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Variations in the friction coefficients of tablet lubricants and relationship to their physicochemical properties

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Abstract—A previously described modified annular shear cell (MASC) has been used to measure the friction coefficients of some powdered tablet lubricants on a steel surface. Commonly used lubricants, as well as others belonging to the stearate group, differed in their friction coefficients at equivalent sample sizes and in the degree of their ability to reduce friction with increasing amounts when evaluated by the apparatus. In all comparisons, magnesium stearate had the lowest friction coefficient. Divalent salts of stearic acid appeared to be better than the other lubricants tested, and among themselves differed only in the extent of their ability to decrease friction. The lubricants also differed in their physical and chemical properties. On evaluation by stepwise regression analysis, such physical properties as projected surface area of lubricant particles, Martin's diameter and bulk density accounted for most of the variation in friction coefficients of the lubricants rather than moisture content or melting point. It could therefore be suggested that particle size and/or surface area parameters be incorporated in product specifications to ensure reproducible functionality.

Variations in the physical, chemical and lubricative properties of pharmaceutical lubricants have been demonstrated by various test methods (Hanssen et al 1970; Butcher & Jones 1972; Holzer & Sjogren 1981). While some investigators have traced variation in lubricant efficiency to morphology (Miller et al 1983; Butcher & Jones 1972) and surface area (Frattini & Simioni 1984), others were unable to explain similar variations on the basis of measured physical properties such as particle size, bulk density and specific surface area (Hanssen et al 1970). There is, therefore, as yet no unified basic understanding about the relation of physicochemical properties of lubricants to their function. One factor which has impeded progress in the functional evaluation of lubricants has been the lack of an appropriate and reliable test for lubricity. A basis for such an evaluation wherein powder lubricants can be spread over a non-interacting standard substrate and their friction coefficients at the powder/metal interface calculated is provided by the modified annular shear cell (MASC). The development and validation of this analytical tool and the test procedure employed for this purpose have been previously described by Baichwal & Augsburger (1985). The present investigation deals with the use of the shear cell in evaluating the frictional properties of some common lubricants and attempting to relate them to their physicochemical properties.

Materials and methods

The materials examined were magnesium, calcium, zinc, aluminium-mono (USP/NF grade, Mallinckrodt Inc.) and sodium stearates (NF, Witco Chemical Corp.), stearic acid (USP, J. T. Baker Chemical Co.); and a second group which included sodium lauryl sulphate (NF, Ruger Chemical Co., Inc.), glyceryl behenate (Compitrol 888, Gattefosse Corp.) and polyethylene glycol 8000 (PEG 8000, E. I. DuPont DeNemours and Co., Inc.).

Friction coefficients were calculated as the regression slopes of plots of shearing stress against normal load following the procedure described earlier (Baichwal & Augsburger 1985).

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Particle dimensions, length (Martin's diameter) and projected area (A_p) were measured by microscopy using a microcomputer image analysis system (Bioquant II microcomputer system, Apple IIe computer) and their values and those of derived parameters are listed in Table 1.

Bulk and apparent particle densities were measured respectively with a Scot Volumeter (Fisher Scientific Co., Fair Lawn, NJ) and by pyncnometry using decalene as the fluid, melting points on a differential scanning calorimeter (Model DSC-4, Perkin Elmer Corporation, Norwalk, CT) and moisture contents on a Karl Fisher titrimeter (Titrimeter II, Fisher Scientific Co.). The results are included in Table 1.

Results and discussion

The shearing stress versus normal load plots for 10 g samples of some common lubricants are presented in Fig. 1. Generally, these plots were linear ($R^2 > 0.9$). Statistically significant differences (one-way ANOVA, $P < 0.05$) in the values of the slopes of these lines were observed in most cases. Based on this analysis, a rank order of the lubricants in terms of their decreasing friction coefficients (regression slopes) was as follows: magnesium stearate < stearic acid < polyethylene glycol 8000 (PEG) = glyceryl behenate (GB) < sodium lauryl sulphate.

