Effects of coating the powder on the tensile strength, disintegration and dissolution of lactose tablets

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Summary

A study has been made of the effects produced on the tensile strength, disintegration and dissolution of lactose tablets by coating the powder with increasing amounts of paraffins.

Addition of paraffins reduces the tensile strength and prolongs the disintegration and dissolution times. Silicones produce similar effects on the disintegration times. The disintegration and dissolution results have been explained in terms of the changes produced by the coatings on the wettability of the powder.

Introduction

The bioavailability of drugs that are administered orally in solid form is controlled by their rates of disintegration and dissolution (Nelson and Schaldemose, 1959; Levy, 1961). The wettability of solids—their hydrophobicity—plays an important role in the disintegration and dissolution processes and subsequent release of the active ingredient.

Excipients applied to a pharmaceutical powder alter its hydrophobic nature and thus affect the wetting process (Zografi and Tam, 1976). The wettability of solids can be estimated by measuring the contact angle of water on their surface (Kossen and Heertjes, 1965). An angle of 0° signifies complete wetting; an angle approaching 180°, negligible wetting. The contact angles of other liquids besides water can be

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used to provide further information about the free energies of surfaces (Zografi and Tam, 1976). Paraffins and silicones are lubricants used in tabletting which make powders strongly hydrophobic (Strickland, 1959).

Previously (Irono and Pilpel, 1982a and b) we coated lactose with increasing concentrations of various paraffins and subjected the powders to tensile and shearing tests at different temperatures. We showed that changes in the processing temperature caused changes in the viscosity of the coatings and affected the mechanical properties of the powders, such as their tensile strengths, cohesion and angle of internal friction.

It is now considered of interest to see firstly whether alterations in temperature have any significant and predictable effects on the tensile strengths of tablets produced from the coated powders and secondly to see how the disintegration and dissolution times of tablets, compressed at different temperatures, depend on the nature and amount of the coating material employed. One might expect some correlation to exist between the disintegration and dissolution times of tablets and the wettability of their surfaces.

Materials and Methods

Materials

Details of coating lactose powder with various paraffins have been given (Irono and Pilpel, 1982a and b).

Samples of lactose were also coated with between 0.5 and 10.0×10^{-5} mol·g^{-1} of 3 types of silicone fluid, DC 200/20 cs, DC 200/50 cs and DC 550 (Hopkin and Williams) using the same technique. These were selected because, like the paraffins, they are hydrophobic, do not react chemically with lactose and their physical properties vary in a regular manner with their molecular weight. The mean molecular weight of each silicone was determined from the viscosity versus $\sqrt{n}$ calibration curve, where n is the number of

$$\left[\begin{array}{c} R \\ | \\ O-Si- \\ | \\ R \end{array} \right] \text{groups}$$
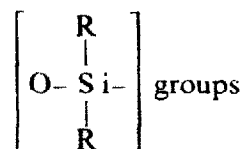
and R is a methyl group in the DC 200 series and a phenyl methyl group in the DC 550 series. The value was confirmed by the viscosity method using Staudinger's equation (Weissberger, 1949). The relevant physicochemical properties of the silicone fluids are listed in Table 1.

Hand press for preparing tablets

This was fitted with a pressure gauge reading up to 5.0 tons (Research and Industrial Instruments, London) and was modified to operate at both low and elevated temperatures (Malamataris and Pilpel, 1981). Before each compression, the

TABLE 1

SOME PHYSICOCHEMICAL PROPERTIES OF THE SILICONE FLUIDS

Properties	DC 200/20 cs	DC 200/50 cs	DC 550
Mean molecular weight	745	3425	5085
Density (g/ml)	0.96–0.97	0.96–0.97	1.06–1.08
Solidifying point (°C)	−60	−55	−50
Viscosity in cs at 25°C ± 2 cs	22	60	110

punches and die were brushed with a 1% w/v suspension of magnesium stearate in chloroform to act as a die lubricant. The die was 10.5 mm diameter and flat-faced punches were used.

Procedure

400 mg of the coated powder was carefully introduced into the die resting on the lower punch. The upper punch was gently placed in position and the whole transferred to the cooling/heating chamber. The required temperature was maintained for 30 min, then the powder was compressed by lowering the pressing head at a constant rate of 0.22 mm/s. The pressure was held for 1 min at a pre-selected level indicated by the gauge. The tablet was carefully removed from the die and subjected to a diametral compression test (Malamataris and Pilpel, 1981) after 24 h storage over silica gel. The storage and test were carried out at the same temperature as used for compression. These tests were only made on powders coated with paraffins.

