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Binder-substrate interactions in wet granulation. 3: The effect of excipient source variation

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Summary

The effect of excipient source variation on the interactions during wet granulation between microcrystalline cellulose and aqueous solutions of two molecular weight grades of two polymer binders has been studied using an instrumented mixer torque rheometer. The wet massing data confirmed previous observations that dissimilar polymers interact differently with cellulose substrates during the wet massing process. In addition, for a second cellulose material, variations were also observed in the pattern of interaction between the binders and the excipient. An examination of particulate and surface energetic properties revealed differences in the cellulose materials which were then related to the observed rheological behaviour.

Introduction

All drug and excipient materials used in pharmaceutical preparations are subjected to full chemical analysis to establish their purity as part of the quality control procedure. However, in recent years, it has been recognised that source and batchwise variability in the solid-state and material properties of both drugs and excipients can have profound effects on final product performance (Butcher and Jones, 1972; Rees and Rue, 1978; Holzer, 1983).

The material properties influencing the granulation process are those of particle size and size distribution, shape, surface area and wettability (surface free energy). A number of studies have examined the relative influences of starting material particle size on the granulation process and the resultant granules produced (Hunter and Ganderton, 1972; Bier et al., 1979; Jaiyoba and Spring, 1979; Holm et al., 1985). Kristensen and Schaefer (1987) concluded that the various observations could be explained in terms of the surface area of the material. In order to achieve the desired level of liquid saturation necessary for agglomeration to occur, an amount of binder is needed which is dependent on the surface area of the powders. A small particle size results in a

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larger surface area and hence a greater liquid requirement. The larger surface area also increases the number of bridges which can form between the particles, thus leading to an increase in granule strength with decrease in particle size.

Hollenbeck et al. (1978) concluded that most problems encountered in the production of solid dosage forms are associated with solid-liquid interactions, and in recent years numerous studies have been carried out in order to characterise specific interactions (Hansford et al., 1980; Zografi et al., 1984; Buckton, 1988).

We have previously used a mixer torque rheometer technique (Parker et al., 1990, 1991) to examine the rheological behaviour of microcrystalline cellulose wet massed with aqueous solutions of commonly used polymer binders. The results indicated that different polymers, and indeed various molecular weight grades of the same polymer, behave differently during the wet massing process. The observed differences, which could only partly be explained on the basis of current theories relating fundamental material properties to final granule properties, were then examined by consideration of possible excipient/binder interactions, and polymer adsorption effects.

The aim of this study is to examine the changes in rheological behaviour when the source of microcrystalline cellulose is changed, and to determine whether previously observed interactions with commonly used polymer binders are maintained with a different source of excipient.

Materials and Methods

Materials

Supplies of microcrystalline cellulose (MCC) were obtained from two sources, Avicel PH 101 (BN:6503) from FMC Corp. (Co. Cork, Ireland) and Unimac MG 100 (BN:5175) from Unitika Rayon Ltd (Osaka, Japan). Polyvinylpyrrolidone (PVP: Kollidon 25 and Kollidon 90, BASF (U.K.) Ltd, Cheadle, Cheshire, U.K.) and hydroxypropyl methylcellulose (HPMC: Pharmacoat 603 and Pharmacoat 606, Shin-Etsu Chemical Co., Tokyo, Japan) were used as the representative polymer binders.

Methods

Material characterisation

The material properties influencing granulation processes are those associated with fundamental bulk properties such as particle size, shape, surface area and wettability. The characterisation of the cellulose excipients was therefore tailored to examine these properties.

Particle size

The particle size distribution and median particle size of each cellulose were determined by a standard sieve analysis technique, using an Endicott Test Sieve Shaker (Endicott Ltd, London) and a nest of Endicott Test Sieves.

Bulk density

The tapped bulk density of each cellulose material was measured in accordance with BS 1460, by repeatedly dropping a known mass of powder in a measuring cylinder through 25 mm. The tapped volume was noted after 500 taps. These data, together with the initial poured bulk volume, were used to calculate the bulk and tapped densities, and to determine the indices of flowability and compressibility derived by Hausner (1967) and Carr (1970).

Scanning electron microscopy (SEM)

Samples of each powder were prepared and examined using a Hitachi S2300 scanning electron microscope (Hitachi Ltd, Tokyo, Japan). Samples to be studied were mounted on double-sided tape on aluminium stubs and coated with gold under vacuum.

Specific surface area determination

The specific surface area of each sample was determined using an Orr Surface Area, Pore Volume Analyser (model 2100, Micromeritics Instruments Corp., U.S.A.), using the B.E.T. method of nitrogen adsorption. Samples of microcrystalline cellulose for analysis were first degassed under vacuum at 70°C for 24 h.

