects the rheological heterogeneity of the mass. The mean torque was chosen since the torque range showed the same effects as the mean torque. All the wet massing experiments were performed in triplicate and a mean torque value and a standard deviation were calculated. The baseline response was deducted from torque responses. Curve fittings (three parameter log normal) were made by SigmaPlot 4.0 to the figures in which the mean torque values are as a function of mixing time.

3. Results and discussion

3.1. Particle size

The results of the particle size analysis are summarized in Table 1. There was no significant difference between cellulose samples.

3.2. Specific surface area and pore size distribution

The specific surface area data for the three celluloses are presented in Table 2. The surface area of Emcocel was slightly greater than that of Avicel, but the specific surface area of SMCC was about five times greater than that of regular microcrystalline cellulose. This is consistent with Staniforth et al. (1997). The results obtained for

Table 1
Particle size distribution[a]

	Mean diameter (μm)	*D* (*v*, 0.1)	*D* (*v*, 0.5)	*D* (*v*, 0.9)
Avicel PH 101	59.7 ± 0.5	25.3 ± 0.1	60.2 ± 1.0	93.6 ± 0.4
Emcocel 50	59.6 ± 0.2	25.1 ± 0.7	59.9 ± 0.2	93.5 ± 0.2
Prosolv 50	58.6 ± 0.3	24.0 ± 0.7	58.8 ± 0.6	93.1 ± 0.2

[a] *D* (*v*, 0.1) = 10 percentile, *D* (*v*, 0.5) = 50 percentile and *D* (*v*, 0.9) = 90 percentile of the particles.

Table 2
Specific surface area and pore volume of cellulose samples

	BET surface area (m^2 g^{-1})	Angle of repose (°)
Avicel PH 101	1.14 ± 0.04	39.3 ± 1.3
Emcocel 50	1.33 ± 0.01	38.6 ± 2.3
Prosolv 50	6.34 ± 0.10	33.2 ± 1.3

Avicel PH 101 agree as well with those reported in the literature (Hancock et al., 1992; Landín et al., 1993a). The specific surface area of Emcocel is greater than in earlier studies by Landín et al. (1993a,b). This could be partly explained by the change in the source of wood pulp.

The pore volume size distributions calculated from the nitrogen adsorption isotherms showed that the total pore volume was quite similar between Avicel PH 101 and Emcocel 50 but much greater for Prosolv 50 (Fig. 1). The pore volume size distributions explain also the greater specific area of Prosolv 50. Edge et al. (1998) and Tobyn et al. (1998) found that silicon dioxide particles cause an extensive surface texturisation of SMCC. Colloidal silicon dioxide has a very large specific surface area and the differences in specific surface area as well as in the pore distribution are ascribed primarily to the silicon dioxide on the surface of the SMCC.

Tobyn et al. (1998) determined pore size distributions for MCC 90 and SMCC 90 using a mercury porosimeter. They found the pore size characteristics to be very similar for MCC 90 and SMCC 90, and explained this by the similarity in envelope surface. Their method detected pores larger than 28 nm in diameter. In this study, however, the main difference in pore size distribution between MCC and SMCC is seen in the smaller pores.

3.3. Flowability and density

The flowability and density data can be seen in Tables 2 and 3. Prosolv showed better flowability than Avicel and Emcocel ($P < 0.0001$). SMCC showed also greater bulk and tapped densities than the regular MCC grades which is probably due to improved flowing and packing characteristics. These findings agree with those reported by Sherwood et al. (1996). The MCC grades had very similar flowability and density values.

