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The effect of temperature on the plasto-elasticity of some pharmaceutical powders and on the tensile strengths of their tablets

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Measurements have been made of the stress relaxation (SR) during, and of the elastic recovery (ER) after, compression of four directly compressible excipients, and of chloroquine diphosphate and of a paracetamol tablet formulation at temperatures between −10 and +65 °C and of the tensile strengths of the tablets produced. It was found that at a fixed packing fraction, the stress relaxation and tensile strength of all the materials increased and the ratio ER/SR decreased as the compression temperature was raised. Tensile strength was inversely proportional to ER/SR at all the temperatures studied. Values for the activation energies (Eo) of bonding between particles for all the materials were derived from plots of the log of tensile strength and of log SR/ER versus the reciprocal of the absolute temperature. The values of Eo obtained from the latter plots tended to be higher than from the former by a factor of between 1·5 and 4·5.

Various studies have been made on the effects of temperature on the mechanical properties of tablets (Jayasinghe et al 1969; York & Pilpel 1972; Pilpel & Esezobo 1977; Britten & Pilpel 1978; Malamataris & Pilpel 1981; Adeyemi & Pilpel 1984). They showed that at a fixed packing fraction the tensile strengths and disintegration times of the tablets increased as the temperature at which they were prepared was increased.

During the tableting of pharmaceutical powders and/or granules, temperatures of 5–30 °C above ambient occur due to the generation of frictional heat at points of contact between particles (Nelson et al 1955; Hanus & King 1968; Travers & Merriman 1970). Particles deform elastically and plastically and there may also be local melting of asperities at the contact points between them due to the combination of frictional heat and the lowering of the melting point of the material caused by high pressure (Rankell & Higuchi 1968; York & Pilpel 1972). When this pressure is released, welded bonds form and these contribute to the subsequent strength of the tablets.

It is now well established (Hiestand et al 1977; David & Augsburger 1977; Rees & Rue 1978; Bangudu & Pilpel 1985; Ejiofor et al 1986) that the greater the stress relaxation (SR) or 'plasticity' of a material the greater the number and strength of particle bonds formed during compression. Both elastic recovery, ER, and SR should be affected by temperature and the purpose of the present work has been to investigate the matter in relation to the resulting strength of tablets.

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MATERIALS AND METHODS

The materials used were some directly compressible excipients—Avicel PH101 (Honeywell and Stein Ltd), Emcompress (Albright and Wilson Ltd), Sta-Rx 1500 (Colocron Ltd), spray dried lactose (McKesson and Robbins Ltd), a pure drug, chloroquine diphosphate (ICI Pharmaceuticals Division) and a paracetamol tablet formulation. This consisted of 70% w/w paracetamol powder (Cambrian Chemicals Ltd), 20% w/w 70 Avicel PH101 20 and 10% w/w potato starch BP (BDH Chemicals Ltd) which had been granulated with 5% w/w aqueous PVP or gelatin binder solutions.

All the materials were classified either on a Zig-Zag classifier (Alpine Multiplex, W. Germany) or on sieves (Endecott Co) to obtain the size range 1–33 μm for chloroquine diphosphate, 1–63 μm for the excipients and 355–710 μm for the granules. They were dried at 60 °C for 24 h and stored in sealed jars until required. Their moisture contents were less than 3% w/w measured with a vacuum tester (Townson and Mercer Ltd, Croydon). Relevant physicochemical properties are listed in Table 1, particle densities being by liquid immersion.

Table 1. Physicochemical properties and activation energies (Eo) of the materials.

Material	M.p. (°C)	Particle density ($g\ cm^{-3}$)	Particle size range (μm)	Packing fraction of tablets (ρ_f)	Calculated activation energy (Eo) $kJ\ mol^{-1}$ from measurements of: Tensile strength	Plasto-elasticity
Avicel	c 230 decomp.	1·52	1–63	0·95	—	6·0
Sta-Rx	c 230 decomp.	1·48	1–63	0·91	10·1	17·7
Emcompress	>1500	2·15	1–63	0·70	3·6	4·5
Spray dried lactose	204	1·55	1–63	0·90	5·8	5·4
Chloroquine diphosphate	193–218	1·58	1–33	0·85	1·4	6·3
Paracetamol formulation + 5% w/w PVP	c 150 decomp.	1·29	355–710	0·85	2·7	8·1
Paracetamol formulation + 5% w/w gelatin	c 150 decomp.	1·29	355–710	0·85	3·0	7·3