Disintegration and dissolution tests

The disintegration times of tablets made from lactose which had been coated either with a paraffin or with a silicone were measured in distilled water at $37 \pm 1°C$ in a Manesty disintegration tester using the B.P. (1973) method.

The dissolution rates of the former tablets only were determined at the same temperature in 1 litre of standard pH 6 buffer solution (B.P., 1973) in a round-bottomed flask, employing a two-bladed paddle fitted 2 cm below the surface of the liquid and a stirring speed of 100 rev·min^{-1}. The amount of lactose that had dissolved in the medium after a certain period was determined by measuring the optical rotation in a polarimeter (Bellingham and Stanley) using a calibration curve made under the same conditions from a sample of pure lactose dissolved in the pH 6 buffer solution. All measurements were made in triplicate or more and the results given are the means of several determinations.

Contact angle determinations

The contact angles of water and methylene iodide on the coated powders were determined as described by Kossen and Heertjes (1965) and by Lerk et al. (1976)

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calculating the values from the following equation:

$$\text{Cos}\,\theta = 1 - \sqrt{\frac{Bh^2}{3(1-\epsilon v)(1-Bh^2/2)}} \tag{1}$$

(for $0 < \theta < 90°$), where h is the height of the drop in cm, ϵv is the porosity of the compact and B is $\rho_L g/2Y_L$, where ρ_L is the density of the liquid in $g \cdot cm^{-3}$, g is 981

TABLE 2

CONTACT ANGLES OF WATER AND METHYLENE IODIDE ON THE COATED POWDERS

Lactose + coating	Coating content (mol g^{-1} × 10^6)	Water (saturated with lactose			Methylene iodide		
		Drop Height, h (cm)	Porosity, ϵ_v	θ°	Drop height, h (cm)	Porosity, ϵ_v	θ^0
Lactose (blank)	0.00	0.0791	0.227	30.7	0.0425	0.248	32.9
Light liquid paraffin	10.00	0.0996	0.242	34.9	0.0440	0.246	33.5
	20.00	0.1186	0.238	38.3	0.0460	0.242	34.2
	50.00	0.1315	0.234	40.5	0.0485	0.240	35.2
	100.00	0.1432	0.214	42.2	0.0536	0.236	37.1
Liquid paraffin	10.00	0.1045	0.240	35.8	0.0490	0.245	35.4
	20.00	0.1296	0.232	40.1	0.0520	0.240	36.5
	50.00	0.1445	0.226	42.6	0.0580	0.238	38.7
	100.00	0.1500	0.222	43.4	0.0591	0.226	39.0
White soft paraffin	10.00	0.1920	0.234	50.5	0.0750	0.236	44.7
	20.00	0.2096	0.228	53.2	0.0812	0.231	46.8
	50.00	0.2300	0.210	56.2	0.0995	0.222	52.8
	100.00	0.2431	0.205	58.3	0.1055	0.209	54.6
Paraffin wax	10.00	0.2920	0.230	67.5	0.1125	0.230	57.4
	20.00	0.3165	0.222	72.1	0.1295	0.225	63.4
	50.00	0.3310	0.219	75.1	0.1440	0.220	68.9
	100.00	0.3450	0.216	78.2	0.1592	0.220	75.4
Silicone DC 200/ 20cs	10.00	0.1012	0.236	35.1	0.0442	0.234	33.4
	20.00	0.1172	0.230	37.9	0.0490	0.228	35.2
	50.00	0.1375	0.226	41.4	0.0572	0.224	38.2
	100.00	0.1496	0.221	43.3	0.0630	0.220	40.3
Silicone DC 200/ 50cs	10.00	0.1745	0.235	47.6	0.0770	0.230	45.3
	20.00	0.1984	0.228	51.4	0.0855	0.228	48.2
	50.00	0.2105	0.225	53.3	0.0910	0.224	50.0
	100.00	0.2511	0.224	60.0	0.1130	0.215	57.3
Silicone DC 550	10.00	0.2755	0.222	64.2	0.1235	0.226	61.2
	20.00	0.2980	0.216	68.3	0.1385	0.220	66.7
	50.00	0.3280	0.208	74.1	0.1510	0.215	71.6
	100.00	0.3511	0.210	79.4	0.1665	0.206	78.5

$cm \cdot s^{-2}$, Y_L is the surface free energy of the liquid against its vapour in $mJ \cdot m^{-2}$ which was measured with a Du Nouy tensiometer (Cambridge Instruments). The values are given in Table 2 as averages of triplicate determinations and are considered accurate to $\pm 0.5°$.

