Comparative Evaluation of Tablet Lubricants: Effect of Application Method on Tablet Hardness and Ejectability after Compression

YOSHIHISA MATSUDA ˣ, YUHKO MINAMIDA, and SHIN-ICHI HAYASHI *

Abstract □ The effect of four lubricants (stearic acid, magnesium stearate, calcium stearate, and talc) on the ejectability and hardness of statically compressed tablets of a lactose granulation was examined. Two methods of application of these lubricants, incorporation into the granulation and mixing with the granulation, were compared. In both methods, the energy consumption curves during ejection and the hardness curves with lubricant concentration were similar and showed complicated behavior at a lower concentration. The mixing method gave better results for ejectability and hardness than the incorporation method.

Keyphrases □ Tablet lubricants—effect on ejectability and tablet hardness, comparison of mixing and incorporation methods of formulation □ Lubricants, tablet—effect on ejectability and tablet hardness, comparison of mixing and incorporation methods of formulation □ Dosage forms—tablet lubricants, effect on ejectability and tablet hardness, comparison of mixing and incorporation methods of formulation

It is customary to add lubricants as the last step in tablet formulation before compression, because they must be present on the surface of the granules and between them and the parts of the tableting machine. Nevertheless, in some formulas, the lubricants are added before wet granulating (1). One reason for this approach is that the intragranular addition (incorporation into the granulation) of the lubricants guarantees their uniform distribution within the granulation. Consequently, stable physical properties may be expected for the compressed tablets. This approach also has the advantages of eliminating the process of dry blending granulations and lubricants before compression and of preventing subsequent generation of "fines."

However, most reports concerning the addition of a lubricant to a granulation were about extragranular addition (mixing with the granulation) (2–12); little work has been reported on the behavior and effect of the lubricant added into the granulation *via* the binder solution (13).

The purpose of the present investigation was to evaluate the behavior and effect of four widely used lubricants, added by means of the described application methods, from the points of ejection force and tablet hardness, which are dynamic and static factors respectively, relating to compression in tablet formation.

EXPERIMENTAL

Preparation of Granulations and Application of Lubricants—Four kilograms of spray-dried lactose JP, under 100 mesh in size, and 600 g of 13% (w/w) ethanol solution of hydroxypropylcellulose[1] as a binding agent were kneaded thoroughly in a kneading machine[2] and then extruded through a 0.5-mm screen on a rotary-type granulator[3]. The granulations were dried for 30 min at 40° in a fluidized bed-type dryer[4], and the 24–48-mesh fraction was used.

These samples were blended for 20 min in a given mix ratio in a twin-shell-type mixer[5] with each lubricant, stearic acid, magnesium stearate, calcium stearate, and talc JP. The concentrations of the lubricant added were 0.1, 0.2, 0.5, 1.0, 2.0, and 5.0% (w/w) in every test granulation (mixing method).

Each lubricant was added beforehand to the same binder solution in a given concentration and dispersed thoroughly using a homogenizer[6]. In this case, stearic acid clarified the binder solution at a lower concentration due to its solubility in ethanol, while the other lubricants did not dissolve and remained dispersed. These binder solutions were kneaded with lactose in the same manner as in the mixing method and then granulated (incorporation method).

The concentrations of each lubricant contained in each test granulation were the same as in the mixing method. A granulation without any lubricant also was prepared as a control. These samples were stored in tightly stoppered containers until weighed for compression tests. The micromeritic characteristics of the powders are shown in Table I.

Compression of Granulations and Ejection—To control the compression operation closely, an accurate compression/tension testing machine[7], with rates of compression many times slower than those of commercial units, was used. Prior to each compression, the die wall and punches were cleaned with water and acetone and then dried to equalize experimental conditions.

Each 260 ± 0.7 mg of test granulation was filled into a single set of 8-mm flat-faced punches and die and compressed under the compression rate of 25 mm/min. The upper and lower punch forces during compression were detected by load cells and recorded by an electromagnetic oscillograph[8]. The displacement of the upper punch was followed by a differential transformer.