Powder X-ray diffraction

X-ray diffraction spectra of powder samples were obtained using an X-ray diffractometer (PW 1130/90, Philips, The Netherlands) with a proportional detector probe. The X-ray source was CuKα radiation with a wavelength of 1.541 Å. A scanning rate of 0.25° 2θ/min over the range 4–50° 2θ was used to produce the spectra. Samples for analysis were prepared by pressing the powder into the cavity in a metal sample holder, and smoothing with a glass slide.

Immersion calorimetry

The solid-liquid interactions occurring during granulation processes depend partly on the surface energetics of the solid substrates, and more precisely on the wettability of the materials. Buckton and Beezer (1988) have observed that the surface energetics of a powder are, at least in part, a measure of its past history. In this study the technique of immersion calorimetry has been used to examine the surface energetics of the cellulose substrates.

The immersion calorimetry studies were carried out on prepared microcrystalline cellulose samples using a Tronac Solution Calorimeter (model 458 Tronac Inc., UT, U.S.A.), which has been described fully elsewhere (Lindenbaum, 1990; Parker and Rowe, 1991).

Samples of microcrystalline cellulose of varying moisture content were prepared by storing the material over saturated salt solutions or in glass desiccator jars. For the immersion study the sample was poured into the previously tared, glass ampoule and sealed with a silicon rubber bung. The ampoule was placed in the holder/stirrer assembly and the Dewar flask containing 50 ml of distilled water carefully raised and clamped in position. The whole assembly was then lowered into the water bath, and equilibrated to a temperature of 25°C. The experimental run, calibration run, data capture and subsequent processing were then carried out using an IBM XT personal computer linked to the calorimeter via an interface.

The experimental procedure was carried out in triplicate for each level of moisture. From the results, graphs of enthalpy of immersion against moisture content of the sample could be plotted.

Binder characterisation

The dynamic viscosity and surface tension of aqueous solutions of each binder were determined using capillary viscometry and a Du Nuoy tensiometer respectively, as described by Parker et al. (1990). The data have been presented elsewhere (Parker et al., 1991).

The molecular weight distributions of each polymer, and possible interaction phenomena with Avicel PH 101, have been investigated using a gel permeation chromatography technique described by Parker et al. (1990, 1991). The approach has been extended here to examine possible interactions between the polymer binders and Unimac MG 100.

Wet massing studies

The rheological profiles of wet masses of Unimac MG 100 with different amounts of aqueous solutions of each binder were monitored using the mixer torque rheometer technique described elsewhere (Rowe and Sadeghnejad, 1987; Parker et al., 1990). The equilibrium torque value, reflecting the rheology of the wet mass, was determined three times for each volume of binder. From these data, rheological profiles of torque against proportion of binder were generated for different concentrations of each binder.

Results

Wet massing studies

Fig. 1 shows the rheological profiles for the two MCC materials using distilled water as the binder. The error bars represent the standard deviation of the mean. Each of the materials exhibited a characteristic rheological profile with increasing water content, as described by Rowe and Sadeghnejad (1987) and Parker et al. (1990).

It can also be seen that the two cellulose materials exhibited differences in terms of both the torque values obtained and the liquid levels required throughout the profiles. The Unimac MG 100 has a reduced peak torque and liquid

TABLE 1

Torque rheometer data for microcrystalline cellulose mixes with PVP grades

Binder (% w/v)	Viscosity (cP)	Maximum torque (Nm)		Liquid content at maximum torque (ml/g)	
		Avicel	Unimac	Avicel	Unimac
Water	1.00	0.5280	0.3693	1.33	1.06
1% K25	1.19	0.4988	0.3572	1.33	1.06
3% K25	1.58	0.4887	0.3855	1.33	1.06
5% K25	2.25	0.5345	0.4601	1.33	1.06
8.24% K25	3.82	0.6186	–	1.33	–
12.78% K25	6.87	0.6427	–	1.20	–
0.3% K90	1.54	0.5756	–	1.20	–
1% K90	3.82	0.5826	0.6156	1.27	1.06
3% K90	16.49	0.6336	0.9329	1.20	1.06
5% K90	41.95	0.6723	1.0054	1.20	0.93

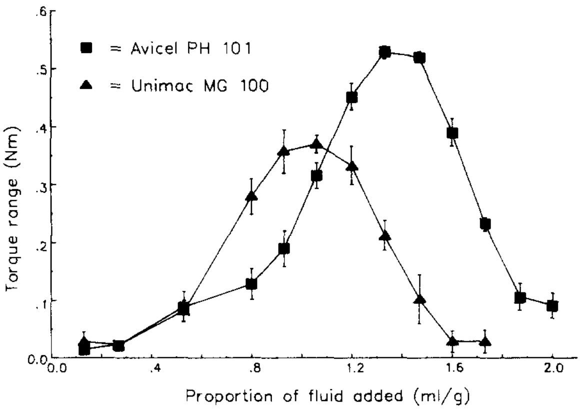

Fig. 1. Rheological profiles for Avicel PH 101 and Unimac MG 100 with water.

requirement at the peak compared to the Avicel PH 101.