Results

The results of the tensile tests on the tablets made from lactose coated with the paraffins at all the temperatures investigated were found to fit the general equation:

$$\log T = KP_f + C \tag{2}$$

Fig. 1.
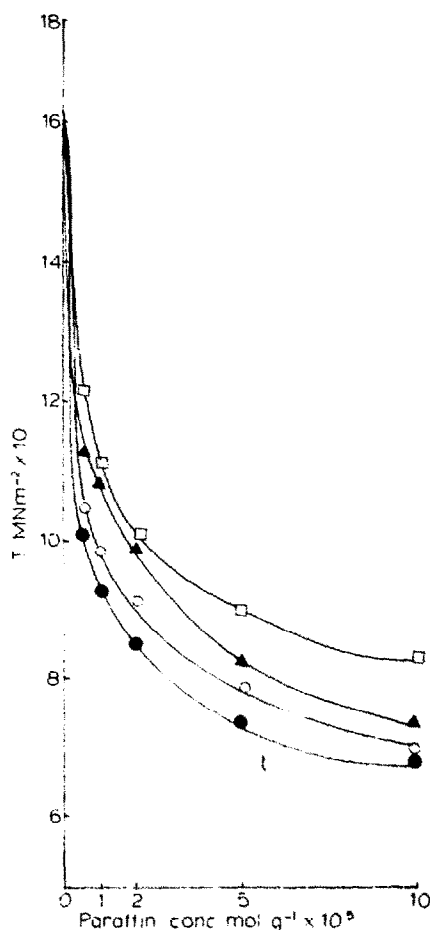
Fig. 2.

Fig. 1. Tensile strength $(MN \cdot m^{-2})$ (P_f 0.86) versus paraffin concentration for tablets compressed at 35°C. ●, light liquid paraffin; O, liquid paraffin; ▲, white soft paraffin; □, paraffin wax.
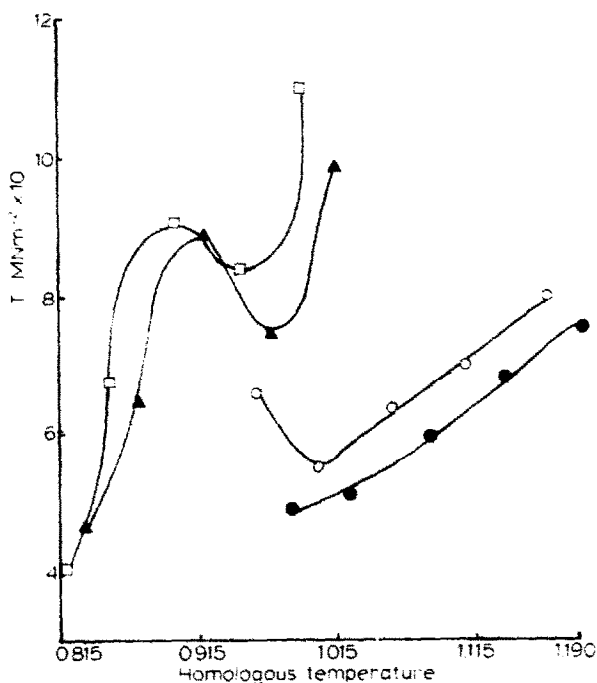
Fig. 2. Tensile strength $(MN \cdot m^{-2})$ (P_f 0.86) versus homologous temperature of compression/testing for tablets containing 10.0×10^{-5} $mol \cdot g^{-1}$ of the paraffins. ●, light liquid paraffin; O, liquid paraffin; ▲, white soft paraffin; □, paraffin wax.

Fig. 3.

Fig. 4.

