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Effects of temperature on the tensile strength of pharmaceutical powders

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Measurements have been made of the tensile strengths of fatty acids, lactose and of an oxtetracycline and a paracetamol tablet formulation at temperatures between −20 and +90°. The measurements were made on compressed tablets and on consolidated beds of powders, using a diametral compression tester and a split plate tensile tester which had been designed to operate over this range of temperature. The tensile strengths of all the materials increase with temperature and values are given for the activation energies of bonding between particles.

Measurement of the tensile strengths of pharmaceutical powders provides useful information on how they are likely to behave during storage, transportation, mixing, granulating, filling into capsules or forming into compressed tablets. Increasingly, specifications for the quality control of such powders include some reference to their tensile strength at a particular packing fraction Pf (= bulk density/particle density) (Walton & Pilpel, 1972, 1974; Esezobo & Pilpel, 1974).

Operations on pharmaceutical powders are nominally carried out at temperatures close to ambient in the range about 5 to 40°. Relatively few powders exhibit measurable changes in tensile strength over this range and there has consequently been less interest in the effect of temperature on the tensile strengths of pharmaceutical powders than on those of other powders such as plastics, coal, metals, ceramics, which are generally handled and processed over a much wider range of temperature, up to 1000° or more (Goetzel, 1949, 1963; Jayasinghe & Pilpel, 1970).

Nevertheless there are reasons why it is now becoming desirable to obtain more information on the way in which the tensile strengths of pharmaceutical powders vary with temperature. Firstly, the range of temperatures over which they are processed has been extended in recent years. At the low end there is the process of freeze drying and the increasing practice of storing powders in bulk at low temperatures in order to preserve them chemically and/or microbiologically. At the high end flash drying, sterilization and high-speed tableting all involve exposing pharmaceutical powders (if only momentarily) to temperatures above 100°. It has been estimated that during tableting, local temperatures at the points of contact between particles in a powder can be as high as several hundred degrees Celcius (Hanus & King, 1968), sufficient to cause the material to melt and subsequently form welded bonds (Rankell & Higuchi, 1968).

Secondly, many powder formulations for capsules and tablets contain ingredients whose melting/softening points are sufficiently close to maximum ambient temperatures for one to expect their contribution to the overall tensile strength of the formulation to change quite noticeably between a high summer and a low winter temperature. Such ingredients include glyceryl esters, commercial fatty acids, hydrated sugars, gums, gelatin and other binding agents.

Some data have been reported on the tensile strengths of pharmaceutical powders at temperatures above ambient (Jayasinghe, Pilpel & Harwood, 1969; York & Pilpel, 1972) but very little has been published on this property at temperatures below 20° (Britten & Pilpel, 1977).

The main difficulty arises from the need to exclude moisture while carrying out the measurements. Otherwise, at temperatures below the dew point, water or frost will deposit on the particles and this will lead to unreliable results.

This paper describes a modified split-plate tensile tester which has been employed in conjunction with a diametral compression tester to measure the tensile strengths of representative pharmaceutical powders over the temperature range −20 to +90°. More elaborate equipment would be needed to extend this range but by using materials of widely differing melting/softening points, it should be possible to relate their tensile strengths to their homologous temperatures (defined as the ratio of the temperature

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of measurement in degrees K to the melting point of the material).

MATERIALS AND METHODS

Materials

The materials were selected to cover a range of softening/melting points between about 40 and 200° and included single pure chemicals like stearic acid and formulated powders for tablets such as the oxytetracycline formulation. Wherever possible they were classified into narrow size fractions using an airjet sieve or a Microplex classifier. All materials were dried at appropriate temperatures and stored in sealed jars over phosphorus pentoxide or silica gel until required. Some of their relevant physicochemical properties are listed in Table 1.

Table 1. *Physicochemical properties of materials.*

Material	m.p. °C	Particle density kg m^{-3} $\times 10^{-3}$	Mean particle/granule diameter (μm)
Glyceryl monostearate	54	1·03	280
Stearic acid	70	0·99	50
Behenic acid	80	0·98	20
Oxytetracycline formulation[1]	c 150 decomp	1·46	powder 7 granules 600
Paracetamol formulation[2]	c 150 decomp	1·29	powder 5 granules 700
Lactose	204	1·54	powder 20 granules 500

[1] A commercial formulation from ICI Ltd.; 90% oxytetracycline, 7% Avicel, 3% alginic acid + 5% gelatin.
[2] A commercial formulation from Winthrop Ltd; 90% paracetamol, 10% maize starch + 5% PVP.

