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The adhesion of film coatings to tablet surfaces - the effect of some direct compression excipients and lubricants

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The effect of some direct compression excipients and lubricants on the adhesion of hydroxypropyl methyl cellulose films has been examined using a specially designed tensile testing apparatus (Fisher & Rowe, 1976). The adhesion was found to be influenced by both the roughness, including microporosity, of the tablet surface and its polarity. Tablets prepared from microcrystalline cellulose showed very high adhesions despite having relatively smooth surfaces, owing to the surface being saturated with hydroxyl groups able to form hydrogen bonds with the corresponding groups on the polymer. The addition of magnesium or calcium stearate to the tablet was found to decrease the adhesion, but the addition of stearic acid caused a significant increase. The effect of lubricant concentration on the adhesion could be expressed by an equation similar to that proposed by Hofrichter & McLaren (1948) for the adhesion of vinyl chloride/vinyl acetate copolymers to regenerated cellulose.

A major pre-requisite for pharmaceutical film coatings is good adhesion to the tablet substrate. Previous studies in tablet film adhesion (Wood & Harder, 1970, Nadkarni, Kildsig & others, 1975; Fisher & Rowe, 1976) have concentrated on the effect of film forming variables (coating solvents, fillers, plasticizers and polymer molecular weight) and, although different substrate formulations were used, little work has been done on the direct effect of the various excipients involved. However, data on tablets prepared from acetylsalicylic acid coated with methyl cellulose films (Wood & Harder, 1970) have shown that added excipients can have a significant effect on the adhesion which in some cases, can far surpass the effect of the film forming variables. I have examined the effect of some direct compression excipients and lubricants on the adhesion of hydroxypropyl methyl cellulose films.

MATERIALS AND METHODS

Tablets (11·11 mm diameter, flat faced) of the materials microcrystalline cellulose (Avicel PH 101, FMC Corporation, Pennsylvania, U.S.A.), spray dried lactose (Makesson and Robbins Ltd., Kent) anhydrous lactose (U.S.P. grade, Sheffield Chemical, New Jersey, U.S.A.) and direct compression forms, of sucrose (Di. Pac, Amstar Corporation, New York, U.S.A.), dextrose monohydrate (Cellutab, Kingsley and Keith (Chemicals) Ltd., Croydon) and dicalcium phosphate dihydrate (Encompress special, Kingsley and Keith (Chemicals) Ltd., Croydon), all lubricated with 0·5% magnesium stearate, were prepared on an instrumented single punch machine (Type F3 Manesty Machines Ltd). Compression pressures in excess of 300 MPa were used, giving porosities of $5 \pm 1\%$ for all tablets except those prepared from the dicalcium phosphate dihydrate which had a porosity of 10%.

In the study of the effect of lubricants and lubricant concentration, a standard placebo granule consisting of lactose and starch as used previously was used as a base and the lubricants added before compression. Stearic acid, magnesium stearate, calcium stearate, hydrogenated castor oil (Cutina H.R. Henkel and Cie, G.M.B.H. Dusseldorf) and vegetable stearin (Duratex, SCM-Glidden International Co., Ohio, U.S.A.) were included. The tablets were compressed at 250 MPa to give porosities of between 8 and 10%.

The tablets were coated with a film formulation consisting of a mixture of four parts hydroxypropyl methyl cellulose (Pharmacoat 606, Shinetsu Chemical Co. Ltd., Japan, or Methocel 60 HG viscosity 50, Dow Chemical Co. Ltd., U.S.A.), and one part ethyl cellulose (Grade N7 Hercules Powder Co. Ltd) with 20% w/w glycerol as plasticizer, applied as a 2·5% w/v solution dissolved in a dichloromethane-methanol (70:30% v/v) solvent mixture using a 24 inch Accelacota (Manesty Machines Ltd). The coated tablets were stored at room temperature and 50°RH for two weeks before testing using the specially designed tensile testing apparatus (Fisher & Rowe, 1976). Ten tablets were used for each measurement and the

mean and standard deviation calculated. The surfaces of the tablets were examined using scanning electron photomicrographs (Stereoscan S11A).