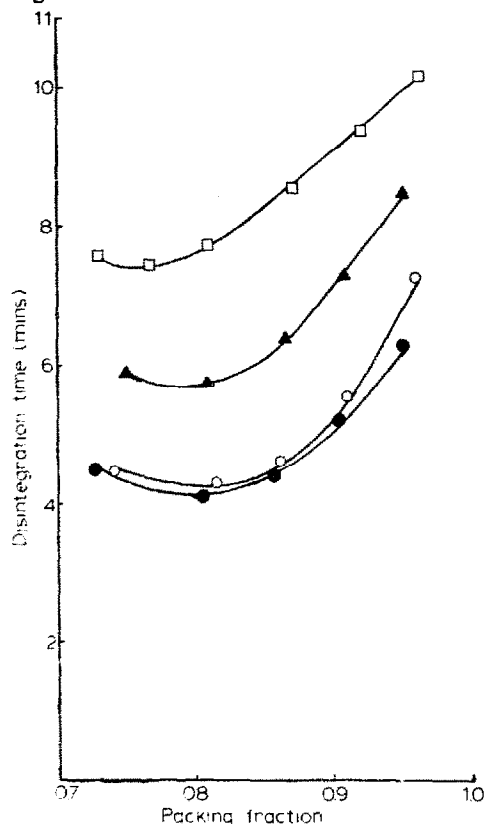Fig. 3. Disintegration time (min) versus packing fraction (P_f) for tablets containing 0.5×10^{-5} mol·g^{-1} of the paraffins compressed at 20°C. ●, light liquid paraffin; ○, liquid paraffin; ▲, white soft paraffin; □, paraffin wax.
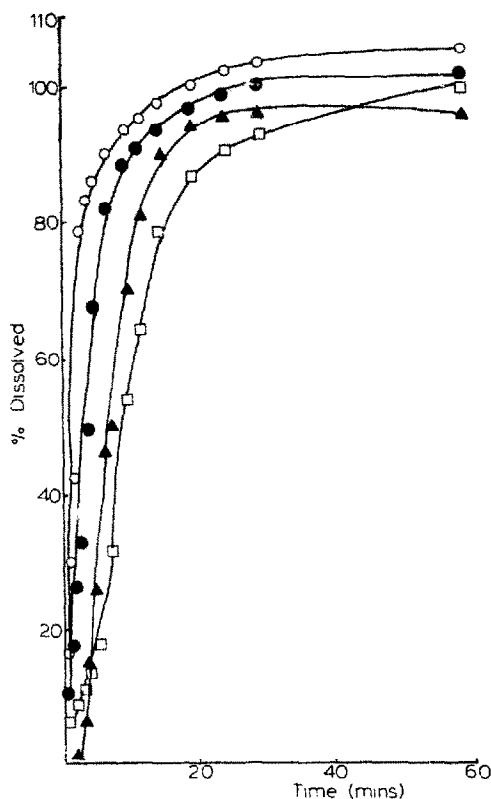
Fig. 4. Effect of packing fraction on the dissolution profiles of tablets containing 10.0×10^{-5} mol·g^{-1} of light liquid paraffin compressed at 20°C. Mean P_f: ●, 0.772; ○, 0.807; ▲, 0.862; ■, 0.891.

with a correlation coefficient of > 0.95. P_f is the packing fraction, K and C were constants which depended on the temperature of the measurement and on the nature and amount of the paraffin used.

In Fig. 1, the tensile strengths of these tablets at 35°C and a fixed P_f of 0.86 (selected because it involved minimum extrapolation of the linear plots of log T versus P_f) are plotted against the concentration of the paraffin. It is seen that the tensile strengths decreased with increase in paraffin concentration.

Representative graphs of tensile strength versus the homologous temperature [1] of compression/testing are illustrated in Fig. 2 for lactose coated with 10.0×10^{-5} mol·g^{-1} of the paraffins. The tensile strengths initially increased with increase in

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[1] Ratio of the temperature of compression/testing in degrees Kelvin to the melting/softening point of the coating material in degrees Kelvin.

the homologous temperature (it was not possible to observe this for the paraffins which are liquid at room temperature because the measurements would have had to be made at very low temperatures), then decreased at homologous temperatures close to 1.00 and finally increased again as the temperature was further increased.

The disintegration times were plotted as a function of packing fraction for all the samples investigated and the values at a fixed packing fraction of 0.86 (the same as used for comparing the tensile strengths) were determined. Representative graphs for tablets containing 0.5×10^{-5} mol $\cdot$ g^{-1} of the various paraffins compressed at 20°C are given in Fig. 3. The disintegration times exhibited minima at packing fractions between 0.75 and 0.83.

Typical dissolution profiles for tablets containing 10.0×10^{-5} mol $\cdot$ g^{-1} of light liquid paraffin compressed to different packing fractions at 20°C are shown in Fig. 4. From these cumulative percentage dissolved versus time plots the values of t_{50}, t_{90} and in some cases t_{100} (the time required for 50%, 90% and 100% of the lactose to be released) were calculated.