Similar results were obtained by Rowe and Sadeghnejad (1987) using a range of other microcrystalline celluloses. This behaviour was explained on the basis of particle size, since it was observed that the maximum torque and water content at the maximum torque decreased with decreasing particle size. It is important, therefore, to examine whether a similar relationship exists in this study.

The rheological profiles obtained for Avicel PH 101 with different concentrations of the polymer binders have been presented elsewhere (Parker et al., 1990, 1991). The profiles for Uni-

TABLE 2

Torque rheometer data for microcrystalline cellulose mixes with HPMC grades

Binder (% w/v)	Viscosity (cP)	Maximum torque (Nm)		Liquid content at maximum torque (ml/g)	
		Avicel	Unimac	Avicel	Unimac
Water	1.00	0.5280	0.3693	1.33	1.06
1.3% 603	2.26	0.4299	0.3203	1.33	1.06
3% 603	5.41	0.5596	0.5024	1.27	1.06
5% 603	12.56	0.6839	0.6260	1.20	0.93
1% 606	2.71	0.4990	0.5318	1.33	1.06
3% 606	12.24	0.5671	0.9128	1.20	0.93
5% 606	39.27	0.7954	1.2502	1.27	0.93

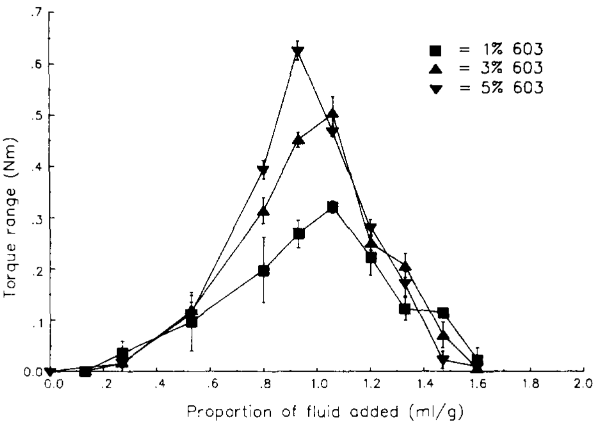

Fig. 2. Rheological profiles for Unimac MG 100 with HPMC 603.

mac MG 100 with different concentrations of the HPMC grades are shown in Figs 2 and 3. Similar profiles were obtained using different concentrations of PVP. The peak torque and proportion of liquid required at the peak are presented for both MCC sources with each binder concentration in Tables 1 and 2. The general form of the results is comparable to that seen with Avicel PH 101. The liquid requirement at the peak torque for each of the polymer grades is similar to that seen for Unimac MG 100 and water, reinforcing the previously observed differences in liquid requirement between Unimac MG 100 and Avicel PH 101. Once again the general trend throughout both polymer systems is one of increasing torque and decreasing liquid requirement at maximum torque with increasing binder viscosity.

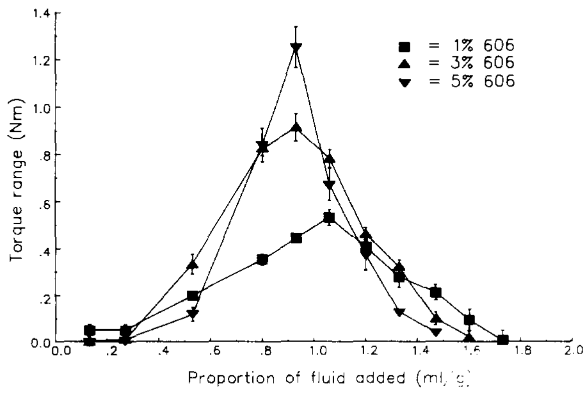

Fig. 3. Rheological profiles for Unimac MG 100 with HPMC 606.

