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EVALUATION OF SOME PROPERTIES OF POWDER MIXTURES

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ABSTRACT

Following previous work on the relation between tablet weight variation and the measured flow properties of direct tabletting vehicles, a study was made on binary powder mixtures. Two different tablet vehicles were used, Dipac and lactose while the added drug was fine aspirin.

Flow properties of various mixtures (up to 40% aspirin by weight) were measured in a Flow Factor Tester and tablet weight variation was also established. It was found that little inter-relationship exists between the shear cell parameters (flow factor and effective angle of friction) and the coefficient of tablet weight variation. It is suggested that one reason for the lack of correlation is the mixtures are complex and in addition have angles of friction which vary considerably with consolidating load.

INTRODUCTION

The need for more study on factors affecting the flow properties of mixtures of powders has been emphasised by Kocova and Pilpel (1,3,3) because mixtures rather than pure powders are more generally used in pharmaceutical manufacture. In studies of failure properties (1,3), tensile strength (2,3,4,5) apparent particle diameter, packing fraction and angle of internal flow (4,5) of mixtures of fine powders anomalies were observed in that rarely was the value of the property proportionally intermediate between that of its constituents. The results are generally ascribed to changes in the packing arrangements of particles on admixture (4). Mixtures also can frequently show 'complex' rather than 'simple' failure.

The use of mixtures of a fine drug powder with a coarse diluent has been suggested in pharmaceutical practice as they frequently form an ordered mixture possessing good homogeneity (6,7). However few studies appear to have been made of the shear properties and flowability of such mixtures particularly in relation to the properties of the pure components. It has been suggested previously that the shear cell can predict the flowability of powder during tabletting (8) and it is the purpose of this paper to examine the usefulness of shear cell parameters in describing the behaviour of powder mixtures.

EXPERIMENTAL

Materials

The drug used was aspirin (Prosana, Australia) and the diluents were Dipac, a sucrose/dextrin co-crystallisation prodcut (Amstar, U.S.A.) and spray-dried lactose (Wyndale, N.Z.). The particle density of aspirin was taken as 1.35 g.m., $^{-1}$ Dipac as 1.52 g.ml^{-1} (9) and lactose as 1.54 g.ml^{-1} (9). The particle size distributions determined by vibrational sieving and air-jet sieving are represented as log-probability plots in Fig. 1.

Methods

Mixing

Approximately 1 Kg lots were mixed for one hour in an Erweka stainless steel cube mixer (capacity 8ℓ) rotating at 20 rpm. This mixing time had been established in preliminary mixing studies.

Bulk Density and Porosity

These values were determined from the weight of powder filling a 100m. graduated cylinder after filling via a funnel. Porosity (ε) was calculated from $\varepsilon = \frac{\rho - \rho_\beta}{\rho}$ .....(1)

where ρ is the true density of the solid and ρ_β is the bulk density.

