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Effect of Compression Speed on the Tensile Strength of Tablets of Binary Mixtures Containing Aspirin

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Abstract—Mixtures of aspirin with sodium chloride, sucrose, Starch 1500 or Emcompress have been compressed to two maximum upper punch pressures at two compression speeds. Non-linear relationships between tensile strength and composition, and tablet porosity and composition were found in all cases. Tablets of the individual materials compressed at fast speed showed either little change or a reduction in tensile strength when compared with those compressed at slow speed. For mixtures of aspirin with Starch 1500, tablets compressed at fast speed were weaker and more porous than those compressed at slow speed. However, some mixtures of aspirin with sodium chloride, sucrose or Emcompress gave tablets with greater tensile strength and lower porosity when prepared at fast compression speed compared with tablets prepared at slow speed. This behaviour was attributed to the modification of the consolidation behaviour of the aspirin by the second material.

The importance of the rate of application and duration of the compression force in tableting has been recognized for many years. Problems associated with changing from single punch to rotary tablet machines during the development of tablet formulations have been attributed to the differences in the rates of compression and decompression, and the time over which the compression force is applied to the powder (Armstrong 1982). Time-dependent factors involved in powder compression have recently been reviewed by Armstrong (1989), who noted that virtually all data in the literature relate to single component systems.

Early investigators (Baba & Nagafuji 1965; Seitz & Flessland 1965) found that the crushing strength of tablets was reduced when the rate of tablet production was increased. An increase in the incidence of capping and lamination of some materials has been found when the tableting rate was increased and Ritter & Sucker (1980) related this to the deformational properties of the materials. Fell & Newton (1971) showed that the consolidation of lactose was affected by the compression speed, tablets prepared using a mechanical press having a greater density than tablets compressed to the same maximum force using a single punch tablet machine. More recently Roberts & Rowe (1985) investigated the effect of punch velocity on the densification of a variety of materials. Using the Heckel equation (Heckel 1961a, b) they showed that an increase in the mean yield stress with increasing punch velocity was exhibited by some plastically deforming materials. This was attributed to a change from plastic to more brittle behaviour or a reduction in the amount of plastic deformation. Materials consolidating primarily by fragmentation showed no change in the mean yield stress with increasing punch velocity.

Commercial tablets usually contain more than one component but little information has been published on the effect of changes in the compression rate on the properties of compacts of different compositions. Sheikh-Salem & Fell (1982) examined the variation in tensile strength of sodium chloride–lactose tablets prepared at three compression speeds. They found that tablets prepared using a single punch tablet machine (upper punch speed about 3000 mm min^{-1}) were weaker than those prepared using a mechanical press (crosshead speeds of 1 mm min^{-1} and 20 mm min^{-1}) and that sodium chloride tablets showed a greater reduction in strength than lactose tablets, which reflected the greater tendency of sodium chloride to consolidate by plastic deformation. The mixtures showed a similar relationship between the tensile strength and composition at each compression speed and each maximum compression force used in the range 40–160 MPa. Changes in the compression speed, although altering the relative efficiencies of the fragmentation and plastic flow consolidation mechanisms, did not alter the overall behaviour of the system studied.

The purpose of this study was to examine the variation in tensile strength of tablets prepared from binary mixtures containing aspirin produced at a slow compression speed using a mechanical press and a relatively fast speed using a single punch tablet machine.

Materials and Methods

Materials

The characteristics of the powders used are shown in Table 1. Aspirin (Crystals 7016 grade, Monsanto Plc, Basingstoke) was chosen as a model drug. This was mixed with four other materials chosen for their different consolidation properties, namely sodium chloride (GPR grade, BDH Chemicals Ltd, Poole), sucrose (Bextra 'F' caster sugar, The Chemical Milling Co., Milton Keynes), Emcompress (Albright & Wilson Ltd, Warley) and Starch 1500 (Colorcon Ltd, Orpington). The sucrose and Emcompress were expected to consolidate principally by fragmentation while sodium chloride and Starch 1500 are believed to consolidate by time-dependent plastic deformation. The 90–125 μm sieve fraction of each material was used in this study, the aspirin and sodium chloride being ball milled before sieving. True densities were determined using an air comparison pycn-

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Table 1. Characteristics of the 90–125 μm sieve fractions of the materials used in this study.