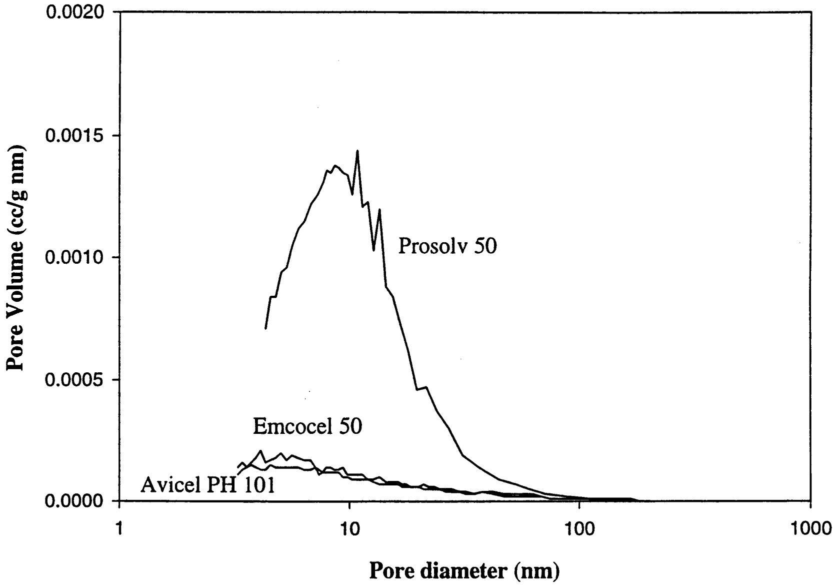

Fig. 1. Pore volume size distributions measured by nitrogen adsorption.

Table 3
Density and swelling volume measurements

	Poured/tapped density ($g\ cm^{-3}$)	True density ($g\ cm^{-3}$)	Swelling volume ($ml\ g^{-1}$)	Relative increase on swelling (%)
Avicel PH 101	0.31/0.42	1.54	4.8 ± 0.2	48.6
Emcocel 50	0.31/0.41	1.54	4.7 ± 0.1	45.5
Prosolv 50	0.35/0.47	1.55	4.3 ± 0.1	50.3

3.4. Swelling volume

Table 3 includes the swelling volume of the powder samples in water. The swelling volume was larger for MCC grades than for SMCC grade. However, the poured bulk volume of SMCC grade (2.86 ml g^{-1}) is smaller than the bulk volume of MCC grades (3.23 ml g^{-1}), so the relative increase on swelling was larger for SMCC grade. The difference between Emcocel and Prosolv was 4.8%. Podczeck and Révész (1993) have previously reported that the relative increase on swelling varied from 27 to 44% between different microcrystalline cellulose grades.

3.5. Wet massing

All the material exhibited an increase in torque with increasing water content rising to a maximum, thereafter decreasing as the material became overwetted (Fig. 2). It has been suggested (Alleva, 1984; Rowe and Sadeghnejad, 1987) that this behaviour is consistent with the different states of liquid saturation (pendular, funicular and capillar) as defined by Newitt and Conway-Jones (1958). The transition between different states of liquid saturation is usually induced by increasing the level of binder liquid but an identical effect can be obtained also by consolidating the agglomerates by further mixing (Newitt and Conway-Jones, 1958; Kristensen and Schæfer, 1987).

3.5.1. Peak torque location

When a binder liquid is added to a solid material, it is gradually distributed throughout the powder bed by the mixing process. With increasing liquid content the number and extent of the liquid bridges increases and a funicular state is formed. A further addition of liquid fills all the interparticulate voids, and the torque reaches a peak (capillary state). Prolonged mixing is assumed to cause a densification of the mass, and this should increase the liquid saturation causing a peak torque at a lower liquid amount. However, prolonged mixing will cause an increased absorption of water giving rise to a lower liquid saturation causing a peak torque at a higher liquid amount. The effect of mixing time on the peak torque location can be seen in Fig. 2a–d. With a shorter mixing time, the peak torque was achieved with a lower amount of liquid. With Emcocel, for instance, the peak torque location shifts during mixing from 1.1 ml g^{-1} (Fig. 2b) to 1.3 ml g^{-1} (Fig. 2d). The effect of absorption seemed to be larger than the effect of densification since a higher peak torque location was seen at prolonged mixing.

The mean torque profiles of MCC grades were quite similar after 1 min of mixing (Fig. 2a). When mixing time was increased to 3.5 min, the mean torque profile of Avicel was very close to the profile of SMCC grade (Fig. 2b). Further increase in mixing time decreased the difference between Emcocel and Prosolv and distinguished them from Avicel (Fig. 2c–d). In general, the mean torque values were smaller and the liquid requirement at peak torque was higher for Avicel (1.4 ml g^{-1}) than for Emcocel or Prosolv (1.3 ml g^{-1}). According to Ek and Newton (1998), variations in the performance of different sources of MCC is associated with the different interactions between the particular grade of MCC and water due to different pore structures. Staniforth et al. (1988) used a sandwich rheometer to measure the cohesiveness of microcrystalline celluloses. In their study Avicel PH 101 was found to be more cohesive than Emcocel. Rowe and Sadeghnejad (1987) reported as well both higher torques and higher water contents for Avicel than for Emcocel. However, these studies were conducted with Emcocel grades which are not equivalent to the currently used Emcocel 50.

