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Brittle/ductile behaviour in pharmaceutical materials used in tabletting

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Summary

Brittle/ductile transitions of several pharmaceutical materials used in tabletting have been determined by measuring the yield pressure during compression of different particle sizes of the materials. The data generated are consistent with the known compaction behaviour of the materials and can be used to calculate fracture energies.

Introduction

Pharmaceutical materials used in tabletting vary from those that are brittle and consolidate by fracture or fragmentation (e.g. calcium carbonate, magnesium carbonate) (Roberts and Rowe, 1985; Armstrong and Haines-Nutt, 1979) to those that are ductile and consolidate by plastic deformation (e.g. microcrystalline cellulose) (David and Augsberger, 1977). However, some materials consolidate by both fragmentation and plastic flow (e.g. lactose) (Hersey et al., 1973; Cole et al. 1975). Particle size effects are important in all three groups of materials. Fig. 1 shows schematically the effect of particle size on both the fracture stress and the stress to cause plastic flow in an ideal body (Atkins and Mai, 1986). It can be seen that where the former decreases with increasing particle size the latter is essentially independent of particle size. Applying the concept to tabletting using the term "compressibility" to denote the ease of consolidation (Leuenberger, 1982; Jetzer et al., 1983; Leueneberger and Jetzer, 1984), it can be seen that for a brittle material the compressibility would decrease with decreasing particle size, whereas for a plastic deforming material compressibility will be independent of particle size. However, for a material that exhibits both brittle and ductile behaviour the situation will be more complex involving an initial decrease in compressibility as particle size decreases until a transition point (x) where flow supervenes fracture, above which the compressibility will be independent of any further decrease in particle size. A composite curve would be expected for a material of a specific median size with a distribution of sizes. In this case the brittle/ductile transition occurs at the point x intermediate between the two inflection points.

This approach has been used in this paper as a means of both distinguishing between the compac-

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tion behaviour of materials and producing data on their brittle/ductile transitions.

Experimental

Implicit in the approach is an accurate reproducible method of assessing the compressibility of materials. In this respect Leuenberger (1982) and Jetzer et al. (1983) have used a $1/\gamma$ function determined from indentation hardness measurements on ejected compacts at varying porosities. As stated recently (Leuenberger and Jetzer, 1984), this function is numerically the same as the yield pressure, P_y, determined from the gradient of the Heckel plot (Heckel 1961a and b). Rather than use this indirect route of determining compressibility we have measured yield pressures under load conditions at a punch velocity of 0.033 $mm \cdot s^{-1}$ (Roberts and Rowe, 1985).

The materials studied include a pure form of dolomite – a double carbonate containing not less than 99% $CaMg(CO_3)_2$ (Microdol, A/S Norwegian Talc, Bergen, Norway) to represent a brittle material; microcrystalline cellulose (FMC International, Food and Pharmaceutical Products, Little Island, Cork, Eire) to represent a plastic-deforming material and crystalline lactose (Dairy Crest, Industrial Division, Milk Marketing Board, Thames Ditton, Surrey, U.K.) and a propanolamine derivative (ICI Pharmaceuticals Division, Cheshire, U.K.) to represent materials exhibiting both brittle and ductile behaviour. Whereas a range of particle sizes of dolomite, microcrystalline cellulose and lactose were obtained by selecting suitable grades from the respective manufacturers, that for the propanolamine derivative were obtained by comminution. In addition a batch of lactose was fluid energy milled (4 inch microniser, F.W. Berk and Co., London, U.K.) to obtain a smaller partice size than those supplied. Median sizes for dolomite, lactose and the propanolamine derivative were evaluated by using an image analyser (Quantimet Model 720, Cambridge Instruments, Cambridge, U.K.). The median size of the microcrystalline cellulose grades were evaluated using an air jet sieve (Alpine Model 320LS, Alpine Process Technology, Runcorn, Cheshire, U.K.).