Preparation of tablets

Oxytetracycline, paracetamol and lactose granules were formed into 5 g 2·54 cm diameter tablets at temperatures between −18° and +90° in a punch and die using a hand press and a procedure which has been described elsewhere (York & Pilpel, 1973; Pilpel & Esezobo, 1977).

Particular care was taken to avoid condensation of water vapour at temperatures below the dew point. The tablets were then subjected to a diametral compression test at as near as possible the same temperature as had been used in their preparation.

Tensile tests

The apparatus consisted of a split brass cell of the Warren Springs type, 9·5 cm internal diameter, 1·1 cm deep with one half free to move on ball bearings. The base of the cell was a removable stainless steel mesh, pore size 10 μm, through which pre-heated or pre-cooled dry nitrogen gas could be passed. The cell was enclosed in an insulating jacket.

Samples of powder were introduced into the cell, brought to the required temperature by passing nitrogen gas through for 10 min and then consolidated by means of the plunger attached to the load platform. Their tensile strength at the packing fraction achieved during consolidation was obtained by measuring the force required to split the bed at the same temperature. Fuller details of the theory and operation of this type of equipment have been published (Ashton, Farley & Valentin, 1964; Britten & Pilpel, 1977).

Diametral compression tests

The apparatus consisted of a flat horizontal plate which was driven downwards at 0·1 cm min^{-1} by a constant speed motor onto the tablet which was positioned on its edge on a lower plate and which was enclosed in a plastic bag. Cardboard padding strips were used to distribute the applied load evenly across the edge (Rudnick, Hunter & Holden, 1963). The temperature during the test was kept within ±10° of that used during preparation of the tablet by blowing pre-heated or pre-cooled dry nitrogen gas through the bag.

Provided the tablet breaks cleanly into halves

$$T = \frac{2P}{D\pi t}$$

where T is the tensile strength, P is the applied load, and D and t are the diameter and thickness respectively of the tablet (Fell & Newton, 1970).

RESULTS

The results of the tensile tests on all the materials at all the temperatures examined followed the expected pattern (York & Pilpel, 1972) yielding straight lines when the log of tensile strength was plotted against packing fraction. Typical results for glyceryl monostearate, stearic and behenic acids at Pf between 0·5 and 0·6 and temperatures between −10° and +35° are shown in Fig. 1 (a,b,c). The results for the lactose, oxytetracycline and paracetamol tablets at Pf 0·75 to 0·95 at temperatures between −18° and +90° are shown in Fig. 2 (a,b,c). It was not possible to achieve packing fractions greater than 0·6 in the tensile tester or to produce coherent tablets with packing fractions less than 0·7 with the punch and die. Thus the linear relations between log T and Pf only held over relatively narrow ranges of Pf.

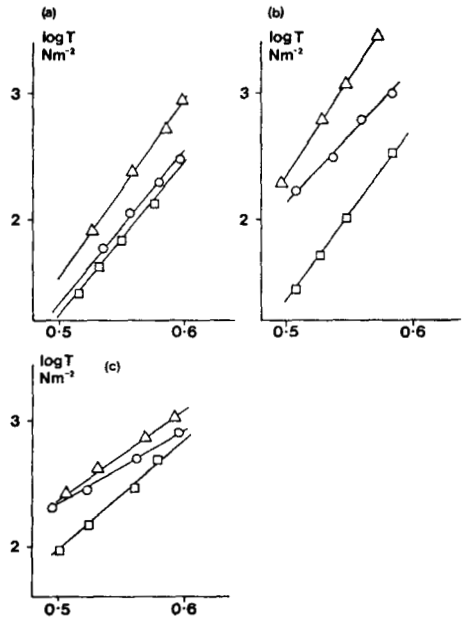

FIG. 1. Log tensile strength (Log T) *vs* packing fraction (Pf). (a) Glyceryl monostearate. (b) Stearic acid. (c) Behenic acid. □ −10°. ○ +20°. △ +35°. Ordinate: Log T (Nm^{-2}). Abscissa: Pf.

