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The tensile strengths of mixtures of oxytetracycline and lactose powders

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Summary

Measurements have been made of the tensile strengths of physical and formulated mixtures of oxytetracycline and lactose, varying the particle size, temperature and compositions of the mixtures.

At a constant packing fraction the tensile strengths of formulated mixtures were higher than those of physical mixtures and both deviated from those expected theoretically; the maximum deviation occurred with the 50 : 50 mixtures.

The tensile strengths of the single powders and the mixtures could be predicted with an average accuracy of ± 10% by the use of equations due to Cheng (1968, 1970) and Kocova and Pilpel (1973).

Introduction

The tensile strength of a bed of powder is the force per unit area required to split it in tension; it is affected by the particle size distribution (Cheng, 1968, 1970; Walton and Pilpel, 1972), particle shape and rugosity, packing fraction (Ashton et al., 1965) and by the temperature of the bed (Jayasinghe et al., 1969/70; York and Pilpel, 1972).

Relatively little work has been reported on the tensile strengths of mixtures of powders (Kocova and Pilpel, 1973; York and Pilpel, 1973; Varthalis and Pilpel, 1976; Chan et al., 1983). The powders can be either mixed physically or granulated

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as a formulation and then milled back to their original size (Kurup and Pilpel, 1979). In the former case the component particles remain discrete. In the latter, any soluble component tends to coat the other(s) and when dry form solid bridges between the particles. Some of the coating may persist even after milling and is visible under the electron microscope. It can affect the range and magnitude of the forces acting between the particles. These forces are: (a) Van der Waals; (b) electrostatic; (c) frictional and mechanical; and (d) surface tension and capillary.

Kocova and Pilpel (1973) extended Cheng's original theory (1968) of tensile strength to try to deal with real systems of powders either containing a wide range of sizes of particles of one material or containing narrow size ranges of particles of different materials.

The purpose of the present work has been to test the validity of this theory for binary mixtures. Tensile tests were carried out at different temperatures on 3 narrow size fractions of oxytetracycline and lactose powders when mixed physically or granulated together in various proportions. The predicted tensile strengths were compared with those obtained experimentally.

The effects of and interaction between particle size, temperature and composition of the mixtures on the tensile strengths were studied by performing the experiments in a factorial design.

Materials and Methods

The two materials used were oxytetracycline dihydrate powder, supplied by ICI Pharmaceuticals Division which complied with the official standard EP 11 (1971), and lactose powder BP from Whey Products.

Granulation of mixtures

250 g batches of the oxytetracycline and lactose powders in appropriate proportions were dry-mixed for 5 min in a Kenwood planetary mixer. 40 ml of water was added and massing continued for 2 min. The wet masses were forced through a no. 24 sieve in an Erweka granulator and the granules were dried in a hot-air oven for 12 h at 55°C. They were then milled down to less than 33 μm in a Teema swing mill.

Classification and particle size determination

The two individual powders and the milled formulated mixtures were freed from particles > 33 μm using an Alpine airjet siever and were then classified on a Microplex zig-zag classifier into 3 different size fractions, 0–10, 10–20 and 20–30 μm. They were stored in airtight glass jars and their particle sizes were confirmed by optical microscopy.

Preparation of physical mixtures

The two powders in the 3 different size fractions were mixed in appropriate proportions in a planetary mixer for 5 min. They were dried and stored as before. Representative samples were assayed spectrophotometrically for oxytetracycline at

TABLE 1

SAMPLES

Material	Weight fraction (W)	Code no.	Particle density (g/cm^3)
Oxytetracycline	1.0	Y	1.454
Lactose	1.0	L	1.554
Physical mixtures			
Oxytetracycline	0.75	M_1	1.525
Lactose	0.25		
Oxytetracycline	0.50	M_2	1.502
Lactose	0.50		
Oxytetracycline	0.25	M_3	1.477
Lactose	0.75		
Oxytetracycline	0.70	M_7	1.522
Lactose	0.30		
Oxytetracycline	0.30	M_8	1.482
Lactose	0.70		
Formulated mixtures			
Oxytetracycline	0.75	M_4	1.525
Lactose	0.25		
Oxytetracycline	0.50	M_5	1.502
Lactose	0.50		
Oxytetracycline	0.25	M_6	1.477
Lactose	0.75		
Oxytetracycline	0.70	M_9	1.522
Lactose	0.30		
Oxytetracycline	0.30	M_{10}	1.482
Lactose	0.70		

353 nm. The index of mixing in all the mixtures, defined by $1 - \sigma/\sigma_0$ where σ is the standard deviation for analyzed samples and σ_o is the standard deviation for the unmixed system, was found to be > 0.95.

