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The tensile strength and consolidation of lactose coated with non-ionic surfactants
I. Powder

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Summary

The tensile strength and the resistance to consolidation by pressure or tapping of fine lactose powder coated with increasing amounts of a series of non-ionic surfactants were examined.

At a constant packing fraction, both the tensile strength and the resistance to consolidation initially decreased to minima when the coating was monomolecular and then increased as the additive formed pendular bonds between the particles.

The packing fraction of the powder after 100 taps increased to a maximum, and then decreased as the amount of the coating material present was increased.

Cheng's expression for tensile strength has been used to compare the forces that operate between the particles of the coated and the uncoated powders.

Introduction

The tesile strength and the packing characteristics of a powder under the action of a consolidating stress provide useful information on how it is likely to behave during packing, storage, filling into capsules or forming into tablets.

Although a good deal of work, has been done on the effect of moisture (Dollimore and Gregg, 1955; Cheng, 1970; Walton and Pilpel, 1972; Eaves and Jones, 1972) and fatty acids (Pilpel and Hepher, 1977; Malamataris and Pilpel, 1980) on the mechanical properties of fine powders, much less has been reported on the

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effect produced by adding other liquids of pharmaceutical interest to powders.

When a liquid is added to a powder with which it does not react chemically, it may form an adsorbed film one or a few molecules thick (Read and Kitchener, 1967), or it may form pendular, funicular or capillary bonds between the particles (Newitt and Conway, 1958; Rumpf, 1962). The behaviour will depend on the amount, the cross-sectional area of the liquid molecules, and the way in which the liquid has been added.

Expressions have been developed for the tensile strengths of powders when the water or liquid fatty acids are in the adsorbed, pendular or capillary state (Derjaguin, 1961; Rumpf, 1962; Cheng, 1970), but few attempts have been made to check the validity of the expressions for other liquids.

The mechanical properties of a powder result from the operation of several types of forces between the constituent particles. These forces can be sub-divided into Van der Waal's, London and other types (Krupp, 1967).

It is presumed that the addition of a liquid to a drug powder alters the magnitude of one or more of these forces, and thereby produces an overall change in its mechanical properties (Pilpel and Hepher, 1977).

Cheng's theory (1968) provides a means for calculating the magnitude and the range of these interparticle forces from measurements of the tensile strength of the powder at different packing fractions. It has been employed in the present work to follow the changes that occurred in the interparticle forces when increasing amounts of a series of non-ionic surfactants (Sorbitan fatty acid esters (Spans)) were added to powdered lactose, and its tensile strength measured in a split-plate apparatus (Ashton and Valentin, 1964).

Lactose was selected since it is insoluble in and apparently unaffected chemically by the surfactants employed. These range from liquids to waxy solids, whose physical properties and the cross-sectional area of their molecules vary with their molecular weights and chemical structures. In the past years they have been included in many pharmaceutical tablet formulations as lubricants, dispersing aids (Schick, 1967) and for controlling wettability and absorption of various drugs (Kreutler and Davis, 1971).

Materials and methods

Materials

The materials used in this study were: lactose powder (BP grade from Evans medical), the non-ionic surfactants, Sorbitan (S) monolaurate (Span 20), Sorbitan monostearate (Span 60), Sorbitan mono-oleate (Span 80), and Sorbitan trioleate (Span 85) (all from Atlas Chemicals), diethyl ether and carbon tetrachloride (both analytical reagents from Fisons). Fig. 1 and Table 1 show, respectively, the chemical structures and some of the physicochemical properties of the surfactants used.

The lactose powder was ground and classified into the range of particle sizes from 30 to 50 μm, using an Alpine zig-zag classifier. 250-g batches were dried in an oven over-night at 100°C and were then coated with between 0.5×10^{-5} and 10×10^{-5}

