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# Effects of composition, moisture and stearic acid on the plasto-elasticity and tableting of paracetamol-microcrystalline cellulose mixtures

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Measurements were made under various conditions of the stress relaxation (SR) and elastic recovery (ER) of mixtures of paracetamol and microcrystalline cellulose (Avicel) and of the tensile strengths (T) of their tablets. T was inversely proportional to ER/SR. Tablets laminated or capped when they contained less than 25% w/w of cellulose and the value of ER/SR measured at 20 kN over a compression/decompression/ejection cycle of 2 min, was greater than 9. Addition of between 2 and 4% w/w of water increased the tensile strengths of tablets, provided they contained less than 75% w/w of cellulose, but more water caused decreases in T. Additions of up to 10% w/w stearic acid also caused decreases in T. Explanations are provided for the results.

The mechanisms responsible for the behaviour of powders during consolidation into tablets have been widely studied (de Blaey & Polderman 1971; Hiestand et al 1977; Leuenberger 1982). The ability of formulated powders to form satisfactory tablets depends on their plastic deformation during compression and on their elastic recovery during decompression (Armstrong & Haines-Nutt 1972; David & Augsburger 1977; Hiestand & Smith 1984). It is well known that paracetamol does not form satisfactory tablets—due to lamination and capping—without the addition of excipients (Leigh et al 1967; Krycer et al 1982) which modify its plastic and elastic characteristics.

The stress relaxation of the powder, SR, is the percentage reduction in force that occurs when, as a result of plastic compression, the applied force decays with time. The stress relaxation has been defined (Malamataris et al 1984) as

$$SR = [(H_p - H_t)/H_t] \times 100\% \quad (1)$$

where $H_p$ and $H_t$ are the thicknesses of the tablet respectively at maximum pressure and after being held for 30 s at maximum pressure. The value of SR will be influenced by a number of experimental variables including the rate of loading, the magnitude of the applied force, the length of time for which it is held, the dimensions and state of the punches and die employed. In a similar manner the elastic recovery of the powder, ER, has been defined (Krycer et al 1982) as

$$ER = [(H_o - H_p)/H_p] \times 100\% \quad (2)$$

where $H_o$ is the thickness of the tablet after final decompression.

While it could be argued that the stress relaxation or 'plasticity' of a powder is unlikely to be related only to changes in tablet thickness, and that the expression for elastic recovery does not allow for the possibility of recovery in a radial direction, nevertheless it seems reasonable to expect that SR and ER as defined above should provide some comparative measure of the changes that occur in the 'plasto-elastic' properties of a powder as increasing amounts of a second ingredient are added to it. The values may not be absolute values but they should be comparative and they will depend on the experimental conditions employed.

In the present investigation a study has been made of the effects produced on the ratio ER/SR and on tablet strengths by varying the weights and compositions of mixtures of paracetamol and Avicel, adding up to 6% w/w of water or up to 10% w/w of stearic acid and varying the compression/decompression/ejection cycle used for forming the samples into tablets.

## MATERIALS AND METHODS

Paracetamol powder (BP, Cambrian Chemicals, mean projected diameter 7·7 μm) and microcrystalline cellulose (Avicel pH 101, mean projected diameter 16·8 μm measured by microscopy) were mixed together in different proportions as previously reported (Bangudu & Pilpel 1984); the compositions of the mixtures are given in Table 1. Additional samples were prepared from these containing up to

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Table 1. Composition, plasto-elastic parameters and tensile strength of paracetamol-(P) cellulose (C) mixtures.

| Code | % w/w of cellulose | Elastic recovery (%) | Stress relaxation (%) | Ratio ER/SR | Tensile strength at $\rho_F$ 0·89 ($MNm^{-2}$) |
|---|---|---|---|---|---|
| P | 0 | 11·7 | 0·8 | 14·1 | cap |
| C | 100 | 9·0 | 2·2 | 4·1 | >6 |
| $M_1$ | 5 | 11·3 | 0·9 | 12·3 | 1·44 |
| $M_2$ | 10 | 11·2 | 1·1 | 9·9 | 2·20 |
| $M_3$ | 15 | 11·0 | 1·2 | 9·5 | 2·02 |
| $M_4$ | 20 | 10·5 | 1·2 | 9·0 | 2·32 |
| $M_5$ | 30 | 10·3 | 1·6 | 6·6 | 3·12 |
| $M_6$ | 50 | 9·7 | 1·8 | 5·4 | 4·56 |
| $M_7$ | 75 | 9·3 | 1·9 | 4·8 | >6 |
| $M_8$ | 90 | 9·2 | 2·1 | 4·3 | >6 |

6% w/w of added water, or up to 10% w/w of added stearic acid BP by mixing in a rotating jar with baffles for 5 min. The uniformity of the mixtures was monitored by determining the moisture or acid contents.