The particle densities of the individual components and of the mixtures were determined by the Beckman air comparison pycnometer method, (Model 930, Beckman Instruments) and the results are recorded in Table 1.

Tensile tests

The tensile strengths of the samples were measured in a split nickel-plated cell of the Warren Spring type (Ashton et al., 1964), 9.5 cm internal diameter, 1.1 cm deep, which had been adapted for use at low or elevated temperatures by enclosing it in an insulating jacket and the samples were maintained at the required temperature for 10 min while checking by means of sensitive miniature bead thermistors (RS Components). Details of its design and operation have been published (Britten and Pilpel, 1977).

In order to study the effects of the variables on the tensile strengths of the samples the experiments were performed in a factorial design. Each of the 3 variables: particle size fraction (D), temperature (U) and proportion of added lactose (P) was employed at a 'high' level (denoted by the subscript H), a 'low' level (subscript L) and a 'medium' level (subscript M)[1]. A 2^3 (= 8) factorial design was used and a total of 24 sets of measurements of tensile strength was analyzed.

For the high and low levels the combinations of tensile strengths selected were: $D_HU_HP_L$, $D_HU_HP_H$, $D_HU_LP_H$, $D_HU_LP_L$, $D_LU_LP_H$, $D_LU_LP_L$, $D_LU_HP_L$ and $D_LU_HP_H$.

For high and medium levels the combinations were: $D_HU_HP_M$, $D_HU_HP_H$, $D_HU_MP_H$, $D_HU_MP_M$, $D_MU_MP_H$, $D_MU_MP_M$, $D_MU_HP_M$ and $D_MU_HP_H$.

For medium and low levels the combinations were: $D_MU_MP_L$, $D_MU_MP_M$, $D_MU_LP_M$, $D_MU_LP_L$, $D_LU_LP_M$, $D_LU_LP_L$, $D_LU_MP_L$ and $D_LU_MP_M$.

By grouping the tensile strength results into different sets it was possible to examine the effect that each variable had had on tensile strength and also to test whether the variables were acting independently or interacting with each other.

For example, the effect on tensile strength of increasing D from its low level to its high level was found by summing all tensile strength results from samples containing high levels of D and subtracting from the total, the sum of the tensile strength results from the samples containing low levels of D and then dividing by 4:

$$\tfrac{1}{4}\left[(D_HU_HP_L + D_HU_HP_H + D_HU_LP_H + D_HU_LP_L) - (D_LU_LP_H + D_LU_LP_L + D_LU_HP_L + D_LU_HP_H)\right] \quad (1)$$

Similarly, the effects of increasing U and P were calculated, respectively, from:

$$\tfrac{1}{4}\left[(D_HU_HP_L + D_HU_HP_H + D_LU_HP_L + D_LU_HP_H) - (D_HU_LP_H + D_HU_LP_L + D_LU_LP_H + D_LU_LP_L)\right] \quad (2)$$

and

$$\tfrac{1}{4}\left[(D_HU_HP_H + D_LU_HP_H + D_HU_LP_H + D_LU_LP_H) - (D_HU_HP_L + D_LU_HP_L + D_HU_LP_L + D_LU_LP_L)\right] \quad (3)$$

The combinations for medium to high and low to medium levels were treated in the same way.

To test whether or not any two variables were interacting and to determine the extent of such interaction, e.g. for D and U, the results were grouped as:

$$\tfrac{1}{4}\left[(D_HU_HP_L + D_HU_HP_H + D_LU_LP_H + D_LU_LP_L) - (D_HU_LP_H + D_HU_LP_L + D_LU_HP_L + D_LU_HP_H)\right] \quad (4)$$

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[1] Mixtures M_1 and M_4 contained the low (L) level of lactose. Mixtures M_2 and M_5 contained the medium (M) level of lactose. Mixtures M_3 and M_6 contained the high (H) level of lactose.