	True density g cm^{-3}	Bulk density g cm^{-3}	Tap density g cm^{-3}	Loss on drying %
Aspirin	1·40	0·62	0·77	0·020
Sodium chloride	2·16	0·93	1·13	0·012
Sucrose	1·60	0·70	0·84	0·015
Starch 1500	1·48	0·61	0·73	7·383
Emcompress	2·32	0·69	0·85	0·481

ometer (Beckman Model 930). Bulk densities were measured by pouring an excess of the powder from a glass funnel into a duralumin cylinder of known volume, scraping the surface level and determining the weight of powder. Tap densities were measured using a jolting volumeter, readings being taken at a limiting volume (250 taps). The loss on drying was determined after drying in a vacuum oven at 50°C for 48 h. Binary mixtures were prepared by tumbling the two materials in the proportions 80:20, 60:40, 40:60, and 20:80 by weight. The homogeneity of the mixtures was checked using a suitable chemical assay. All powders were conditioned before use by storage at 43% relative humidity, 20°C for 14 days. Full details of the preparation and characterization of the materials are given elsewhere (Cook 1987).

Compression details

Tablets were prepared using 12 mm diameter plane-faced punches. Before each compression the die wall was lubricated with a 5% w/v solution of stearic acid in chloroform. The die was filled manually, sufficient powder being used to give a compact 3 mm thick at zero porosity. Tablets were compressed at a slow speed using a Caleva COMP 2500 mechanical press (G. B. Caleva Ltd, Sturminster Newton) operating at a crosshead speed of 1 mm min^{-1}. This was fitted with a load cell to measure the upper punch force and a control unit allowing automatic reversal of the crosshead on reaching the required load. Tablets were compressed at a fast speed using a Manesty E2 single punch tablet machine (Manesty Machines Ltd, Speke) fitted with strain gauged punches and a displacement transducer, with data collection by a microcomputer-based system (Huckle 1985). The tablet machine was operated at a rate equivalent to 68 tablets min^{-1}. On each piece of equipment tablets were prepared at two maximum upper punch pressures of 75 and 162·5 MPa. Unlike the mechanical press the speed of the upper punch of the single punch tablet machine is not constant during the compression phase, falling from about 6000 mm min^{-1} to zero. A consequence of compressing fixed quantities of material is that the speed of the upper punch at the point when it contacts the powder will vary if maximum upper punch pressure is varied or if the bulk volume of powder varies from material to material. This is due to the differences in punch travel required to consolidate the powder into a tablet. In this study the speed of the upper punch of the tablet machine on contacting the powder was estimated to vary between 5500 and 7500 mm min^{-1}, the slower speed still being very much greater that the 1 mm min^{-1} crosshead speed of the mechanical press.

Tablet characterization

Tablets were stored for 7 days at 43% relative humidity, 20°C before testing. The thickness and diameter were measured to 0·01 mm using a micrometer and the weight measured to 0·1 mg. The percentage porosity, P, was calculated from:

$$P = \frac{V - V_0}{V} \times 100$$

where V is the tablet volume and V_0 the volume of material at zero porosity. The diametral crushing strength was determined using a Caleva tensile tester at a crosshead speed of 1 mm min^{-1} and the tablet tensile strength, σ_t, calculated from:

$$\sigma_t = \frac{2F}{\pi DT}$$

where F is the crushing force and D and T are the tablet diameter and thickness, respectively. The tensile strength used was the mean value of 5 tablets which failed in tension.

Heckel analysis

Sufficient material to give a compact 2·0 mm thick at zero porosity was compressed as described above. Heckel plots were constructed in which the volume of the tablet was calculated from the diameter of the die and measurements of the tablet thickness determined under load by monitoring the distance between the punches. From regression analysis of the linear portion of the plot the mean yield stress for each material was derived.