*Moisture sorption and desorption isotherms*

Samples of paracetamol and Avicel were dried over phosphorous pentoxide (no sign of decomposition), divided and transferred to desiccators at 20 °C and relative humidities of 20, 44, 65 and 85% provided respectively by saturated solutions of potassium acetate, potassium carbonate, sodium nitrite and potassium chloride. After standing for 5 days, their equilibrium moisture contents were determined in triplicate to within ±0·5% with a vacuum moisture tester (Townson and Mercer Ltd, Croydon) operating at 90 °C and 25 inches mercury pressure. The results yielded the sorption isotherms. A similar procedure was followed for determining the desorption isotherms, this time initially equilibrating samples over saturated potassium chloride, rh 85%.

*Tablet preparation*

A DARTEC 100KN M2501 universal testing machine (DARTEC Ltd) was used to measure the plasto-elasticity of the powders by forming them into tablets. It consisted of a load cell with a sensitivity of ±0·001 kN and a displacement transducer attached to a straining frame activated by a hydraulic power unit; a static control panel and a BRYANS X–Y recorder.

After preliminary experiments to determine the effects of varying the weight of sample, the compression pressure and the loading/unloading cycle had been made, a weight of powder (ca 450 mg) sufficient to produce a tablet ca 4·5 mm thick (at a packing fraction of about 0·9) was introduced into the 10·00 mm diameter die. It was compressed at a rate of 0·667 kN for 30 s between flat faced punches lubricated with 1% w/v magnesium stearate dispersion in acetone. The load was maintained at 20 kN for 30 s, then released at the same rate over 30 s and the tablet was finally ejected over a further 30 s by inverting the die and using the upper punch. The whole cycle occupied 2 min.

Four tablets were prepared from each sample. Their tensile strengths were determined by diametral compression (Fell & Newton 1970) using a CT 40 tester (Engineering System, Nottingham) and applying the equation

$$T = 2P/\pi DH \quad (3)$$

where T is the tensile strength ($Nm^{-2}$), P = load in Newtons causing fracture, D = tablet diameter (m), H = tablet thickness (m). Tablets containing added water were tested immediately after preparation, the others after storing for 24 h over silica gel at room temperature (20 °C).

The dimensions and the weights, Wg of the tablets were determined to within 0·01 mm and ± 1 mg and their packing fractions, $\rho_F$ were calculated using the equation

$$\rho_F = W/V_t \rho_s \quad (4)$$

where $V_t$ = volume of tablet ($cm^{-3}$), and $\rho_s$ = particle density of the powder or mixture (g $cm^{-3}$).

## RESULTS AND DISCUSSION

Fig. 1 is a schematic record of the behaviour of a sample while being formed into a tablet on the Dartec where: 0 = original position of the upper punch at the top of the die before compression, a = position of upper punch at maximum load of 20 kN; b = position of upper punch after being held for 30 s at 20 kN; c = position of upper punch after decompression; d = maximum displacement of upper punch i.e. the distance between the two punches.

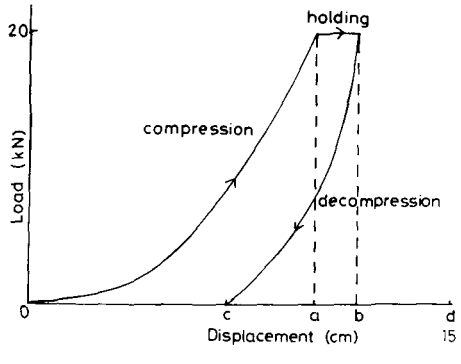


FIG. 1. Force-displacement plot.

Applying equation 1 and 2 respectively, (SR) = [(b −a)/(d − b)] × 100% and (ER) = [(a − c)/(d − a)] × 100%.

It was found that the packing fractions of typical samples weighing ca 450 mg approached a limiting value of about 0·90—the usual commercial value—at the selected compression load of 20 kN. This is expected from the theory of the mechanisms operating during compression (Heckel 1961). The tensile strengths of the resulting tablets each also approached a limiting upper value at this load, further justifying its selection. Besides being dependent on the weight of sample used (and therefore on the thickness of the resulting tablet) as illustrated typically in Fig. 2, the values that were obtained for ER, SR and the ratio ER/SR also depended on the duration of the compression cycle (David & Augsburger 1977). Fig. 3 shows that the values of ER/SR became minimal at the selected loading/holding/unloading cycle of 90 s. As will be seen later, Fig. 4, low values of ER/SR correspond to high tensile strength tablets and it may therefore be inferred that these will be best produced by using relatively slow rates of compression, allowing opportunity for elastic and plastic deformation and for bond formation between particles.

