

Tensile strength and compression of coated pharmaceutical powders: tablets

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A study has been made of the tensile strength and compression during tableting of lactose, sodium chloride and calcium phosphate powders after they had been coated with small amounts of stearic acid, polyethylene glycols and polyvinylpyrrolidones. The properties of the systems were measured over a range of temperatures. The tensile strength and the compression behaviour depended not only on the amount and type of the coating material but also on the homologous temperature of processing. The changes in tensile strength have been explained in terms of changes in interparticle separation, changes in interparticle forces and the formation of welded bonds by the coatings. The compression results have been analysed in terms of the Heckel and the Cooper & Eaton equations.

The effect that the coating of fine powders has on their tensile strength and increase in density when they are loosely packed at different temperatures, was reported previously (Malamataris & Pilpel 1980, 1982). It was shown that both properties depended on the content, the homologous temperature and hardness of the coating material and on the surface energies of the coated powders.

In order to produce tablets in practice, higher compression pressures are needed than those used in the work cited above. At these higher pressures various mechanisms have been proposed to account for the bonding that occurs between particles (Goetzl 1949). They include mechanical interlocking, deformation and fragmentation of particles, and the generation of heat at points of contact (Travers & Merriman 1970) resulting possibly in the melting and subsequent resolidification of asperities at temperatures below the conventional melting points of the materials concerned (York & Pilpel 1973). It was therefore considered appropriate to see whether changes produced by temperature on the properties of the coatings employed during the tableting would have significant and quantitatively predictable effects on the compression and resulting tensile strength of the tablets.

The same coated powders as used in the previous work (Malamataris & Pilpel 1982) were tableted at different temperatures and the tensile strengths of the tablets were measured by diametral compression at the same temperatures. By applying Cheng's (1968) theory, the results were used to calculate the

interparticle separation and the range of the interparticle forces. The compression behaviour of the materials was also analysed in terms of two equations, one proposed by Heckel (1961), the other by Cooper & Eaton (1962). The aim was to see whether at various homologous temperatures‡ any correlations could be found between interparticle separation, range of interparticle forces, properties of the coatings, the tensile strengths of the tablets and the values of the numerical terms in the above compression equations. Such correlations might provide information about the bonding mechanisms that occur during a compression process and assist formulators in the choice of excipients and manufacturing conditions so as to avoid problems which sometimes arise during routine production of commercial tablets.

MATERIALS AND METHODS

The materials employed were the same as in the previous investigation (Malamataris & Pilpel 1982). Sodium chloride was chosen as a substrate representative of materials which on tableting bond by plastic deformation (Cole et al 1975). Calcium phosphate dihydrate ($\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$) was representative of those bonding by fragmentation (Khan & Rhodes 1972) and lactose of those bonding by both mechanisms (Hersey & Rees 1973). Stearic acid, polyethylene glycols (PEG) and polyvinylpyrrolidones (PVP) were applied as coatings because they are frequently employed as lubricants and binders for pharmaceutical formulations.

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‡ (Defined as the ratio of the temperature of measurement to the melting point of the material both in degrees K).

The coated powders were formed into tablets in a hydraulic press (Research and Instrument Company) using 10.3 mm diam. flat faced punches and a die which were lubricated with a suspension of magnesium stearate in chloroform. The resulting tablets were subjected to a diametrical compression test at different temperatures either immediately after preparation or after 24 h storage. Fuller details of the equipment and procedures have been given elsewhere (Malamataris & Pilpel 1981).

RESULTS

The tensile strengths, T , of the tablets made from all the samples at all the temperatures were found to fit the general equation:

$$\text{Log } T = A \rho_f + B \quad (1)$$

with a highly significant correlation (>0.95 correlation coefficient for at least six measurements) over the range of packing fractions, ρ_f , from 0.7 to 0.9 which is typical of commercial tablets. A and B are numerical terms which, for each sample, depended on the nature and amount of the coating material and on its homologous temperature during compression and testing (Malamataris 1981).