3.5.2. Mixing kinetics

The correlation coefficients of curve fittings varied between 0.999 and 0.968 for Avicel PH 101, 0.998 and 0.987 for Emcocel 50 and 0.999 and 0.987 for Prosolv 50. The typical relative standard deviations of mean torques were less than 10%, with the exception of the lowest liquid level (0.8 ml g^{-1}) which showed much higher variations. At low liquid amounts (0.8–1.2 ml g^{-1}), all the mean torque curves were descending after 4 min of mixing (Figs. 3a, 4a and 5a). At the lowest liquid amount the initial torque peaks were higher for the MCC grades (Figs. 3a and 4a) than for the SMCC grade (Fig. 5a). Alleva (1984) observed an initial force peak at low to intermediate liquid contents and attributed this to the uneven distribution of the granulating liquid and the formation of large unstable agglomerates.

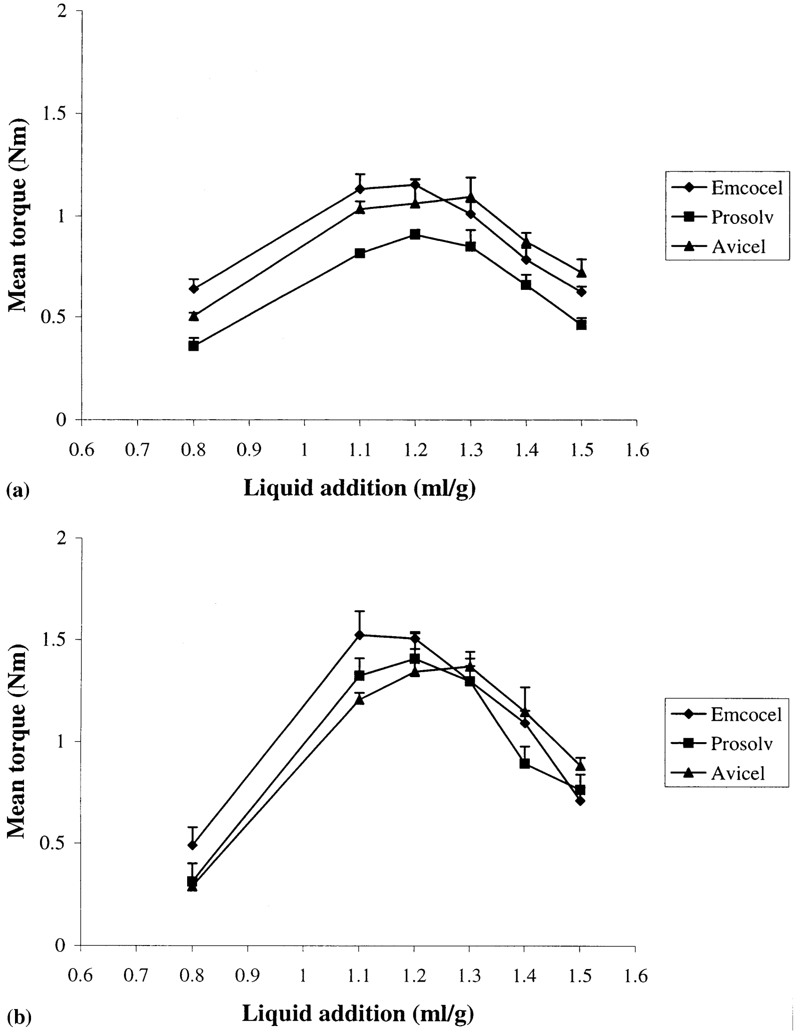

Fig. 2. Effect of mixing time on mean torque profile (a) 1 min (b) 3.5 min (c) 6 min (d) 12.25 min.