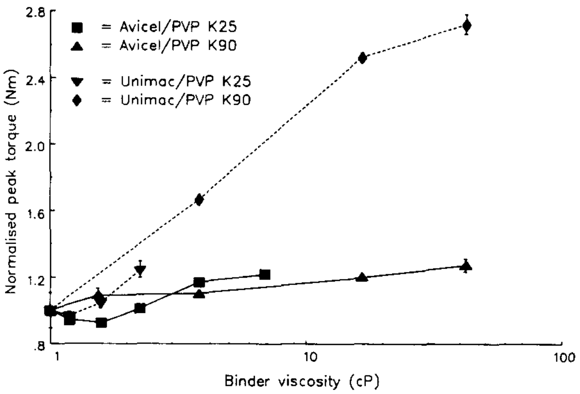

Fig. 4. Effect of excipient source variation on torque development with PVP systems.

The data in Tables 1 and 2 indicate that the lower molecular weight grades of each polymer follow similar trends with each cellulose substrate. However, the results for the PVP K90 and HPMC 606 show considerable differences between the Unimac and Avicel substrates. The peak torque developed with each polymer is much higher for the Unimac substrate, possibly reflecting a different balance of interactions compared to Avicel PH 101.

In order to clarify these observations and to compare source variation effects on the interaction between the excipient and the binder, the peak torque results from Tables 1 and 2 were normalised with respect to the torque obtained with water and plotted against the binder viscosity for each excipient/binder combination. The graphs are presented in Figs 4 and 5.

Considering the curves for the Unimac substrate, it can be seen that a similar pattern of behaviour is exhibited by the two polymer systems studied. In both cases, the curve for the lower molecular weight grade polymer exhibits a minimum followed by a rise as the binder concentration, and hence viscosity, increases. However, in neither system does the curve for the lower molecular weight grade cross that of the higher molecular weight grade, as seen with the polymers and the Avicel substrate. For the PVP curves further experiments at higher viscosity levels

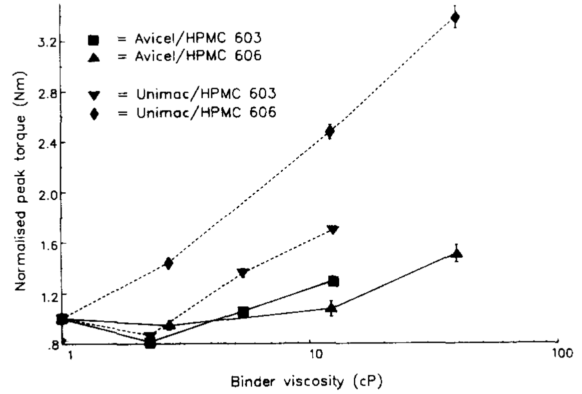

Fig. 5. Effect of excipient source variation on torque development with HPMC systems.

would be necessary before being able to establish whether or not the K25 curve would cross the K90 curve as seen in the Avicel/PVP system. For the Unimac/HPMC curves it is clear that there are distinct differences in the rheological behaviour at equivalent viscosity between the two grades of the same material.

Considering both sets of curves in Figs 4 and 5, it can be seen that for the low molecular weight polymers there is a similar pattern of interaction between the binder and the two microcrystalline celluloses, as demonstrated by the almost parallel profiles for the Avicel and Unimac curves for PVP K25 and HPMC 603. For the high molecular weight grades the figures clearly show the differences in interaction between Avicel PH 101 and Unimac MG 100 with both PVP K90 and HPMC 606.

It is also interesting to note that for both grades of the two polymer binders, the magnitude of the torque changes relative to that obtained with water are greater in the Unimac study than in the Avicel study.

These variations in rheological behaviour can be attributed to differences in the degree, or balance, of interaction between the excipient material and the polymer molecules. Additional contributory factors are likely to be differences in the particulate, surface characteristics and energetics of the different celluloses.

TABLE 3

Particulate properties of microcrystalline celluloses

	Avicel PH 101	Unimac MG 100
Median particle size (μm)	59	53
Specific surface area ($m^2\ g^{-1}$)	1.18	1.24
Bulk density ($g\ cm^{-3}$)		
Poured	0.32	0.33
Tapped	0.45	0.50
Hausner ratio	1.41	1.51
Carr's compressibility index (%)	29.0	33.9

Particle size

The median particle sizes of the microcrystalline cellulose materials are listed in Table 3. In general the results agree well with the manufacturers' literature.

Fig. 6 presents the frequency distribution curves for the two cellulose materials. The curves show that the two materials have broadly similar distributions, with the Unimac MG 100 having a greater percentage of particles at the peak frequency. It can also be seen that the Avicel PH 101 has a second frequency peak at the 60–80 μm size fraction which is not seen with the Unimac MG 100. Thus, the Unimac material may be considered to have a more monodisperse distribution.