In order to determine the effect of increasing the amount of the coating material on the tensile strength of the different types of tablets (lactose, NaCl, $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$) at 20 °C, the values of $\text{Log } T$ at a fixed ρ_f 0.82 (selected because it involved minimum extrapolation of the experimental data) were plotted against the Log molar content per g of

powder, C , of the stearic acid I, PEG (20 000) and PVP (40 000) in Fig. 1 (a-c). It is seen that the tablets' tensile strengths altered rectilinearly as the amounts of the coatings were increased from 0.1% w/w (i.e. $2.5 \text{ mol} \times 10^{-6} \text{ g}^{-1}$ for stearic acid, $0.05 \text{ mol} \times 10^{-6} \text{ g}^{-1}$ for PEG (20 000) and $0.025 \text{ mol} \times 10^{-6} \text{ g}^{-1}$ for PVP (40 000)) to 3.0% w/w and obeyed the general relationship:

$$\text{Log } T = Q_1 \text{Log } C + Q_2 \quad (2)$$

where Q_1 and Q_2 are constants whose values can be found in Malamataris (1981).

The tensile strengths of tablets at ρ_f 0.82, obtained by compressing at various homologous temperatures and then tested immediately at these same temperatures, are plotted in Fig. 2 (a-c) versus the homologous temperature of compression/testing. With a stearic acid coating, Fig. 2a, increasing the compression/testing temperature initially produced increases in the tensile strength, followed by decreases to minima at homologous temperatures between 0.95 and 1.0 and then further increases when the temperature exceeded the melting point of the acid. With PEG (20 000), Fig. 2b, the tensile strengths exhibited maxima at homologous temperatures around 0.9 but no subsequent minima near the coating's melting point. With the PVP (10 000), Fig. 2c, the tensile strengths also increased up to an homologous temperature of about 0.9 which was the limit for measurements because of the material's relatively high m.p.

Fig. 2 (a-c) also show that with a fixed ρ_f and any

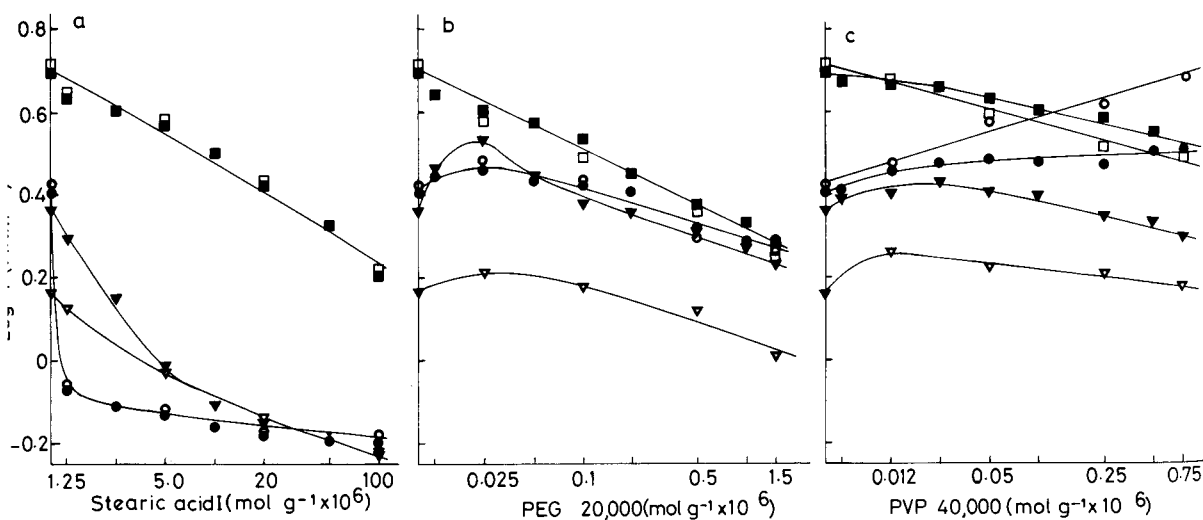


FIG. 1 (a-c). $\text{Log } T$ at ρ_f 0.82 and 20 °C vs the molar concentration of coating for lactose (\circ unstored, \bullet stored for 24 h), NaCl (∇ unstored, \blacktriangledown stored for 24 h) and $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ (\square unstored, \blacksquare stored for 24 h). (Coatings: a, stearic acid I; b, PEG 20 000; c, PVP 40 000).

