J. Pharm. Pharmacol. 1984, 36: 616–617
Communicated January 24, 1984

Plasto-elasticity and tableting of paracetamol, Avicel and other powders

S. MALAMATARIS†, S. BIN BAIE‡, N. PILPEL*, *Department of Pharmacy, Chelsea College, University of London, Manresa Road, London SW3 6LX, UK*

The plasto-elasticity of mixtures of paracetamol and Avicel powders and the tensile strengths of their tablets varied with the sizes of the particles and with the compositions of the mixtures. Tests made on these and other tablets showed that the logarithms of their strengths were inversely proportional to the ratios of the samples' elastic recovery : plastic compression; they exhibited lamination or capping when this ratio was greater than 9.

The incidence of capping and lamination during the production of pharmaceutical tablets by compression, followed by ejection from the die, depends on the plastic and elastic behaviour of the material used (Shotton & Obiorah 1975; Hiestand et al 1977: David & Augsburger 1977). Its plastic compression

$$PC = \frac{H_O - H_L}{H_O} \times 100\% \quad (1)$$

and its elastic recovery

$$ER = \frac{H_R - H_L}{H_L} \times 100\% \quad (2)$$

H_O, H_L and H_R are respectively the thicknesses of the tablets when first formed, at the end of the loading period and after ejection from the die (Armstrong & Haines-Nutt 1972). A study has been made of the changes produced in the ratio ER/PC (which is a combined measure of plasto-elasticity) and in the tensile strengths of paracetamol tablets by incorporating powdered Avicel and by changing the sizes of both species of particles.

Materials and methods

Paracetamol powder B.P. (Cambrian Chemical Co) and Avicel PH 101, microcrystalline cellulose (Honeywell & Stein Ltd) were ballmilled, then sieved and classified on a Zig Zag classifier (Alpine Multiplex, W. Germany) to give three fractions of paracetamol (P_1 (0–15), P_2 (10–30) and P_3 (15–40) μm) and two of Avicel (A_1 (0–15) and A_2 (15–40 μm)).

Batches (300 g) of the fractions were mixed together in the proportions shown in Table 1 by tumbling for 20 min in a jar fitted with a baffle. Their degrees of mixedness (Rose 1959) were determined from uv analysis of the paracetamol at 249 nm and were >0·96. The mixtures were dried at 60 °C for 24 h and their moisture contents, measured with a vacuum tester (Townson & Mercer), were <2% w/w. They were stored in airtight jars.

Preparation and testing of tablets. An amount of 500 mg of each mixture was formed into a tablet in a Dartec M2501 universal tester (Dartec Ltd) using flat faced lower and upper punches—the latter connected to a load cell—and a die of 10·5 mm diameter. The limit ramp was set to 20% and the load rate to 0·667 kN s^{-1} resulting in the application of loads up to 20 kN over 30 s. The loads were adjusted to give tablets with a packing fraction of 0·85. These were held manually for 30 s, then released automatically over 30 s. The tablet was ejected and the whole cycle ocupied 2 min. The apparatus was connected to a Bryan X–Y recorder which plotted the load versus the displacement of the upper punch. The length of the horizontal portion of the trace was a measure of the plastic compression (PC) and the horizontal distance between the top of the compression curve and the bottom of the release curve yielded the elastic ratio (ER). After the tablets had been stored for 24 h in a desiccator to allow for any further elastic recovery, their dimensions and weights were accurately determined to within 0·01 mm and ±1 mg to give their packing fractions. Their tensile strengths were measured by diametral compression using a CT 40 tester (Engineering Systems, Nottingham), their moisture contents were <2% w/w.

Results and discussion

It was found that, in general, the incidence of capping and lamination of tablets was greatest in mixtures containing mass fractions of Avicel ≤0·25. Mixtures containing paracetamol P_2 had the greatest tendency to cap and laminate. For the remaining tablets, it was found that, as expected (York & Pilpel 1973), their tensile strengths, T, fitted the general equation

$$\log T = Ap_f + B \quad (3)$$

with a highly significant correlation over the range of packing fractions, p_f, between 0·60 and 0·95, where A and B are constants.

Using this equation, values of T were obtained at a fixed packing fraction of 0·85 (selected because it involved minimum extrapolation of the plots of log T

* Correspondence.
† Department of Pharmacy, University of Thessaloniki, Greece.
‡ Department of Pharmacy, University of Sains Malaysia, Penang, Malaysia.

versus p_f and because it was representative of commercial tablets).

The results are given in Table 1. It is seen that the tensile strengths of the tablets decreased with decrease in the amount of Avicel and increase in the particle size of the paracetamol. Changing the amount of Avicel had less effect when it was coarse (A_2) then when it was fine (A_1). increasing the particle size of the paracetamol produced a slightly larger effect with coarse Avicel than with fine.

By inference from the results for the mixtures, Avicel had a higher value of PC and a lower value of ER than paracetamol. The values for Avicel were hardly affected by particle size but for paracetamol ER appeared to increase slightly and PC (by inference) to decrease slightly with increasing size.