These differences in the particle size distribution between the materials of different source may influence the packing behaviour of the mate-

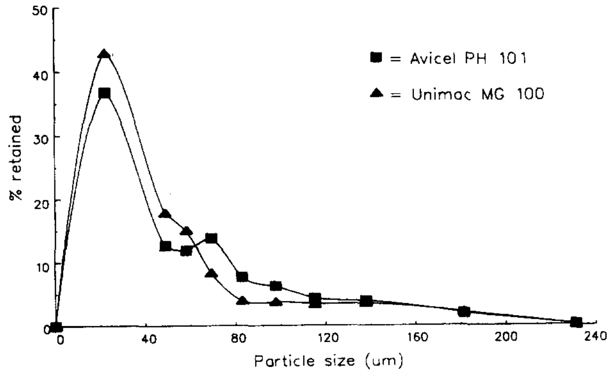

Fig. 6. Particle size distributions for Avicel PH 101 and Unimac MG 100 by sieve analysis.

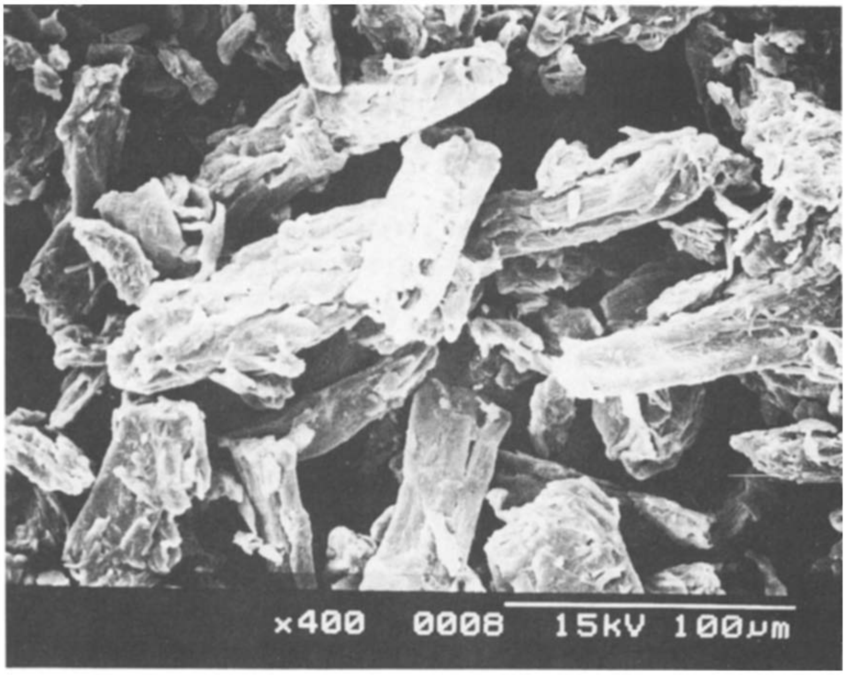

Fig. 7. SEM photomicrograph of Avicel PH 101.

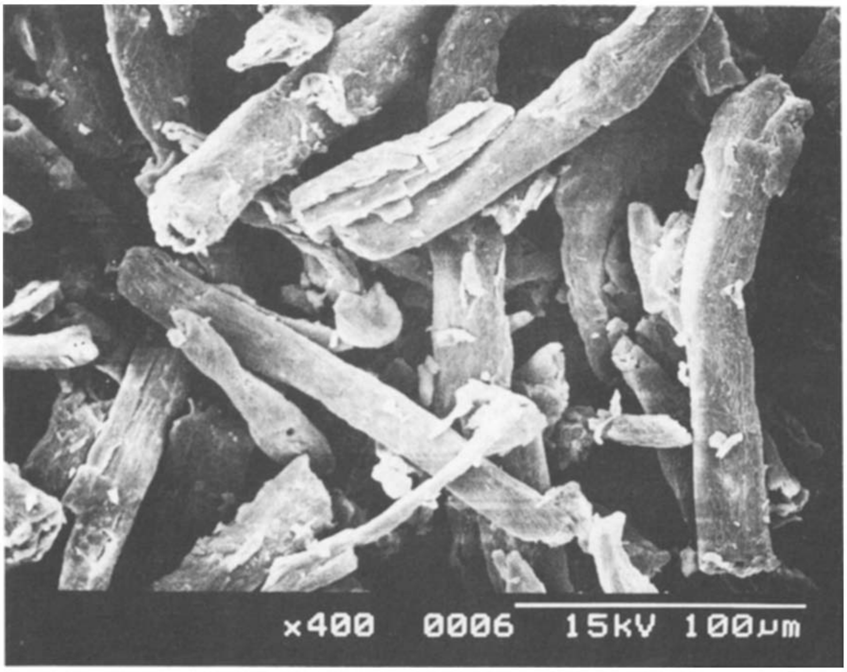

Fig. 8. SEM photomicrograph of Unimac MG 100.

rials, and hence the liquid requirements and material performance during granulation.