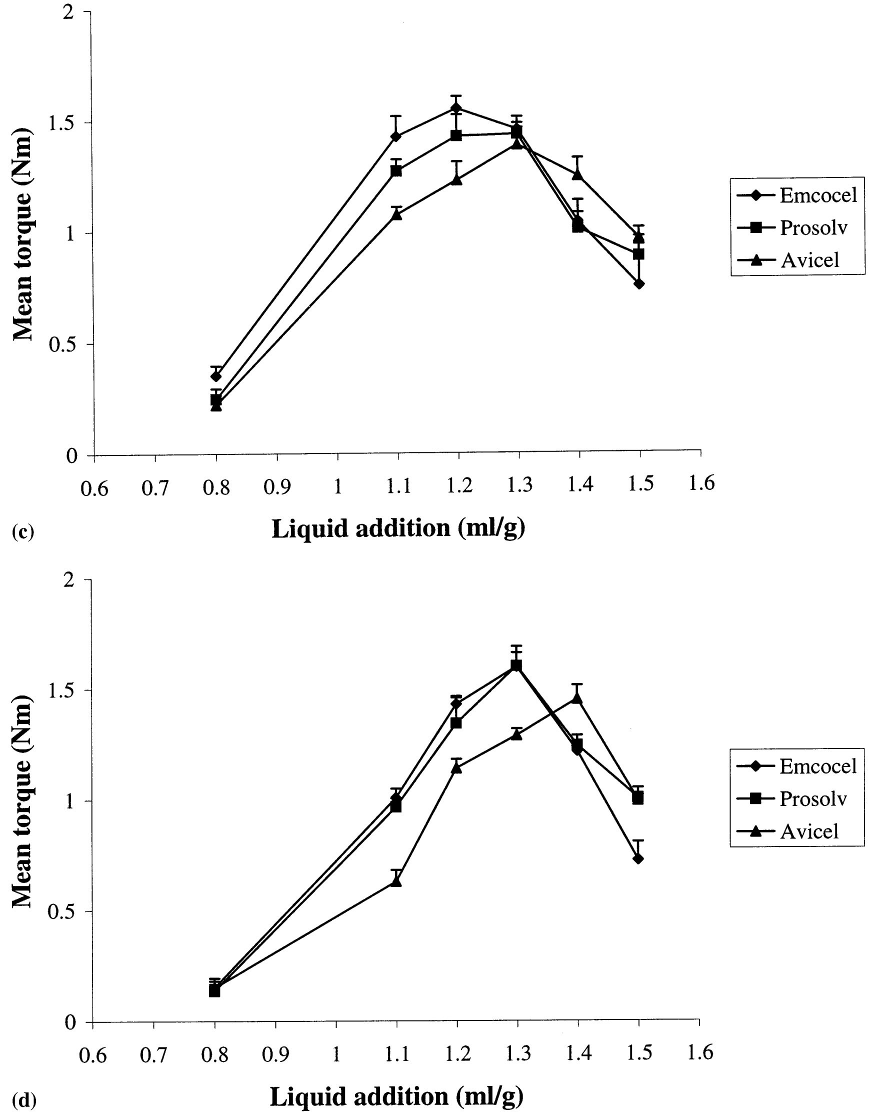

Fig. 2. (*Continued*)

When the wet masses achieved the peak torque (capillary state), the curves turned into ascending (Figs. 3b and 4b). With overwetted masses of MCC grades (1.5 ml g^{-1}), the torque responses achieved a plateau level after a few minutes of mixing whereas the overwetted SMCC masses did not (Fig. 5b).

Li et al. (1992) attributed water in the cellulose samples to the bulk water between fibres and to water in pore within the fibres. The amount of water absorbed by cellulose fibres will reduce the amount of free liquid being able to form liquid bridges and will thus affect agglomerate growth by affecting the liquid saturation. Khan et al. (1988) reported that the first 3% of moisture is strongly bound into internal structure of MCC without any change in volume, but at higher water levels the particles swell increasing the particle volume. According to Davidson et al. (1994), both swelling of the cellulose fibres and increase in the voidage of the matrix were taking place when Avicel matrices were immersed in water. Westermarck et al. (1998) found as well that with increasing moisture the size of the MCC particles increased and the voids between particles became larger. Hence, during the swelling the interparticulate voids will enlarge and the microcrystalline cellulose needs more water to fill them. Consequently, the differences both in the void volume and in the amount of water absorbed inside the cellulose fibres are able to affect the liquid saturation.