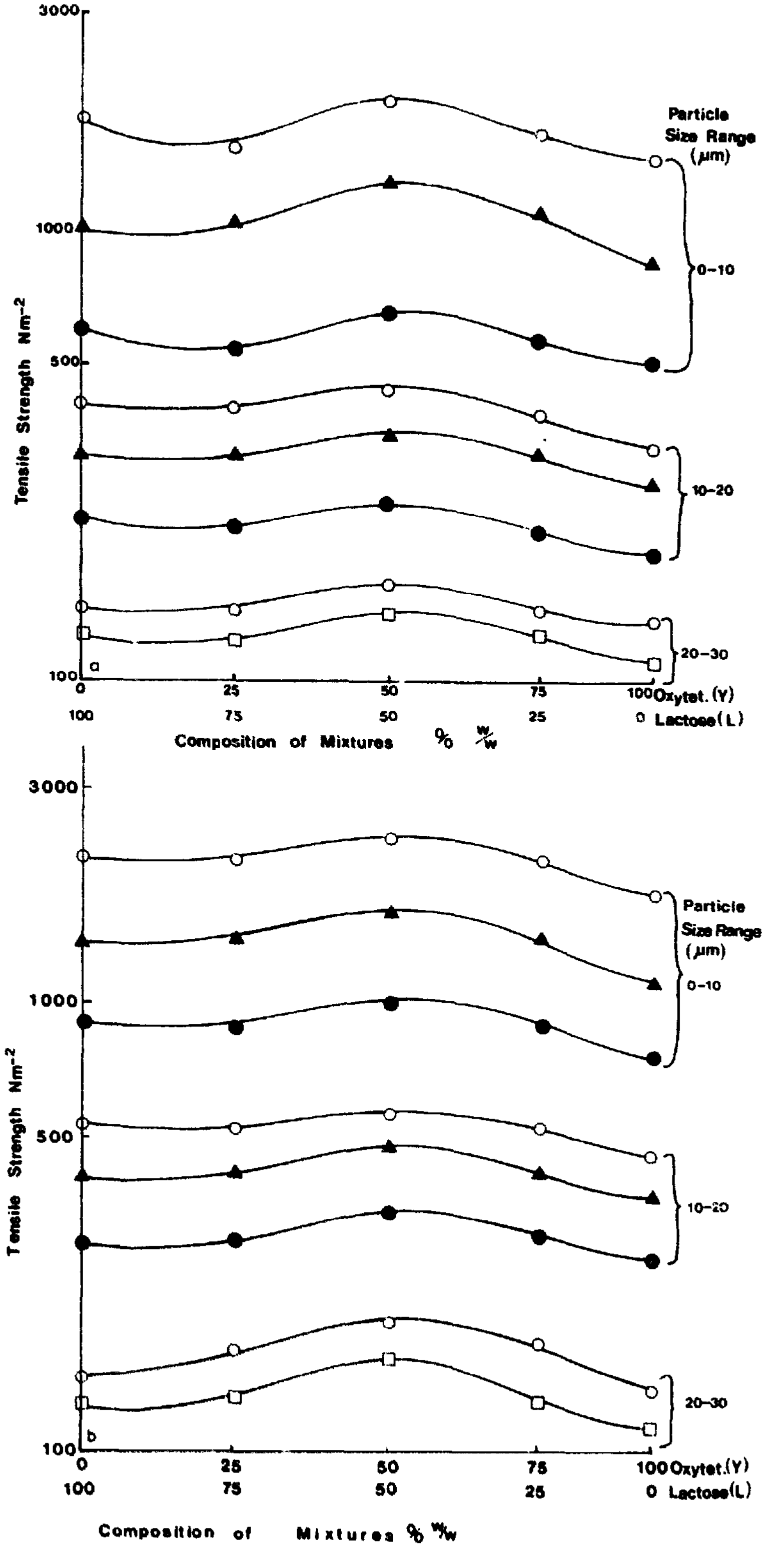

Fig. 1. a: log tensile strength versus composition of physical mixtures (ρ_f 0.45) at different temperatures and particle size fractions. ○, 50°C; □, 35°C; ▲ 20°C; ●, −10°C. b: log tensile strength versus composition of formulated mixtures (ρ_f 0.45) at different temperatures and particle size fractions. ○, 50°C; □, 35°C; ▲, 20°C; ●, −10°C.

Similarly for D and P:

$$\tfrac{1}{4}[(D_H U_H P_H + D_H U_L P_H + D_L U_L P_L + D_L U_H P_L) - (D_H U_H P_L + D_H U_L P_L + D_L U_L P_H + D_L U_H P_H)] \qquad (5)$$

and for U and P:

$$\tfrac{1}{4}[(D_H U_H P_H + D_H U_L P_L + D_L U_L P_L + D_L U_H P_H) - (D_H U_H P_L + D_H U_L P_H + D_L U_L P_H + D_L U_H P_L)] \qquad (6)$$

A summation result of zero indicated that there was no interaction between the variables; the amount of departure from zero was a measure of the amount of interaction (Woolfall, 1964).