Results and Discussion

The variation in tensile strength with composition for each mixture is shown in Figs 1–4. Each point is the mean tensile strength with the bars showing the standard deviation. It can be seen that a non-linear relationship was obtained at both compression speeds and maximum compression pressures with each binary mixture. If the data for the tablets made from a single material are examined it can be seen that the results reflect the deformational behaviour of the material. Thus Emcompress and sucrose, expected to consolidate primarily by time-dependent fragmentation, form tablets which show little difference in tensile strength when compressed at slow or fast speed. By contrast sodium chloride and Starch 1500 tablets produced at the fast compression speed have much lower tensile strengths than those produced at slow speed, illustrating the importance of time-dependent plastic deformation in the development of strong interparticulate bonds and hence strong tablets, for these materials. Aspirin also shows a significant reduction in tablet tensile strength with increase in compression speed, suggesting that time-dependent deformation is also important in the formation of strong aspirin tablets. This relationship between the deformational properties of materials and the effect of compression speed on tablet tensile strength is in agreement with the findings of previous workers (Baba & Nagafuji 1965; Sheikh-Salem & Fell 1982).

If two materials exhibiting time-dependent deformation properties were mixed together and compressed it might be expected that the mixed composition tablets would also have lower tensile strength when compressed at the faster speed. All mixtures of aspirin with Starch 1500 (Fig. 3) conform to

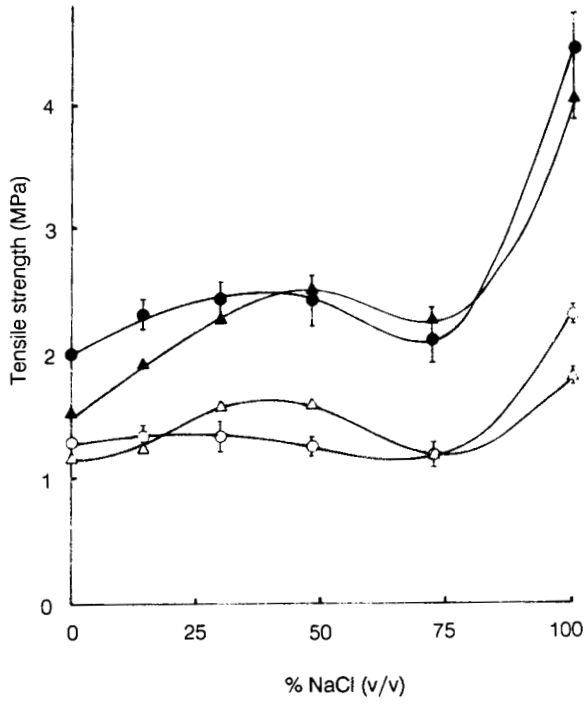

FIG. 1. The tensile strength of aspirin–sodium chloride tablets prepared at two compression speeds. 75 MPa maximum upper punch pressure (open symbols). 162·5 MPa maximum upper punch pressure (closed symbols). ○ ● Slow compression speed (mechanical press). △ ▲ Fast compression speed (single punch tablet machine).

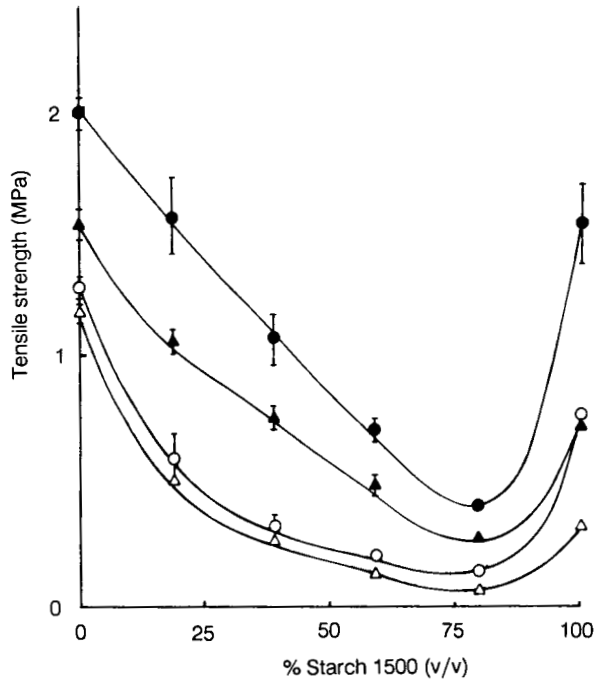

FIG. 3. The tensile strength of aspirin–Starch 1500 tablets prepared at two compression speeds. 75 MPa maximum upper punch pressure (open symbols). 162·5 MPa maximum upper punch pressure (closed symbols). ○ ● Slow compression speed (mechanical press). △ ▲ Fast compression speed (single punch tablet machine).