Preparation of tablets

A Dartec 100 KN M2501 universal testing machine (Dartec Ltd) whose operation has been described elsewhere (Bangudu & Pilpel 1985; Bangudu 1985; Ejiofor et al 1986) was used to measure the plasto-elasticity of the powders/granules at temperatures between −10 and +65 °C by forming them into tablets, using 10·5 mm diameter upper and lower flat-faced punches and a die which were lubricated with 1% w/w suspension of magnesium stearate in acetone. To minimize the effects of temperature on the zeroing and output of the measuring load cell of the machine it was thermally insulated with plastic sheet. The following procedure was adopted. Samples (500 mg) of each of the test materials in glass containers, were placed together with the die and upper punch in plastic bags containing silica gel and were heated or cooled for 30 min either in an oven or in solid carbon dioxide, until they had reached the required temperature. The lower punch within the adaptor plate of the Dartec was brought to the same temperature using a hot air blower or solid carbon dioxide.

Material was quickly emptied into the die, its temperature was measured, and then it was compressed for 30 s to form a tablet of the required packing fraction. Pressure was held manually for 30 s and then released automatically over 30 s. By starting with the sample up to 5 °C above or below the required temperature, it was ensured that over the period the average temperature remained within a few degrees of that recorded in Table 2. The tablet

Table 2. Effect of temperature on the plasto-elasticity parameters and tensile strengths for spray dried lactose, chloroquine diphosphate and the paracetamol formulation containing 5% w/w PVP.

Applied load (kN)	−10 °C Packing fraction (ρ_f)	ER (%)	SR (%)	ER/SR	T (MN m^{-2})	+23 °C Packing fraction (ρ_f)	ER (%)	SR (%)	ER/SR	T (MN m^{-2})	+65 °C Packing fraction (ρ_f)	ER (%)	SR (%)	ER/SR	T (MN m^{-2})
						Lactose									
10	0·824	2·11	1·38	1·53	0·60	0·841	2·56	1·74	1·47	1·22	0·856	1·90	1·71	1·11	1·71
15	0·856	4·50	1·37	3·28	1·20	0·868	4·67	1·91	2·45	1·80	0·903	3·51	1·79	1·96	2·50
20	0·892	6·73	1·46	4·61	1·35	0·897	5·85	1·67	3·51	2·15	0·916	5·12	1·36	3·76	3·10
25	0·907	7·32	1·49	4·91	1·76	0·293	7·84	1·49	5·26	2·62	0·943	7·15	1·45	4·93	3·45
						Chloroquine diphosphate									
7·5	0·807	2·20	1·57	1·40	1·05	0·799	1·72	1·47	1·17	1·08	0·816	0·90	1·78	0·51	1·79
10	0·821	3·25	1·54	2·11	1·45	0·818	2·56	1·74	1·47	1·52	0·837	1·35	1·73	0·78	2·55
15	0·849	5·07	1·54	3·29	2·06	0·844	4·11	1·62	2·54	2·43	0·862	3·43	1·92	1·79	2·96
20	0·854	7·04	1·53	4·90	2·16	0·863	6·05	1·42	4·26	2·64	0·876	5·55	1·12	4·96	3·47
						Paracetamol formulation with 5% w/w PVP									
7·5	0·809	2·70	1·97	1·37	1·28	0·810	2·38	2·31	0·98	1·46	0·809	0·76	3·12	0·24	1·66
10	0·833	3·59	2·03	1·77	1·58	0·839	3·41	2·04	1·67	2·06	0·840	2·67	2·74	0·97	2·75
15	0·871	5·58	1·75	3·19	2·53	0·877	5·56	2·19	2·54	3·45	0·878	4·20	1·93	2·34	3·85
20	0·891	7·69	1·38	5·57	3·31	0·891	7·08	1·80	3·93	4·44	0·903	6·08	2·07	2·94	5·63

was ejected over a further period of 30 s and stored in a sealed pill-vial at ambient temperature (23 °C) for 24 h.

Diametral compression test

The tensile strengths of the tablets were measured in triplicate by diametral compression using a CT40 tester (Engineering System, Nottingham) (Fell & Newton 1970).