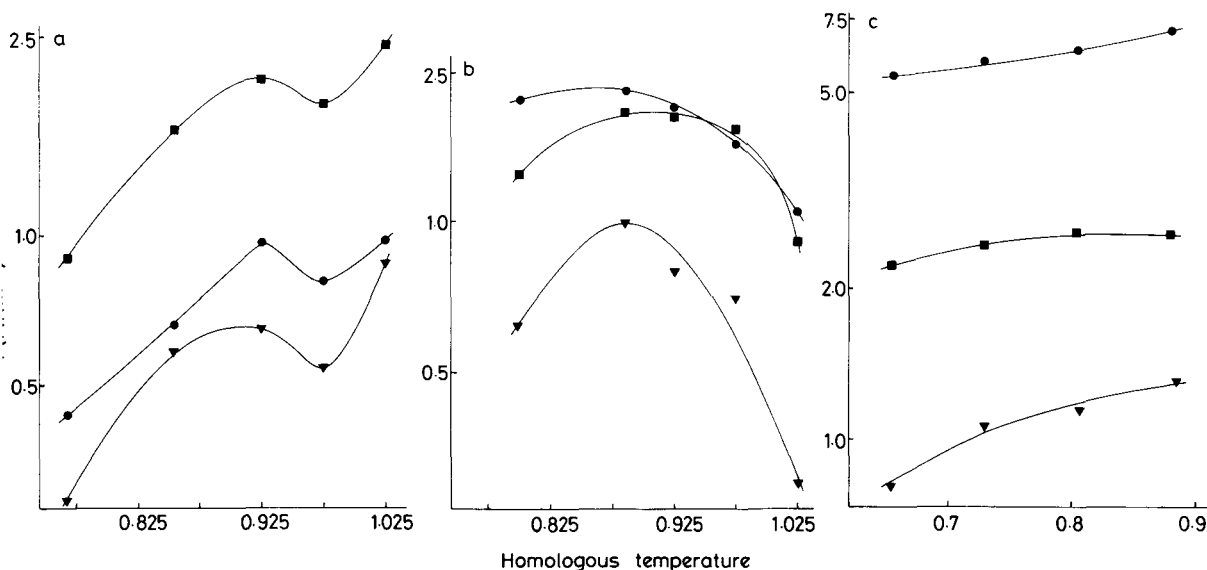


FIG. 2 (a-c). Tensile strength of tablets (ρ_f 0.82) vs homologous temperature of compression/testing, ● lactose, ▼ NaCl and ■ $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ all coated with: a, $100.0 \text{ mol g}^{-1} \times 10^{-6}$ stearic acid I; b, $1.5 \text{ mol g}^{-1} \times 10^{-6}$ PEG 20 000; c, $3.0 \text{ mol g}^{-1} \times 10^{-6}$ PVP 10 000.

selected homologous temperature < 0.9 the tensile strengths of the tablets were in the same order as the m.p.s of the coating materials employed and incidentally of their Brinell hardnesses and moduli of elasticity (Malamataris & Pilpel 1981). Smooth curves were obtained when $\text{Log } T$ at ρ_f 0.82 and homologous temperature 0.85 was plotted vs the Brinell hardness of the coating materials employed (Malamataris 1982).

The effect of coating and storage on the tensile strength of the tablets was that with NaCl the coatings generally caused the strength to increase on storage, but with lactose coated with PVP, to decrease. The effect of storage on the strengths of tablets made from other coated powders was small and these results are seen in Fig. 1 (a-c) and from the values of Q_2 .

The relations between applied pressure, P , and the resulting packing fraction, ρ_f , of the uncoated and of some representative coated powders were next analysed to test the validity of the Heckel (1961) equation:

$$\text{Log} \frac{1}{1 - \rho_f} = K_H P + A_H \quad (3)$$

and of the Cooper & Eaton (1962) equation:

$$\frac{\frac{1}{\rho_{fco}} + \frac{1}{\rho_f}}{\frac{1}{\rho_{fco}} - 1} = a_1 \exp \frac{-Ck_1}{P} + a_2 \exp \frac{-Ck_2}{P} \quad (4)$$

K_H , A_H , a_1 , a_2 , Ck_1 and Ck_2 are physical constants for each material under certain compression conditions. ρ_{fco} is the packing fraction at zero compressive stress. Graphs of:

$$(i) \text{Log} \frac{1}{1 - \rho_f} \text{ vs } P \text{ and}$$

$$(ii) \text{Log} \left[\frac{\frac{1}{\rho_{fco}} - \frac{1}{\rho_f}}{\frac{1}{\rho_{fco}} - 1} \right] \text{ vs } \frac{1}{P}$$

were plotted (Malamataris 1981). The values of K_H and A_H are listed in Table 1. For all the coated powders the values of K_H and A_H were higher than those for the uncoated powders and increased as the temperature was increased up to the melting points of the coatings beyond which the Heckel graphs began to deviate from linearity.