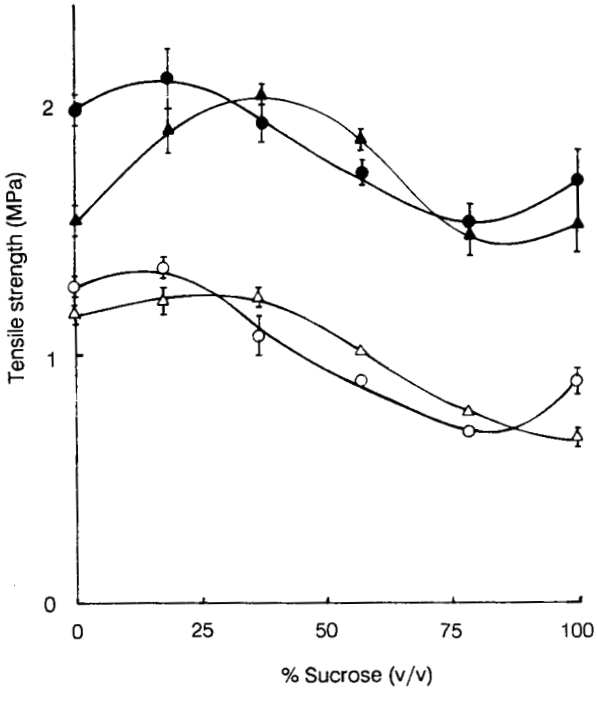

FIG. 2. The tensile strength of aspirin–sucrose tablets prepared at two compression speeds. 75 MPa maximum upper punch pressure (open symbols). 162·5 MPa maximum upper punch pressure (closed symbols). ○ ● Slow compression speed (mechanical press). △ ▲ Fast compression speed (single punch tablet machine).

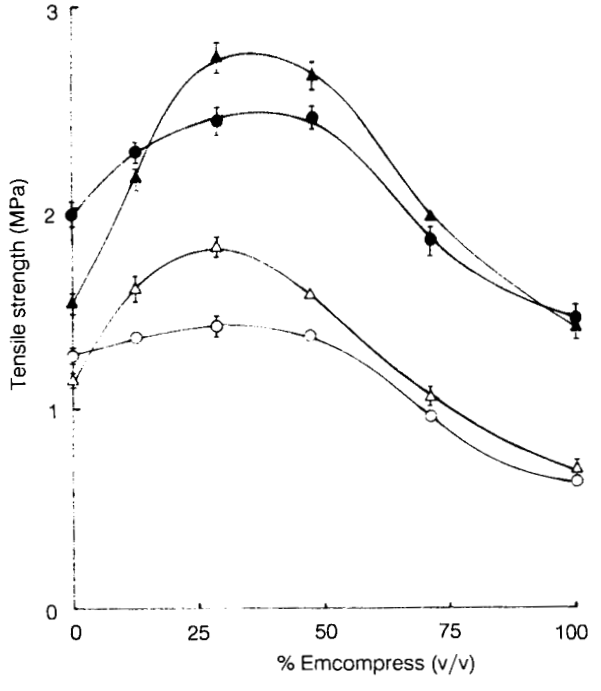

FIG. 4. The tensile strength of aspirin–Emcompress tablets prepared at two compression speeds. 75 MPa maximum upper punch pressure (open symbols). 162·5 MPa maximum upper punch pressure (closed symbols). ○ ● Slow compression speed (mechanical press). △ ▲ Fast compression speed (single punch tablet machine).

this pattern indicating that time-dependent deformation was the primary consolidation mechanism. However, mixtures of sodium chloride with aspirin show different behaviour (Fig. 1). At the 75 MPa maximum compression pressure tablets containing about 30 to 60% v/v sodium chloride had greater tensile strengths when compressed at the faster speed, while at the 162·5 MPa maximum compression pressure tablets containing about 30 to 70% v/v sodium chloride were of similar tensile strength whichever compression speed was used.

An increase in tablet tensile strength with an increase in compression speed was also exhibited by certain aspirin–sucrose and aspirin–Emcompress mixtures. Tablets containing 40 to 60% v/v sucrose were found to have greater tensile strengths when compressed at the faster speed at both compression pressures (Fig. 2). The effect was even more marked with the aspirin–Emcompress mixtures (Fig. 4), where increased tensile strength was found with tablets containing about 15 to 60% v/v Emcompress at 75 MPa compression pressure and 20 to 50% v/v Emcompress at 162·5 MPa compression pressure.

