J. Pharm. Pharmacol. 1980, 32: 386–388 Received November 22, 1979

The granulation of ternary mixtures: the effect of the wettability of the powders

K. T. JAIYEOBA† AND M. S. SPRING*

Department of Pharmacy, University of Manchester, Manchester M13 9PL, U.K.

Granules have been prepared by a standard method from ternary mixtures of lactose, boric acid and either sulphanilamide, heavy kaolin or salicylic acid, using an aqueous solution of polyvinylpyrrolidone as binder. The granules were examined for size distribution and for the work required to crush larger granules from each batch. For the same binder volume the mean granule sizes and resistance to crushing of the granules increased as the wettability of the third component increased. The detailed results are discussed in relation to powder wetting and the packing properties of powder mixtures.

The first stage in the process of granulation is the wetting of the powder mixture (Carstensen et al 1976), how this is achieved will affect the uniformity of moisture distribution and thus the properties of the final granules. Hunter (1972), using single powder systems, found that the amount of liquid required to form satisfactory granules from different grades of lactose was inversely related to the mean particle size. In multi-component systems the proportion of each component can be varied, affecting both packing and wetting, and these can have a significant effect on the nature of the granules produced.

In the present investigation the effects of wetting ternary powder mixtures were examined in relation to the properties of granules. For this purpose blends of lactose with boric acid and third components of differing aqueous wettability and particle size were used. The third component replaced an equal weight of the appropriate lactose: boric acid blend. The hydrophilicity of this blend alters as the proportion of lactose content varies from 90%–10%. To minimize the effects of solubility three materials were chosen with low water solubility but differing greatly in their affinity for water: they were sulphanilamide, heavy kaolin and salicylic acid.

MATERIALS AND METHODS

The mean particle sizes and true densities of the powders used were determined as previously reported (Jaiyeoba & Spring 1979) and had the values: lactose B.P. (BDH) 31 μm, 1·54 g cm^{-3}; boric acid B.P. (BDH) 12·6 μm, 1·51 g cm^{-3}; heavy kaolin B.P. (BDH) 1·7 μm, 2·54 g cm^{-3}; sulphanilamide (BDH) 21·1 μm, 1·51 g cm^{-3}; salicylic acid (Fisons Scientific Apparatus, England) 23·0 μm, 1·40 g cm^{-3}.

The kaolin, sulphanilamide and salicylic acid powders were individually mixed with blends of lactose and boric acid, and granules were prepared from 1 kg of the blended powders using a 5% w/v aqueous solution of polyvinylpyrrolidone PVP, (Plasdone K29–32. GAF, U.K. Ltd.) as binder. The methods of granulation and determination of granule properties were as described (Jaiyeoba & Spring 1979). An example of a granulation would be lactose 81%, boric acid 9%, kaolin 10% to give 1 kg, granulated with 150 g of the binder solution.

RESULTS AND DISCUSSION

The results of the size analyses of the various batches of granules prepared are given in Tables 1 and 2. The results of tests to determine the work required to crush granules taken from the 1·4–1·2 mm size fractions are listed in Table 3.

Examination of these results indicates a very complex pattern of behaviour due to the fact that changing the third component changes the wettability, packing, solubility, density and surface area of the powder bed which is to be granulated. The components differed in aqueous wettability; the contact angles are kaolin 0°, lactose 30°, sulphanilamide 64°, boric acid 74°, salicylic acid 103°. These values give an indication of the ease of wetting with water. The surface tension of the PVP solution was 45 mJ m^{-2}, as determined by the drop weight technique. It would therefore be anticipated that with this solution the contact angles will be reduced, but the order of wetting will be retained.

* Correspondence.
† Present address: Department of Pharmaceutics, University of Ife, Ile-Ife, Nigeria.

Table 1. Size distributions of granules prepared using 15% w/w binder solution expressed as percentage finer than the stated sieve size.

Lactose : boric acid ratio blend	Two component 1·4	1·2	1·0	710	500	355	210	180	75
90:10	100	79·8	46·9	34·0	28·0	22·8	18·0	13·7	4·7
75:25	100	68·8	32·4	21·9	17·0	12·0	8·2	5·1	0·9
50:50	100	75·9	39·3	21·9	16·4	11·4	7·0	3·9	0·8
10:90	100	99·2	93·2	75·0	55·7	43·8	32·5	18·2	0·8
	Kaolin as third component								
90:10	100	33·1	13·7	7·0	4·5	3·1	2·3	1·8	1·2
75:25	100	42·5	21·2	13·1	9·0	5·8	3·9	3·9	1·5
50:50	100	65·1	33·5	17·6	12·3	8·2	5·2	3·1	1·0
10:90	100	98·9	91·4	65·7	61·4	49·5	37·3	20·2	2·7
	Sulphanilamide as third component								
90:10	100	66·0	41·4	28·8	22·0	16·2	11·9	8·3	2·9
75:25	100	65·4	44·2	33·2	27·6	22·1	17·2	12·3	3·9
50:50	100	72·6	43·3	27·6	21·9	16·5	11·4	7·2	1·9
10:90	100	99·2	86·9	67·0	52·8	43·2	32·3	19·3	2·7
	Salicylic acid as third component								
90:10	100	61·4	34·1	25·8	32·8	19·1	15·2	11·2	4·1
75:25	100	91·6	59·2	38·6	32·0	24·9	18·6	12·2	3·0
50:50	100	97·0	74·5	49·0	38·2	30·0	22·3	15·2	5·3
10:90	100	99·9	91·6	74·2	61·6	52·6	45·5	36·3	11·6