RESULTS AND DISCUSSION

The plasto-elasticity and tensile strength results for representative samples at different compression loads and temperatures are listed in Table 2. It is seen that at any given compression load, the packing fraction tended to increase with increase in temperature; ER tended to decrease, SR to increase and the ratio ER/SR to decrease. Representative graphs of ER/SR vs ρ_f at the three different temperatures are illustrated in Fig. 1. The graphs for the other materials showed similar trends. These results are as expected. They confirm the choice of SR as a measure of plasticity (which increases with temperature), of ER as a measure of elasticity (which decreases with temperature), and generally support the theory of asperitic melting at high pressures (Jayasinghe et al 1969; York & Pilpel 1972; Britten & Pilpel 1978; Malamataris & Pilpel 1981).

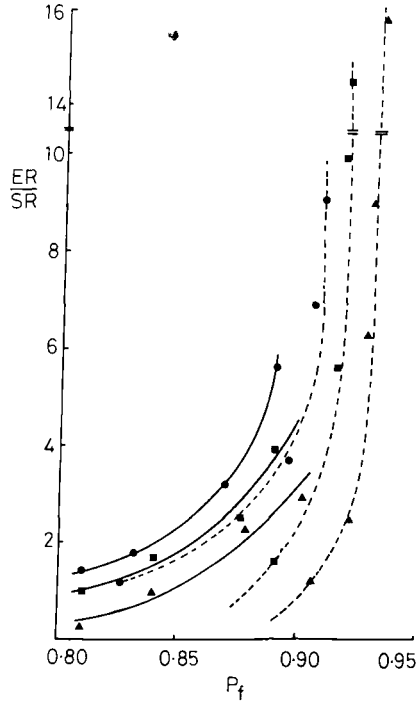

FIG. 1. ER/SR versus ρ_f at different temperatures. —— Paracetamol formulation + 5% w/w PVP; - - - Sta-Rx; ○ −10 °C; □ +23 °C; △ +65 °C.

As expected (York & Pilpel 1973), there was a log linear relationship between the tensile strength and packing fraction, ρ_f, for all the tablets at all temperatures investigated and this is illustrated typically in Fig. 2. The values of the tensile strength for all the materials at fixed packing fractions of 0·91 for Sta-Rx, 0·90 for lactose and 0·85 for the remaining materials (selected because they involved no extrapolation of the experimental data) are

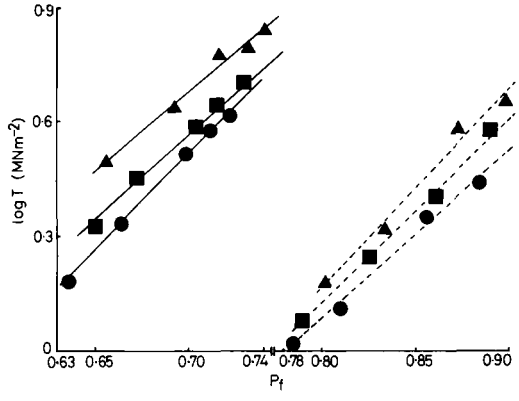

FIG. 2. Log tensile strength (T) versus ρ_f at different temperatures for Emcompress and paracetamol formulation +5% w/w gelatin. —— Emcompress; - - - Paracetamol + 5% w/w gelatin. Symbols as in Fig. 1.

plotted against the homologous temperature during compression (i.e. the temperature of the measurement/melting point of the material concerned both in degrees K) in Fig. 3. The marked increase in tensile strength with homologous temperature is again ascribed to a combination of increased plasticity, asperitic melting and the formation of strong welded bonds beween particles (Pilpel & Britten 1979).

Fig. 4 shows that there is an inverse relationship between the values of ER/SR for the samples and the tensile strengths of their tablets at fixed packing fractions at all the temperatures investigated. The results may be compared with those of Malamataris et al (1984) and Bangudu & Pilpel (1985) for mixed powders and with those of Ejiofor et al (1986) for coated powders.