The relationship between the porosity of the ejected tablets and their composition is shown in Figs 5–8. In general a non-linear relationship was found although the relationship for aspirin–Emcompress tablets compressed at slow speed approaches linearity at both compression pressures (Fig. 8). Tablets containing 100% Starch 1500 show much lower porosities when compressed at the slower speed (Fig. 7) as the more extensive time-dependent deformation results in denser tablets. Aspirin, sodium chloride and sucrose show similar behaviour although the magnitude of the difference is somewhat smaller. Emcompress forms slightly denser tablets when compressed at the faster speed (Fig. 8) suggesting that consolidation of the material may be slightly enhanced.

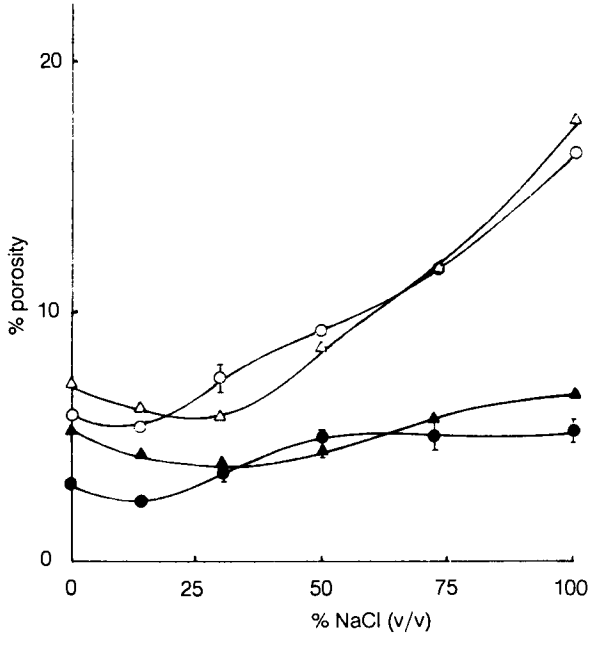

FIG. 5. The porosity of aspirin–sodium chloride tablets prepared at two compression speeds. 75 MPa maximum upper punch pressure (open symbols). 162·5 MPa maximum upper punch pressure (closed symbols). ○ ● Slow compression speed (mechanical press). △ ▲ Fast compression speed (single punch tablet machine).

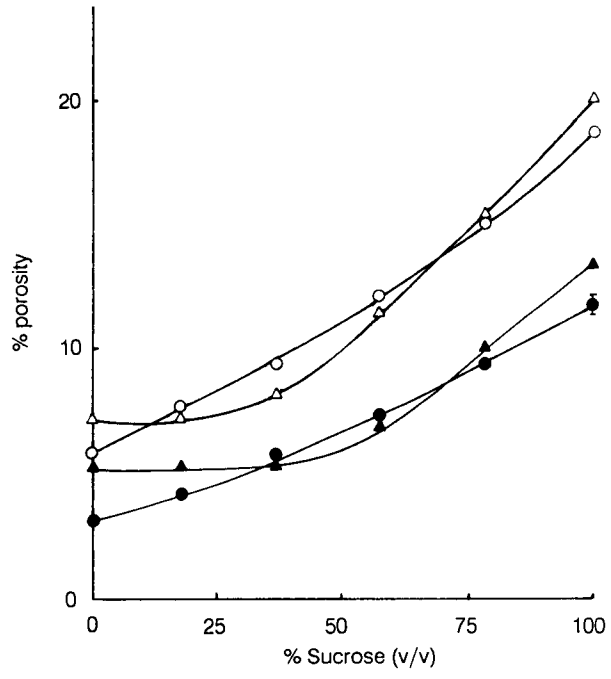

FIG. 6. The porosity of aspirin–sucrose tablets prepared at two compression speeds. 75 MPa maximum upper punch pressure (open symbols). 162·5 MPa maximum upper punch pressure (closed symbols). ○ ● Slow compression speed (mechanical press). △ ▲ Fast compression speed (single punch tablet machine).