While the regression slopes of shearing stress versus normal load varied for these materials, the y-intercepts were similar and close to the origin. These intercept values were not as reproducible as the regression slopes and hence no physical interpretation could be attached to them. According to the friction model, these

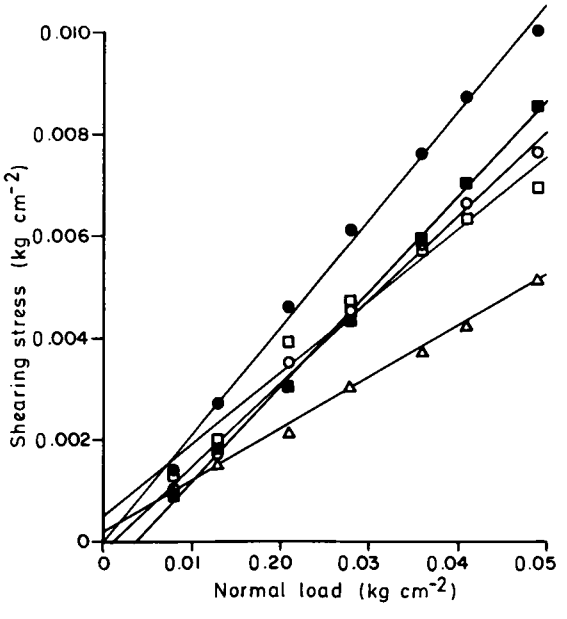

FIG. 1. Shearing stress versus normal load for 10 g samples of common lubricants. Key: ○ Polyethylene glycol. ■ Glyceryl behenate. ● Sodium lauryl sulphate. □ Stearic acid. △ Magnesium stearate.

Table 1. Physical and chemical properties of lubricants.

Material	Friction coeff. (μ) 10 g	15 g	d_a (μm)	Specific surface Areas ($M^2 g^{-1}$) S_{wa} B	S_{wa} T	Densities ρ_B	ρ_T	%MC	mp(°C)	d_M(μm)
Glyceryl Behenate	0·1862	0·2513	11·27	1·212	0·531	0·439	1·003	0·072	68·7	12·9
PEG 8000	0·1632	0·1414	11·09	1·058	0·448	0·511	1·206	0·117	60·5	15·1
Sodium lauryl Sulfate	0·2100	0·2073	21·67	0·513	0·225	0·540	1·229	1·453	188	52·1
Stearic Acid	0·1399	0·1489*	46·93	0·249	0·135	0·514	0·945	0·000	60·0	49·5
Magnesium Stearate	0·0991	0·1154	17·88	1·875	0·314	0·179	1·069	4·985	119	18·8
Calcium Stearate	0·1247	0·1180	11·92	2·190	0·482	0·230	1·044	3·294	162	13·1
Zinc Stearate	0·0997	0·1263	13·08	3·131	0·411	0·147	1·115	0·086	122	12·7
Sodium Stearate	0·1180	—	14·11	0·995	0·405	0·427	1·050	2·328	198	10·2
Aluminium Monostearate	0·2497	0·3121	6·16	3·012	0·915	0·323	1·065	1·090	155	8·7

* Sample size 13 g
d_a = projected area diameter = $(4A_p/\pi)^{1/2}$, where A_p is the projected area.
ρ_B = bulk density of the powder
ρ_T = true density of the solid
S_{wa}.B = a weight-specific surface area (projected) calculated from the volume-specific surface area (projected) and the bulk density of the powder, i.e., S_{va}/ρ_B.
S_{wa}.T = a weight-specific surface area (projected) calculated from the volume-specific surface area (projected) and the true density of the solid, i.e., S_{va}/ρ_T,
%MC = Moisture content
mp = Melting point
d_M = Martin's diameter

intercepts, which represent the shearing stress under zero normal load, should be a measure of the adhesive interaction between the test surface and the metal surface. Possibly such intercepts would have provided a measure of the anti-adherent property of lubricants. A similar analysis made with 15 g samples of these lubricants revealed the expected differences in regression slopes, but their rank order had changed slightly.