*Effect of composition*

Table 1 gives mean values for four replicates which agreed to within ± 10%. It shows that while the elastic recoveries of paracetamol and cellulose powders were comparable, the latter had a much higher value of stress relaxation. This greater plasticity results in the formation of strong (hydrogen) bonds during compression. These can resist the elastic recovery which would otherwise disrupt the tablets on ejection. It is seen from Table 1 that as the proportion of cellulose in the mixtures was increased, the values ER/SR decreased and the tensile strengths of the tablets increased. This inverse relation between ER/SR and tensile strength is shown in Fig. 4. It may be concluded that if the

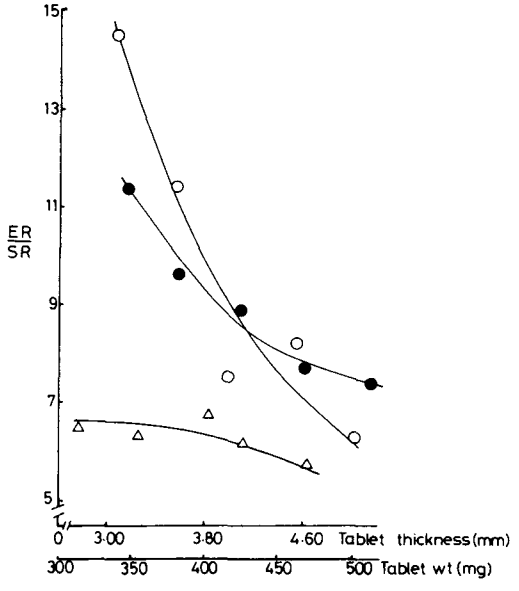


FIG. 2. ER/SR versus tablet thickness; ●—● $M_5$, ○—○ $M_6$, △—△ C (see Table 1).

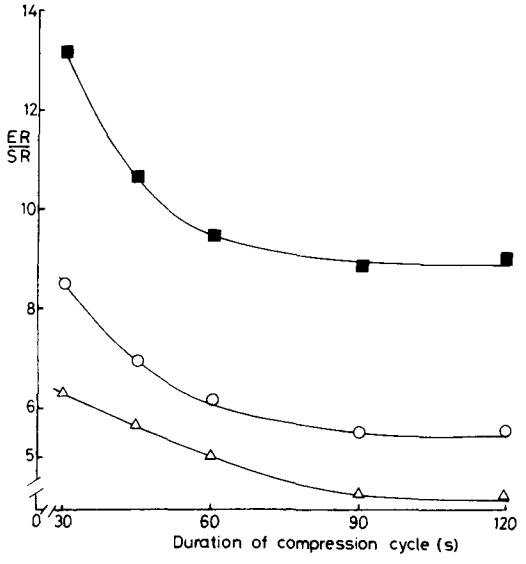


FIG. 3. ER/SR versus duration of compression cycle; ■—■ $M_4$, ○—○ $M_6$, △—△ C.

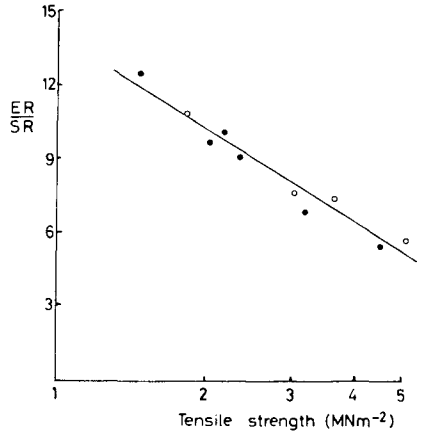


FIG. 4. ER/SR versus tensile strength at $\rho_F$ 0·89 for ● paracetamol-Avicel mixtures, ○ paracetamol-Avicel-stearic acid mixtures.

ratio of ER/SR is greater than about 9, capping/lamination of tablets will occur and this accounts for the commercial use of about 25% w/w of Avicel as an excipient for paracetamol tablets (Lieberman & Lachman 1980).

*Effect of moisture*

Analysis showed that after the initial drying over phosphorus pentoxide all samples contained less than 2% w/w of moisture. Fig. 5 shows that subsequently paracetamol, had little tendency to absorb moisture but that cellulose slowly absorbed up to 14% w/w at 20 °C and 85% rh over 5 days. The relative ease with which this can be desorbed (shown by the narrow hysterisis loop) accounts for the ready reversibility of the softening that occurs at high relative humidities in tablets containing more than 25% w/w of cellulose when they are subsequently dried (Reier & Shangraw 1966).