Most of the Cooper & Eaton plots for the coated powders at different temperatures exhibited curvature but they tended to become rectilinear as the amounts of the coatings and the temperature were increased. This tendency was most pronounced in the case of NaCl and least with $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$. The relative magnitudes of the dimensionless coefficients, a_1 and a_2 in equation 4, indicating the fraction of theoretical compaction that would be achieved at infinite pressure by the filling of the holes of the same size (a_1) and or smaller size (a_2) than the particles, are given in Table 1. Approximate values of

Table 1. Constants in Heckel and Cooper & Eaton compression equations, interparticle separation and range of forces for coated powders.

Coating and content (mol g ⁻¹ × 10 ⁶)	Temperature/Homologous	Lactose					t ₀ ' (μm)	t' at ρ _f 0.82 (μm)					
		A _H	K _H	a ₁	a ₁ + a ₂	ρ _{f0}							
None	20 °C	0.52	1.65	0.84	1.02	0.470	3.0	1.0					
Stearic acid I (100.0)	0.767	0.59	1.43	0.82	1.02	0.485	2.6	0.7					
	0.860	0.60	1.67	0.85	1.01	0.404	3.8	1.0					
	0.925	0.57	2.12	0.86	1.01	0.410	4.0	1.2					
	0.975	0.62	2.54	0.89	1.00	0.395	4.3	1.3					
Stearic acid II (100.0)	1.025	—	—	—	—	0.345	5.1	1.4					
	20 °C	0.58	1.69	0.87	1.02	0.395	4.3	1.3					
	0.800	0.52	1.59	—	1.01	0.380	4.3	1.1					
PEG 20 000 (1.5)	0.885	0.58	1.84	—	—	0.390	4.4	1.3					
	0.925	0.58	2.21	0.91	1.02	0.340	5.3	1.4					
	0.975	0.62	1.93	1.00	1.00	0.320	5.9	1.6					
	1.025	—	—	—	—	0.310	6.3	1.8					
PEG 1500 (20.00)	20 °C	0.56	2.00	0.91	1.02	0.375	4.8	1.5					
	0.656	0.40	1.94	0.85	1.03	0.375	4.1	0.8					
PVP 10 000 (3.0)	0.730	0.45	2.13	0.86	1.01	0.340	5.2	1.4					
	0.805	0.46	2.45	0.90	1.03	0.320	5.4	1.1					
	0.880	0.46	2.65	1.00	1.00	0.310	5.5	1.0					
PVP 40 000 (0.75)	20 °C	0.48	1.99	0.89	1.02	0.410	4.1	1.3					
	—	—	—	—	—	—	—	—					
None	20 °C	NaCl					0.42	2.64	0.92	1.01	0.345	5.3	1.4
	Stearic acid I (100.0)	0.767	0.42	3.62	—	—	1.06	0.510	3.1	1.4			
		0.860	0.43	3.81	1.00	—	1.03	0.465	4.3	2.1			
		0.925	0.53	4.25	—	—	1.03	0.430	5.1	2.6			
		0.975	0.58	3.81	—	—	1.03	0.440	4.5	2.1			
1.025	—	—	—	—	—	0.300	6.6	1.7					
Stearic acid II	20 °C	0.53	3.76	—	1.03	0.465	3.9	1.7					
	—	—	—	—	—	—	—	—	—				
PEG 20 000 (1.5)	0.800	NaCl					0.55	2.59	0.90	1.02	0.395	4.6	1.5
	0.885	0.49	3.70	—	—	—	0.385	4.9	1.7				
	0.925	0.53	4.10	0.95	1.03	0.380	5.0	1.8					
	0.975	0.51	4.15	—	—	1.02	0.370	5.4	2.0				
	1.025	—	—	—	—	0.360	4.9	1.3					
PEG 1500 (20.0)	20 °C	0.44	4.33	0.92	1.03	0.320	6.6	2.2					
	0.656	0.42	2.85	0.87	1.05	0.440	3.7	1.2					
PVP 10 000 (3.0)	0.730	0.42	3.60	—	—	1.02	0.430	3.9	1.3				
	0.805	0.42	4.20	1.00	1.05	0.425	4.1	1.4					
	0.880	0.38	5.27	1.00	1.05	0.420	4.2	1.5					
PVP 20 000 (0.75)	20 °C	0.42	3.10	0.89	1.03	0.425	4.0	1.4					
	—	—	—	—	—	—	—	—	—				
None	20 °C	CaHPO ₄ ·2H ₂ O					0.45	0.92	0.76	1.00	0.420	2.9	0.3
	Stearic acid I (100.0)	0.767	0.55	1.18	—	—	1.00	0.495	2.4	0.6			
		0.860	0.51	1.29	0.81	1.00	0.420	3.3	0.8				
		0.925	0.58	1.48	0.85	1.02	0.390	4.0	1.0				
		0.975	0.55	1.28	0.85	1.01	0.480	3.4	0.8				
1.025	—	—	—	—	0.390	3.6	0.7						
Stearic acid II (100.0)	20 °C	0.52	1.32	0.85	1.01	0.425	3.2	0.7					
	0.800	0.54	1.11	—	—	1.00	0.390	3.7	0.7				
PEG 20 000 (1.5)	0.885	0.54	1.19	—	—	1.00	0.345	4.5	0.8				
	0.925	0.56	1.27	—	—	1.00	0.340	4.8	1.0				
	0.975	0.52	1.37	0.87	1.01	0.330	5.0	1.0					
	1.025	—	—	—	—	0.325	5.0	0.9					
PEG 1500 (20.0)	20 °C	0.50	1.26	0.82	1.02	0.350	4.3	0.7					
	0.656	0.46	1.02	—	—	1.00	0.410	3.1	0.5				
PVP 10 000 (3.0)	0.730	0.47	1.08	—	—	1.00	0.410	3.2	0.5				
	0.805	0.48	1.10	—	—	1.00	0.400	3.4	0.5				
	0.880	0.47	1.18	0.85	1.00	0.395	3.5	0.6					
PVP 40 000 (0.75)	20 °C	0.45	1.11	0.79	1.00	0.415	3.0	0.4					
	—	—	—	—	—	—	—	—	—				

