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Changes in the particle size distribution during tableting of sulphathiazole powder

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Five size fractions of sulphathiazole powder (volume surface mean diameter 155, 133, 86, 50 and 41 μm) were compressed into 12 mm diameter tablets on an instrumented single punch tablet machine. The size analysis of the tablet material after compression showed an attrition of the coarser fraction and an agglomeration of the finer fraction. It is postulated that there is a critical particle size where the effects of crushing and bonding cancel each other. The changes in particle size are discussed in relation to some of the compressive characteristics of the powder.

The changes in surface area of a powder after compression have been studied by Higuchi, Rao & others (1953) and Armstrong & Haines-Nutt (1970, 1972a,b). These workers found that as compaction pressure increased, the surface area first increased but subsequently decreased at higher pressures. Armstrong & Griffiths (1970) have shown that if the compaction pressure is raised above 250 MN m^{-2} a second increase in surface area occurs and is associated with elastic recovery of the compact. These studies are of significance in tablet dissolution as an increase in surface area will increase the rate of dissolution of tablets made from drugs of low solubility. Surface areas were measured by nitrogen adsorption (Higuchi & others, 1953; Armstrong & Griffiths, 1970; Armstrong & Haines-Nutt, 1970, 1972a, b), which also measures the internal surface area contributed by cracks and fissures in the particle (Gregg, 1961). According to Armstrong & Haines-Nutt (1973) the dissolution rate remained constant for the tablet compressed above 250 MN m^{-2} as 'most of the surface detected by nitrogen adsorption is inaccessible to the solvent.' There is also lack of correlation between surface area (nitrogen adsorption) and mean particle size after compaction for magnesium carbonate fractions compacted at 62·5 MN m^{-2} (Armstrong & Haines-Nutt, 1970). Thus it appears more relevant to determine the particle size distribution of the disintegrated/deaggregated particles, because the surface of such particles will be directly available to the dissolution medium. An increase in the mean particle size with corresponding increase in the mean disintegration time as compaction pressure was increased was reported by Shotton & Leonard (1972). Although the agglomeration of the particles during compaction is well documented (Rumpf, 1962; Train & Lewis, 1962), the distribution of the deaggregated particles from a tablet has not been studied extensively. However, the importance of particle size distribution was emphasised by Riley & Hausner (1970) in characterizing the powder mass for the calculation of specific surface area.

In this study the mean volume surface diameter (d_{vs}) was determined from the whole distribution using equation (1)

$$d_{vs} = \frac{\Sigma nd^3}{\Sigma nd^2} \quad .. \quad .. \quad .. \quad .. \quad (1)$$

where n is the number of the particles having diameter d at each size interval. d_{vs} is converted directly to specific surface assuming that the particles are spheres, by applying equation (2)

$$\text{Specific surface} = 6/d_{vs}\rho \quad .. \quad .. \quad .. \quad (2)$$

where ρ is the density of the solid. Since comparative changes in surface areas are being studied in this work, the introduction of a particle shape factor was not considered necessary.

The breaking strength of the tablet was determined using an Erweka hardness tester (Summers, 1971) and the tensile strength was calculated from equation (3) proposed by Rowe, Elworthy & Ganderton (1973).

$$S = 2P/\pi\,(Dt\,(1-\epsilon) \quad .. \quad .. \quad .. \quad .. \quad (3)$$

where P = applied load (N); D = diameter of the tablet (m); t = thickness of the tablet (m); ϵ = porosity of the tablet; S = tensile strength N m^{-2}.

MATERIALS AND METHODS

Sulphathiazole B.P.C. (May and Baker batch No. 913) melting point 199° determined by hot stage micoscope (Mettler); density 1·58 g cm^{-3} determined by the specific gravity bottle method (B.S. 733) using water saturated with sulphathiazole. The fractions were separated by B.S. sieves into five different batches and the size distribution of each was determined by Coulter Counter analysis. The volume surface mean diameter of the batches were 155, 133, 86, 50 and 41 μm respectively and their corresponding specific surfaces were 245, 285, 441, 758 and 923 $cm^2\,g^{-1}$ (Table 1).