The effect of the silicification process on the rheological profiles is shown in Fig. 2a–d. The difference between Emcocel and Prosolv mixing kinetics can be seen in the early stages of mixing (Fig. 2a). According to Alleva (1984) and Rowe and Sadeghnejad (1987) bigger torque value is

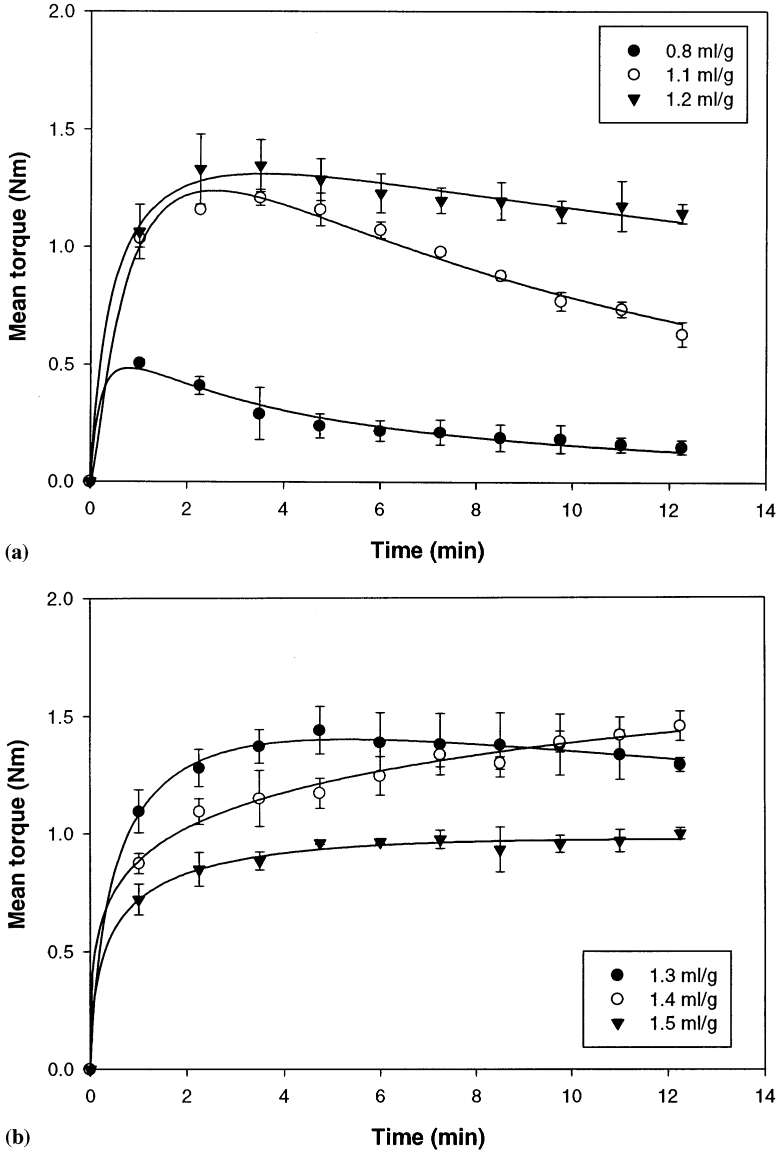

Fig. 3. Mixing kinetics of Avicel PH 101 (a) 0.8–1.2 ml g^{-1} (b) 1.3–1.5 ml g^{-1}.

