

The use of surface energy values to predict optimum binder selection for granulations

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Summary

The surface energy of microcrystalline cellulose (Avicel PH101), was assessed using a Wilhelmy plate technique. Using values for the surface energy of binders that are available in the literature, it was possible to predict the spreading behaviour of binder over powder and vice versa. This was taken as a method by which the optimum binder for the powder might be selected. To test the prediction, granulations of microcrystalline cellulose were made using hydroxypropylmethylcellulose (HPMC), polyvinylpyrrolidone (PVP) and water as binding agents. The granulations were tested for friability, density, bulk density, tapped bulk density, angle of repose and size distribution. The variables that were considered were the binder used, the volume and concentration of binder solution, the particle size of the powder to be granulated and the quantity of powder to be granulated. The major conclusions were that the granulation was poor if a small quantity of powder was placed in the mixer, the particle size of the powder did not alter the size of the granules that were produced, but did alter the other properties (e.g. friability): an increase in concentration of the binder solution does not necessarily result in improved binder performance, but an increase in the volume of the binder solution produced a significant improvement in granule properties. The prediction of binder performance based on surface free energies and polarity proved reliable in that HPMC was superior to PVP as a binding agent for this powder.

Introduction

Granulation is a process which is used regularly to improve the properties of powders which have poor flow and compression behaviour. There are many acceptable excipients which are used in the

process of wet granulation as binders; these include hydroxypropylmethylcellulose (HPMC), methylcellulose, polyvinylpyrrolidone (PVP), starch and acacia. With some products the selection of a suitable binder will be easy; however, with other products the choice of binder is critical as an inappropriate selection would not produce a workable formulation.

The aim of this work is to use predictions of binder performance based on powder surface energetics and to test these predictions to see if the correct binder was indicated. Wells and Walker (1983) have reported that the wetting of a powder

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by the granulating fluid is an important factor in controlling the granulation process. Rowe (1989) produced a theoretical paper to show how the selection of binders may be made on the basis of a knowledge of surface energetics.

Predictions of Binder Performance Based on Surface Energetics

The interaction between any two components of a system will be controlled, initially, by an interfacial process. Wu's equation (Wu, 1971) links the interfacial energy between any two phases to the relative polar and dispersion components of the surface energies of the two individual phases:

$$\gamma_{12} = \gamma_1 + \gamma_2 - 4 \left[\frac{\gamma_1^d \gamma_2^d}{\gamma_1^d + \gamma_2^d} - \frac{\gamma_1^p \gamma_2^p}{\gamma_1^p + \gamma_2^p} \right] \quad (1)$$

where γ_{12} = the interfacial energy between phases 1 and 2 which each have a surface energy consisting of a polar (p) and dispersion (d) component.

A spreading coefficient of phase 1 over phase 2 (λ_{12}) and phase 2 over phase 1, can be calculated by taking the difference between the work of adhesion between the two phases and the work of cohesion of the phases that is being tested for spreading:

$$\lambda_{12} = 4 \left[\frac{\gamma_1^d \gamma_2^d}{\gamma_1^d + \gamma_2^d} + \frac{\gamma_1^p \gamma_2^p}{\gamma_1^p + \gamma_2^p} - \frac{\gamma_1}{2} \right] \quad (2)$$

$$\lambda_{21} = 4 \left[\frac{\gamma_1^d \gamma_2^d}{\gamma_1^d + \gamma_2^d} + \frac{\gamma_1^p \gamma_2^p}{\gamma_1^p + \gamma_2^p} - \frac{\gamma_2}{2} \right] \quad (3)$$

It follows that from a knowledge of the polar and dispersion components of the powders and the binders surface energies, it is possible to calculate the spreading coefficient of either phase over the other. In this work, the surface energy of a model solid (microcrystalline cellulose) has been determined and literature values for the surface energies of the binders have been used to predict spreading.