Table 1. *Change in specific surface of sulphathiazole powder after compression to a maximum pressure of 237 MN m^{-2}.*

Sp. surface cm^2g^{-1}			Yield stress MN m^{-2}	Residual die-wall stress MN m^{-2}	Tensile strength kN m^{-2}
Initial	Final	Inference			
245	330	Fracturing	82·1	6·9	6·97
285	345	Fracturing	86·0	7·7	8·60
441	500	Fracturing	90·0	8·0	9·84
758	632	Bonding	113·0	8·7	8·72
923	730	Bonding	125·0	12·3	8·85

Equipment

A Manesty E2 single-punch tablet machine fitted with 12 mm flat faced punches was instrumented according to Leigh (1969) to enable the upper punch pressure and die wall pressure to be monitored. Four strain gauges (Budd Type C6 121A Meta Film foil gauges) were bonded around the shank of the upper punch in a Poisson arrangement and connected as a Wheatstone bridge. Similarly, four gauges (Micro Measurements Type EA-06-125AD-120) were mounted on the cut away die wall to monitor the transmitted radial force. Displacement of the upper punch was measured using a Honeywell Type LD11 linear displacement transducer. The signals from these systems were amplified with Honeywell Type CA 2506 carrier amplifiers and recorded on a Honeywell 1706 Visicorder.

Coulter Counter model B with 400 μm orifice. Ultrasonic probe-type bath (MSE). Erweka tablet hardness tester with flat platens as modified by Summers (1971).

Methods

All the samples were dried at 60° for 1 h and stored over silica gel in a desiccator. Assuming zero porosity of the tablet at maximum compression of 237 MN m^{-2} the amount of sulphathiazole necessary to produce a 4 mm thick and 12 mm diameter tablet was calculated from a knowledge of the crystal density.

The required amount of powder to give a compact height of 4 mm was transferred to the die cavity with the help of a vibrating spatula. The compression was carried in pressure increments of 11·05 MN m^{-2} every second to the maximum of 237 MN m^{-2} applied by the upper punch. The axial, radial stresses and the linear thickness were read from their relative tracings on the chart. The yield stress was estimated from the axial pressure *vs* radial stress plot (Carless & Leigh, 1974).

Size analysis

Sulphathiazole powder was dispersed in a medium of 0·9% sodium chloride and 0·059% Nonex 52 (Shell Chemicals) in water saturated with sulphathiazole. The suspension was agitated with the ultrasonic probe before size analysis in Coulter Counter. For size analysis of the tableted sulphathiazole, 120 mg of the tablet was added to 200 ml of the electrolyte medium and after 15 min, the aggregates were broken mechanically with a scalpel. The suspension was then agitated with the ultrasonic probe for 5 min and subjected to size analysis in the Coulter Counter.