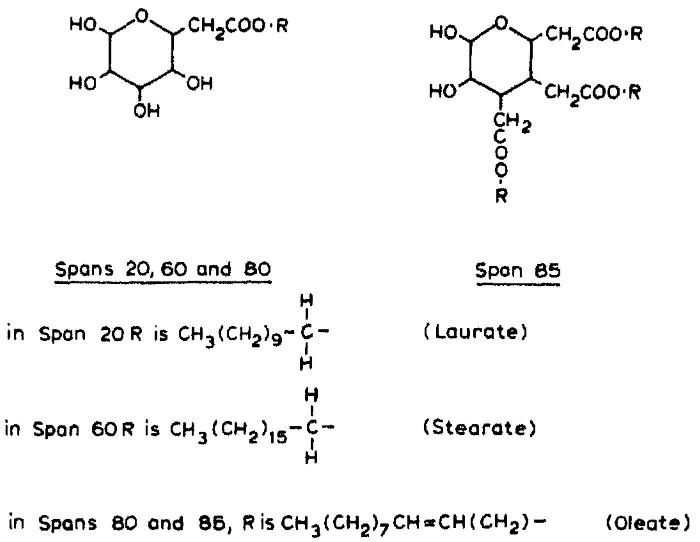


Fig. 1. The chemical structures of the surfactants.

mol · g^{-1} of the different surfactants by mixing in a 1-litre flask with 0.5 litre diethyl ether containing the appropriate amount of surfactants. One batch was treated with the same amount of ether alone to provide a blank (the ether was recovered by distillation with continuous stirring from a water bath at 40°C). The coated lactose was stored over-night in a dry chamber to ensure the removal of any residual solvent. The samples were then passed through a nylon mesh of 90 μm aperture to break down aggregates, then stored in air-tight containers until ready for testing.

Determination of cross-sectional areas of surfactant molecules

These experiments were carried out at the carbon tetrachloride–triple distilled water interface. The surfactants, at concentrations ranging betwen 10^{-2} and 10^{-7} g · mol · l^{-1}, were dissolved in carbon tetrachloride to form the adsorbed films. Interfacial tensions were measured at 20°C with a Du Noüy tensiometer using a platinum ring. The scale reading at rupture of the interfacial film was converted into interfacial tension by substituting into the following equation (Zuidema and Waters,

TABLE 1

SOME OF THE PHYSICOCHEMICAL PROPERTIES OF SPANS

Surfactant	Chemical name	Nature	Density (g/ml^3)	Viscosity at room temp. Cp	Mol. wt.
Span 20	Sorbitan monolaurate	liquid	$\simeq 1$	4500	346.5
Span 60	Sorbitan monostearate	solid	–	–	430.6
Span 80	Sorbitan mono-oleate	liquid	$\simeq 1$	1550	428.6
Span 85	Sorbitan trioleate	liquid	$\simeq 1$	200	957.5

1941):

$$\gamma = R\left\{0.725 + \left(0.0145R/\theta^2(D-d)\right)^{1/2}\right\} \quad (1)$$

where γ = interfacial tension in $mN \cdot m^{-1}$; R = scale reading at rupture in $mN \cdot m^{-1}$; θ = circumference of the platinum ring in cm; D = density of water at 20°C $g \cdot cm^{-3}$; and d = density of sample at 20°C $g \cdot cm^{-3}$. The values of γ were used to determine the area per molecule of surfactants as shown in the results section.

Tensile tests

The tensile strengths of the samples were measured in a split-plate tensile tester at the packing fractions produced by consolidating them at stresses from 0.709 to 5.679 $kN \cdot m^{-2}$. Fuller details of the equipment and measuring technique have been published (Kočova, 1973; Britten and Pilpel, 1977).

Resistance to consolidation

This is defined as the stress P required to consolidate the samples to a particular packing fraction, namely 0.54, and the values were obtained during preparation of the samples for the tensile tests.

Tapping tests

A known weight of each sample was poured into a 100-ml cylinder in a standard tap density apparatus (Scientific Developments, Romford) and then subjected to tapping. The equipment and the technique for measuring the resulting tap density have been described elsewhere (Neumann, 1967; Varthalis and Pilpel, 1976).

Results

Table 2 shows the interfacial tension results from which the areas per molecule (A) of the surfactants were calculated.