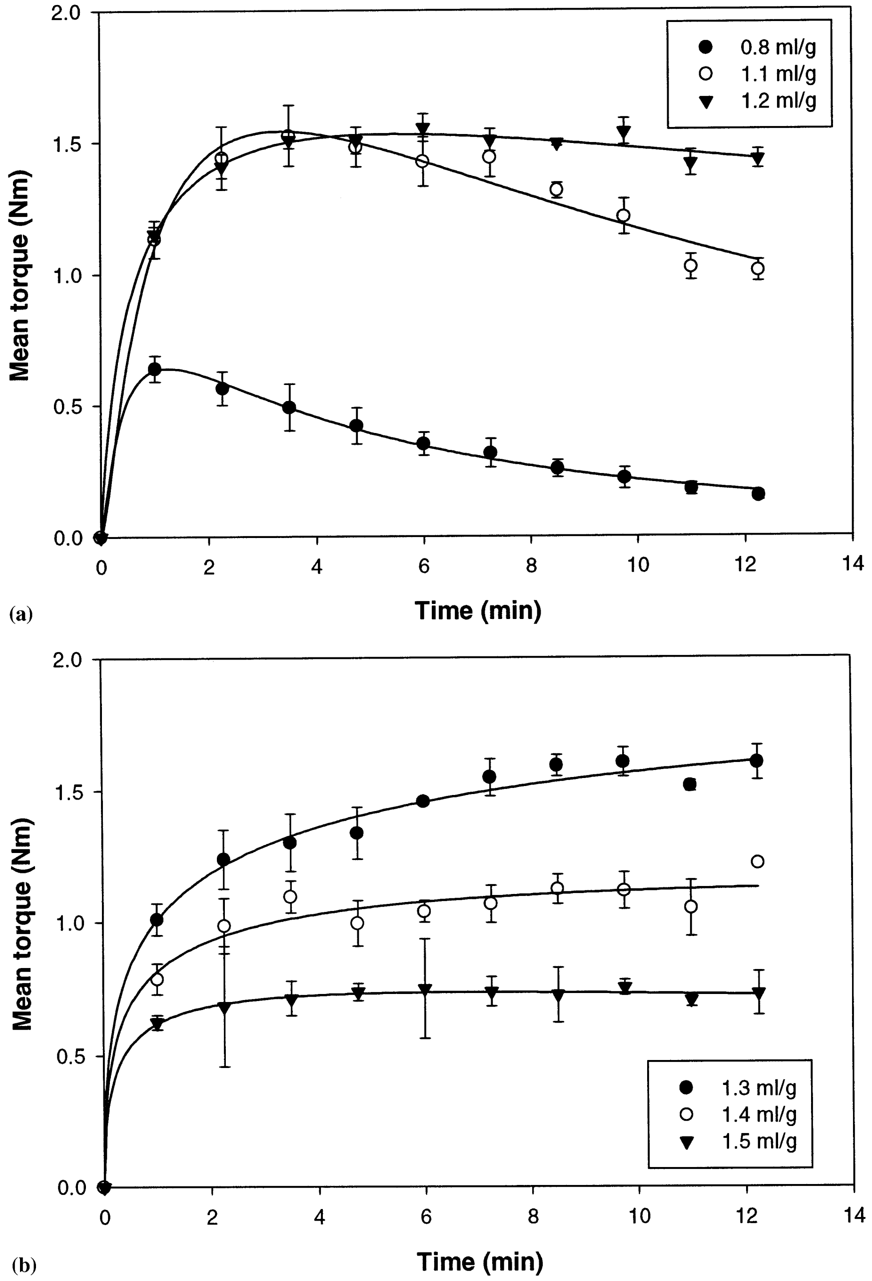

Fig. 4. Mixing kinetics of Emcocel 50 (a) 0.8–1.2 ml g^{-1} (b) 1.3–1.5 ml g^{-1}.

consistent with the higher liquid saturation. Since the relative increase on swelling was larger for Prosolv (50.3%) than for Emcocel (45.5%), the most likely explanation for the observed differences in the mean torque is that more water is absorbed by the Prosolv causing a lower liquid saturation. After 12.25 min of mixing Emcocel and Prosolv have similar rheological profiles (Fig.

2d). This can be explained by the densification of the moist agglomerates which is said to be the most important process during granulation (Kristensen et al. 1985).

3.5.3. Effect of surface area

According to Kristensen and Schæfer (1987), the surface area of a powder material influences the amount of liquid required during wet massing,