Scanning electron photomicrographs

Figs 7 and 8 show the SEM photomicrographs of the two cellulose excipients. These figures show the typical elongated, fibrous particle shape, of the microcrystalline cellulose particles, and indicate the general similarities in particle size between the Avicel and Unimac materials. However, differences in the surface morphology of the particles may be observed. The Unimac MG 100 particles appear to be more elongated, with a smoother surface than the Avicel PH 101 particles.

Bulk density

The density results and derived data are presented in Table 3, and for Avicel PH 101 they are in good agreement with data presented in the literature (Krycer et al., 1982; Parvez, 1985). It can be seen that the Unimac MG 100 has both a greater Hausner ratio and compressibility index, indicating a greater degree of consolidation on tapping, and hence poorer flow properties compared to the Avicel PH 101.

The differences in the surface morphology of the Avicel PH 101 and Unimac MG 100 particles observed from the SEM photographs, i.e., the apparently smoother surfaces of the Unimac MG 100 particles, may help to explain the observed differences in densification of the two materials.

Specific surface area

The specific surface area data for the two substrates are also presented in Table 3. The results for Avicel PH 101 correlate well with data reported elsewhere in the literature [1.0 m^2 g^{-1} (Nakai et al., 1977); 1.3 m^2 g^{-1} (Zografi et al., 1984)]. Although the results indicate that the cellulose samples have similar surface area values, it is interesting to note that the rank order of surface areas of Unimac MG 100 > Avicel PH 101 follows the pattern expected from the median particle size data by sieve analysis.

The surface area of a powder material will also influence the liquid requirement during granulation, since a larger surface area increases the number of bridges which can form between particles, thus leading to an increase in the liquid requirement and granule strength (Kristensen and Schaefer, 1987). In this study, the small differences in surface area between the Avicel and Unimac materials do not reflect the observed differences in liquid requirement of the two materials. These differences in surface area may be cancelled out by the possibly greater degree of densification occurring within the Unimac powder bed during wet massing, and the resultant reduction in the liquid requirement that this produces.

Powder X-ray diffraction spectra

The powder X-ray diffraction spectra for the two cellulose materials are presented in Figs 9

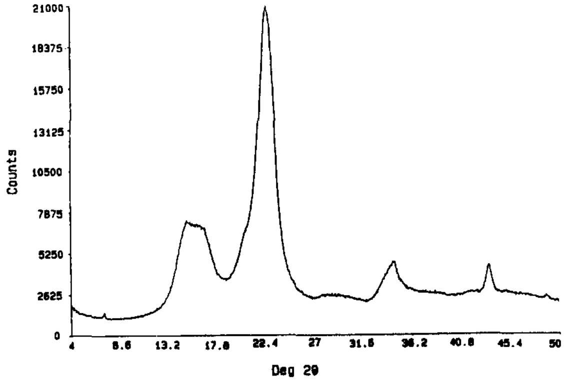

Fig. 9. Powder X-ray diffraction spectrum for Avicel PH 101.

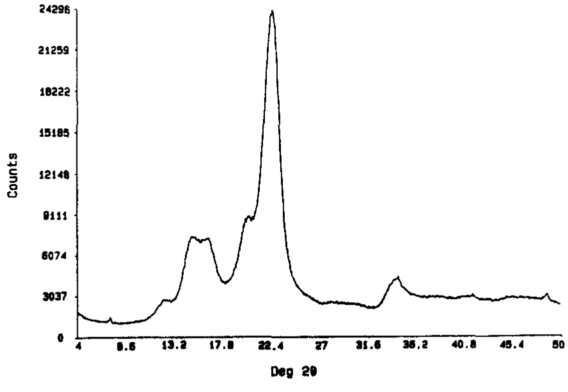

Fig. 10. Powder X-ray diffraction spectrum for Unimac MG 100.

and 10. The spectra are different from those normally obtained from true crystalline materials, with the occurrence of very broad peaks. The spectrum for Avicel PH 101 is comparable to that presented by Nakai et al. (1977).