Results

The tensile strength results for all the samples (L, Y, M_1–M_6) at all the temperatures studied fitted the general equation:

$$\log T = K \cdot \rho_f + B \qquad (7)$$

TABLE 2

THE EFFECT ON TENSILE STRENGTH OF VARYING PARTICLE SIZE (D), TEMPERATURE (U) AND PROPORTION OF LACTOSE (P)

Sample system	Effect on tensile strength of increasing from low to high level of:		
Table 2a	D (Nm^{-2})	U (Nm^{-2})	P (Nm^{-2})
Physical mixtures	−1047	593	49
Formulated mixtures	−1357	623	8
	Effect on tensile strength of increasing from low to medium level of:		
	D (Nm^{-2})	U (Nm^{-2})	P (Nm^{-2})
Physical mixtures	−572	301	87
Formulated mixtures	−837	320	100
	Effect on tensile strength of increasing from medium to high level of:		
	D (Nm^{-2})	U (Nm^{-2})	P (Nm^{-2})
Physical mixtures	−243	63	25
Formulated mixtures	−330	76	24
	Interaction coefficient for tensile strength between:		
Table 2b	D and U	D and P	P and U
Physical mixtures	5.01	0.24	0.12
Formulated mixtures	5.60	0.14	0.11

with a correlation coefficient > 0.98 where T was the tensile strength, K and B were constants for each material and ρ_f was the packing fraction (Farley and Valentin, 1967/68).

The tensile strength values at different temperatures at a fixed ρ_f 0.45 (selected because it involved minimum extrapolation of the rectilinear plots of log T versus ρ_f) were determined. The formulated mixtures had higher tensile strengths than the physical mixtures and Fig. 1a and b show how log T varied as the composition, temperature and particle size of the samples were changed. It is seen that in all cases T was a maximum for the 50:50 mixtures deviating from the theoretical straight lines obtained by joining the ends of the curves. It is also seen that the tensile strength increased with increase in temperature (Jayasinghe et al., 1969) and with decrease in particle size.

The results of the factorial experiment given in Table 2a and b show that particle size had a bigger effect on tensile strength than temperature or composition of the mixture.

Discussion

The higher tensile strengths of the formulated mixtures than of the physical mixtures at all temperatures studied can be ascribed to the greater likelihood in the former systems of solid bonds forming between neighbouring particles (all the other forces listed in the introduction probably remain the same). During granulation some lactose could dissolve in the water and then crystallize on drying to form solid bonds between oxytetracycline particles thus increasing the tensile strength. Solid bonds could only form in the physical mixtures by plastic deformation of particles when consolidating the samples for testing (Kurup and Pilpel, 1979).

Test of theory

There is a tensile strength equation [2] (Kocova and Pilpel, 1973) which can be employed for analyzing the present results. This is:

$$T = h\left[t_0 - \frac{\bar{d}_{mix}}{3}\left(\frac{\rho_f}{\rho_0} - 1\right)\right] \cdot \frac{abc}{2\bar{v}_{mix}} \cdot \frac{\rho}{\rho_s} \cdot M\left[\bar{S}_Y W^2 + 2\,\bar{S}_{YL} W(1 - W) + \bar{S}_L (1 - W)^2\right] \tag{8}$$

where W is the weight fraction of oxytetracycline; a and b are constants; c is the co-ordination number; T is the tensile strength; h is the inter-particle force per unit area; ρ is the bulk density of the powder; ρ_s is the particle density of the mixture;

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[2] The justification for employing this equation for the present mixtures is that the two component powders had the same particle size ranges and very similar densities. Thus their weight fractions were virtually the same as their number fractions. E.g. in mixtures M_7 and M_8 the weight fractions of oxytetracycline are 0.70 and 0.30, respectively, and their number fractions are 0.73 and 0.28.

$\rho_f = \rho/\rho_s$ is the packing fraction; t_0 is the effective range of the inter-particle forces; ρ_0 is the packing fraction when $T = 0$; M is the index of mixing; $\bar{d}_{mix}$ is the mean particle diameter of the mixture (i.e. about 4.3, 15 or 25 μm); $\bar{V}_{mix}$ is the mean particle volume of the mixture (i.e. about 80, 1800 or 8200 μm^3); $\bar{S}_L$ is the mean surface area of lactose; $\bar{S}_Y$ is the mean surface area of oxytetracycline; and $\bar{S}_{YL}$ is the mean surface area of the mixture. (Clearly for single-component powders the terms with the subscript 'mix' will be replaced by the corresponding terms for the individual components.)