Fig. 2 illustrates the effects of varying the concentration of Span 60 (as a representative surfactant) on the interfacial tensions at the carbon tetrachloride–water interface. The slopes of the interfacial tension γ versus log concentration curves (Fig. 2) were used to calculate the surface excess Γ (i.e. the number of molecules of surfactant in 1 cm^2 of interface at a given interfacial pressure π, in excess of that in 1 cm^2 of the bulk solution), and the areas A available for each molecule in the interface by means of the Gibbs equation (Davies and Rideal, 1963).

$$\Gamma = -\frac{1}{2.303RT} \times \frac{d\gamma}{d\log c}\, mol \cdot m^{-2} \quad (2)$$

where $d\gamma/d\log c$ is the slope of γ versus $\log c$; T is the absolute temperature (293°K); R is the gas constant (8.4×10^3 $mN \cdot mmol^{-1}$ $°K^{-1}$); and

$$A = \frac{2.303RT \times 10^{18}}{6.03 \times 10^{23} \times \frac{d\gamma}{d\log c}} \quad (3)$$

TABLE 2

DATA OBTAINED FROM THE MEASUREMENT OF THE INTERFACIAL TENSION BETWEEN CARBON TETRACHLORIDE CONTAINING SPAN 60 AND WATER

Concentration of SAA (gmol/l)	10^{-7}	10^{-6}	10^{-5}	10^{-4}	10^{-3}
Log concentration (M)	−7	−6	−5	−4	−3
γ ($mN \cdot m^{-1}$)	45.0	41.5	35.5	28.0	17.5
π ($mN \cdot m^{-1}$)	2.2	5.2	10.7	22.0	29.2
$\text{Slope} = -\frac{d\gamma}{d \log c}$	3.7	6.3	8.6	10.5	11.0
A (nm^2)	2.5	1.5	1.1	0.9	0.9
πA ($mN \cdot m^{-1} \cdot nm^2$)	5.6	7.7	11.7	19.8	25.0

Data obtained from the measurements of the area per mol for Span 60.

where 6.03×10^{23} is the Avogadro's number; and c is the molar concentration of the surfactant in the bulk carbon tetrachloride phase.

The differences between the interfacial tensions $\gamma_0 - \gamma_c$ between the clean interface, concentration of surfactant = 0, and the interface with surfactant concentration = c, was a measure of the interfacial pressure π; the π–A curves were then obtained from the data shown in Table 2, and are presented in the form of plots πA versus π in Fig. 3. These gave straight lines whose intercepts on the ordinate at $\pi = 0$ yielded a value of πA at around 4. This confirmed that the adsorbed films of the surfactants were ideally gaseous (Pithayanukul, 1981).

The limiting area of each surfactant molecule, A_0, was then obtained from the slopes of the lines in Fig. 3. The values are included in Table 3.

Coating thickness

To calculate the surfactant coating thickness on each particle of lactose, the following steps were followed.

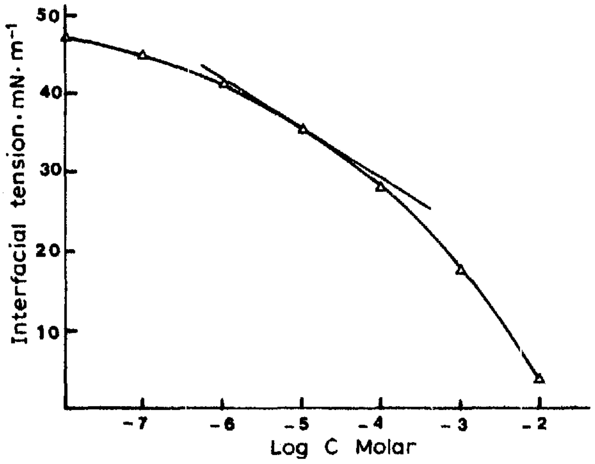


Fig. 2. Interfacial tension vs log surfactant concentration for Span 60. Ordinate: interfacial tension γ($mN \cdot m^{-1}$); abscissa; log c (M).