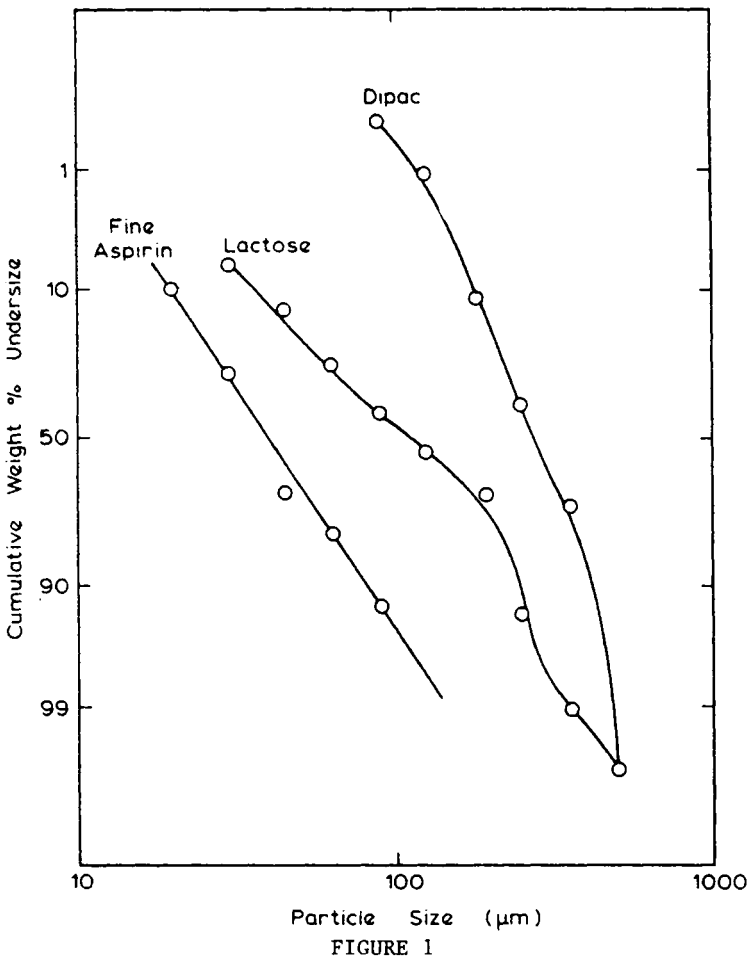


FIGURE 1

PARTICLE SIZE DISTRIBUTION

Shear Cell Studies

Values for the reciprocol of flow factor, 1/FF, and the effective angle of friction, δ, under normal consoliditing stresses of 31.3 gcm $^{-2}$, 50.5 gcm $^{-2}$ and 88.8 gcm $^{-2}$ were determined using a Jenike shear cell as described previously (9). The porosity of the powder bed under each consolidating stress was estimated from volume and weight measurements.

Tablet Compression

To each mix, 1% magnesium stearate was added as a lubricant. Tablets were compressed on a Manesty SP1 single punch tablet machine producing 3600 tablets/hour using 10mm punches at constant die volume. Compression was allowed to proceed before tablets were collected. Samples of 100 tablets were weighed and the coefficient of variation (CV) of weight estimated.

RESULTS AND DISCUSSION

Values for bulk densities and porosities for Dipac containing up to 40% aspirin and lactose containing up to 30% aspirin are summarised in Table 1. The sample of aspirin had the low loose poured bulk density of 0.37 corresponding to a porosity of 0.73 and therefore it might be expected that on its addition to the coarse powder porosity would increase according to the formula

$$\text{Porosity of mixture} = x\,\varepsilon_x + y\,\varepsilon_y \quad \ldots.(2)$$

where x and y are the proportions of each component and ε_x and ε_y their corresponding porosities. Such estimates are included in Table 1 for comparison. Although the porosities of the lactose/aspirin mixtures correspond to those predicted this was not true for the Dipac/aspirin mixtures. Addition of up to 30% aspirin did not cause any increase in porosity which even decreased slightly. Only after addition of 40% aspirin did porosity increase. This can be explained on the basis of ordered mixing of aspirin and Dipac (6,7). The aspirin is adsorbed onto the surface of the course. Dipac particles causing

TABLE 1

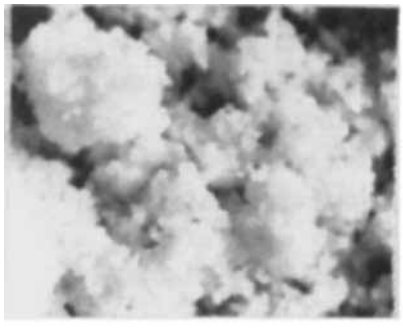
Bulk Density Data of the Powders

Material	True Density	Consolidating Stress g/cm^2 (Loose Poured) Bulk Density	Actual	Predicted	31.3 Bulk Density	50.5 Bulk Density	88.8 Bulk Density
Dipac	1.52	0.66	57	57	0.82	0.82	0.83
Dipac + 10% Aspirin		0.67	55	59	0.85	0.84	0.86
Dipac + 20% Aspirin		0.65	56	60	0.89	0.90	0.90
Dipac + 30% Aspirin		0.64	56	62	0.95	0.94	0.93
Dipac + 40% Aspirin		0.57	60	63	0.92	0.92	0.94
Lactose	1.54	0.68	56	56	1.01	1.01	1.09
Lactose + 10% Aspirin		0.65	57	58	1.02	1.02	1.05
Lactose + 20% Aspirin		0.62	59	59	0.96	0.96	0.99
Lactose + 30% Aspirin		0.58	61	61	0.94	0.94	0.95
Aspirin	1.35	0.37	73	73	0.74	0.74	0.80