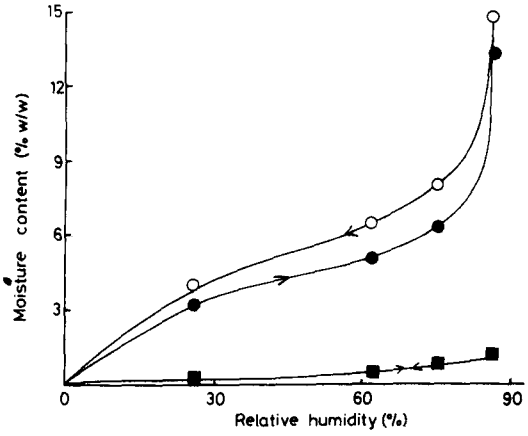


FIG. 5. Moisture sorption and desorption isotherms of paracetamol and cellulose powders at 20 °C. ●—● sorption, ○—○ desorption for cellulose, ■—■ sorption and desorption, for paracetamol.

Fig. 6 shows that for all the mixtures adding small (<4% w/w) amounts of water caused a decrease in the ratio ER/SR but that at higher levels there was an increase. With cellulose alone, there was only an increase. The initial decrease is presumably due to the development of surface tension and pendular bonds which hold the particles together (Newitt & Conway-Jones 1958; Young & Nelson 1967a, b). It can be inferred from Figs 4 and 6 that mixtures of paracetamol and cellulose containing between about 2 and 4% w/w of water (depending on their composition) will form stronger tablets than those without moisture. The reason why the values of ER/SR

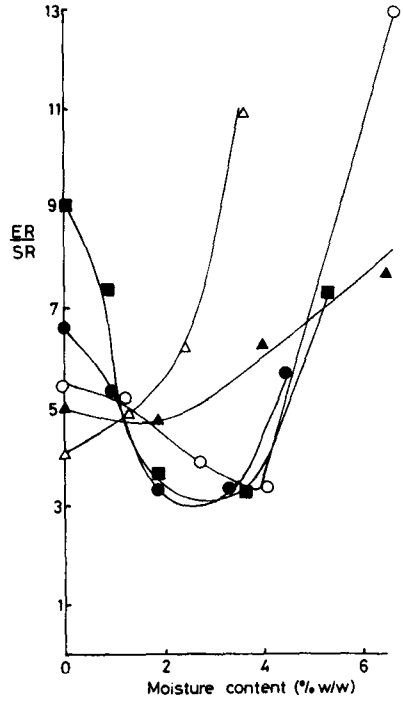


FIG. 6. ER/SR versus moisture contents of some samples; ■—■ $M_4$, ●—● $M_5$, ○—○ $M_6$, ▲—▲ $M_7$, △—△ C.

increase when more water is added and why the tensile strengths of the tablets then decrease is that at these levels the water is probably beginning to form multilayers on the surface of the particles (Zografi et al 1984) acting as a lubricant and therefore reducing the frictional forces responsible for attraction between particles (Coelho & Harnby 1978). Liquid water also tends to rupture the hydrogen bonds between cellulose particles (Reier & Shangraw 1966) which contribute to its tensile strength. This explains why samples containing 75% w/w or more of cellulose exhibited virtually no decrease in the ratio ER/SR (and consequent increase in tensile strength) when up to 2% w/w of water was added to them.

*Effect of stearic acid*

Fig. 7 shows that adding up to 10% w/w of stearic acid which is frequently used as a lubricant in tablet formulations (Little & Mitchell 1963) and which because of its hydrophobicity can also affect disintegration and dissolution rates (Levy & Gumtow 1963) caused increases in the values of ER/SR and reduced the tensile strengths of all the present mixtures. This is because stearic acid is a lubricant and is inherently less cohesive than the two other materials at a fixed

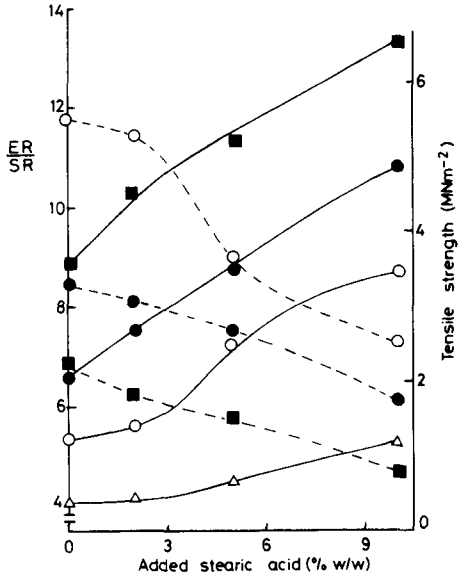


FIG. 7. ER/SR and tensile strength versus % w/w of added stearic acid; ——ER/SR, - - - Tensile strength, ■ ■ $M_4$, ● ● $M_5$, ○ ○ $M_6$, △ △ C. T values of C $\gg$6·0 $MNm^{-2}$, limit of tester.

packing fraction. The presence of such a lubricant in the form of a surface film or as particles could influence the bonding mechanism between particles and thus account for the changes observed in T and in ER/SR.

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