Fig. 5 shows how the disintegration times and t_{90} values of the tablets containing the various paraffins at P_f 0.86 and compressed at 20°C varied with the paraffin
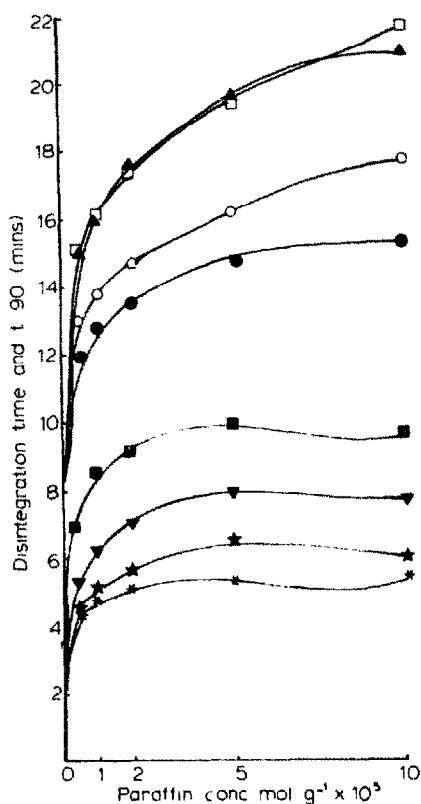

Fig. 5. Disintegration time (min) versus paraffin concentration for tablets (P_f 0.86) compressed at 20°C. ●, light liquid paraffin; ★, liquid paraffin; ▼, white soft paraffin; ■, paraffin wax. Time required for 90% dissolution (min) versus paraffin concentration for tablets (P_f 0.86) compressed at 20°C. ●, light liquid paraffin; ○, liquid paraffin; ▲, white soft paraffin; □, paraffin wax.
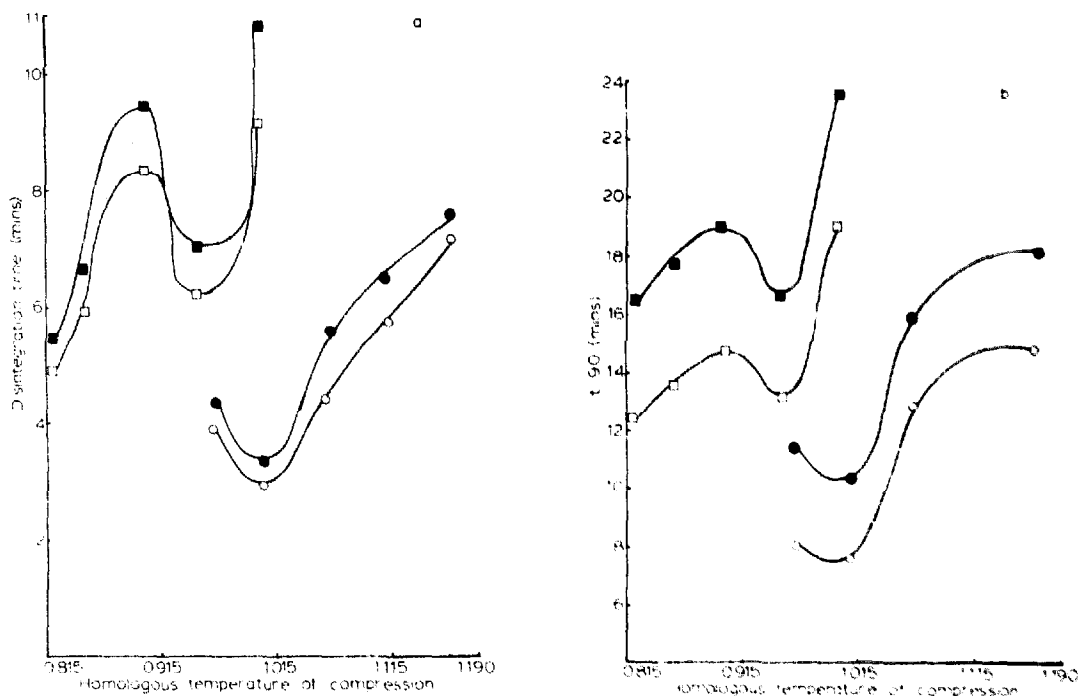
Fig. 6. a: disintegration time (min) versus homologous temperature of compression for tablets (P_f 0.86) containing 0.5 and 5.0×10^{-5} mol·g^{-1} of liquid paraffin and paraffin wax. 0.5×10^{-5} mol·g^{-1}: ○, liquid paraffin; □, paraffin wax. 5.0×10^{-5} mol·g^{-1}: ●, liquid paraffin; ■, paraffin wax. b: time required for 90% dissolution (min) versus homologous temperature of compression for tablets (P_f 0.86) containing 0.5 and 5.0×10^{-5} mol·g^{-1} of liquid paraffin and paraffin wax. 0.5×10^{-5} mol·g^{-1}: ○, liquid paraffin; □, paraffin wax. 5.0×10^{-5} mol·g^{-1}: ●, liquid paraffin; ■, paraffin wax.

concentration (the shapes of the graphs of t_{50} versus paraffin concentration were similar). Both the disintegration and dissolution times increased with paraffin content.