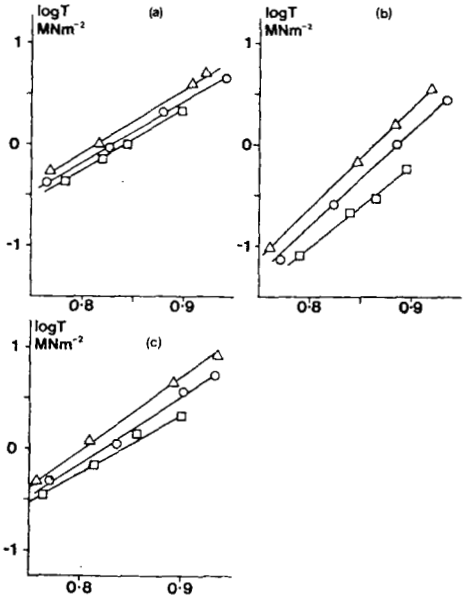

FIG. 2. Log tensile strength *vs* packing fraction. (a) Lactose. (b) Paracetamol formulation. (c) Oxytetracycline formulation. □ −18°. ○ +20°. △ +90°. Ordinate and abscissa as for Fig. 1.

DISCUSSION

It is apparent from the results in Figs 1 and 2 that the tensile strengths of all the materials tested increased as their temperature was raised: conversely at low temperatures the tensile strengths all became very small. The effects produced depended on the packing fraction of the sample and also on the temperature of the material in relation to its melting/softening point (homologous temperature). To demonstrate this graphically we have selected two convenient packing fractions of 0·5 and 0·6 for the results obtained in the tensile tester and 0·75 and 0·90 for those obtained by diametral compression and then plotted tensile strength versus homologous temperature in Figs 3 (a,b) and 4 (a,b).

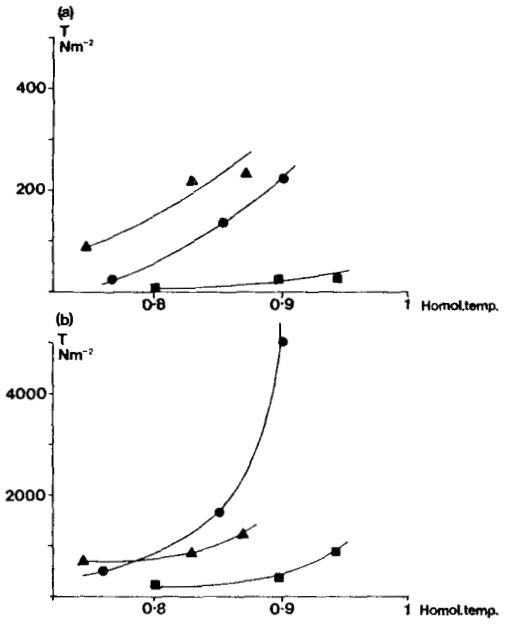

FIG. 3. Tensile strength (Nm^{-2}) (ordinate) *vs* homologous temperature (abscissa). (a) Pf 0·5; (b) Pf 0·6. ■ Glyceryl monostearate. ● Stearic acid. ▲ Behenic acid.

On comparison of Figs 3a with 3b and 4a with 4b (and noting the different scales on the ordinates) it is seen that the effect of temperature on tensile strength becomes increasingly marked as the packing fraction of the sample is increased.

The tensile strengths of the powders arise from physical and mechanical forces that act between their constituent particles and it is now well established that in a moderately packed bed (Pf 0·5 to 0·9) there is only a relatively small area of actual contact

between asperities on the surfaces of neighbouring particles.

The pressure that is exerted on the powder in preparing it for the tensile test thus becomes localized at these points of contact and may amount to several hundred atmospheres (Jayasinghe & others, 1969; York & Pilpel, 1972). Under these conditions the asperities may deform by plastic flow. As the temperature is raised, the amount of deformation and hence the area of contact between the particles increases (Gane, Pfaelzer & Tabor, 1974) resulting in the increases in tensile strength that have been observed above.

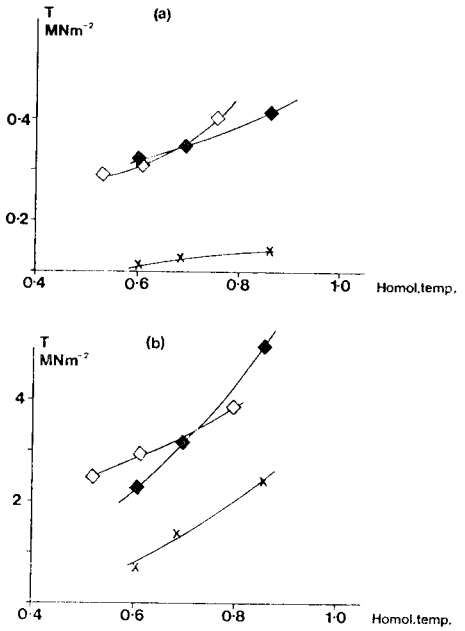

FIG. 4. Tensile strength (MN m^{-2}) (ordinate) *vs* homologous temperature (abscissa) (a) Pf 0·75; (b) Pf 0·9. ◇ Lactose. ◆ Oxytetracycline formulation. × Paracetamol formulation.