RESULTS AND DISCUSSION

It is now generally accepted that adhesion is due to the interaction of intermolecular bonding forces (hydrogen bonding, dipole-dipole and dipole-induced dipole) involving such functional groups as -OH, -COOH, -C=O and -$COCH_3$ (Pritchard, 1971). Therefore, for hydroxypropyl methyl cellulose films containing both primary and secondary hydroxyl groups in the molecule, adhesion should be enhanced by the presence of hydroxyl groups in the substrate. This is the case with the excipients used here (Table 1) with the adhesion being highest for

Table 1. *The effect of excipients on the measured adhesion of hydroxypropyl methyl cellulose films (tablet diameter 11·11 mm).*

Excipient	Measured adhesion (kPa) Pharmacoat 606	Methocel 60HG Viscosity 50
Microcrystalline cellulose	65·4 ± 6·3	77·7 ± 9·9
Sucrose	44·5 ± 7·9	42·4 ± 8·4
Anhydrous lactose	51·2 ± 4·3	39·9 ± 5·5
Spray dried lactose	24·5 ± 2·7	23·4 ± 2·4
Dextrose	33·5 ± 9·5	20·7 ± 4·6
Dicalcium phosphate dihydrate	29·9 ± 3·4	22·0 ± 4·0

tablets prepared from microcrystalline cellulose, the surface of which is known to be saturated with hydroxyl groups (Battista & Smith, 1962). Unfortunately the tablets prepared from the inorganic dicalcium phosphate dihydrate cannot be directly compared with those prepared from the carbohydrate derivatives because of their higher overall porosity, a factor known to increase the measured adhesion by increasing the rate and depth of penetration of the polymer solution during the coating process (Fisher & Rowe, 1976). However, even allowing for this, the measured adhesion for these tablets is relatively low.

Lubricants will interfere with the bond formation by presenting a surface consisting mainly of non-polar hydrocarbon groups and the measured adhesion will be lowered. The extent to which interference occurs will be dependent on the nature of the lubricant and on its concentration in the tablet. If the lubricant itself has polar groups on the molecule then some interaction will occur between these groups and the film, and the measured adhesion will be less affected. This is the case with tablets lubricated with stearic acid (Table 2, Fig. 1)

Table 2. *The effect of lubricants on the measured adhesion of hydroxypropyl methyl cellulose films (lubricant concn 1% w/w, tablet diameter 11·11 mm).*

Lubricant	Measured adhesion (kPa) Pharmacoat 606	Methocel 60HG Viscosity 50
Stearic acid	44·4 ± 6·5	51·7 ± 5·7
Vegetable stearin	39·1 ± 5·2	32·9 ± 2·0
Hydrogenated castor oil	37·9 ± 5·7	36·2 ± 3·0
Magnesium stearate	25·3 ± 3·1	24·7 ± 4·7
Calcium stearate	21·4 ± 5·4	26·3 ± 4·9

with its free polar carboxyl group. When this group is combined with glycerol (to form the glyceryl esters as present in hydrogenated castor oil and vegetable stearin) or inorganic bases (to form the calcium and magnesium salts) the measured adhesion is progressively lowered. The intermediate adhesions shown by tablets lubricated with hydrogenated castor oil and vegetable stearin are due to free hydroxyl groups from either the partially esterified glycerol and/or the 12-hydroxystearic acid present in large concentrations in these materials.

In an investigation of the fundamentals of adhesion, Hofrichter & McLaren (1948) found that the adhesion of a polymer containing polar carboxyl groups to regenerated cellulose increased in a manner expressable by the equation:

$$\text{adhesion} = k\,(\text{COOH})^n \quad \ldots \quad \ldots \quad (1)$$

where k and n were constants.

The equation is analogous to the Freundlich adsorption isotherm. If it is assumed that a similar

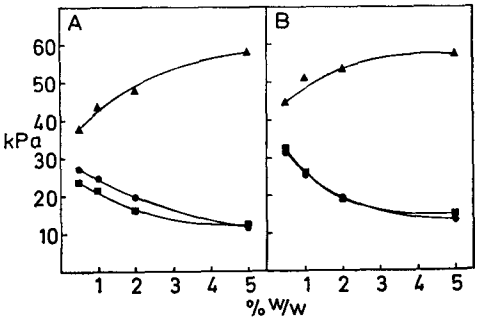

FIG. 1. The effect of lubricant concentration (% w/w) on the measured adhesion (kPa) of hydroxypropyl methyl cellulose films. A—Pharmacoat 606 and B—Methocel 60 HG viscosity 50 (tablet diameter 11·11 mm). ▲ Stearic acid. ● Magnesium stearate. ■ Calcium stearate.