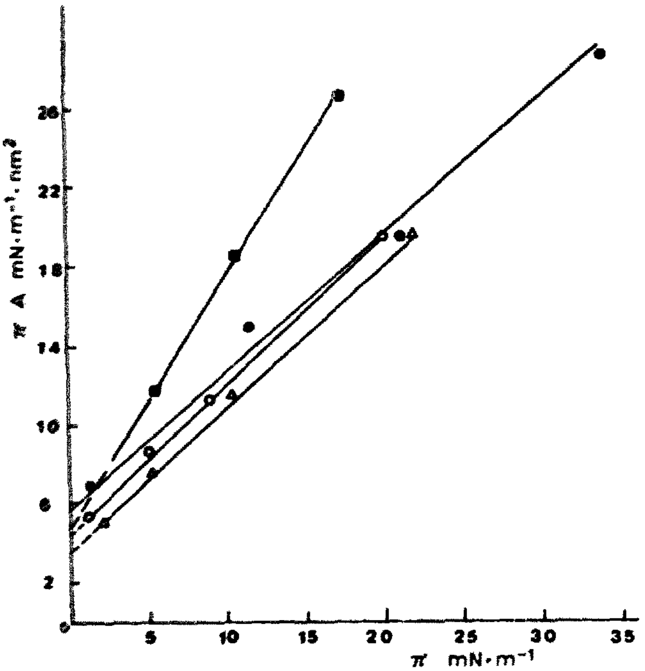


Fig. 3. Plots of πA(mN · m^{-1} · nm^2) (ordinate) vs π (mN · m^{-1}) (abscissa). Key: ○, Span 20; Δ, Span 60; ●, Span 80; ■, Span 85.

The particle size parameters $\bar{d}$ (mean effective diameter), $\bar{s}$ (mean effective surface area per particle), and $\bar{v}$ (mean effective volume per particle) were calculated from the particle size analysis of the powder using an optical microscope. The equations for calculating these parameters are given elsewhere (see Esezobo and Pilpel, 1977).

Density of lactose is 1.53 g · cm^{-3};

therefore

volume of 1 g lactose $= 0.653\ \text{cm}^3 = 653 \times 10^9\ \mu\text{m}^3$

Mean effective volume per particle $(\bar{v}) = 37725\ \mu\text{m}^3$; (4)

therefore number of particles per g of lactose $= 1731 \times 10^4$ particles.

Total surface area per 1 g lactose $= \bar{s} \times 1731 \times 10^4 = 2.23 \times 10^{18}\ \text{nm}^2$ (5)

Since 1 g · mol of a surfactant contains Avogadro's number, i.e. 6.03×10^{23} molecules, then the number of molecules for each concentration of surfactant per gm of lactose can be calculated. Multiplying this number by the cross-sectional area of the surfactant molecule, and dividing by the surface area of 1 g lactose, yields the number of molecular layers in the coating.

Table 3 shows the coating thickness obtained for different concentrations of each

TABLE 3

DATA USED FOR CALCULATING THE COATING THICKNESS PRODUCED BY DIFFERENT CONCENTRATIONS OF EACH SURFACTANT (SPANS) FOR A GIVEN SURFACE AREA OF 2.23×10^{18} nm^2 FOR 1 g OF LACTOSE

Surfactant	Area per molecule (nm^2)	Concentration (mol·g^{-1} $\times 10^5$)	Area per molecule $\times$ no. of molecules (nm^2 $\times 10^{18}$)	Coating thickness (molecules thick)
Span 20	$\simeq 0.68$	0.5	2.00	$0.91 \simeq 1$
		1.0	4.10	$1.83 \simeq 2$
		2.0	8.20	$3.67 \simeq 4$
		3.0	12.00	$5.56 \simeq 6$
		5.0	20.00	$9.17 \simeq 9$
		10.0	41.00	$18.32 \simeq 18$
Span 60	$\simeq 0.73$	0.5	2.19	$0.98 \simeq 1$
		1.0	4.39	$1.97 \simeq 2$
		2.0	8.78	$3.94 \simeq 4$
		3.0	13.10	$5.91 \simeq 6$
		5.0	21.90	$9.85 \simeq 10$
		10.0	43.90	$19.70 \simeq 20$
Span 80	$\simeq 0.75$	0.5	2.25	1
		1.0	4.51	$2.02 \simeq 2$
		2.0	9.02	$4.04 \simeq 4$
		3.0	13.50	$6.07 \simeq 6$
		5.0	22.50	$10.12 \simeq 10$
		10.0	45.10	$20.24 \simeq 20$
Span 85	$\simeq 1.35$	0.5	4.05	$1.82 \simeq 2$
		1.0	8.12	$3.64 \simeq 4$
		2.0	16.20	$7.28 \simeq 7$
		3.0	24.30	$10.92 \simeq 11$
		5.0[a]	–	–
		10.0[a]	–	–

[a] Concentrations of Span 85 at which the results of the experiments on the powder were unreproducible.

surfactant. It can be seen that the thickness varied with the cross-sectional area of the molecules and with their concentration.