Using the experimental results from samples L, Y and M_1–M_6, the values of ρ_0 were obtained by plotting tensile strengths against packing fraction and extrapolating to $T = 0$. Representative graphs are shown in Fig. 2.

To evaluate values of t_0, the range of the inter-particle force, graphs were plotted of:

$$F = \frac{1}{2} \cdot \frac{\bar{S}_{YL}}{\bar{V}_{mix}} \cdot \frac{\rho_f}{T} \tag{9}$$

versus

$$G = \frac{\bar{d}_{mix}}{3} \cdot \left(\frac{\rho_f}{\rho_0} - 1 \right) \tag{10}$$

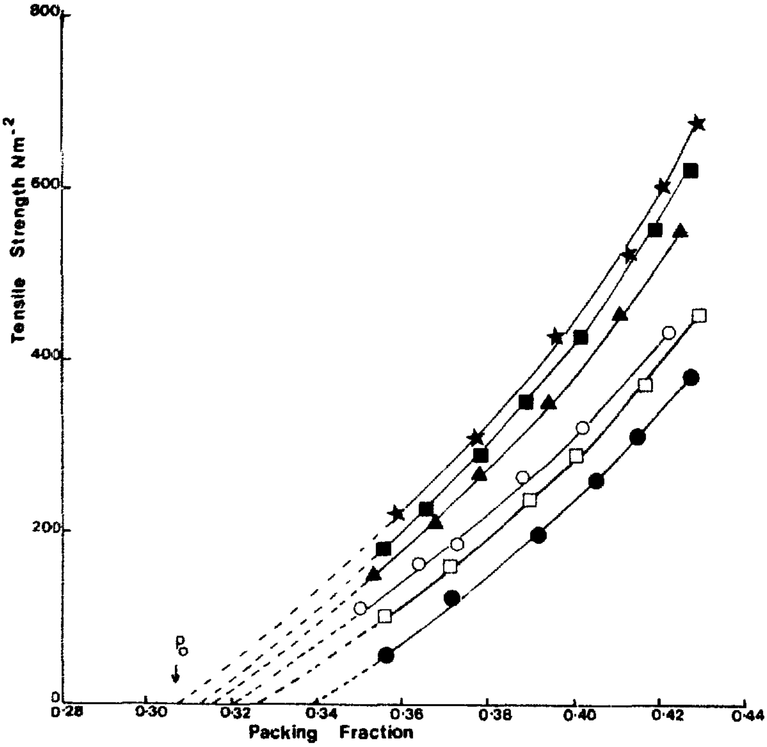

Fig. 2. Tensile strength versus packing fraction for physical and formulated mixtures at −10°C and 0–10 μm. □, L; ○, M_2; ●, M_3; ▲, M_4; ★, M_5; ■, M_6.

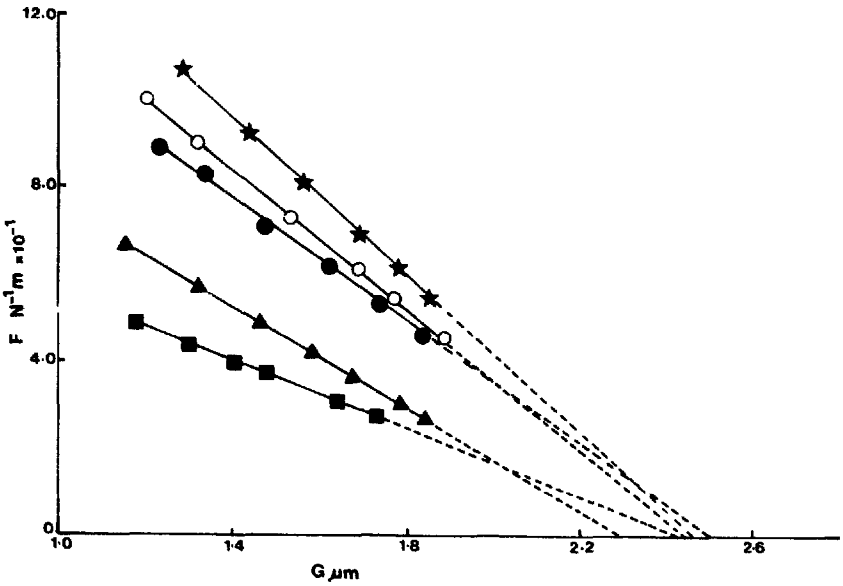

Fig. 3. Plots of F versus G. ★, M_1; ○, M_2; ●, M_3; ▲, M_4; ■, M_6.