When comparing the two spectra the peaks appear very similar in terms of relative peak height and position, reflecting gross similarities in the degree of crystallinity of the materials. However, a shoulder can be seen in the Unimac spectrum at a 2θ of approx. 22°. Thus, although the materials are chemically equivalent, some minor crystallographic differences are identified, which may reflect differences in the pretreatment and manufacturing processes of the two celluloses.

This has implications in the interactions of the materials with water, since it is now accepted that water interacts with the anhydroglucose molecules in the amorphous regions of the cellulose molecule. A more crystalline cellulose material will therefore have a reduced interaction with water, requiring a lower amount of water to saturate the system, to a point where multi-molecular layers of free water (the immediate precursor to pendular bridges) are formed.

Immersion calorimetry

The graphs of enthalpy of immersion against moisture content for the two celluloses are presented in Fig. 11. The shape of the curves correlates well with those presented by Hollenbeck et al. (1978), and has been explained by these workers and by Zografi et al. (1984). At low levels of moisture, water is thought to interact in a 1 : 1 stoichiometric ratio with the anhydroglucose units in the amorphous regions of the cellulose chain. As the moisture content rises, water interacts in a less strongly bound, 2 : 1 stoichiometric ratio with each repeating unit, subsequently followed by less well defined multilayers of water molecules. Hollenbeck suggested a change in the mechanism occurred at moisture levels of 3% w/w, with a further change apparently taking place at around 8% w/w moisture.

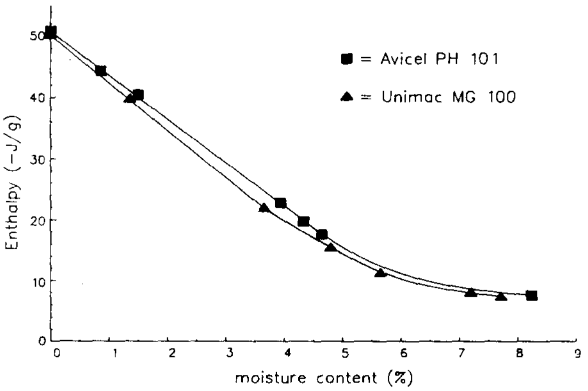

Fig. 11. Immersional isotherms for Avicel PH 101 and Unimac MG 100.

From Fig. 11 it can be seen that the two isotherms are displaced vertically, with the enthalpy of immersion values for Unimac MG 100 lower than those for Avicel PH 101. This suggests that there is a difference in the surface properties or energetics between the two celluloses in terms of their interaction with water. If water interacts with the anhydroglucose units in amorphous regions of the cellulose, then a cellulose with a smaller amorphous component will at equivalent moisture content react to a lesser degree on immersion in water. Thus, the observed immersional behaviour of the two celluloses may correlate with the X-ray diffraction spectra, where the shoulder in the Unimac spectrum could reflect an increased level of crystallinity, and hence a reduced amorphous component.

Excipient / binder adsorption

Data presented elsewhere (Parker et al., 1990, 1991) have indicated that adsorption of the polymers used in this study can occur onto Avicel PH 101. Table 4 presents the GPC analysis data for the different binders after equilibration with Unimac MG 100. As seen with the previous data, the results for the PVP materials are rather inconclusive. For the PVP K25 grade there is no change in the weight average (M_w) or peak molecular weight values after equilibration with the cellulose. The decrease in the number average molecular weight (M_n) is not considered significant, since this value is likely to be affected by peak tailing in the GPC analysis. For the K90 grade the data show no clear patterns to indicate adsorption is taking place.

TABLE 4

GPC data for Unimac substrate

Sample	Weight average molecular weight (M_w) ($\times 10^3$)	Number average molecular weight (M_n) ($\times 10^3$)	Peak molecular weight ($\times 10^3$)
PVP			
3% K25 (control)	30	3.6	24.9
3% K25/Unimac	30	1.7	25.0
1% K90 (control)	2250	174	809.8
0.3% K90/Unimac	2400	148	1144.0
2.5% K90/Unimac	1940	191	959.0
HPMC			
1% 603 (control)	45	3.5	33.3
5% 603/Unimac	36	2.6	22.7
1% 606 (control)	93	11.0	51.6
3% 606/Unimac	90	8.5	47.4

Examination of the HPMC data gives a more positive indication of polymer adsorption. There are clear reductions in all three measured parameters for both the low and high molecular weight grades of polymer.

These data correlate well with conclusions derived elsewhere for Avicel PH 101 (Parker et al., 1990, 1991) that there is a greater interaction between HPMC and microcrystalline cellulose than between PVP and microcrystalline cellulose.