Rowe (1989) observed that for low polarity surfaces (e.g. griseofulvin) HPMC would be an

inappropriate choice of binder as spreading would not occur, but that PVP would be a good binder as a positive value was obtained for one of the spreading coefficients. For polar solids, this situation should be reversed, with HPMC being the binder of choice. In this work, HPMC, PVP and water are used as binders.

Materials and Methods

The materials used were MCC (Avicel PH101, FMC Corp., USA; Lot 6052), HPMC (Sigma), PVP (kollidon 17, BASF UK Ltd.), glycerol (Sigma), ethylene glycol (BDH), methylene iodide (Fluka, Switzerland) and decane (BDH, Analar). Water was purified by reverse osmosis and collected into clean glass bottles immediately prior to use.

Assessment of the surface energy of MCC

Compacts of the powder were prepared in a highly polished stainless steel punch and die assembly, which had the approximate dimensions of 5 cm length, 1 cm width and 0.8 mm thickness. The punch and die could be unbolted to allow easy removal of the compacts. The perimeter of the plates was measured using a micrometer.

The formed plates were suspended from an electronic microbalance (CI Electronics) and used as the plate in the manner of a surface tension measurement: a Wilhelmy gravitational method. The balance head and the suspended plate were housed in a perspex cabinet to allow the vapour to equilibrate with the sample.

The test liquids of known surface free energy (reverse osmosis water, methylene iodide, glycerol and ethylene glycol) were placed in a clean glass dish and raised by means of a motorised platform to contact the suspended powder plate. The balance was connected to a chart recorder and a typical trace is shown in Fig. 1, where AB is a baseline section prior to contact between the plate and the liquid; when the liquid reaches the plate a deflection is observed to point C. The platform continues to move up at the same speed and the line CD is produced. Any deviation from a straight line for CD represents either a change in contact

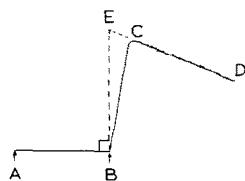


Fig. 1. A typical trace from the Wilhelmy plate apparatus. AB, baseline response prior to contact between the liquid and the plate. As the powder makes contact with the liquid a deflection is observed to point C. Continued raising of the liquid results in the production of line CD. Extrapolation of CD to the perpendicular to AB gives the true force (BE).

angle along the length of the plate, or a variation on the perimeter. Extrapolation of line CD to meet the perpendicular to AB, drawn at point B, gives the true displacement force (f) as BE. From this force measurement it is possible to obtain the contact angle (θ) for that particular liquid on the solid:

$$f = \frac{p \gamma_L \cos \theta}{g} \quad (4)$$

where p is the perimeter of the plate and g is the acceleration due to gravity. Water was the only liquid to cause deformation of the MCC plate.

Results quoted are averages from five separate plates.

As well as using this Wilhelmy plate technique, a contact angle was also determined by liquid penetration. The experimental technique was exactly as described previously (Buckton and Newton, 1985). Surface tensions were measured using the Wilhelmy plate technique, and viscosities were determined by use of U-tube viscometers and specific gravity bottles for densities.

The penetrating liquids were: water, 1.63, 2.04 and 6.00 % w/v aqueous solutions of PVP, and a 2.00% w/v aqueous solution of HPMC. Decane was arbitrarily selected as the perfectly wetting liquid (Buckton and Newton, 1985).

Preparation of the granules

Granules were prepared from either as received MCC or a sieved size fraction (Endecotts test sieve shaker for 30 minutes). The particle size of the powders was measured using a laser diffraction

technique (Malvern 2600C). The median size of the original powder was 72.5 μm , and for the 45–63 μm and 125–150 μm size fractions it was 66.2 and 175.8, respectively. It can be seen from these data that the original powder has a median particle size more like that of the small size fraction than the large.