(Esezobo, 1976) and each curve was extrapolated to the point where $F = 0$ giving t_0. Typical graphs of F versus G are illustrated in Fig. 3.

Cheng (1968) derived a law of corresponding states between h(t), t and ϵ_0 as:

$$\frac{t_0^3}{\epsilon_0} h(t) = \phi\left(\frac{t}{t_0}\right) \qquad (11)$$

where t is the average surface separation of particles, t_0 is the range of the interparticle force, ϵ_0 is the energy of the particle surface and ϕ is the functional relationship between them. It follows from Cheng's treatment that

$$t = t_0 - \frac{\bar{d}_{mix}}{3}\left(\frac{\rho_f}{\rho_0} - 1\right) = t_0 - G \qquad (12)$$

and

$$h_{(t)} = \tfrac{1}{2} M \frac{\bar{S}_{YL}}{\bar{V}_{mix}} \cdot \frac{\rho_f}{T} = F \qquad (13)$$

(Kocova and Pilpel, 1973). Plotting F versus t/t_0 on a logarithmic scale (Fig. 4), gives curves which have approximately the same shapes and are parallel to each other, proving the validity of the law of corresponding states in the mixtures M_1–M_6 and the applicability to them of the common function ϕ.

TABLE 3

VALUES OF t, t_0 AND ϵ_0 DERIVED FROM TENSILE TESTS

Material code no. [a]	Particle size range (μm)								
	0–10			10–20			20–30		
	t (μm)	t_0 (μm)	ϵ_0 at ρ_f 0.45	t (μm)	t_0 (μm)	ϵ_0 at ρ_f 0.45	t (μm)	t_0 (μm)	ϵ_0 at ρ_f 0.45
Temp. – 10°C									
Y	0.130	0.89	0.344	0.94	1.69	0.98	3.30	3.89	1.15
L	0.110	0.58	1.000	0.91	1.55	1.00	3.20	3.77	1.00
Physical mixtures									
M_1	0.100	0.60	0.312	0.98	1.76	1.20	3.30	4.47	2.11
M_2	0.085	0.56	0.243	0.85	1.70	0.99	3.00	4.40	1.35
M_3	0.100	0.59	0.350	0.92	1.84	1.37	3.20	4.36	1.74
Formulated mixtures									
M_4	0.095	0.48	0.120	0.88	1.64	0.85	3.00	4.12	1.05
M_5	0.070	0.46	0.090	0.78	1.63	0.72	2.78	4.00	1.22
M_6	0.085	0.53	0.150	0.86	1.70	0.93	3.05	4.15	1.08

Temp. 20°C								
Y	0.160	0.77	0.990	1.01	1.00	0.99	3.70	4.17	1.00
L	0.140	0.68	1.000	0.99	1.15	1.00	3.60	4.08	1.11
Physical mixtures									
M_1	0.150	0.78	0.480	0.91	1.96	1.20	3.56	4.71	1.22
M_2	0.120	0.76	0.430	0.80	1.88	0.96	3.30	4.49	1.30
M_3	0.140	0.95	0.970	0.90	1.77	0.89	3.75	4.81	1.65
Formulated mixtures									
M_4	0.110	0.70	0.290	0.80	1.60	0.50	3.21	4.09	0.83
M_5	0.090	0.70	0.270	0.71	1.50	0.41	3.00	4.52	0.97
M_6	0.100	0.77	0.380	0.81	1.60	0.55	3.30	4.77	1.30
Temp. 50°C									
Y	0.340	1.40	0.650	1.11	2.36	1.10	3.79	4.68	1.05
L	0.310	1.12	1.000	1.00	2.24	1.00	3.62	4.57	1.00
Physical mixtures									
M_1	0.390	1.35	1.000	1.04	2.46	1.19	3.60	4.75	1.06
M_2	0.300	1.43	1.200	0.90	2.40	1.04	3.52	4.70	1.01
M_3	0.380	1.30	0.890	0.99	2.50	1.20	3.80	4.99	1.26
Formulated mixtures									
M_4	0.320	1.21	0.580	0.93	2.20	0.73	3.34	4.64	0.84
M_5	0.270	1.20	0.530	0.78	2.13	0.69	3.20	4.60	0.73
M_6	0.260	1.27	0.680	0.82	2.22	0.86	3.58	4.75	0.96