Discussion

The material characterisation data have indicated several relevant differences between the cellulose substrates in terms of their particulate and energetic properties. Although the particle size data indicate that Avicel PH 101 and Unimac MG 100 are of equivalent median particle size, differences can be seen in their size distribution. Slight differences can also be observed in the surface morphology of the two celluloses using SEM, and differences are also seen in the bulk density behaviour consistent with the predicted packing behaviour from the size distribution profiles and SEM photomicrographs.

These observed differences in particulate properties will influence the densification behaviour of these materials during wet massing. Densification of a powder bed reduces the liquid requirement in granulation processes by its effects on the liquid saturation (Kristensen et al., 1984; Schaefer et al., 1986a–c). Therefore, if the Unimac MG 100 consolidates to a greater degree in the mixing bowl of the rheometer, this may help to explain the reduced liquid requirement of this material at all points along the rheological profiles. Furthermore, the X-ray powder diffraction and immersion calorimetry studies indicate differences in the crystallographic nature and surface energetics of the two celluloses, which may also influence the liquid requirement for granulation.

The arguments developed elsewhere for Avicel PH 101/binder interactions (Parker et al., 1990, 1991) do not take into account the effects of substrate source variation on the degree of interaction. It is reasonable to suggest, however, that particulate and surface energetic differences between materials of different source will lead to differences in excipient/binder interaction and hence differences in the observed rheological behaviour. Examination of the changes in peak torque with increasing binder viscosity for the Unimac MG 100 experiments (Figs 4 and 5) also shows distinct differences in rheological behaviour in comparison with Avicel PH 101. For the Unimac/PVP system the general pattern of behaviour for the two grades of polymer is similar to that seen with Avicel PH 101 and PVP (Fig. 4 and Parker et al., 1991). The major difference between them is the generally higher torque values for Unimac/PVP system.

Data from the polymer adsorption experiments yield no conclusive information to suggest that there is perhaps greater adsorption of PVP onto Avicel PH 101 than onto Unimac MG 100. However, this pattern of rheological behaviour is consistent with the immersion calorimetry data on the two materials. From these calorimetric data, it can be concluded that the Avicel PH 101 has a more energetic surface than the Unimac MG 100. As a result there is a greater potential for interaction of the PVP molecules with Avicel PH 101 than with Unimac MG 100. This would then lead to lower peak torque values for the Avicel/PVP system due to the effect on the intra-granular viscosity (Parker et al., 1991).

For the Unimac/HPMC system, examination of Fig. 5 indicates a different balance of interactions between the two molecular weight grades when compared with the Avicel/HPMC curves. The curve for the HPMC 603 grade does not cross that of the 606 grade, and as seen with the Unimac/PVP system, the torque values for the high molecular weight grade are much higher than those of the comparable Avicel data.

The GPC data in Table 4 confirm that adsorption of HPMC onto Unimac MG 100 does occur. The torque rheometer data backed up to a certain extent by the GPC results indicate a greater degree of interaction between the Unimac MG 100 and HPMC 603 than with the 606 grade. This would result in a greater effect on the intra-granular viscosity, and hence produce the torque differences seen in Fig. 5.

A comparison of the torque rheometer data in Tables 1 and 2 shows that for the low molecular weight grades, the peak torque values for HPMC 603 are lower than those of the PVP K25. This suggests a similar balance of interactions between the polymers and the substrate to that described by Parker et al. (1990) for Avicel PH 101.

On inspection of the torque rheometer data for the high molecular weight grades of each polymer (Tables 1 and 2), it can be seen from comparison with the pattern of behaviour seen with Avicel PH 101, where the curve for the HPMC 606 was generally lower than that of PVP K90, that for the Unimac substrate, the two sets of data are very similar. This is consistent with the proposal that there is a lower degree of interaction between HPMC 606 and Unimac MG 100 compared with Avicel PH 101.

The observed differences between the PVP K90 curve and the HPMC 606 curve at the highest viscosity may be explained in a similar manner to that for the Avicel systems (Parker et al., 1991) where it was proposed that differences in the spreading coefficients of the two polymers affect the distribution of the binder throughout the mass, and hence the torque developed.

Fig. 5 also shows that in general the torque changes relative to that of water are higher for Unimac MG 100 than for Avicel PH 101. This may also be explained in a similar manner to that developed for the PVP systems above by relating the differences in the surface energetics of the two celluloses to observed differences in torque.

Conclusions

The rheological profiles presented in this study clearly demonstrate the effect of source variation on the rheological behaviour during wet granulation of two microcrystalline celluloses. They also highlight the influence that relatively modest differences in solid-state, energetic and particulate properties can have over the processibility of chemically equivalent excipients.

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