Granulations were prepared using a planetary mixer (Kenwood Chef) which was operated at a constant speed (setting 2.5). The granulation process was controlled by dividing the granulating fluid into equal aliquots and adding each aliquot gradually over a 90 s period. This continued for the first 6 min of the process. A further 3 min of mixing was allowed, followed by 1 min of kneading at which stage the wet mass was forced through a screen (1 mm apertures) by hand and the resultant granules were dried in a fluid bed drier at 60 °C (Model FBD/L70, PRL Engineering Ltd., UK) until they reached constant weight. Granules were formulated to allow the study of the effect of

TABLE 1

The composition of the granulations used in this work

Particle size of powder (μm)	Weight of powder (g)	Quantity of binder solution (g)	Conc. of binder (%)
For PVP			
(1) 45–63	100	100.0	6.00(5.7)
(2) 45–63	200	200.0	6.00(5.7)
(3) 45–63	250	312.5	1.63(2.0)
(4) 45–63	250	250.0	2.04(2.0)
(5) 45–63	250	250.0	6.00(5.7)
(6) 125–150	100	100.0	6.00(5.7)
(7) *	250	250.0	2.04(2.0)
(8) *	250	250.0	6.00(5.7)
For HPMC			
(9) 45–63	250	250.0	2.04(2.0)
(10) 45–63	250	312.5	1.63(!)
(11) *	250	250.0	2.04(2.0)
For water			
(12) 45–63	250	250.0	–
(13) *	250	250.0	–
(14) *	250	312.5	–

Values in parentheses indicate % binder calculated as weight of binder added/total final dry weight, values not known for water; *, original unfractionated powder; !, formed a paste and could not be granulated.

starting particle size of the MCC, and the quantity, concentration and type of binder fluid added. Table 1 shows the composition of the batches of granules that were formed. The numbers given to each granulation in Table 1 will be used to describe each formulation in the discussion section.

Each batch of granules was then tested as follows.

Particle size analysis

The granules were sized by shaking the entire batch of granules in an Endecotts test sieve shaker for 15 min. Size fractions of less than 90, 90–125, 125–212, 212–355, 355–500, 500–710, 710–1000 and greater than 1000 μm were collected. For each sieve size range, the cumulative % undersize was plotted as a function of probability on a log-probability scale.

Density

The true density was measured using an air compression pycnometer (Beckman). Results are averages of four replicate determinations.

Bulk density

A loose bulk density was measured by gently and slowly passing 30 g of the sample through an 11.5 cm diameter (1 cm orifice diameter) short stemmed funnel into a 100 ml graduated cylinder. The orifice of the funnel had been aligned with the 100 ml mark on the cylinder. The volume occupied by the granulation was read to the nearest 0.5 ml and the bulk density recorded in g/ml. Results quoted are averages of three replicate determinations.

Tapped bulk density

The same sample used for the bulk density measurement was retained in the measuring cylinder and subjected to 100 taps in a mechanical tester which moved the sample through a vertical displacement amplitude of 1 cm. The results, which are averages of three replicates, are quoted as g/ml.

Angle of repose

The flowability of the granules was assessed by use of a purpose built angle of repose tester. The

sample was placed in a cylinder which covered a horizontal plate of diameter 2 cm. The apparatus was levelled by use of adjustable feet. The powder was allowed to escape from the cylinder by sliding a base support and the height of the granules that were retained on the circular horizontal support was measured by use of a travelling microscope.

Results quoted are averages of five determinations.

Friability

Approximately 10 g of a 355–500 μm fraction of granules, accurately weighed, were placed in a 350 ml wide mouthed jar, together with 10 plastic balls of 2.0 cm diameter with an average weight of 1.015 g. The jar was then placed in a rotating shaker mixer (Turbula T2C, W A Bachofern, Basel, Switzerland) for 20 min. The abraded samples were sieved on a 250 μm mesh sieve for 2 min. The amount retained on the sieve was weighed and the friability percentage was calculated [(weight passing through the sieve/total weight) $\times 100$].