[a] Refer Table 1

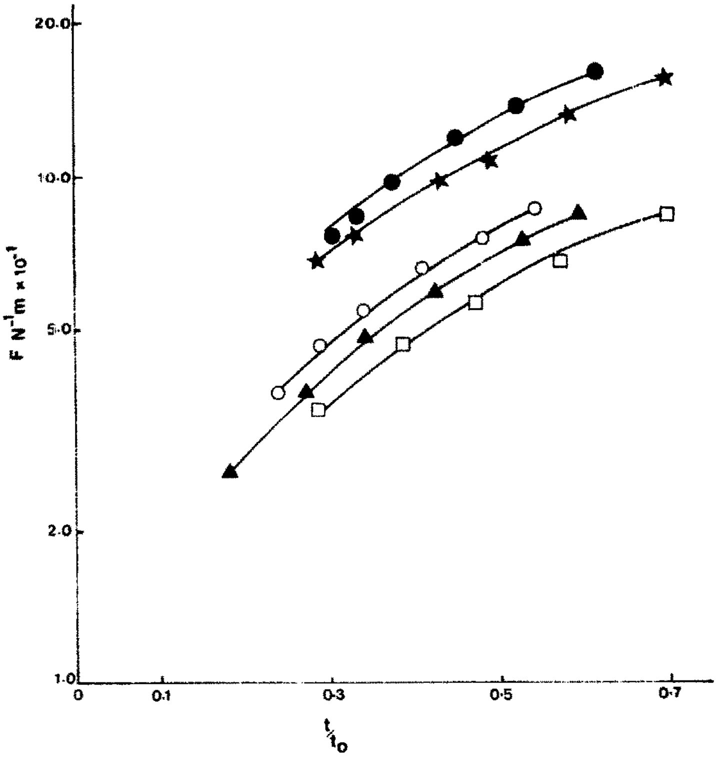

Fig 4. Test of the law of corresponding states. Particle size fraction 20–30 μm. ★, M_1; ○, M_2; ●, M_3; ▲, M_4; □, M_5.

For two surfaces designated 1 and 2, Cheng (1968) showed that:

$$\frac{\epsilon_{0_1}}{\epsilon_{0_2}} = \frac{(t_{0_1})^3}{(t_{0_2})^3} \cdot \frac{F_1}{F_2} \tag{14}$$

where F is given by Eqn. 9. Since the same function ϕ applies to all the systems investigated, ϵ_{0_1} was identified with lactose and arbitrarily assigned a value of unity. The values of ϵ_{0_2} (at a fixed ρ_f) for the mixtures were then calculated relative to lactose. They are listed for samples Y, L and mixtures M_1–M_6 in Table 3 together with the values of t and t_0.

Making use of the law of corresponding states, Eqn. 8 can be rewritten (Kocova and Pilpel, 1973) as:

$$T = \phi\left(\frac{t}{t_0}\right)\frac{\epsilon_0}{t_0^3} \cdot \tfrac{1}{2} M \frac{\bar{S}_{YL}}{\bar{V}_{mix}} \cdot \rho_f \tag{15}$$

Its validity was tested on some further mixtures M_7–M_{10} whose compositions are given in Table I, and whose values of t, t_0 and ϵ_0 were taken as the average of those in Table 3 for the appropriate type of mixture. The values of ϕ were obtained from

TABLE 4

TEST OF EQNS. 8 AND 15 FOR MIXTURES M_7–M_{10}

Mixture code number	Particle size range (μm)											
	0–10				10–20				20–30			
	Packing fraction	T (predicted) (Nm^{-2})	T (observed) (Nm^{-2})	Percent error	Packing fraction	T (predicted) (Nm^{-2})	T (observed) (Nm^{-2})	Percent error	Packing fraction	T (predicted) (Nm^{-2})	T (observed) (Nm^{-2})	Percent error
Temp. – 10°C												
M_7	0.352	104.0	97.0	+6.7	0.482	330.0	366.4	−11.0	0.508	180.1	164.6	+8.6
M_8	0.405	277.0	264.0	+4.6	0.438	170.5	142.1	+16.0	0.514	169.0	185.0	−9.4
M_9	0.353	135.0	148.3	+9.6	0.466	341.1	385.7	−13.0	0.480	190.0	169.8	+10.0
M_{10}	0.365	273.0	225.0	−17.5	0.480	448.5	439.7	+1.9	0.511	195.0	217.7	−11.0
Temp. 20°C												
M_7	0.352	175.2	201.2	−14.0	0.447	312.9	300.1	+4.0	0.481	130.2	145.6	−11.0
M_8	0.347	230.4	243.2	5.5	0.428	159.0	185.4	−16.0	0.522	216.0	200.1	+7.3
M_9	0.346	375.4	429.8	−14.0	0.440	336.2	325.6	+3.1	0.494	235.0	202.0	+14.0
M_{10}	0.351	352.0	309.1	+12.0	0.431	264.2	282.6	−6.9	0.481	150.7	161.41	−10.0
Temp. 50°C												
M_7	0.329	400.0	330.8	+17.0	0.415	162.0	182.5	−12.0	0.478	152.0	165.0	−8.5
M_8	0.357	461.0	448.6	+2.6	0.419	250.0	222.0	+11.0	0.518	250.0	206.0	+17.0
M_9	0.335	502.0	570.0	−13.0	0.436	330.0	365.5	−10.0	0.489	196.0	211.0	−7.6
M_{10}	0.333	530.0	589.0	−11.0	0.428	325.0	302.6	+6.8	0.479	200.0	182.0	+9.0