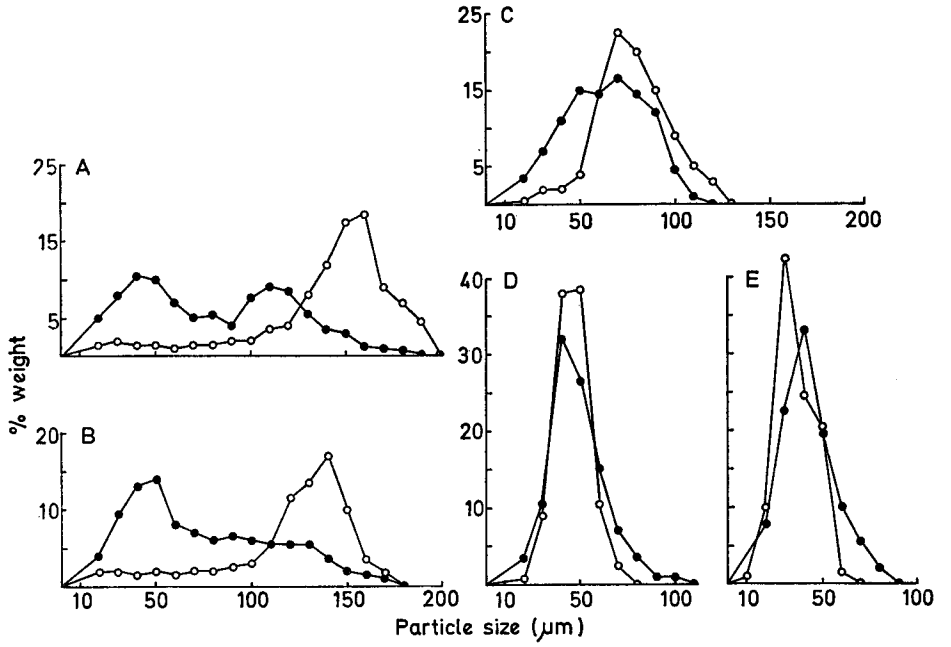

FIG. 1. Particle size distribution before and after compression. A: ○—○ = original d_{vs} 155 μm. ●—● = after compression d_{vs} 115 μm. B: ○—○ = original d_{vs} 133 μm. ●—● = after compression d_{vs} 110 μm. C: ○—○ = original d_{vs} 86 μm. ●—● = after compression d_{vs} 76 μm. D: ○—○ = original d_{vs} 49 μm. ●—● = after compression d_{vs} 60 μm. E: ○—○ = original d_{vs} 41 μm. ●—● = after compression d_{vs} 52 μm.

RESULTS

The changes in the distributions for all the size fractions before and after compression are depicted in Fig. 1. The results of specific surface change, yield stress, residual die-wall stress and tensile strength are tabulated in Table 1. The compression cycles for three size fractions are illustrated in Fig. 2. The relation percentage change in specific surface and original specific surface is shown in Fig. 3. The plot of log yield stress against original specific surface is given in Fig. 4.

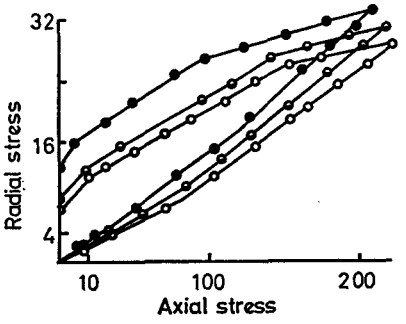

FIG. 2.

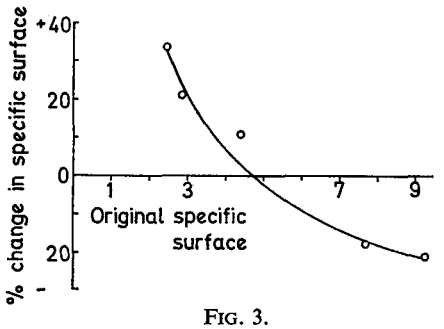

FIG. 3.

FIG. 2. Compression cycles—axial stress (MN m^{-2}) against radial stress (MN m^{-2}). ○—○ = sulphathiazole powder d_{vs} 155 μm. ◒—◒ = sulphathiazole powder d_{vs} 87 μm. ●—● = sulphathiazole powder d_{vs} 41 μm.

FIG. 3. % change in specific surface due to compression against original specific surface ($\times 10^2$ cm^2 g^{-1}) of sulphathiazole.

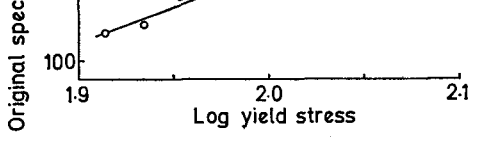

FIG. 4. Log yield stress against original specific surface (cm^2 g^{-1}) of sulphathiazole.

DISCUSSION

Particulate and compressional characteristics

It is seen from Table 1 that on decreasing particle size, there are increases of yield stress and residual die wall stress. There appears to be a trend towards increase in tensile strength as the particle size is reduced. The higher value of tensile strength for fine particle tablets suggested stronger particle-particle bonding. This is in accordance with Shotton & Ganderton (1961). Leigh, Carless & Burt (1967) and Hersey, Rees & Cole (1973) have also expressed the view that there is a tendency for increased yield with decreased particle size. Similarly, a higher residual die wall stress signifies a harder tablet formed by strong bonding, so also the result of size

analysis in this experiment (Table 1—Fig. 3) has clearly depicted the agglomeration of the finer particles. The mechanisms of bonding are possibly due to (a) interparticular shearing and shearing along the die wall (Train & Lewis, 1962); (b) interparticular van der Waals force of attraction (Rumpf, 1962); (c) the asperitic melting of the local surfaces (York & Pilpel, 1972). Whatever may be the cause, all of these views support the suggestion that the larger surface area creates a greater number of contacts and facilitates the bonding between particles. Particle-particle binding is assumed to have occurred when the agglomerate withstands the standardized shearing and handling, in the preparation of the sample for particle size analysis.