The effect of kaolin as third component

The kaolin used was very readily wetted and had a small mean particle size. Its chief effect was to produce granules of greater resistance to crushing than those made without a third component. The granules were also larger than the control granules except when made with the 10:90 lactose : boric acid blend. As kaolin is practically insoluble in water, the increase in granule strength must be the result of closer packing of the component particles. This could result from the smaller, kaolin, particles going into the voids between the lactose and boric acid particles. Alternatively, the kaolin particles could promote closer packing of the larger particles. In the latter case, this will be the result of better wetting increasing the total inter-particulate cohesion by the formulation of more pendular bonds within the damp mass. Closer packing will also result in the formation of larger granules provided sufficient liquid is available to produce the damp granule mass. The mean size diminishes with increasing boric acid content, and reduction in binder volume results in smaller granules for all blends; indeed, at 10% binder for the 10:90 lactose : boric acid blend, the bed was too dry to granulate.

The effect of sulphanilamide as third component

The results of replacing 10% of the lactose : boric acid blend with sulphanilamide were small. The contact angle of sulphanilamide lies between those of lactose and boric acid, as did the mean particle size of the material used in this work. The replacement of 10% boric acid by sulphanilamide in binary mixtures with lactose gave granules with similar sizes and strengths, as measured by the work required to crush them (Opakunle & Spring 1976). Components

Table 2. Mean granule size of blends containing lactose, boric acid and 10% of different third components using various binder concentrations.

	Mean granule size (μm)									
Third component	Control*		Kaolin			Sulphanilamide			Salicylic acid	
% w/w binder	15	10	12·5	15	10	12·5	15	12·5	15	17·5
Lactose : boric acid										
90:10	1050	560	1150	1300	710	800	1100	660	1100	1150
75:25	1180	330	1000	1200	620	900	1050	600	880	1200
50:50	940	280	600	1150	360	840	1050	420	720	1100
10:90	410	—	240	360	—	380	450	280	320	500

* Control. Binary blends of lactose : boric acid.

Table 3. Mean work required to crush granules from blends containing lactose, boric acid and 10% of different third components granulated with 15% w/w PVP binder solution,

Lactose: boric acid ratio	Mean work required to crush granules ($\times 10^4$ J)			
	Control*	Kaolin	Sulphanilamide	Salicylic acid
90:10	6·27 ± 1·22	7·55 ± 0·88	6·76 ± 1·13	3·79 ± 0·50
75:25	6·20 ± 0·80	7·69 ± 1·04	7·09 ± 0·87	5·90 ± 0·52
50:50	4·47 ± 0·61	6·54 ± 0·86	4·58 ± 0·50	5·36 ± 0·57
10:90	3·30 ± 0·36	3·36 ± 0·58	3·33 ± 0·48	3·98 ± 0·52

* Binary mixture of lactose and boric acid.

can therefore, be substituted without changing the size and strength of the granules, if their physical properties are similar.

The effect of salicylic acid as third component

Salicylic acid is not wetted by water and replacement of 10% of the lactose: boric acid blend with it resulted, in general, in smaller granules, which were weaker than the control granules for the 90:10 and 75:25 blends but stronger for the 50:50 and 10:90 blends. The salicylic acid used had a similar mean size to the sulphanilamide, and both form acicular crystals, so that the packing properties should be similar. It would appear therefore that as the proportion of lactose falls below 50%, poorer wetting results in smaller granules but the improved packing causes them to have a greater resistance to crushing.

DISCUSSION

The results show that granule properties are altered by changing the wettability of a component present at only the 10% level. The wettability of the powders will influence the distribution of the binder liquid over their surfaces, and processes such as dispersion and dissolution can only take place after a sufficient degree of wetting has occurred. Thus, in wet granulations, after sufficient massing, liquid bridges are formed, which hold the particles together by surface tension. The tensile strength of a granule in this state has been related by Rumpf (1958) to the contact angle between the solid and the liquid by:

$$\text{Tensile strength} = 6 \frac{(1-\epsilon)}{(\ \epsilon\ )} \frac{T}{d} \cos\theta$$

d = particle diameter, ϵ = void fraction, T = surface tension of the liquid θ = contact angle.

This equation gives a measure of the strength of the damp granules. Their dry strength will depend largely on the strength of the bonds formed by the drying of the liquid bonds, which results in the deposition of any dissolved materials. In the present case the bonds will contain PVP, lactose and boric acid with only minute proportions of the third components. As the amount of the soluble components is the same in all the granulations, differences in hardness measured by resistance to crushing must be due to differences in the natures of the damp granules and the liquid bonds formed during massing. From the equation of Rumpf, given above, a powder with a low contact angle with water would give strong damp masses, and kaolin is an example of such a powder. The presence of kaolin at 10% in the lactose: boric acid blends gives granules that, after drying, are resistant to crushing and have a large mean size. In contrast, salicylic acid is hydrophobic and gives smaller, weaker granules. The third component must therefore affect the damp granule in such a way that its effect is also seen in the properties of the dried granule. This can either be by the formation of liquid bonds that dry to give weak intragranule bonds or by affecting the packing of the particles such that more open granular structures are formed which yield weaker dry granules.

Thus fine particle hydrophils result in stronger, larger granules being formed and coarser hydrophobes result in the production of weaker granules. The properties of granulations can therefore be altered by the substitution of some 10% of the granulation with an excipient chosen to produce the desired effect.

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