Results and Discussion

Contact angle, surface energies and spreading coefficients

The Wilhelmy plate results proved to be extremely reproducible for water, glycerol and ethylene glycol, with a total range of $\pm 1^\circ$. This is particularly encouraging as contact angles this low (20° and below) are extremely difficult to measure by sessile drop techniques. The results for methylene iodide showed more variation, in the region of $\pm 6^\circ$. Table 2 shows the mean values of the contact angle obtained for the various liquids on the MCC plates, together with the polar and dispersion components of the surface energies of the liquids that were used.

By using the contact angle data for any two liquids of known surface energy and polarity it is possible to calculate the surface energy of the solid (as described by Zografi and Tam, 1976). Table 3 shows the values obtained for the surface energy and its polar and dispersion forces, calculated using each combination of the liquid pairs.

TABLE 2

The contact angles obtained for MCC using the Wilhelmy plate technique, and the surface energies of the liquids used

Liquid	$\cos \theta$	Surface free energy (mN/m)	Dispersion component (mN/m)	Polar component (mN/m)
Water	0.930	72.0	23.2	48.8
Glycerol	0.954	63.7	32.0	31.7
Ethylene glycol	0.957	48.9	33.4	15.5
Methylene iodide	0.652	50.4	50.4	0

(Surface free energy values from Zografi and Tam (1976))

Both the harmonic and geometric mean values have been calculated. The values for the surface energy of MCC are dependent upon the choice of the liquids used in their calculation; this is not an unusual finding (e.g. Zografi and Tam, 1976). Despite the variation in the values of surface energies, the calculated spreading coefficients (Table 4) show the same predictive trends irrespective of the liquids used in the calculations.

From the data presented in Table 4 it is possible to make the prediction that HPMC will be the binder of choice for MCC. PVP is not going to

spread over the MCC and neither is the MCC going to spread over the PVP, if the geometric data is considered, but the harmonic mean data leads to the conclusion that even though both binders may spread over the MCC, the HPMC will be preferred. The PVP will therefore, be a comparatively poor binder. It would also be predicted that the interaction between water and MCC will be of a different type, with the MCC attempting to spread over the water.

Liquid penetration

Wells and Walker (1983) argued that liquid penetration is the technique of choice for assessing the wettability of powders when considering granulation, because it is analogous to the addition of water in a planetary mixer during wet massing. The results in Table 5 show that particle size does not alter the contact angle to any significant effect. HPMC has a higher contact angle than that of PVP, suggesting the inverse of the result indicated by the Wilhelmy plate technique.

Granule assessment

Angle of repose The differences between the angles of repose that were measured for the vari-

TABLE 3

The surface energies of the binders used, and the calculated surface energies for MCC obtained by solving the equations using different combinations of the liquid pairs

	Liquids used	Surface free energy (mN/m)		Dispersion component (mN/m)		Polar component (mN/m)	
		A	B	A	B	A	B
PVP ^a	—	53.6		28.4		25.2	
HPMC ^b	—	48.4		18.4		30.0	
MCC	water						
MCC	methylene iodide	69.2	71.4	34.4	35.5	34.8	36.0
MCC	glycerol						
MCC	methylene iodide	61.0	61.5	34.4	35.5	26.6	26.0
MCC	ethylene glycol	47.5	47.3	34.4	35.4	13.1	11.9
MCC	methylene iodide						
MCC	water/glycerol	68.9	67.3	12.4	19.2	56.5	48.1
MCC	ethylene glycol						
MCC	glycerol	80.7	67.3	5.6	19.2	75.1	48.1
MCC	ethylene glycol						
	water	71.9	67.3	8.1	19.2	63.8	48.1

^a Data from Krycer et al. (1983); ^b data from Rowe (1989); A, calculated using a geometric mean approach; B, calculated using a harmonic mean approach.