Lubricants belonging to the stearate group were also characterized by the lubricity test and the data for 10 g samples are summarized in Table 1. Again, there were statistically significant differences (one way ANOVA, $P < 0{\cdot}05$) in the regression slopes (coefficients of friction) from the shear stress vs normal load plots. Aluminium mono-stearate had the highest friction coefficient (0·2497) followed by stearic acid (0·1399), calcium stearate (0·1247), magnesium stearate (0·0991) and zinc stearate (0·0997). The latter two values did not differ within themselves.

The amount of lubricant used is not only an important consideration in the uniformity of the test, but also reveals differences in the ability of lubricants to cover a given substrate. Hence, these test lubricant samples were evaluated (shearing stress vs normal load plots) at least at three sample sizes. The

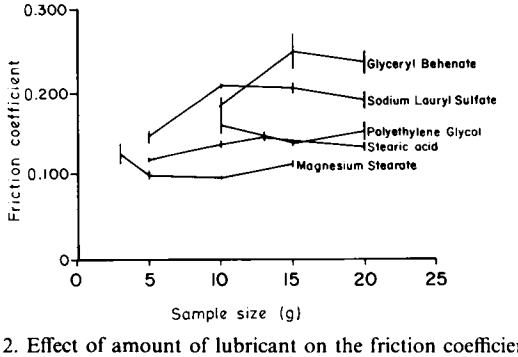

FIG. 2. Effect of amount of lubricant on the friction coefficient of some common lubricants (vertical lines, s.e. bars).

averages of the regression slopes from these experiments (friction coefficients) were plotted against amount of lubricant. Representative plots are shown in Fig. 2.

It has been suggested (Bowden & Tabor 1950) that boundary lubricant molecules consist of a long backbone of carbon atoms with an active polar group. Such molecules readily adsorb on a metal surface to form essentially an oriented monolayer. The best protection is therefore provided by a solid consisting of long chain molecules possessing the following properties: (a) low shear strength to give a low friction coefficient ('true lubricity'), (b) strong lateral attraction between the carbon chains to resist penetration by surface asperities, thus reducing surface damage, amount of wear and providing a thin strong film ('covering potential'), and finally (c) high melting point so that it provides solid-film protection up to high temperatures.

From the graphical representation (for instance, Fig. 2), friction coefficients at equivalent sample sizes can be considered as an indication of 'true lubricity' for differentiating various lubricants. The change in friction coefficient with increasing amount of lubricant can be viewed as an indirect measurement of the 'covering potential' of the lubricant. On the basis of such an evaluation, it can be observed that tablet lubricants vary both in their 'true lubricity' and their 'covering potential'. Divalent salts of stearic acid vary only in their 'covering potential' and are equivalent in terms of friction coefficients on a well lubricated substrate. Glyceryl behenate, on the other hand, exhibits neither good 'true lubricity' nor good 'covering potential'. Of all the lubricants studied, magnesium stearate resembles most closely an ideal lubricant with a low friction coefficient, a large 'covering potential' and a fairly high melting point (cf. Table 1).

Differences in the performance of various lubricants are not surprising since they vary in both their physical and chemical properties, as shown in Table 1. To establish any possible functional relationship between their friction coefficients and the selected physicochemical properties, a stepwise multiple regression analysis model was used (Software Tape No. 0982515044

and desktop calculator/computer model No. 9825T Hewlett-Packard, Palo Alto, CA). Here, the friction coefficients for either 10 or 15 g sample sizes were treated as the dependent (response) variables and the physicochemical properties in Table 1 as the predictor variables (though, strictly speaking, not all are independent variables).