The tensile strength, T, results for all samples were found to fit the general equation (Malamataris and Pilpel, 1980):

$$\log T = K\rho_F + B \tag{6}$$

with a correlation coefficient > 0.9 for at least 5 measurements. ρ_F is the packing fraction and K and B are numerical constants which depend on the nature and the amount of the surfactant employed. The values obtained by regression analysis to a limit of 0.999 are listed in Table 4.

Fig. 4 shows representative results on the effect of packing fraction on the tensile strengths of lactose coated with different concentrations of Span 80.

TABLE 4

PARAMETERS DERIVED FROM TENSILE TESTS AND CHENG'S EQUATION

Non-ionic surfactant	Concentration ($mol \cdot g^{-1} \times 10^5$)	A	B	t_0 (μm)	Σ_0 at ρ_F 0.54	Surfactant concentration at which maxima occur — C crit. ($mol \cdot g^{-1} \times 10^5$)
Blank	0.0	13.6	−5.00	2.5	1.37	–
Span 20 (liquid)	0.5	12.6	−4.60	2.0	0.76	0.5
	1.0	10.9	−3.40			
	2.0	9.7	−2.60	2.8	0.77	
	3.0	5.4	−0.20	3.4	0.97	
	5.0	4.8	0.60	6.9	2.62	
	10.0	3.3	1.40	11.0	10.30	
Span 60 (solid)	0.5	9.9	−3.10	1.4	0.46	0.5–1
	1.0	11.6	−4.00	1.3	0.32	
	2.0	16.5	−6.40	1.1	0.07	
	3.0	15.5	−5.60	1.1	0.03	
	5.0	20.4	−7.60	1.1	0.01	
	10.0	13.4	−3.80	1.2	0.01	
Span 80 (liquid)	0.5	20.7	−9.20	1.5	0.41	0.5
	1.0	13.9	−5.16			
	2.0	10.8	−3.30	2.8	0.85	
	3.0	7.7	−1.49	4.5	2.47	
	5.0	6.2	−0.30	6.6	3.46	
	10.0	4.7	0.63	10.5	9.29	
Span 85 (liquid)	0.5	8.4	−2.00	3.7	2.00	None
	1.0	8.9	−2.00	6.9	7.70	
	2.0	3.7	1.20	11.9	12.80	
	3.0	3.1	1.50	14.5	21.00	

From these results one could determine the tensile strengths of all the samples at a fixed packing fraction of 0.54 (selected because it involved minimum extrapolation of the experimental data). The tensile strengths of the samples at packing fraction 0.54 are plotted against their surfactant contents in Fig. 5, and it is seen that excluding Span 85, addition of surfactant initially produced a decrease in the tensile strength followed by an increase.

Dealing with the resistance of the samples to consolidation by the application of stress P, a highly significant correlation (> 99% certainty) was found between the packing fraction achieved and the log of the applied stress at all concentrations. The correlation fitted the equation

$$\log P = K_1 \rho_F + B_1 \tag{7}$$

where again K_1 and B_1 are constants and depended on the nature and the amount of the surfactant employed.

Fig. 6 shows the stress required to achieve a packing fraction 0.54 plotted against

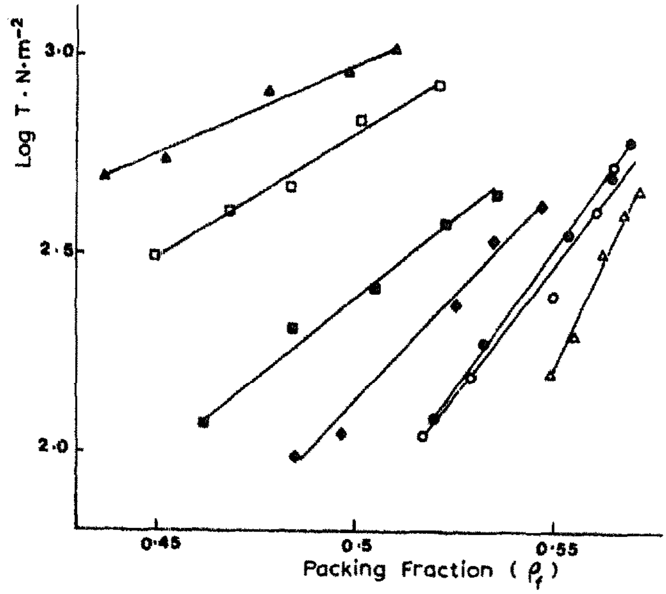


Fig. 4. Log tensile strength T (N·m^{-2}) (ordinate) vs packing fraction ρ_F (abscissa) of lactose coated with different amounts of Span 80. Key: ○, lactose alone (L); Δ, L+0.5×10^{-5}; ●, L+1×10^{-5}; ◆, L+2×10^{-5}; ■, L+3×10^{-5}; □, L+5×10^{-5}; ▲, L+10×10^{-5} mol·g^{-1} Span 80.