interaction is taking place between the hydroxyl groups on the hydroxypropyl methyl cellulose film and those of the unlubricated substrate, and that lubricants act as monolayers at the interface, then the same equation should apply to the adhesion data shown in Fig. 1. If the equation is rewritten:

Table 3. *Constants calculated for equation 2 using the method of least squares.*

	Pharmacoat 606			Methocel 60HG Viscosity 50		
	Calculated values for					
Lubricant	k	n	c. coeff.	k	n	c. coeff.
Stearic acid	43·15	0·174	0·991	49·31	0·095	0·945
Magnesium stearate	23·17	−0·380	0·956	24·60	−0·371	0·999
Calcium stearate	20·04	−0·294	0·987	25·66	−0·296	0·960

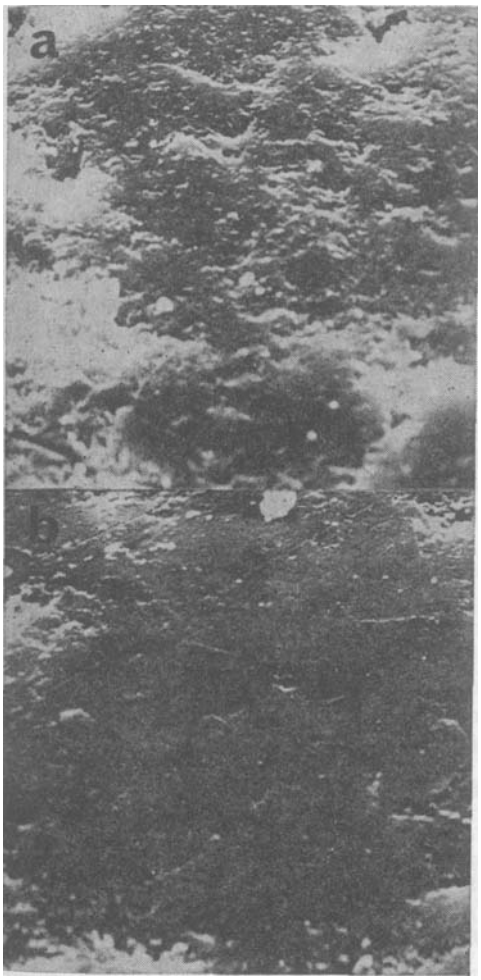

FIG. 2. Scanning electron photomicrographs of the surfaces of tablets prepared from a—anhydrous lactose, b—spray dried lactose (× 500).