These high pressures, acting selectively at the points of actual contact, may cause them to melt even though the temperature may be below the conventional melting point of the material at atmospheric pressure (Jayasinghe & others, 1969). The amount of this 'pressure melting' will depend on the ambient temperature and on the localized pressure that has been generated in preparing the sample for test. Once it has occurred the area of true contact between the particles increases, the localized pressure falls and the previously melted material may then resolidify to form welded bonds.

However, if the ambient temperature is below that at which 'pressure melting' can occur then no (or at least fewer) welded bonds will be formed.

These mechanisms would explain the low tensile strengths of the powders at low temperatures, the increases that occur as their homologous temperatures are raised towards unity and the larger effects that are produced by temperature on the tensile strengths of the powders at high packing fractions than at low ones (cf. Figs 3a and 3b).

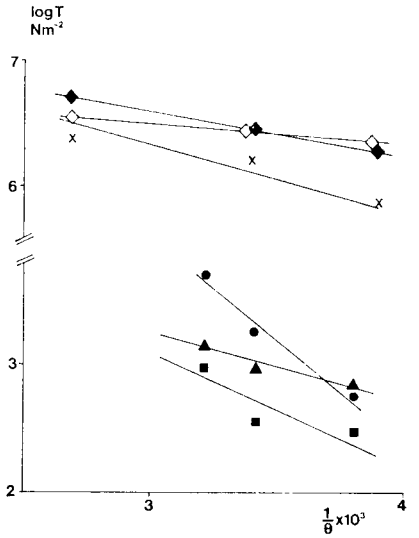

FIG. 5. Log tensile strength (Log T) *vs* reciprocal absolute temperature ($1/\theta$). ■ Glyceryl monostearate. ● Stearic acid. ▲ Behenic acid. ◇ Lactose. ◆ Oxytetracycline formulation. × Paracetamol formulation. Ordinate: Log T (Nm^{-2}). Abscissa: $1/\theta \times 10^3$.

When the homologous temperatures are increased to unity any welded bonds that may have been formed melt and the tensile strengths of the materials then decrease, presumably to the work of adhesion of the liquid melt.

On the basis of the theory of sintering (Kuczynski, 1950) in which it is assumed that sintering occurs by atomic transport and diffusion mechanisms whose rates are determined by the ambient temperature, a relation between tensile strength and temperature might be expected which follows a form of the Arrhenius equation

$$T = ke^{-Eo/R\theta}$$

where R = 8·3 J mol^{-1}; E_0 = activation energy of bonding; k = a constant for each material at each packing fraction; θ = temperature in degrees K.

Arrhenius plots for representative materials are shown in Fig. 5. Their slopes ($= -E_0/2{\cdot}303R$) give the values of E_0 listed in Table 2.

Table 2. *Activation energies.*

Material	Pf	Eo kJ mol^{-1}	Material	Pf	Eo kJ mol^{-1}
Glyceryl monostearate	0·6	18·8	Lactose	0·9	5·0
Stearic acid	0·6	32·8	Paracetamol form.	0·9	9·2
Behenic acid	0·6	9·4	Oxytet. form.	0·9	5·9

These are of the magnitude expected for welded bonds, the values of E_0 for the paracetamol and oxytetracycline being similar to those reported in previous work (Pilpel & Esezobo, 1977).

The potential applications of these findings to the handling and processing of pharmaceutical powders may now be outlined.

(a) Powders that have a tendency to cake when stored for long periods at ambient temperatures, due to plastic deformation of particles and the formation of welded bonds between them, might be better stored (in the dry state) at low temperatures.

(b) The decrease that is observed in the tensile strengths of powders as their temperature is reduced below ambient should make them flow more easily through pipes and orifices provided that appropriate precautions are taken to keep them dry at temperatures below the dew point.

(c) The large increases that occur in the tensile strengths of powders when they are heated (which is the basis of the sintering process for metals, plastics, ceramics) might be usefully applied also to the compression and tableting of pharmaceutical materials and this would call for the exercise of tighter control over the speed and/or temperature of the tableting process.

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