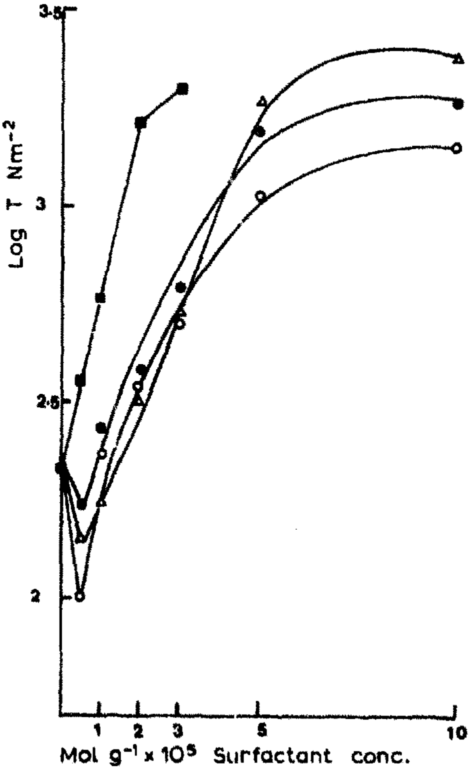
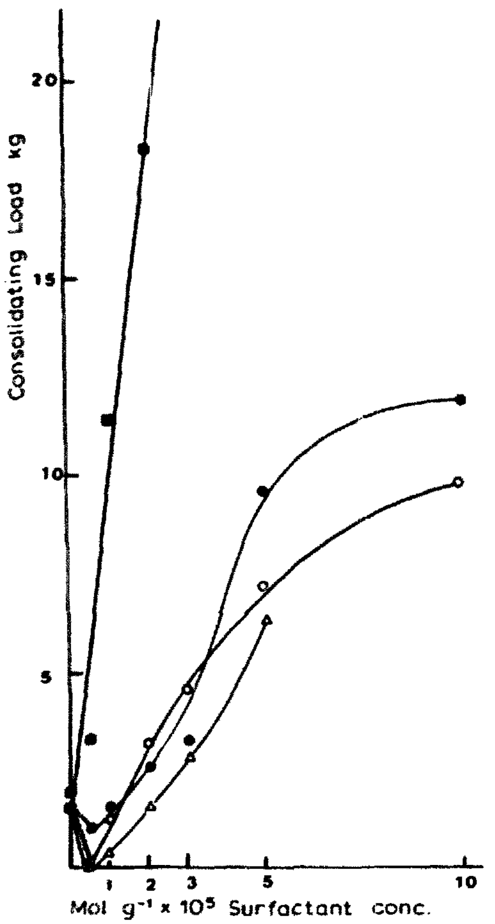


Fig. 5. Log tensile strength T (ordinate) vs surfactant concentrations (abscissa). Key as in Fig. 3.



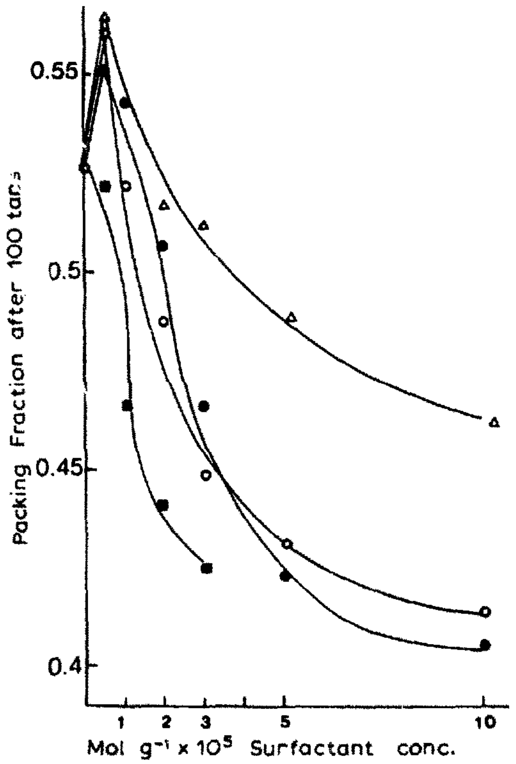


Fig. 6. Consolidation (kg) (ordinate) required to achieve packing fraction 0.54 vs surfactant concentrations. Key as in Fig. 3.