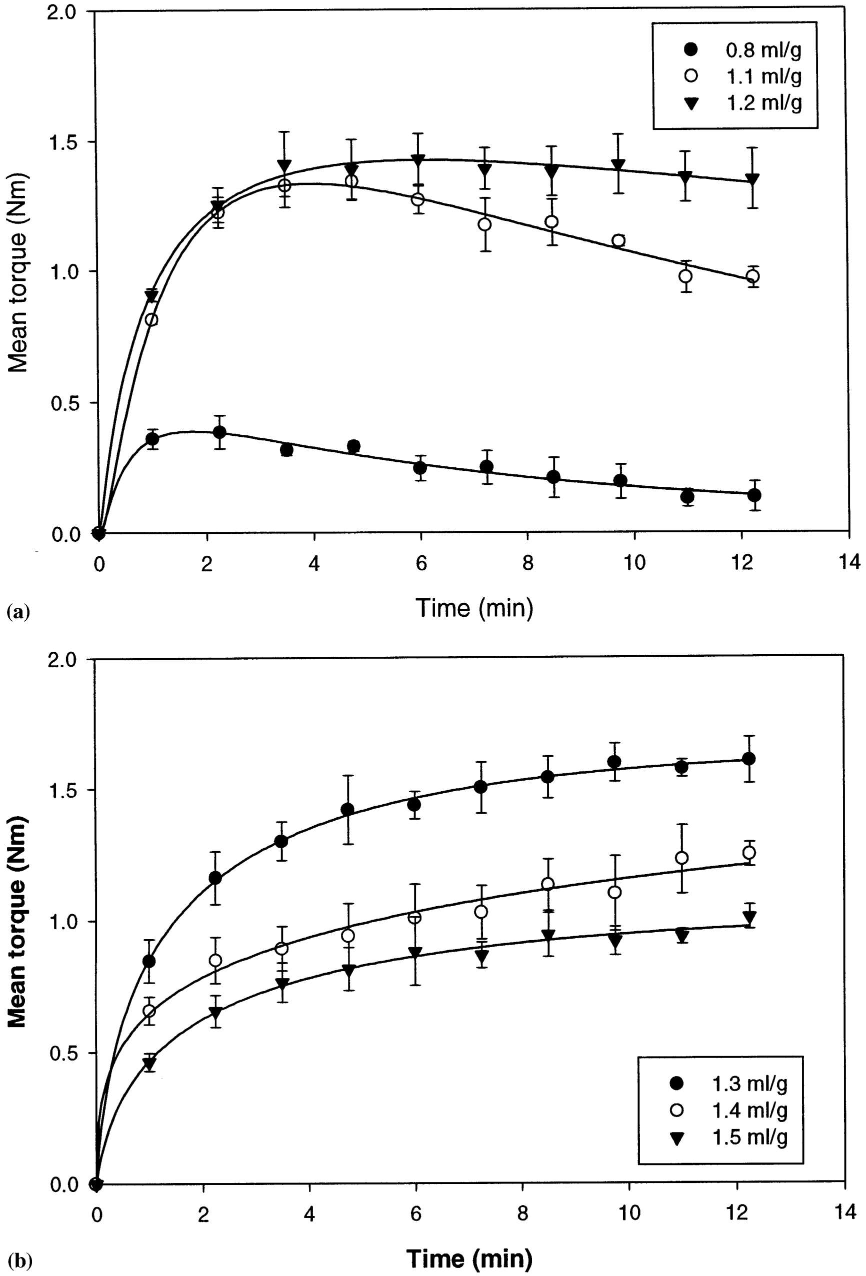

Fig. 5. Mixing kinetics of Prosolv 50 (a) 0.8–1.2 ml g^{-1} (b) 1.3–1.5 ml g^{-1}.

since a larger surface area increases the number of liquid bridges, which can be formed between the particles. In this study, the differences in surface area were not reflected by an increase in the liquid requirement for Prosolv 50. In fact, both Prosolv 50 and Emcocel 50 achieved the maximum torque value at lower liquid level when compared with that of Avicel PH 101. Neither Hancock et al. (1992) nor Chatlapalli and Rohera (1998) could find a correlation between the critical liquid requirement and the surface area. Parker and Rowe (1991), instead, reported that the suggested relationship between liquid requirement and surface area correlated well when the cellulose particles were convoluted in shape, with numerous folds and cavities. The difference between the micromorphology of MCC and SMCC is due to the silicification which does not induce gross changes in the shape and texture of the microcrystalline cellulose particles (Tobyn et al., 1998) and, consequently, does not reflect the liquid requirement at the peak torque.

4. Conclusions

Silicified microcrystalline cellulose exhibited improved flow characteristics and increased specific surface area compared to standard microcrystalline cellulose grades. The effect of the silicification process on the rheological profiles was seen in the early stages of mixing. Since the relative increase on swelling was larger for the SMCC grade than for MCC grades, the most likely explanation for the observed differences in the mean torque is that more water is absorbed by the Prosolv causing a lower liquid saturation. After 12 min of mixing the mean torque profiles of Emcocel and Prosolv were identical whereas Avicel exhibited higher liquid content and lower torque value. Although the silicification process affected the swelling properties and, furthermore, the mixing kinetics of microcrystalline cellulose, the source of the microcrystalline cellulose had a stronger influence than silicification on the liquid requirement at peak torque.

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