TABLE 4

Spreading coefficients of MCC over binder (λ_{12}) and the binder over MCC (λ_{21}), calculated using the different values of the surface energy of MCC presented in Table 3

Liquids used to calculate MCC surface energy	Binder	λ_{12}		λ_{21}	
		A	B	A	B
Water/glycol	PVP	-46.3	-22.6	-9.8	4.8
Water/glycerol	PVP	-33.5	-22.6	-2.9	4.8
Water/methylene iodide	PVP	-17.7	-20.4	13.4	15.2
Glycerol/methylene iodide	PVP	-8.8	-8.7	7.2	7.1
Glycol/glycerol	PVP	-67.2	-22.6	-12.9	4.8
Water/glycol	HPMC	-39.8	-22.6	7.1	14.7
Water/glycerol	HPMC	-29.8	-22.6	11.2	14.7
Water/methylene iodide	HPMC	-26.0	-29.0	15.6	16.2
Glycerol/methylene iodide	HPMC	-18.8	-18.0	7.6	7.2
Glycol/glycerol	HPMC	-58.5	-22.6	6.2	14.7
Water/glycol	water	-9.4	4.2	-9.5	-5.2
Water/glycerol	water	-0.7	4.2	-6.9	-5.2
Water/methylene iodide	water	-23.2	-3.9	-28.8	-5.1
Glycerol/methylene iodide	water	+1.1	-0.3	-19.7	-49.7
Glycol/glycerol	water	-65.8	4.2	-48.2	-5.2

A, calculated using the geometric mean data; B, calculated using the harmonic mean data.

ous granulations (Table 6) seem to be rather small; however, there is a good correlation with the percentage friability. A high value for angle of repose is noted when a high percentage friability exists. A value of less than 39° for angle of repose always corresponds with a very low friability (around 10%).

Angle of repose is not generally regarded to be a good indicator of differences in granule properties, but the results here suggest it has some value.

Effect of weight of sample used With the granules that were prepared using PVP as the binder, weights of 100, 200 and 250 g of powder were used (formulations 1, 2 and 5, respectively from Table 3) whilst the volume of binder fluid was kept at a constant proportion to the powder weight and of constant strength. The results (Table 6) show that the low volumes of fill in the mixer produce granules with a higher percentage friability, indeed, sample 1 (100 g of powder) resulted

TABLE 5

Values for the surface tensions and viscosities of the penetrating liquids, together with the results for rate of penetration (gradient of distance of penetration squared as a function of time) and calculated apparent contact angles, for MCC 45–63 μm powder and the as received powder

Liquid	Surface tension (mN/m)	Viscosity (mN s/m)	45–63 μm		Original	
			grad.	θ	grad	θ
Water	70.4	1.000	0.150	69.2	0.115	69.2
PVP						
1.63%	60.8	1.022	0.143	66.4	0.109	66.5
2.04%	60.5	1.056	0.135	66.9	0.101	67.5
6.00%	60.7	1.440	0.085	70.4	0.061	71.6
HPMC						
2.00%	50.7	69.422	9.3 E-4	77.9	6.9E-4	78.2

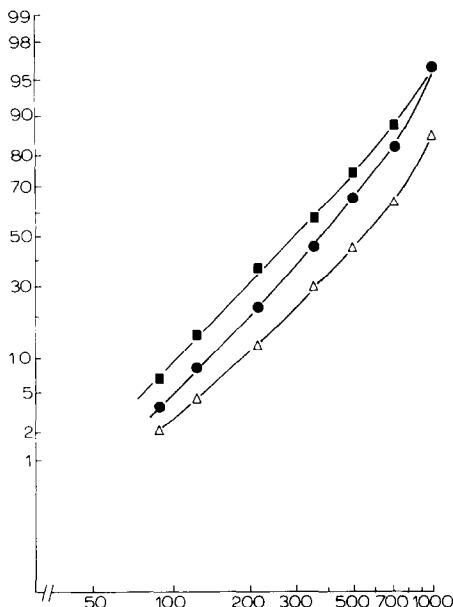


Fig. 2. The particle size distributions of the formed granules, showing the effect of weight of fill of the mixer. x-axis log size; y-axis probability. Δ formulation 1 (100 g load); \blacksquare formulation 2 (200 g load); \bullet formulation 5 (250 g load).

in granules with a low bulk and tapped bulk density, presumably demonstrating poor kneading and that the energy transferred from the mixer was inadequate.