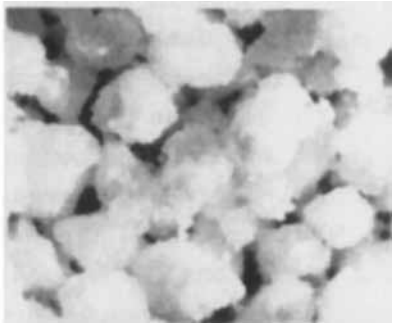
little change in porosity. This phenomenon has been observed by Gunning and Stead (10). On addition of up to 30% fine calcium carbonate to 20-40# starch/lactose granules bulk density was increased. Although calcium carbonate has a high true density ($2.93\ g.ml^{-1}$) this increase is probably greater than would be predicted from simple weight and volume considerations. They confirmed their suspicions of adsorbtion of fines by demonstrating that the mixture did not segregate.

Photomicrographs of the Dipac/Aspirin mixtures shown in Figure 2 suggest that in systems containing up to 30% aspirin most of it is concentrated around the coarse Dipac particles leaving little free in the voids of the mix. From considerations of the surface area of the Dipac particles accommodation of up to 30% aspirin suggests that adsorbtion is multi-layer rather than just mono-layer. From photomicrographs of the lactose/aspirin system (Fig. 3) it appears that no ordered mixing occurs which may explain why the porosities found experimentally are similar to those predicted. It has been demonstrated previously that there are size requirements for ordered mixing to occur (7,10) and therefore the lactose particles are probably too small to accommodate adsorbed aspirin.

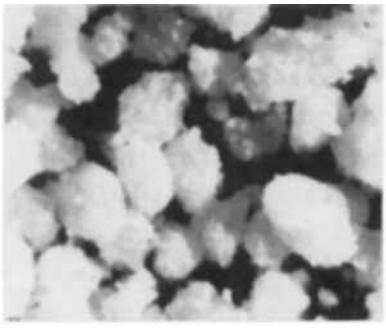
Table 2 summarises shear cell data for the various mixtures of aspirin with either Dipac or lactose together with the corresponding mean tablet weight and tablet weight variation data. It can be seen immediately that there is little interrelationship that can be established between the shear cell parameters 1/FF and δ and the coefficient of tablet