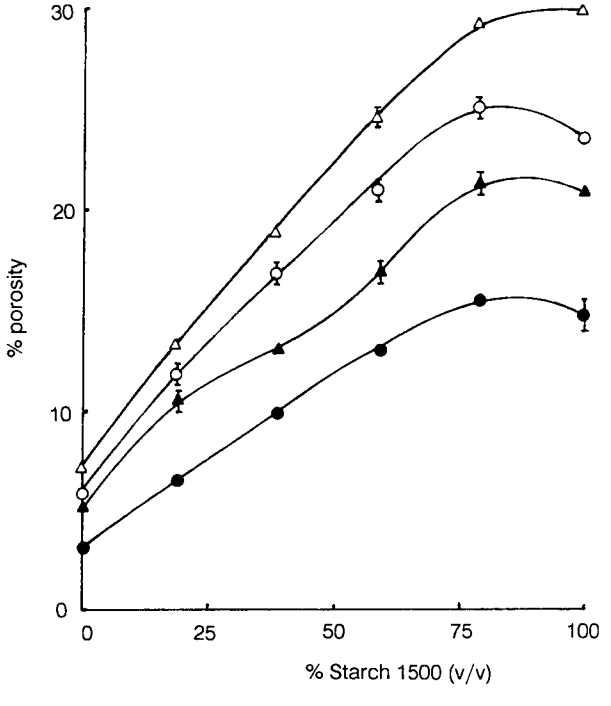

FIG. 7. The porosity of aspirin–Starch 1500 tablets prepared at two compression speeds. 75 MPa maximum upper punch pressure (open symbols). 162·5 MPa maximum upper punch pressure (closed symbols). ○ ● Slow compression speed (mechanical press). △ ▲ Fast compression speed (single punch tablet machine).

Fig. 7 shows that tablets of lower porosity were produced at the faster speed for each aspirin–Starch 1500 mixture tested. However, as with the tensile strength data, the relationships exhibited by the other mixtures were more complex. With aspirin–sodium chloride mixtures containing about 20 to 70% v/v sodium chloride and compressed to 75 MPa pressure, tablets compressed at fast speed had lower or similar porosities to those compressed at slow speed (Fig. 5). At 75 MPa pressure, compression at fast speed also produced denser tablets from aspririn–sucrose tablets containing 40 to 60% v/v sucrose (Fig. 6) and aspirin–Emcompress tablets containing about 20 to 100% v/v Emcompress (Fig. 8). As with the differences in tensile strength, the differences in porosity are affected by compression pressure. The production of tablets with greater density when using the fast compression speed was generally found to occur over a greater range of compositions at the lower maximum upper punch pressure used.

Examination of Figs 1–8 shows that the changes in porosity which result from compression at different speeds can be seen to correlate with the changes in tablet tensile strength. An increase in porosity is generally associated with a reduction in tensile strength, and vice versa. This is probably because an increase in porosity (i.e. a reduction in tablet density) is likely to be associated with less extensive contact and therefore bonding between particles and a greater incidence of flaws within the tablet. The pores within the tablet could act as stress concentrators, reducing the stress required to propagate a crack through the tablet. An increase in the gross porosity is therefore likely to result in a decrease in tablet tensile strength, although a change in the pore size distribution at the same gross porosity might also affect the tensile strength, possibly accounting for the discrepancies in the correlation between changes in the tensile strength and porosity.

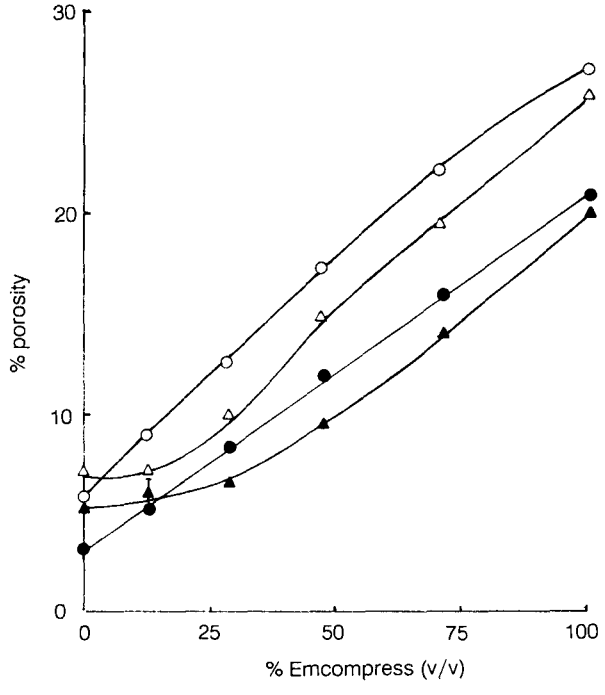

FIG. 8. The porosity of aspirin–Emcompress tablets prepared at two compression speeds. 75 MPa maximum upper punch pressure (open symbols). 162·5 MPa maximum upper punch pressure (closed symbols). ○ ● Slow compression speed (mechanical press). △ ▲ Fast compression speed (single punch tablet machine).