Fig. 7. Relation between packing fraction (ordinate) and surfactant concentrations (abscissa) after 100 taps. Key as in Fig. 3.

the surfactant content for various samples of coated lactose. It is seen that excluding Span 85, the addition of surfactant initially produced a decrease to a minimum followed by an increase in the resistance to consolidation. This pattern is very similar to that obtained in Fig. 5.

Turning next to the tapping results, the packing fraction of each sample after 100 taps (when the sample achieved its maximum packing density), was considered a suitable parameter for assessing the effect of the coating on the consolidation of the samples during tapping.

Fig. 7 shows the packing fraction achieved by each coated sample of lactose after 100 taps plotted against the surfactant content. It can be seen that except for Span 85, addition of surfactant initially produced an increase in the packing fraction followed by a decrease.

Discussion

It is seen from Table 3 that, with the concentrations employed, the surfactant coatings on lactose were between 1 and 20 molecules thick. At any particular concentration Span 85 produced the thickest coating because of its larger molecular cross-sectional area.

It seems from the similar shapes of the curves in Figs. 5 and 6, showing initial decreases in T and P followed by increases as the surfactant content is increased, that a common mechanism may be responsible for the tensile strengths of the samples and their resistance to consolidation (see also Malamataris and Pilpel, 1980).

The initial decreases in Figs. 5 and 6, and the increases in Fig. 7, may be ascribed to smoothing of surfaces of the particles and masking of London or Van der Waal's forces between them due to the formation of a monomolecular layer of the coating material. This appears to act as a lubricant for the particles making it easier for them to slide past each other during the consolidation and tapping processes. These minima and maxima did not appear when the lactose was coated with Span 85, because even at the lowest concentration employed the coating was more than 1 molecule thick due to the large cross-sectional area and the big molecular structure of the Span 85 molecule (Table 3 and Fig. 1).

The subsequent increases seen in Figs. 5 and 6, and the decreases in Fig. 7, at the higher concentrations of the surfactants can be attributed either to the greater area of real contact between the particles due to the soft plastic nature of the coatings, or to the development of capillary or pendular bonds between these liquid or semi-liquid coatings, thereby forming bridges between neighbouring lactose particles. From the relative positions of the curves in Figs. 6 and 7, it seems that Span 60 is more effective as a lubricant than the other surfactants, presumably because the monostearate forms a harder, more stable, durable lubricating coating than the laurate or oleate.

Magnitude of interparticle forces

Several workers (see Kočova and Pilpel, 1973) have proposed theories to explain the tensile strengths of beds of compressed powders in terms of the forces that operate between the constituent particles. The most recent is due to Cheng (1968, 1970). It is now proposed to apply this theory to the tensile strength results that have been obtained on the lactose powder before and after coating it with different amounts of the different surfactants in order to calculate two quantities, t_0 and Σ_0.

t_0 can be identified as the range of the forces that act between the particles of the powder, and cause it to exhibit tensile strength. Σ_0 is the energy of their surfaces.

Cheng's expression for tensile strength T, is

$$T = abc\frac{1}{2}\left\{\left[\frac{\bar{s}}{\bar{v}}\rho_F\right]h\left[t_0 - \frac{\bar{d}}{3}\left(\frac{\rho_F}{\rho_{F0}} - 1\right)\right]\right\} \tag{8}$$

where a and b are constants, c is the co-ordination number, h is the interparticle force per unit area of contact, ρ_F is the packing fraction of the powder bed, ρ_{F0} is the packing fraction when $T = 0$, t_0 is the interparticle attractive force, $\bar{d}$ is the mean particle diameter (here = 33 μm), $\bar{s}$ is the mean effective surface area per particle (here = 1290 μm^2), and $\bar{v}$ is the mean effective volume per particle (here = 37725 μm^3). These values together with the values of tensile strength and of ρ_{F0} (obtained by extrapolating the tensile strength versus packing fraction curves to $T = 0$) were used to calculate the functions:

$$F = \frac{1}{2}\frac{\bar{s}}{\bar{v}} \cdot \frac{\rho_F}{T} \tag{9}$$

and

$$G = \frac{\bar{d}}{3}\left(\frac{\rho_F}{\rho_{F0}} - 1\right) \tag{10}$$

The values of t_0 (see Table 4) were estimated by extrapolating graphs of F versus G to zero as illustrated in Fig. 8.