Fig. 6a and b illustrates the effects produced by the homologous temperature of compression on the disintegration time and t_{90} (the curves for t_{50} were similar) for tablets at P_f 0.86 containing 0.5 and 5.0×10^{-5} mol·g^{-1} of liquid paraffin and paraffin wax. It is seen that the shapes of the curves in Figs. 6 and 2 were generally similar. The correlation between disintegration and dissolution times is shown in Fig. 7.

The dissolution results were subjected to the Wagner (1969) analysis by plotting the percentage of lactose dissolved against time on a log-probability scale; Fig. 8 shows the results for tablets coated with increasing concentrations of light liquid paraffin compressed at 20°C to a fixed P_f 0.86. The plots were rectilinear up to about 20 min.
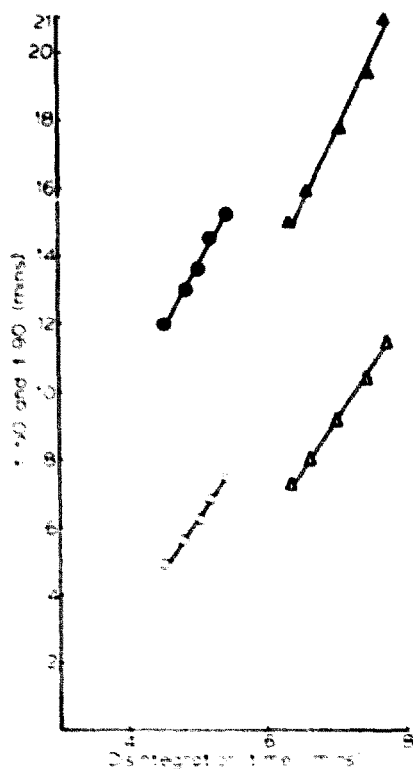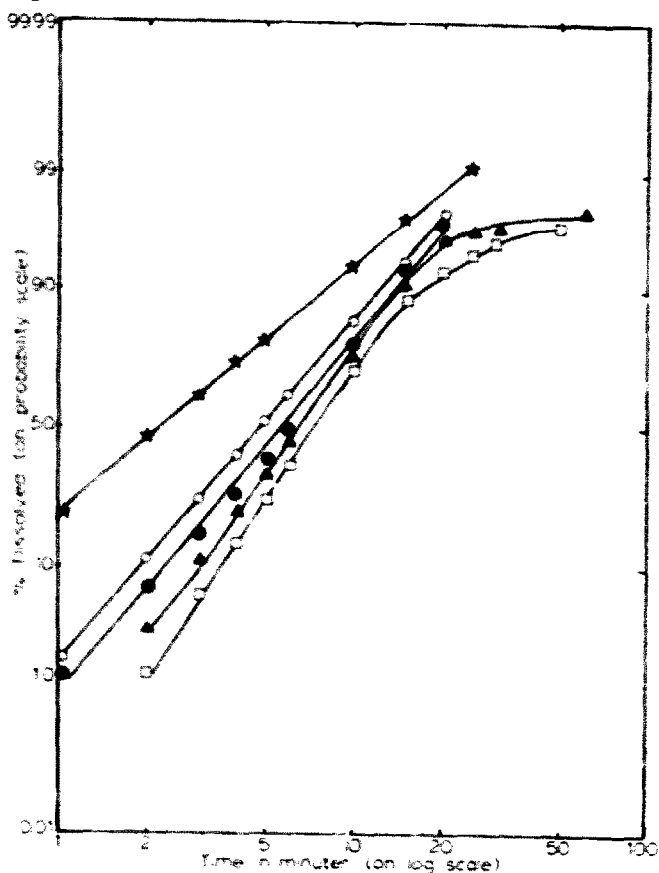
Fig. 7.

Fig. 8.

Fig. 7. Correlation of t_{50} and t_{90} (min) with disintegration time (min) of tablets (P_f 0.86) containing $0.5-10.0 \times 10^{-5}$ mol·g^{-1} of light liquid paraffin and white soft paraffin compressed at 20°C. Light liquid paraffin: O, t_{50}; ●, t_{90}. White soft paraffin: △, t_{50}; ▲, t_{90}.