the average slopes of the graphs in Fig. 4. The resulting predicted values of T for M_7–M_{10} at 3 temperatures are compared in Table 4 with the actual measured values and the average agreement is seen to be within ± 10%. This is considered satisfactory showing that Eqns. 8 and 15 can be used to predict the tensile strengths of binary mixtures of powders from knowledge of their composition and the properties of the components and their particle size distribution.

Conclusions

(1) At a fixed packing fraction, formulated mixtures of oxytetracycline and lactose had higher tensile strengths than physical mixtures.

(2) Eqns. 8 and 15 can be used to predict the tensile strengths of physical and formulated mixtures of oxytetracycline and lactose with an average accuracy of about ±10%.

(3) The effects produced on tensile strength by the 3 variables studied show that particle size has a bigger effect than temperature which has a bigger effect than change in composition of a mixture. The interaction between particle size and temperature is bigger than that between particle size and composition or between temperature and composition.

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References

Ashton, M.D., Farley, R. and Valentin, F.H.H., An improved apparatus for measuring the tensile strength of powders. J. Sci. Instrum., 41 (1964) 763–765.

Ashton, M.D., Cheng, D.C.-H., Farley, R. and Valentin, F.H.H., Some investigation into the strength and flow properties of powders. Rheol. Acta, 4(3) (1965) 206–217.

Britten, J.R. and Pilpel, N., Tensile testing of powders over a range of temperatures. Lab. Pract., 26(3) (1977) 185–186.

Chan, S.Y., Pilpel, N. and Cheng, D.C.-H., The tensile strengths of single powders and binary mixtures. Powder Technol., 34 (1983) 173–189.

Cheng, D.C.-H., The tensile strength of powders. Chem. Eng. Sci., 23 (1968) 1405–1420.

Cheng, D.C.-H., The effect of moisture on the tensile strength of powders. J. Adhes., 2 (1970) 82–92.

Esezobo, S., Mechanical Properties of Some Oxytetracycline Formulations in Relation to Tableting, PhD thesis, University of London, 1976, pp. 110–118.

Farley, R. and Valentin, F.H.H., Effect of particle size upon the strength of powders. Powder Technol., 1 (1967/68) 344–354.

Jayasinghe, S.S., Pilpel, N. and Harwood, C.F., The effect of temperature and compression on the cohesive properties of particulate solids. Mat. Sci. Eng., 5 (1969/70) 287–294.

Kocova, S. and Pilpel, N., The tensile properties of cohesive powders. Powder Technol., 7 (1973) 51–67.

Kurup, T.R.R. and Pilpel, N., The effect of binding agents on the tensile strengths of powders and tablets. Asian J. Pharm. Sci., 1 (1979) 75-90.

Varthalis, S. and Pilpel, N., Anomalies in some properties of powder mixtures. J. Pharm. Pharmacol., 28 (1976) 415-419.

Walton, C.A. and Pilpel, N., The effect of particle size, shape and moisture content on the tensile strength properties of procaine penicillin powders. J. Pharm. Pharmacol., 24 (1972) 10P-16P.

Woolfall, R.C., An approach to product formulation. Soap Perfum. Cosmet., 37 (1964) 965-970.

York, P. and Pilpel, N., The effect of temperature on the mechanical properties of some pharmaceutical powders in relation to tableting. J. Pharm. Pharmacol., 24 (1972) Suppl. 47P-56P.

York, P. and Pilpel, N., The tensile strength and compression behaviour of lactose, four fatty acids, and their mixtures in relation to tableting. J. Pharm. Pharmacol., 25 (1973) 1P-11P.