The results with the 10 g lubricant sample size suggested that 98% ($R^2 = 0.982$, Overall $F = 53.54$, degrees of freedom of denominator and numerator = 4, significant 99%) of the variation in friction coefficients could be accounted for by four variables. These variables were: projected surface area for particles, Martin's diameter, bulk density of powder, and projected area diameter.

Similarly, with the 15 g sample size, 80% ($R^2 = 0.800$, overall $F = 10.02$, degrees of freedom of numerator = 2, degrees of freedom of denominator = 5, significant 95%) of the variation in friction coefficients was explained by two variables, namely, projected surface area for particles and Martin's diameter.

Based on the above results it can be generalized that physical properties, particularly the project surface area of particles and Martin's diameter account for most of the variation in friction coefficients of the lubricants rather than the moisture content or melting point. Hence, to ensure reproducible functionality of tablet lubricants it could be suggested that particle size and/or surface area parameters be incorporated in product specifications, and in-house quality control tests be devised on such parameters.

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Cephaloridine resistance in Gram-negative bacteria isolated in Scotland

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Abstract—The incidence of cephaloridine resistance (minimum inhibitory concentration, MIC > 8mg L^{-1}) in isolates from urinary tract infections was 45·1% in Glasgow, 22·6% in Dundee and 25·9% in Edinburgh. The incidence of ampicillin resistance (MIC > 8 mg L^{-1}) was even higher:- being 45·2% in Dundee and 48·5% in Edinburgh. In Glasgow, the incidence was 71·9% which is the highest proportion of ampicillin resistance reported in the United Kingdom. The cephaloridine resistant strains were examined for β-lactamase production. Amongst these strains 50·8% produced only a chromosomal β-lactamase, whereas 47·9% produced β-lactamases which were potentially plasmid-mediated on the basis of biochemical tests. Only 1% of the resistant strains produced no detectable β-lactamase.

The recent increase in the number of available β-lactam antibiotics highlights the clinical importance of antibacterials. In the Royal Infirmary, Edinburgh, prescriptions for β-lactams accounted for 59% of all antibiotic prescriptions in 1986. Newer β-lactam antibiotics have been chemically manipulated to increase β-lactamase stability. However, a high proportion of older, less stable, compounds such as ampicillin or the 'first generation cephalosporins' are still in widespread clinical use for uncomplicated infections.

Several surveys have been conducted outside Scotland which examined the types of β-lactamase produced by ampicillin-resistant populations of Gram-negative enterobacteria (Simpson et al 1980, 1986; Roy et al 1983; Stobberingh et al 1985). However despite the increase in the use of cephalosporins, no surveys have been undertaken to investigate β-lactamase-mediated resistance to this class of compound.

The objectives of this study were to compare the relative incidences of cephalosporin and penicillin resistance, employing cephaloridine and ampicillin as class representatives, and to investigate the distribution of bacterial species and β-lactamase types within the cephaloridine-resistant strains.

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Materials and methods

Bacterial strains. A random population of 549 Gram-negative strains were collected from hospitals in Edinburgh, Dundee and Glasgow from January to April 1984. Only one isolate per patient was included in the study. Most of the strains (441) were isolated from significant urinary tract infections (UTI). From this population of 549, 164 cephaloridine-resistant (minimum inhibitory concentration, MIC > 8mg L^{-1}) strains were obtained.

A further 70 cephaloridine-resistant, Gram-negative strains selected on the same criteria, were collected from the three centres in April 1984. Thus the total number of cephaloridine-resistant strains studied was 234. The bacterial species of each resistant strain was determined by the API 20E biochemical test system (API system, SA38390, Montalieu-Vercieli, France).

Antimicrobial drug sensitivity testing. Sensitivity-testing and MIC determinations of the antimicrobials were determined as previously described (Amyes & Gould 1984). Resistance to a defined antimicrobial agent was described as an MIC of greater than 8 mg L^{-1}.

β-Lactamase preparation and isoelectric focusing. Cell-free extracts containing β-lactamase for isoelectric-focusing (IEF)