Fig. 8. Wagner plot on dissolution tests of tablets (P_f 0.86) compressed at 20°C containing $0.0-10.0 \times 10^{-5}$ mol·g^{-1} of light liquid paraffin. ★, lactose 'blank' (0.0×10^{-5} mol·g^{-1}); ●, 0.5×10^{-5} mol·g^{-1}; O, 2.0×10^{-5} mol·g^{-1}; ▲, 5.0×10^{-5} mol·g^{-1}; □, 10.0×10^{-5} mol·g^{-1}.

Discussion

The decrease in tensile strength produced by increase in paraffin concentration in Fig. 1 may be attributed to the increasing incidence of paraffin–paraffin bonds which are inherently weaker than the lactose–lactose bonds [2]. The addition of more paraffin tends to smooth out the surface irregularities on the particles and mask the Van der Waal's forces between them. The paraffin acts as a lubricant, making it easier for the lactose particles to slide past each other during compression, prevent-

[2] At ~7°C and a packing fraction 0.65, the tensile strengths of paraffin wax and of lactose tablets were, respectively, 0.130 and 0.481 MN·m^{-2}.

ing them from interlocking and thus decreasing the number and strength of bonds formed between neighbouring particles (York, 1973; Malamataris and Pilpel, 1981). Although the tensile strength of lactose coated with silicones was not measured in this work similar conclusions would be expected (York, 1973).

The changes produced in the tensile strengths in Fig. 2 as the homologous temperature is raised to about 0.95 may be explained by postulating that under the influence of temperature and compression the paraffin which is coating the asperities on the lactose particles may initially melt but then resolidify to form strong welded bonds (Jayasinghe et al., 1969; York and Pilpel, 1972; Pilpel and Britten, 1979). However, at homologous temperatures near unity, welded bonds cannot form and there is a decrease in the tensile strength.

At still higher temperatures, 'liquidified' coating materials may diffuse into the interparticle spaces to form larger areas of true contact between particles with a consequent increase in the tensile strength. The tensile strengths of the coated samples of lactose are lower than that of the pure lactose (see Fig. 1) over the same temperature range. Thus coating powders with paraffins (and presumably also silicones) might, if considered necessary, provide a convenient method for reducing the intrinsic tensile strengths of their tablets.

The plots of logarithm of tensile strengths against the reciprocal of absolute temperatures were approximately linear both for lactose and for lactose containing the various paraffins. This is consistent with the Arrhenius equation (Kuczynski, 1950; Polke, 1969)

$$T = K \, e^{-E_0/RT_1} \tag{3}$$

where T is the tensile strength, E_0 is the activation energy, T_1 is the absolute temperature, R is $8.3 \, J \cdot mol^{-1}$, K is a constant for each material at each packing fraction and e has a numerical value of 2.718. The slopes of the lines are a measure of the activation energy, E_0, of bonding between the particles and the values were all between 5 and 12 $kJ \cdot mol^{-1}$. This is of the order expected for physical bonding between particles.

Turning next to the disintegration and dissolution results, for all the samples investigated the values were minimal at packing fractions between 0.75 and 0.83 as depicted in Figs. 3 and 4. This has been noted by several other workers (Polderman and Braakman, 1968; Esezobo and Pilpel, 1976; Kurup and Pilpel, 1977; Pilpel et al., 1978) and has been explained in terms of the specific surface area of the particles and the rate of penetration of liquid over this particular range of packing fractions.

The addition of paraffin (and presumably silicone) produced a parallel increase in disintegration and dissolution time as illustrated in Fig. 5. (This sort of connection between disintegration and dissolution has been noted before (Schroeter et al., 1962; Esezobo and Pilpel, 1976; Pilpel et al., 1978).) It can be attributed to the fact that the paraffins and silicones not only reduce the wettability of the surface of a tablet by increasing its contact angle with water but also reduce the interparticle friction and change the nature, shape and size distribution of the capillaries which conduct water into it. The presence of a paraffin or silicone in the tablet voids makes the

internal surface more hydrophobic and reduces the number of capillaries which are contributing to the transport of water. The water penetrates as a result of the pressure difference, ΔP, which exists across the entrance to each capillary