The greater densification produced by compression at the fast speed, which was found for some of the mixtures but not shown by the individual components of the mixture, suggests that there is an interaction between the materials resulting in modified consolidation behaviour. There is more efficient packing of the material in the mixed tablet than would have been expected from a simple additive function of the consolidation behaviour of the individual materials. Greater densification at the fast compression speed was found with mixtures of aspirin with sodium chloride, sucrose and Emcompress, but not Starch 1500. This may be related to the consolidation behaviour of aspirin and the relative deformability of the second material. The aspirin used in this study was found to be a soft, readily deformable material consolidating by both plastic deformation and fragmentation (Cook 1987). This was in agreement with the results of previous workers (Leigh et al 1967; Huckle 1985). If a second, harder, less deformable material is mixed with the aspirin it could result in greater fragmentation of the aspirin at the fast compression speed, resulting in more efficient packing of the materials and a denser tablet. The second material modifies the consolidation behaviour of the aspirin, changing the balance between plastic and brittle deformation, in effect comminuting the aspirin. The presence of a second component modifying the consolidation behaviour of a material has been found in binary systems examined by other workers. Tuladhar et al (1983) explained the difference in dissolution of tablets prepared from phenylbutazone with lactose or microcrystalline cellulose (Avicel) by proposing that the lactose, because it was harder than the microcrystalline cellulose, could reduce the particle size of the phenylbutazone during compression. Armstrong & Cham (1986) showed that there was an interaction between microcrystalline cellulose (Avicel) and heavy magnesium carbonate, materials with dissimilar consolidation mechanisms. When mixtures were compressed the size of the particles from disintegrated tablets was different from values expected if each component in the mixture had behaved as if it were being compressed on its own.

Table 2 shows the mean yield stress values obtained from Heckel analysis of the data from compression of the individual materials (Cook 1987). The mean yield stress values for Starch 1500 are consistent with it being a soft, easily deformable material, and lower than the results for aspirin. Thus mixing aspirin with Starch 1500 does not lead to enhanced fragmentation of the aspirin and the mixtures behave in a similar manner to the individual materials when the compression speed is increased. Emcompress and sucrose both have higher values for the mean yield stress than aspirin. Mixing aspirin with these harder, less deformable materials results in enhanced fragmentation of the aspirin at the fast compression speed and the production of a denser, stronger tablet. Like Starch 1500, sodium chloride also undergoes plastic deformation. From the mean yield stress values in Table 2 it is not clear whether sodium chloride is harder or softer than aspirin. However, Ridgway et al (1969) found sodium chloride crystals to be harder than aspirin in

Table 2. Mean yield stress values obtained from Heckel plots.

Material	Mean yield stress (MPa) Slow compression speed (Mechanical press)	Fast compression speed (Single punch machine)
Aspirin	55·7	114·9
Sodium chloride	70·6	86·7
Sucrose	138·8	131·3
Starch 1500	46·4	56·9
Emcompress	276·8	284·6

indentation tests and Aulton & Marok (1981) showed that sodium chloride crystals exhibited work hardening during compression. Thus the results for the aspirin–sodium chloride mixtures might also be explained by this hypothesis.

The effect of compression speed on the tensile strength of tablets prepared from aspirin–sodium chloride, aspirin–sucrose, and aspirin–Emcompress mixtures is different from tablets prepared from aspirin–Starch 1500 mixtures or the sodium chloride–lactose mixtures studied by Sheikh-Salem & Fell (1982). The punch speed of the Manesty E2 single punch tablet machine is somewhat lower than punch speeds attained on large rotary tablet machines. However, our results suggest that the possibility of developing tablet formulations which are less sensitive to the effects of compression rate on tensile strength, by combining the drug with excipients having the appropriate deformational properties is worthy of further investigation.

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