Results and Discussion

Fig. 2 shows the combined data for all 4 materials. As expected the brittle material dolomite showed a decrease in compressibility, i.e. an increase in yield pressure, in accordance with the fracture stress curve shown in Fig. 1. This is indicative of a deformation mechanism involving particle fragmentation. At the other extreme of material behaviour, the microcrystalline cellulose shows the typical behaviour associated with a material deforming by plastic flow, i.e. the yield pressure is independent of particle size. Lactose and the propanolamine derivate both show intermediate behaviour following the composite curve with brittle/ductile transitions at 27.4 μm and 22.1 μm, respectively.

Kendall (1978) has shown that it is impossible to comminute very small particles by compression since when the deformation zone is small enough, even the most brittle of solids will flow. Based on the compression of a specimen of an idealised geometric shape Kendall (1978) derived an equation to calculate the critical particle size below which flow will occur (d_{crit}):

$$d_{crit} = \frac{32ER}{3P_y^2} \tag{1}$$

where E and P_y are the Young's modulus of

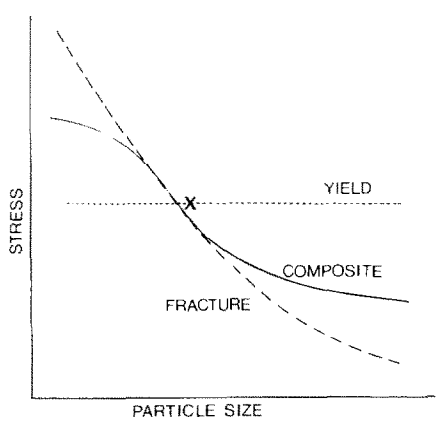

Fig. 1. Schematic diagram showing the effect of the particle size of an ideal material on both yield and fracture stresses. The composite curve is for a material containing a distribution of particle sizes. X is the brittle/ductile transition.

elasticity and yield pressure, respectively, of the material and R is its fracture energy or fracture toughness. Although the shape of the particles compressed in a powder bed is not the same as that used by Kendall (1978) and the effect of adjacent particles in the bed is unknown, it is useful to apply Eqn. 1 in order to analyse our results. The results of the calculations in addition to the values taken for E, P_y and R in the case of the dolomite and the microcrystalline cellulose and E, P_y and d_{crit} from the case of the lactose and the propanolamine derivative are shown in Table 1. Yield pressure values for the lactose and the propanolamine derivative were taken intermediate between the two inflection points on the curves (Fig. 2) while for the microcrystalline cellulose an average value of the 3 grades was used. However, for the dolomite where the yield pressure was still rising even at the lowest particle size, a true yield stress cannot be strictly evaluated. In this case the value for the lowest particle size was used. Values for the Young's modulus of elasticity and fracture energy of the materials were taken from the literature.

For dolomite the value predicted for the brittle/ductile transition is smaller than that reported for the similar material calcium carbonate (approximately 1 μm – Kendall, 1978). This may be due to two factors, firstly the value taken for the fracture energy of the dolomite is too small and secondly the value for the yield pressure is too large. Both may be responsible. For instance, frac-

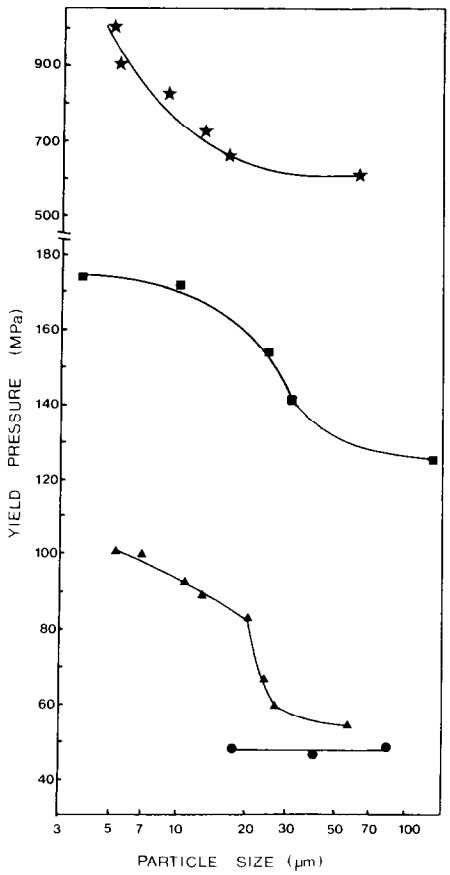

Fig. 2. The effect of particle size on the yield pressure of dolomite (★), lactose (■), propanolamine derivative (▲) and microcrystalline cellulose (●).