From Fig. 2 it can be seen that formulation 1 resulted in larger granules than those produced from the two formulations that were prepared with larger quantities of powder (formulations 2 and 5), this is reflected in the bulk density value.

Particle size of the MCC The effect of altering the initial particle size of the MCC is demonstrated by comparing formulations 1 (100 g of 45–63 μm) and 6 (100 g of 125–150 μm), where it is clear that number 1 produces weaker and less uniform granules with higher friability and angle of repose, and lower bulk and tapped bulk density, this is despite the fact that the particle size distributions of the granules produced from these different sized powders are indistinguishable (Fig. 3). Even though the quantity of fill into the mixer is equally low, formulation 6 has a higher bulk density than formulation 1, which may demonstrate that the difference in surface to mass ratio is a significant factor in binder distribution. A com-

parison of formulations 5 (250 g of 45–63 μm) and 8 (250 g of original) shows that the trends observed when considering formulations 1 and 6 are repeated despite the increased quantity of powder used in the preparation of formulations 5 and 8. Formulation 8 (made with the powder as received) has a slightly lower friability than the comparable granulation made with the 45–63 μm powder (formulation 5).

The effect of starting particle size on granule properties can also be investigated for systems in which HPMC and water were used as the binder. Between formulations 9 (250 g of 45–63 μm) and 11 (250 g of original), where HPMC, and samples 12 (250 g of 45–63 μm) and 13 (250 g of original) where water is the binder, only the size of the MCC has been changed. As with the samples granulated with PVP that have been discussed above, the granules made from the larger particles

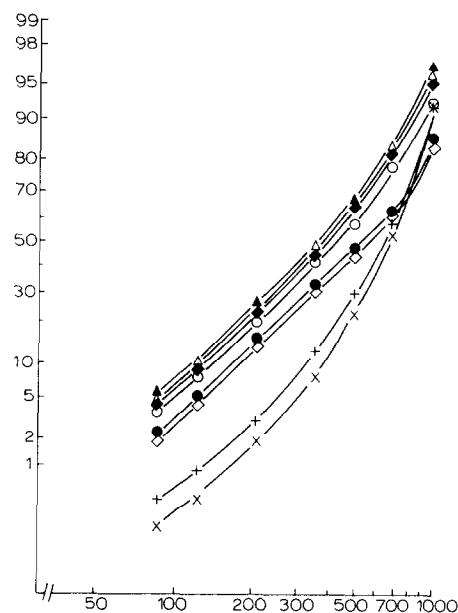


Fig. 3. The particle size distributions of the formed granules, showed the effect of starting particle size of the powder. (x) log size; (y , probability). Formulation number as given in Table 3 (powder size, weight of powder, binder). \bullet , formulation 1 (45–63 μm , 100 g, 6% PVP); Δ , formulation 5 (45–63 μm , 250 g, 6% PVP); \diamond , formulation 6 (125–150 μm , 100 g, 6% PVP); \circ , formulation 8 (original, 250 g, 6% PVP); $+$, formulation 9 (45–63 μm , 250 g, HPMC); \times , formulation 11 (original, 250 g, HPMC); \blacklozenge , formulation 12 (45–63 μm , 250 g, water); \blacktriangle , formulation 13 (original, 250 g, water).

have a lower percentage friability. The size distributions of the formed granulations are similar and converge at the larger particle sizes (Fig. 3).

The effect of changes in the powder particle size shows that for the preferred binder (HPMC) only a very small change in friability is observed, whereas for a less suitable binder (PVP) the stress put on the formulation by increasing the surface area to weight ratio is demonstrated by significant differences in granule properties.