Cheng's expression for tensile strength was originally derived for a single-component powder containing a relatively narrow range of particle sizes, but it is clear from Fig. 8, that it also applied to powders whose particles have been coated with a second component; here this was a non-ionic surfactant.

The same figure shows that the value of t_0 varies with the amount of surfactant in the coating being at a minimum when the coating is monomolecular, and then increasing as the amount of the surfactant is increased. This behaviour is similar to that shown in Figs. 5 and 6, and it can be seen that there is a correlation between t_0,

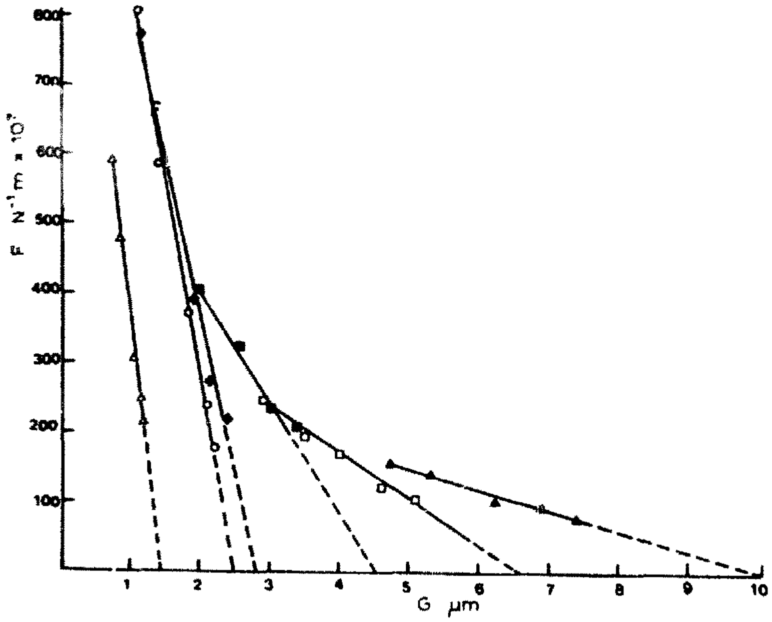


Fig. 8. Plots of F (ordinate) vs G (abscissa). Key as in Fig. 4.

the tensile strength of the powder and its resistance to consolidation.

Table 4 shows that at comparable concentrations Span 60 gives the lowest t_0 values. Span 85 produced no minima in these values which were higher than those produced by the other surfactants at any particular concentration.

The other parameter that can be derived from Cheng's equation is Σ_0 and this can be identified as the energy of the particle surfaces (Cheng, 1968, 1970).

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

$$\frac{\Sigma_{0_1}}{\Sigma_{0_2}} = \frac{(t_{0_1})^3}{(t_{0_2})^3} \frac{F_1}{F_2} \tag{11}$$

where F_1 and F_2 are obtaied fom Eqn. 9. Hence, if the surface energy of the uncoated lactose Σ_{0_1} is taken as unity, that of the coated material Σ_{0_2} can be calculated.

Relative values of Σ_{0_2} at a packing fraction 0.54 for all the samples are given in Table 4. The values for coated lactose are substantially higher than those for uncoated lactose except when the coating is monomolecular. The values for lactose coated with Span 60 are less than for lactose alone. This is thought to be due to the smoothness and durability of Span 60 coatings.

Conclusions

The tensile strength of powdered lactose and its resistance to consolidation after being coated with a series of Spans has been studied.

The existence of a monomolecular coating increases the values of the packing fractions of the samples after 100 taps. Increasing the thickness of the coatings increases the cohesion between the particles, preventing them from slipping and rearrangement. Their packing fractions consequently decrease.

On the basis of Cheng's theory of tensile strength, values are given for the range and magnitude of the physical forces that act between the surfaces of the coated and uncoated particles. Explanations for the results are provided.

At any particular concentration Span 60, which produces a solid coating, is more effective as a lubricant than the Spans which give a 'liquid coating'.

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