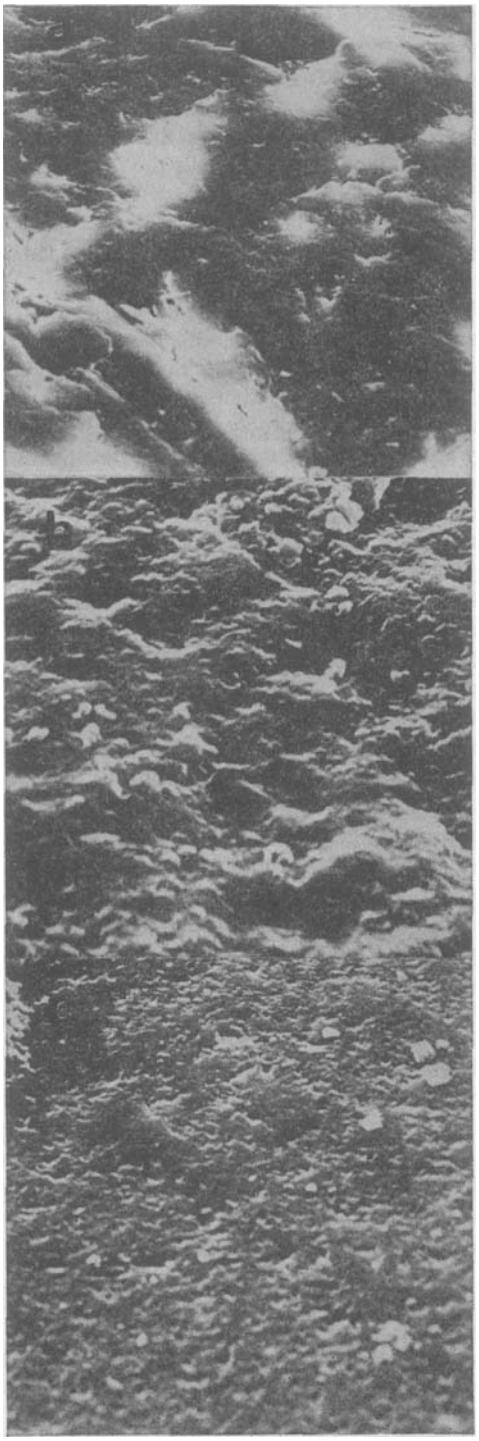

FIG. 3. Scanning electron photomicrographs of the surfaces of tablets prepared from a—microcrystalline cellulose, b—direct compression sucrose, c—direct compression form of dextrose monohydrate (× 500).

log adhesion = log k + n log (concentration of lubricant % w/w) .. .. (2)

then the results (Table 3) show a very good correlation. The positive value for n for tablets lubricated with stearic acid indicates that there is some interaction between it and film while the negative values for n for tablets lubricated with magnesium and calcium stearates indicate that these lubricants interfere with the bond formation between film and the unlubricated substrate.

Further factors must also be considered. The measured adhesion will be dependent on the area over which interaction occurs. Since no surfaces are perfectly smooth, the actual interfacial area in contact between the polymer and substrate will vary according to the surface characteristics (waviness, roughness, and microporosity) of the substrate. In a study involving the adhesion of polyurethanes to metals, Reegen & Ilkka (1962) found a direct correlation between the measured adhesion and the surface roughness as measured using a micro-pickup device. However, only a rank order correlation could be found when tablets were used (Nadkarni & others, 1975) probably due to the fact that, unlike metal surfaces, tablet surfaces are also porous. The differences in the surface characteristics of the tablets prepared from the two grades of lactose (Fig. 2) could well explain the differences in the measured adhesion for these tablets, since those prepared from the anhydrous lactose have a relatively rough surface with many fissures and micropores while those prepared from the spray dried lactose have a much smoother surface with fewer irregularities and fissures. A comparison of the surfaces of the tablets prepared from the other excipients (Fig. 3) shows the wide variation obtained with tablets prepared from microcrystalline cellulose having a relatively smooth undulating surface with few fissures compared to the very rough surface of the tablets prepared from the sucrose. An examination of the surfaces of tablets lubricated with 0·5 and 5% w/w magnesium stearate showed that, although the latter had a marginally smoother appearance overall, both had rough areas.

Interfacial areas of contact will also increase if partial dissolution of the substrate occurs during coating. Stearic acid and, to a lesser extent, hydrogenated castor oil and vegetable stearin are soluble in the dichloromethane-methanol solvent mixture used during the coating process, and an examination of the film after removal from a tablet lubricated with stearic acid showed adhering substrate and subsequent pitting of the tablet surface. No evidence of adhering substrate was seen with tablets lubricated with calcium or magnesium stearate.

The results show the difficulties involved in the prediction of film/substrate adhesion. Contrary to the opinion of Nadkarni & others (1975) the surface characteristics, including roughness and porosity, are important factors in governing the measured adhesion with rougher more irregular surfaces, enhancing the adhesion. However, these changes can, in some cases, be offset by changes in surface polarity. This can be seen in tablets prepared from microcrystalline cellulose which exhibit a high adhesion but have a relatively smooth surface. Since there is no way of quantifying the variations in surface roughness and porosity in terms of their effect on the interfacial area of contact, it is unlikely that the current methods of predicting optimum adhesion from solubility parameters (Engle & Fitzwater, 1962) or surface free energy values (Harder, Zuck & Wood, 1971) will be of any significant value in comparing different substrates. If there is little change in surface roughness the Hofrichter & McLaren equation, as modified here to study changes in lubricant concentration, could well provide useful predictive information, but even in this case an empirical method of measuring the adhesion is needed to provide some initial data.

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