In general, the greater the amount of Avicel in a mixture the higher its plastic compression and the lower its elastic recovery. (System A_1P_3 containing a mass fraction of 0·25 of Avicel appeared to be anomalous in this respect, probably the result of error due to the low value of PC.) This is as expected and is consistent with the use of Avicel as a tableting excipient for paracetamol (Leigh et al 1967; Lamberson & Raynor 1976; Krycer et al 1982).

There appears to be an inverse relation between the ratio ER/PC of the samples and the tensile strengths of their tablets (Table 1). This is plotted semi-logarithmically in Fig. 1, together with experimental results obtained from a variety of other powders in the size range 0–40 μm (Baie 1982).* It is seen that all the points can be reasonably accommodated on a single straight line.

The point of interest is that, in general, samples for which the ratio ER/PC < 9 could be formed into satisfactory tablets with a packing fraction of 0·85 with loads up to 20 kN applied for 30 s, while those for which this ratio was >9 produced tablets which tended to cap or laminate.

Table 1. Composition, plasto-elastic parameters and tensile strengths of paracetamol–Avicel mixtures.

Composition size fraction	Mass fraction of Avicel	Plastic compression %	Elastic recovery %	ER / PC	Tensile strength at p_f 0·85 MN m^{-2}
A_1P_1	0·75	2·4	10·0	4·1	4·7
	0·5	2·1	12·2	5·8	3·9
	0·25	2·0	14·5	7·8	2·6
A_1P_2	0·75	2·2	12·0	5·5	4·0
	0·5	2·0	13·3	6·7	3·8
	0·25	1·4	13·4	9·6	Capped
A_1P_3	0·75	2·0	12·0	6·0	4·2
	0·5	1·5	11·0	7·3	3·2
	0·25	1·1	11·8	10·7	Capped
A_2P_1	0·75	2·2	12·6	5·6	4·1
	0·5	2·1	12·4	5·9	3·3
	0·25	1·5	14·0	9·3	2·3
A_2P_3	0·75	1·9	12·8	6·7	3·4
	0·5	1·5	13·2	8·8	2·5
	0·25	1·3	14·0	10·8	Capped
A_1 and A_2	—	2·5	9·5	3·8	6·0
P_1, P_2 and P_3	—	—	13·5–14·5	—	Capped

* These powders were chloroquine phosphate, dicalcium phosphate, oxytetracycline, mannitol, sodium salicylate, lactose, sulfisoxazole, chloramphenicol, griseofulvin, diazepam, zinc oxide, and aluminium silicate. Results for the first six are plotted in Fig. 1; the values of ER/PC for the remainder were respectively 12·5, 13·5, 14·4, 15·9, 15·9 and 16·0 and their tensile strengths (when measurable) were all below 1 MN m^{-2}.

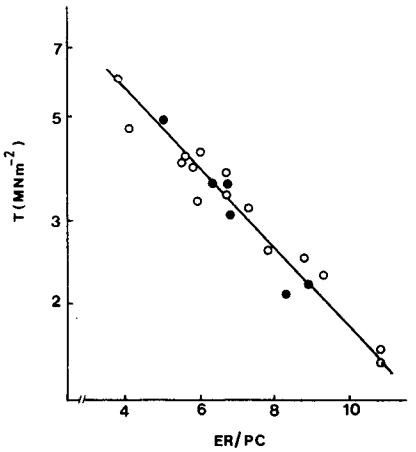

FIG. 1. Tensile strength at p_f 0·85 versus ratio ER/PC for ○ paracetamol–Avicel mixtures, ● other powders.

The absolute values of the ratio may be expected to vary with the test conditions e.g. applied load, duration of loading and unloading cycle (David & Augsburger 1977), tablet size, moisture content etc. But the use of this ratio might prove useful in further preformulation studies.

REFERENCES

Armstrong, N. A., Haines-Nutt, R. F. (1972) J. Pharm. Pharmacol. 24: 135P–136P

Baie, b. S. (1982) Ph.D. thesis, University of London

David, S. T., Augsburger, L. L. (1977) J. Pharm. Sci. 66: 155–159

Hiestand, E. N., Wells, J. E., Peot, C. B., Ochs, J. F. (1977) Ibid. 66: 510–519

Krycer, I., Pope, D., Hersey, J. (1982) Int. J. Pharm. 12: 113–134

Lamberson, R. L., Raynor, G. E. (1976) Manf. Chem. Aerosol News, June 55–61

Leigh, S., Carless, J. E., Burt, B. W. (1967) J. Pharm. Sci. 56: 888–892

Rose, H. E. (1959) Trans. Inst. Chem. Eng. 36: 422–442

Shotton, E., Obiorah, B. A. (1975) J. Pharm. Sci. 64: 1213–1216

York, P., Pilpel, N. (1973) J. Pharm. Pharmacol. 25: 1P–11P