The concentration of binder used

When PVP was used as the binder, the effect of two different concentrations were studied (2 and 6%). This was not possible with HPMC as high viscosity limited the concentration range. Formulations 4 and 5 are identical except for the concentration of PVP used. The bulk and tapped bulk density terms are similar for the two formulations, but the formulation with the higher concentration of binder has the highest friability, suggesting that

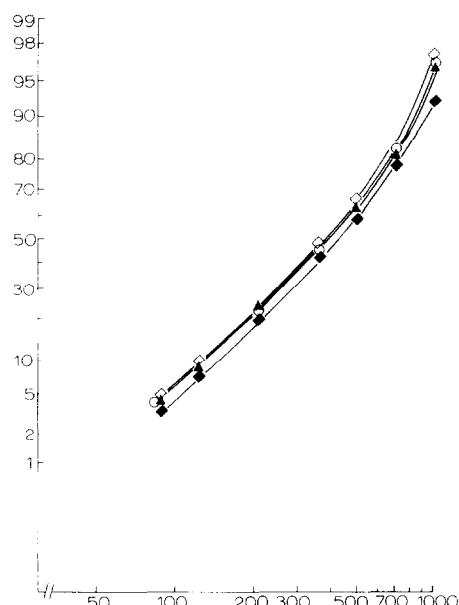


Fig. 4. The particle size distributions of the formed granules, showing the effect of the concentration of binder used (x log size; y probability). Powder size, powder weight, binder strength: \blacktriangle formulation 4 (45–63 μm , 250 g, 2% PVP); \circ formulation 5 (45–63 μm , 250 g, 6% PVP); \diamond formulation 7 (original, 250 g, 2% PVP); \blacklozenge formulation 8 (original, 250 g, 6% PVP).

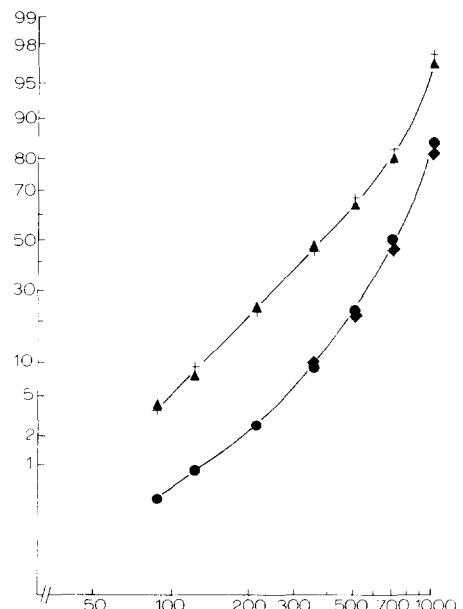


Fig. 5. The particle size distributions of the formed granules, showing the effect of changes in volume of binder solution (x log size; y probability). Powder size, powder weight, binder, weight of binder: \bullet formulation 3 (45–63 μm , 250 g, 2% PVP, 312.5 g); \blacktriangle formulation 4 (45–63 μm , 250 g, 2% PVP, 250 g); $+$ formulation 13 (original, 250 g, water, 250 g); \blacklozenge formulation 14 (original, 250 g, water, 312.5 g).

the presence of larger quantities of binder decreases granule strength. The size distributions of these two formulations are shown in Fig. 4, and are indistinguishable from each other. This situation is also observed for formulations 7 and 8 (2 and 6% PVP respectively, 45–63 μm size).

The volume of the binder solution

The volume of the binder solution has been changed, with simultaneous alteration in concentration such that the final dried weight of binder will be the same. For example, formulation 3 was prepared using 312.5 g of binder solution of concentration 1.63% such that when dried the concentration of PVP (calculated as added PVP/total weight of MCC + PVP expressed as a percentage) was 2.00%. Equally formulation 4 contained 250 g of a 2.04% solution of PVP which when dried equated to 2.00% of total dry weight. On this basis it is possible to effect a comparison between formulations 3 and 4 and from Table 6.

the larger volume of solution is much more effective in terms of reducing the friability, furthermore, the granules formed with the larger volume are of a much larger size (Fig. 5).