(a₁ + a₂) were obtained by extrapolation of the graphs to 1/P = 0 (infinite pressure) and were close to unity as expected. The upper limiting values of a₁ were obtained from the intercepts on the ordinate of the tangents to the curves at the highest values of 1/P,

(i.e. low pressure) and increased with the addition of coating and with increase of temperature (see Table 1).

Turning finally to Cheng's (1968) method for analysing the tensile strength data in terms of particle size parameters, \bar{d} , \bar{s} and \bar{v} , interparticle separation 't' and range of interparticle forces 't₀' (Malamataris & Pilpel 1982), values of $\frac{1}{F} = \frac{1/2(\bar{s}/\bar{v})\rho_f}{T}$ were plotted versus $\text{Log} \frac{\bar{d}}{3} \left(\frac{\rho_f}{\rho_{f0}} - 1 \right)$ (where ρ_{f0} is the packing fraction when T = 0) and the straight lines were extrapolated to the abscissa where 1/F = 0. This procedure avoids the abrupt changes in slope which occur when 1/F is plotted against $\frac{\bar{d}}{3} \left(\frac{\rho_f}{\rho_{f0}} - 1 \right)$ (cf Esezobo & Pilpel 1977; Kurup & Pilpel 1978). The interparticle separations 't' at ρ_f 0.82 were obtained from 't₀' by substituting into the equation:

$$t = t_0 - \frac{\bar{d}}{3} \left(\frac{\rho_f}{\rho_{f0}} - 1 \right) \quad (5)$$

The values of 't₀' and 't' are included in Table 1. It can be seen that with all the powders investigated the values of both 't₀' and 't' increased with the addition of the coating and with increase of temperature up to the melting point of the coating materials. For NaCl and CaHPO₄·2H₂O the 't' values at homologous temperatures above 1.0, when the coating had melted, tended to be lower than those at lower temperatures when the coatings were still solid, see Table 1.