Based on the theory that sintering of powders occurs by atomic diffusion of material across particles' boundaries, it has been shown (Pilpel &

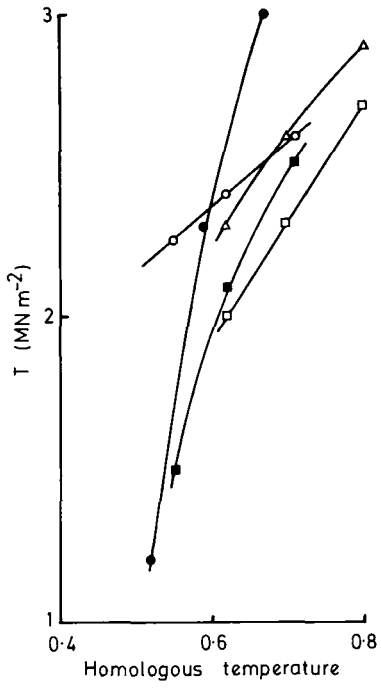

FIG. 3. Tensile strength (T) versus homologous temperature of compression. ● Sta-Rx ρ_f 0·91; ■ lactose ρ_f 0·90; ○ chloroquine diphosphate ρ_f 0·85; △ paracetamol formulation + PVP ρ_f 0·85; □ paracetamol formulation + gelatin ρ_f 0·85.

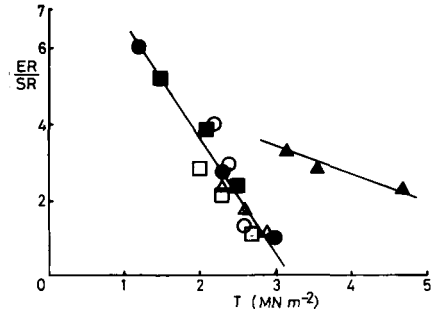

Fig. 4. ER/SR versus tensile strength. ● Sta-Rx ρ_f 0·91; ■ lactose ρ_f 0·90; ▲ Emcompress ρ_f 0·70. ○ Chloroquine diphosphate; △ paracetamol formulation + PVP; □ paracetamol formulation + gelatin all ρ_f 0·85.

Esezobo 1977; Britten & Pilpel 1978; Malamataris & Pilpel 1981) that certain physical and mechanical properties of tablets such as their tensile strength (T), vary with temperature according to the Arrhenius equation

$$T = k\, e^{(-Eo/R\theta)} \qquad (1)$$

where k = a constant for each material at each packing fraction; e = 2·17; Eo = activation energy J mol^{-1}; R = 8·3 J mol^{-1}; θ = temperature in degrees K.

It was thought of interest to see whether the above equation applied to the present tensile strength data and also to the plasto-elasticity data. Inspection of Table 2 showed that the ratio SR/ER rather than ER/SR was more likely to obey equation 1. Plots of log T versus 1/θ and log SR/ER versus 1/θ are given in Fig. 5, the points having been derived from

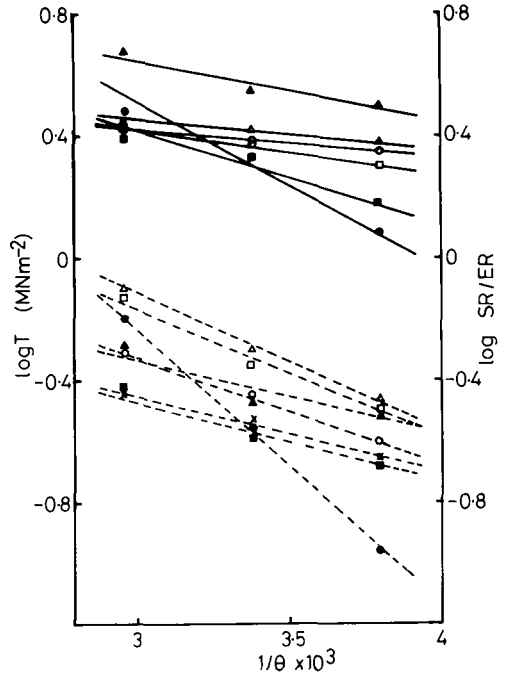

FIG. 5. Log tensile strength and log SR/ER versus 1/θ —— log tensile strength; - - - log SR/ER. Symbols as in Fig. 4 and x Avicel ρ_f 0·95.

appropriate plots (not shown) of log T and logSR/ER against ρ_f. In both cases, good straight lines were obtained for all the materials investigated showing that equation 1 was obeyed. From the values of their slopes (=−Eo/2·303 R), values of the activation energies, Eo, were obtained and these are listed in Table 1. It is seen that although the activation energies derived from SR/ER tended to be between 1·5 and 4·5 times higher than those derived from T, both were of the magnitude expected for interaction between particles to be occurring by physical rather than by chemical processes.

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