A convenient parameter that can be used to quantify size enlargement or size reduction is the percentage change in specific surface (Fig. 3). The specific surface area change with 285 and 441 cm^2g^{-1} fractions are approximately 60 cm^2g^{-1} in both cases, but these are calculated as 21% and 13% increase in surface respectively. Davis, Carithers & Watson (1971) have suggested that the mean or average size has no practical significance in characterizing the compaction of the powder. Alternatively, they have used two extremes of the sizes in a distribution to calculate the specific surface area. The equation (1) used in this paper has more application because it is suitable for use in all types of size distribution (Herdan, 1960).

Size change and compressional force

It is obvious from Table 1 and Fig. 3 that the bigger sizes are crushed, the fines are agglomerated and the intermediate sizes are not significantly affected. Following this trend in Fig. 3 the critical size where the phenomenon of bonding and fragmentation equalize each other, was approximately 76 μm (d_{vs}). The result can be further explained by assuming that the bigger size fraction is broken down under stress to fill the voids and the smaller fraction because of its dimension cannot be broken down further and is forced to fit into the voids. During these operations there is a high degree of shear in the case of fine particles which causes rise of both temperature and pressure within the stressed system, especially at the points of contacts. As a result of this, a local melting of the surface below its melting points occurs at higher pressure. This type of melting under the conditions above is called asperitic melting (York & Pilpel, 1972). On releasing the load the asperitically molten surfaces solidify giving rise to strongly bonded particles. Thus the finer particles having greater surface area and larger number of contact points form bigger particle sizes on compression.

It can be assumed that at a critical size where overall change is insignificant, the situation is dynamic, i.e. smaller particle $\xrightarrow{\text{bonding}}$ large particle $\xrightarrow{\text{fracturing}}$ smaller and thus it is not possible to follow the fate of an individual particle. At what stage the compression stops seems an important factor. In order to check whether the particles in the critical size range were affected by compression, further experimentation was undertaken. A narrow size fraction in the range of 180/200 mesh was chosen as a possible critical size. The size determined experimentally by the Coulter Counter was 67 μm (d_{vs}). The pressures used in the compression were 42, 59, 104, 148, 228, 258 MN m^{-2} and their respective sizes after compression were 63, 64, 74, 81, 74 and 73 μm (d_{vs}). There was a tendency of first fracturing, then agglomerating and subsequent fracturing, as had been observed by Higuchi & others (1953) and Armstrong & Haines-Nutt (1970). The statistical analysis of the whole distribution by χ^2 before and after compression showed no significant difference except in the 81 μm fraction.

Thus it can be concluded that there is no correlation between the compression pressure and final particle size in the range studied. On the other hand, it has been found that the log of yield stress bears a straight line relationship with original specific surface (Fig. 4). The slope of the regression may be a characteristic of the material under compression. The higher yield value of the finer particles can be discussed further as follows. There are mostly rearrangements of the particles at lower pressure and after the yield has occurred most of the applied stress is transferred to the die wall (Carless & Leigh, 1974). It has also been reported by Fell & Newton (1971) and Armstrong & Haines Nutt (1972b) that the rearrangement of the particles was greater for the fine particles. Therefore a higher yield stress for the finer particles is not the matter of controversy. It was interesting to note in this context that even the widely used graphical treatment by Heckel (1961) could not differentiate between the bonded and fractured nature of the compacted mass of particles. The invalidity of Heckel's equation was also observed by Hersey & others (1973) during compression of different size fractions of lactose powder.

It is concluded that the original size is an important factor to consider in the predicdiction of particle size changes. The critical size, where bonding and fragmentation equalize each other may well vary from solid to solid, as a brittle compound is likely to have a lower critical value than more ductile materials. Mixed powders of different particle size are subjected to compression in normal tableting procedures and the changes in particle size of such powders is at present under investigation.

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