Dipac

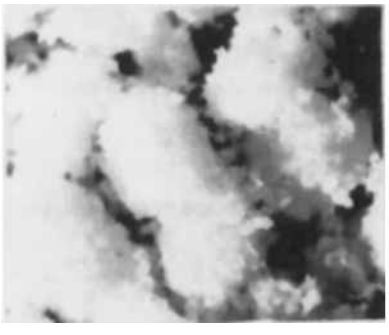


Aspirin

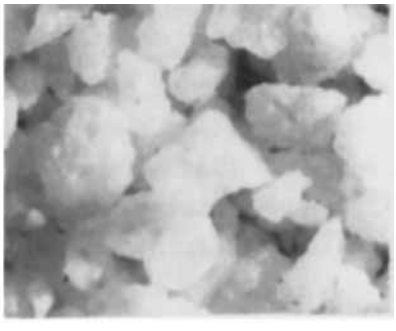


Dipac + 10% Aspirin

Dipac + 20% Aspirin



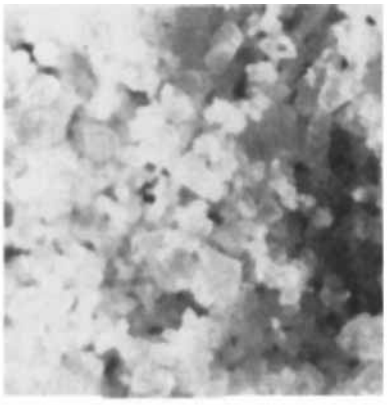
Dipac + 30% Aspirin



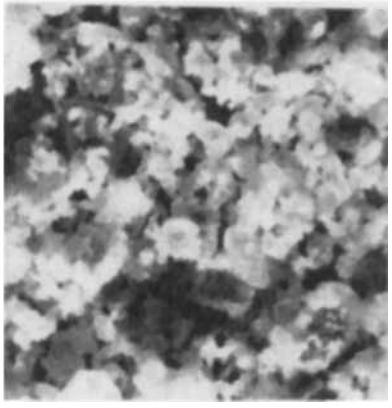
Dipac + 40% Aspirin

FIGURE 2

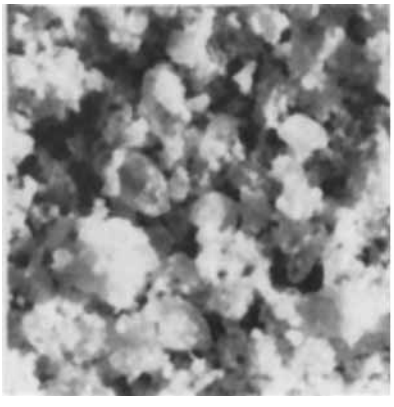
PHOTOMICROGRAPHS OF DIPAC MIXTURES



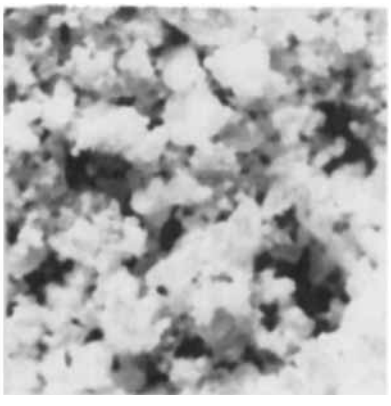
Lactose



Lactose + 10% Aspirin



Lactose + 20% Aspirin



Lactose + 30% Aspirin

Scale for figures 2 and 3

1mm

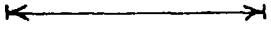


FIGURE 3

PHOTOMICROGRAPHS OF LACTOSE MIXTURES

TABLE 2

Shear Test Data and Tablet Weight Variation

Material	Flow Factor FF			Effective Friction Angle δ			CV%	Mean Tablet Weight mgm
	Consolidating Load			Consolidating Load				
	31.3	50.5	88.8	31.3	50.5	88.8		
Dipac	-	>20	>20	-	37	37	1.88	439
Dipac + 10% Aspirin	>20	>20	>20	33	33	35	0.69	423
Dipac + 20% Aspirin	-	>20	>20	-	33	36	1.09	390
Dipac + 30% Aspirin	18.2	9.0	9.5	35	39	39	3.32	353
Dipac + 40% Aspirin	4.0	5.4	7.5	39	41	44	-	-
Lactose	11.1	10.4	9.0	40	46	43	2.85	424
Lactose + 10% Aspirin	5.0	5.7	7.3	41	41	40	6.29	386
Lactose + 20% Aspirin	8.0	6.5	-	38	41	-	-	-
Lactose + 30% Aspirin	5.0	5.7	-	41	41	-	-	-
Aspirin	1.81	1.84	2.36				-	-

weight variation, CV. The values of 1/FF for Dipac containing up to 20% aspirin were too low to determine accurately. An important point is that for all mixtures where 1/FF could be determined relatively accurately, 1/FF was highly dependent on normal consolidating stress. In some systems 1/FF decreased with normal consolidating stress (Dipac + 40% aspirin, lactose + 10% aspirin) whereas in others 1/FF increased (Dipac + 30% aspirin, lactose + 20% aspirin). Values of 1/FF for the pure materials appear to be relatively constant over the range of consolidating stress as was observed for several tablet vehicles in a previous publication (8).

Variation of shear cell parameters is indicative of "complex" behaviour (11,12). Kocova & Pilpel (1) observed that for many complex powders the angle of internal friction, related to δ in the current work, remained relatively independent of consolidating stress. This does not appear to hold for the systems in Table 2. On examination of the porosities obtained in the shear cell it can be seen that each mixture was consolidated to a different extent under the same normal consolidating stress. The greater the aspirin content the greater the decrease in porosity. While the porosities of all the Dipac/aspirin systems were very similar in the unconsolidated form the values vary markedly after consolidation at 31.3 $g.cm^{-1}$. As a higher normal consolidating stress is applied however porosity does not change further. In the case of the lactose/aspirin systems porosity does decrease progressively with normal consolidating stress.

It seems that consolidation rearranges the packing of the powder mixtures studied such that shear

cell parameters are highly dependent on normal consolidating stress. Such "complex" powder behaviour means that it is difficult to predict flow ability during tabletting from shear cell parameters obtained at relatively high degrees of consolidation unlike the situation with pure tablet vehicles (8). Narrow size fractions of pure powders frequently behave as 'simple' powders whereas mixtures of two different materials often show 'complex' properties (1).

The findings of the present study have been very largely negative, that flow properties are measured with the now standard shear cell do not correlate with tablet weight variation. These conclusions must now be confirmed with other mixtures and then a detailed investigation of the reasons must be made.

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