The quantity of water needed to produce monolayer coverage on the surface of MCC is about 3% (Zografi et al., 1984). The quantity of binder solution used here should be more than adequate to cover the surface with multilayers of sorbed water and/or binder, the improvement in performance shown on increasing the quantity of binder fluid added must be due to increased distribution and hence availability of the fluid, rather than the fact that the lower quantities are inadequate to cover the surface and perform a binding function.

When using water alone, (13 = 250 ml and 14 = 312.5 ml) the high liquid content again produced granules with a much lower friability (9.6 compared to 25.7%) and once again the size of the granules produced with a large volume of solution was significantly greater (Fig. 5).

General Discussion

Changes in the particle size of a powder, the binder used, the concentration and the volume of the binder solution all alter the properties of the granules that are produced.

The predictive test based upon spreading coefficients indicating that HPMC would be better as a binder for MCC. The results presented in Table 6 show that granulations made with HPMC are less friable, have the better flow properties and have higher bulk and tapped bulk densities than granules made using PVP or just water as the binder. The granules produced using HPMC as the binder are also of larger particle size than most of the other granules that were produced (see Fig. 3).

When PVP or water were used as the binding agent it was possible to produce granules of similar quality to those that resulted from granulations with HPMC (for example, formulations 3 and 14),

TABLE 6

The density, bulk density, tapped bulk density, angle of repose and friability of the granulations (formulation numbers refer to Table 1)

Formulation	Density (g/ml)	Bulk density (g/ml)	Tapped bulk density (g/ml)	Angle of repose (°)	Friability (%)
For PVP					
1	1.532	0.366	0.416	43.2 ± 2.9	57.6 (+)
2	1.523	0.455	0.509	42.8 ± 1.9	53.6 (0.8)
3	1.542	0.510	0.573	37.4 ± 1.4	10.0 (1.1)
4	1.530	0.444	0.509	41.5 ± 0.8	40.6 (2.0)
5	1.516	0.444	0.504	40.6 ± 2.0	44.5 (1.3)
6	1.529	0.403	0.462	40.7 ± 1.9	47.9 (+)
7	1.540	0.462	0.515	38.6 ± 7.0	34.6 (0.7)
8	1.522	0.446	0.511	42.3 ± 2.0	42.0 (1.7)
For HPMC					
9	1.527	0.579	0.657	38.8 ± 0.7	10.2 (0.8)
10	*	*	*	*	*
11	1.534	0.548	0.619	38.7 ± 0.1	9.8 (0.3)
For water					
12	1.546	0.433	0.500	43.2 ± 1.4	36.6 (0.6)
13	1.531	0.483	0.544	39.8 ± 3.2	25.7 (2.0)
14	1.523	0.525	0.601	38.8 ± 2.2	9.6 (0.2)

* Produced a solid mass which would not granulate. (+) Only one measurement, for other samples % friability (± S.D.). Standard deviations for density and bulk density values all in the order of ± 0.004.

but this was only under the most advantageous conditions. When similar formulations are compared HPMC is indeed the best binder that has been tested for this powder. It also appears that different formulations prepared using HPMC as the binder (formulations 9 and 11) result in products that are far less likely to show variation than those prepared when PVP or water are used.

The prediction that HPMC would be the binder of choice seems accurate.

Liquid penetration experiments do not correlate with the predictions that were made using the Wilhelmy plate technique or with the behaviour of the respective binders.

Conclusions

The results for the spreading coefficients that were calculated for HPMC, PVP and water with MCC indicated that HPMC would be the binder of choice. The results presented in this work confirm this prediction.

The necessary practical work to allow the calculation of the surface energy of a powder (or indeed powder mix) using a compressed beam of powder and the microbalance can be carried out in a short period of time, and with a suitable computer programme, results can be calculated immediately. It should be possible to optimise the formulation (with respect to binder selection) without the need to make and test the granules.

Further work is required to study the extent of applicability of this predictive method.

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