TABLE 1

Young's modulus (E), yield pressure (P_y), fracture energy (R), and d_{crit} for all the materials in the study

Material	E (GPa)	P_y (MPa)	R (J · m^{-2})	d_{crit} (μm)
Dolomite	29 [a]	1002.1	0.35 [b]	0.11 [c]
Microcrystalline cellulose	8.3 [d]	47.6	30 [e]	1172 [c]
Lactose	14.2 [f]	150.1	4.08 [c]	27.4
Propanolamine derivative	7.0 [f]	74.4	1.63 [c]	22.1

[a] Washburn (1927).
[b] Data for $CaCO_3$—Gilman (1960).
[c] Calculated values using Eqn. 1.
[d] Roberts and Rowe–*Int. J. Pharm.*, in press.
[e] Data for coniferous pine wood—Atkins and Mai (1985).
[f] Roberts and Rowe (1987).

ture energies for other similar inorganic materials have been found to range from 1.2 to 3.0 $J \cdot m^{-2}$. Gilman (1960) and yield pressures for hard, brittle materials determined using the Heckel plot are known to be more variable because of the curvilinear nature of the plots (Roberts and Rowe, 1985). However, as expected, the value for the transition is below the lowest particle size of dolomite used in this study. The predicted value for d_{crit} for the microcrystalline cellulose is reasonable in the light of data predicted and determined experimentally for the polymeric material polystyrene (4.48 mm and 3.6 mm, respectively) (Kendall, 1978). Furthermore, the data for the fracture energies of the lactose and propanolamine derivative are reasonable in the light of literature data (Gilman, 1960; Lawn and Wilshaw, 1975; Atkins and Mai, 1985). For highly brittle materials where crack propagation occurs via the reversible rupture of cohesive bonds between two atomic planes, the fracture energy is equal to the surface free energy, i.e. $R = 0.5 - 5\ J \cdot m^{-2}$.

For semi-brittle materials where there is some flow at the crack tips, R can be in the range $5 - 50\ J \cdot m^{-2}$ and for non-brittle materials where blunting of crack tips occurs R can be in excess of $5 \times 10^4\ J \cdot m^{-2}$ (Lawn and Wilshaw, 1975). Therefore, based on this classification pharmaceutical materials can be considered to be brittle or semi-brittle in nature.

Since the fracture energy term can be considered to be a measure of the ease of crack propagation and thus the brittleness of materials, it is interesting to note that the expected trend of increasing brittleness microcrystalline cellulose > lactose > propanolamine derivative > dolomite agrees with previous data where the brittle fracture propensity index was used as a measure of brittleness (Roberts and Rowe, 1986).

Finally, it is interesting to note that the existance of brittle/ductile transitions for both drug substances and excipients has been reported previously in the pharmaceutical literature. Alderborn and Nystrom (1985) using an air permeability method, found a transition for lactose in the order of 20–40 μm, comparable with our results and Tuladhar et al. (1983) and Carless and Sheak (1976) using dissolution and disaggregation techniques, respectively, have found transitions for both phenylbutazone and sulphathiazole. In the case of sulphathiazole ($d_{crit} = 76\ \mu m$) where yield pressures were reported (100.1 MPa) it is thus possible to calculate a fracture energy of 7.5 $J \cdot m^{-2}$ (assuming a value of Young's modulus of elasticity of 9.5 GPa). This value is reasonable in the light of the data in Table 1.

In conclusion it can be seen that brittle/ductile transitions of materials can be determined using yield pressure data. The method is relatively easy and rapid to undertake and generates data consistent with known compaction behaviour. Additionally, the data can be used to calculate fracture energies of materials.

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