$$\Delta P = \frac{Y \cos \theta}{m} \quad \text{(Carman, 1941)} \tag{4}$$

where Y is the surface tension of water, θ is its contact angle on the capillary surface and m is the ratio of the cross-sectional area of the capillary to its perimeter. Clearly the penetration is slowest when ΔP is a minimum, i.e. when the contact angle is 90°. This connection between contact angle and disintegration or dissolution time is seen in Fig. 9a and b and it applies to lactose coated both with paraffins and with silicones despite the influence of the other factors that operate during a dissolution process (Wurster and Taylor, 1965; Wood, 1967).
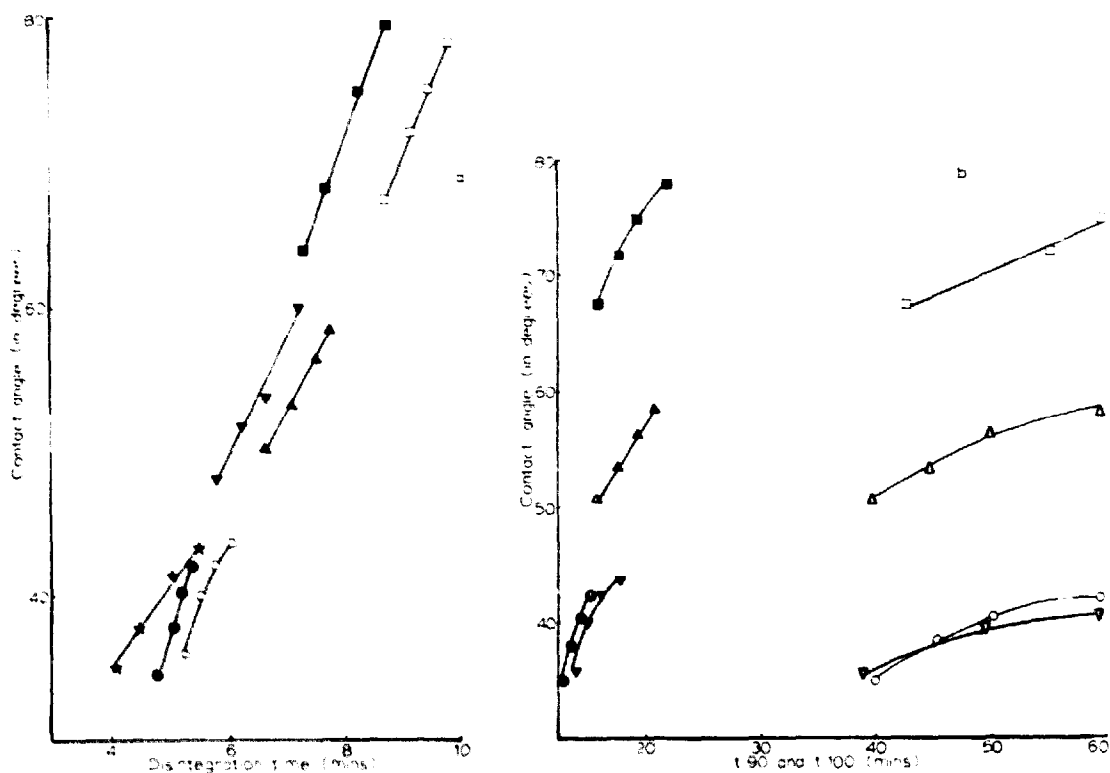

Fig. 9. a: correlation of contact angle of water on the powder compacts containing $0.5-10.0 \times 10^{-5}$ mol·g^{-1} of paraffins and silicones with the disintegration time (min) of the corresponding tablets (P$_f$ 0.86) compressed at 20°C. ●, light liquid paraffin; ○, liquid paraffin; ▲, white soft paraffin; □, paraffin wax; ★, silicone DC 200/20; ▼, silicone DC 200/50; ■, silicone DC 550. b: correlation of contact angle of water on the powder compacts containing $0.5-10.0 \times 10^{-5}$ mol·g^{-1} of paraffins with t$_{90}$ and t$_{100}$ (min) of the corresponding tablets (P$_f$ 0.86) compressed at 20°C. Light liquid paraffin: ●, t$_{90}$; ○. t$_{100}$. Liquid paraffin: ▼, t$_{90}$; ▽, t$_{100}$. White soft paraffin: ▲, t$_{90}$; △, t$_{100}$. Paraffin wax: ■, t$_{90}$; □, t$_{100}$.

Conclusions

Addition of increasing amounts of paraffins to lactose reduces the tensile strengths of its tablets and increases their disintegration and dissolution times: silicones produce similar effects on the disintegration times. These additives inhibit liquid penetration into the tablets by increasing their contact angle with water. Such additives could be considered for controlling the release rates of drugs from tablets.

Acknowledgement

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