DISCUSSION

The changes in tensile strength caused by the addition of coatings and by increasing the temperature during compression as seen in Fig. 1 (a-c) and Fig. 2 (a-c) may be ascribed to masking of the Van der Waals' and interlocking forces between the substrate particles by the adsorbed films of the coatings and the development of additional bonds formed by plastic deformation/melting of the coatings which increase as the temperature is increased up to a homologous temperature of about 0.95. At higher temperatures the coatings begin to melt, the bonds weaken and the tensile strengths decrease. In the case of stearic acid coatings, Fig. 2a, the operation of substrate-substrate bonds after the acid has melted accounts for the subsequent increases in tensile strength and for the observed minima. These minima do not occur with PEG coatings, Fig. 2b, probably because wetting and softening of the substrates' surface prevents the operation of strong

substrate-substrate bonds which would cause a re-increase in tensile strength beyond the melting point of PEG. Wetting and penetration of melted PEG and PVP into the micropore structure of NaCl, lactose and $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ may be causing the tensile strength changes of these tablets during storage, as has been reported for lauric acid on lactose (Pilpel & Hephher 1977; Malamataris & Pilpel 1981).

The initial curved region in the Heckel plots for both the coated and uncoated samples up to a compression force of about 100 MNm^{-2} , followed by a linear section, shows that at low pressures the particles are slipping into a new packing arrangement but that at higher pressures they are deforming plastically and becoming bonded together with or without fragmentation. The shapes of the curves suggest that NaCl is being compressed mainly by plastic deformation and $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ mainly by fragmentation. This could explain why addition of coating material and change in temperature had much less effect on the values of A_H and K_H for $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ than for NaCl, with lactose being intermediate (see Table 1). In the present work both A_H and K_H altered with the addition of coating and with alterations in the temperature (Table 1). The term K_H is the reciprocal of the materials' mean yield pressure and A_H is a measure of densification due to slippage and rearrangement of particles which depend mainly on their size and shape but also on their hardness.

Analysing the compression behaviour by the Cooper & Eaton expression, for a hard material at low pressure (i.e. high values of $1/P$) densification is occurring by particle rearrangement to fill the voids of the same or larger size than the particles. At higher pressures (i.e. lower values of $1/P$) the particles begin to deform plastically or fragment and thereby fill the smaller voids. For the range of pressure investigated the tendency of the Cooper & Eaton plots to become rectilinear with the addition of coatings and increase of temperature indicates the operation of only one mechanism but it would be impossible to fill the smaller voids without first filling the larger ones. It would also be impossible to achieve packing fractions greater than 0.95 by filling the larger voids alone. Thus, it must be concluded that the filling of larger voids is completed at lower pressures when the powders have been coated and/or when the temperature is increased. An alternative explanation for the linear plots could be that both mechanisms are operating simultaneously and cannot therefore be distinguished by the Cooper &

Eaton expression. York & Pilpel (1973) and Kurup & Pilpel (1978) reported similar results for other relatively soft powders.

Considering the increases in the values of ' t_0 ' and ' t ' when the powders are coated and/or when the temperature is increased up to a homologous temperature ≈ 1.0 (Table 1), and the higher values of ' t ' for NaCl than for $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ (Table 1) the following explanation may apply. The coatings are soft and plastic and modify the surface characteristics of the particles. It is therefore to be expected that adding them to the powders will cause systematic alterations in the values of ' t_0 ' and ' t ' since these are measures of the surface characteristics of the particles, the former measuring the range of the interparticle attractive forces and the latter the average height of asperities. In other words ' t_0 ' represents the closest approach of the particles at zero tensile strength and ' t ' is the average interparticle separation of every microcontact at which the interparticle attractive force exists. Similar results have been reported, for example, by Esezobo & Pilpel (1977) and Kurup & Pilpel (1978) who showed that the values of ' t_0 ' increased with gelatin content in an oxytetracycline formulation, and with starch or PVP content in a griseofulvin formulation.

From the above it can be concluded that:

(1) The tensile strengths of tableted pharmaceutical powders that have been coated with a second, lower melting component are likely to be appreciably affected by comparatively small, e.g. 10°C , changes in the temperatures employed during their preparation.

(2) The tensile strength changes can be explained in terms of the masking of Van der Waals' forces between the particles and the formation of welded bonds by the coatings. They arise from changes produced in the interparticle separation and the range of the interparticle forces (as derived from Cheng's theory of tensile strength).

(3) Correlations have been established between the hardness of the coating materials, the terms in the Heckel and Cooper & Eaton equations and the tensile strengths of the tablets.

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