The effect of the lubricants during compression will be reported in a separate paper. According to the described procedures, 980 tablets were compressed in random order to reduce systematic errors. For a single concentration of one lubricant, the compression force ranged from 200 kg (400 kg/cm²) to 2000 kg (4000 kg/cm²); 20 tablets were made at every 100 kg within this range.

After compression, the lower punch was taken down, the die was inverted, and the compressed tablet was ejected downward at the same rate as during compression using the upper punch. The ejection force curve during ejection also was recorded by the electromagnetic oscillograph. The energy consumption for ejection was calculated by integrating the area beneath the force–displacement curve with a planimeter.

The thickness of these compressed tablets was individually measured with a micrometer; it ranged from 4.509 mm for the compression force of 200 kg to 3.631 mm for 2000 kg. The tablets were stored in a desiccator over silica gel until used for hardness tests. To examine the compression state of tablets, porosity (ϵ) was calculated using the apparent volume obtained from the geometric dimensions of the tablets and the particle density of the ingredients given in Table I. The porosity of a tablet composed of more than two ingredients is expressed by (16):

$$\epsilon = 1 - \rho_B \sum \frac{x_i}{\rho_i} \qquad \text{(Eq. 1)}$$

[1] Nisso HPC, Type L, Nihon Soda Co., Niigata, Japan.
[2] Dalton model 5DM, San-ei Manufacturing Co., Tokyo, Japan.
[3] Model RG-5, Kikusui Seisakusho Co., Kyoto, Japan.
[4] Midget dryer model MD-A-200, Fuji Pawdal Co., Osaka, Japan.
[5] Model V-1, Tokuju Kosakusho Co., Tokyo, Japan.
[6] Universal homogenizer (capacity 300 ml, impeller speed 7950 rpm), Nihon Seiki Seisakusho Co., Tokyo, Japan.
[7] Autograph model IS-5000, Shimadzu Co., Kyoto, Japan.
[8] Visigraph model FR-301, San-ei Instrument Co., Tokyo, Japan.

Table I—Micromeritic Characteristics of Sample Powders

Parameter	Lactose	Stearic Acid	Magnesium Stearate	Calcium Stearate	Talc	Hydroxypropylcellulose
Particle density, g/cm^3[a]	1.545	0.998	1.086	1.074	2.703	1.203
Specific surface area, cm^2/g[b]	1.8×10^4	4.0×10^4	6.3×10^4	4.6×10^4	9.2×10^3	—

[a] Measured by Beckmann air comparison pycnometer. [b] This value was calculated from the Kozeny–Carman equation (14) using the air permeability apparatus (15). Each value is the mean of five determinations.

where ρ_B is the bulk density (grams per cubic centimeter) of a compressed tablet, ρ_i is the particle density (grams per cubic centimeter) of the ith ingredient, and x_i is the weight fraction of the ith ingredient.

Tablet Hardness—The diametrical crushing strength of tablets was measured on a hardness tester[9] to the nearest one-fourth of a scale reading. The loading speed was 27.7 kg/min. All measured values fell within the maximum scale reading of this tester.

RESULTS AND DISCUSSION

Ejection Properties—In the compression of a tablet, the lubricant is expected (4) to prevent sticking and binding to the punch faces and die wall and to reduce friction at the tablet–die wall interface during compression and ejection. The latter has usually been considered the true property of a lubricant and has been evaluated in the compression process by the R-value, *etc.* (2, 4, 5, 9, 10, 17–20). When commercial tableting machines were used, a few examples of ejection force curves were presented (2, 3, 21), but these curves did not refer to the relationship between the kind of lubricant used and the shape of the curves or to the energy consumption for ejection.

Accurate ejection force curves can be recorded under a relatively low paper speed (100 mm/min) when the ejection speed is as slow as in the present work. Three ejection force curves recorded for the same kind of test granulation under the same compression conditions are shown in Fig. 1. These curves are close to each other throughout the whole ejection process and show good reproducibility, similar to the results obtained previously (22, 23). Consequently, it was confirmed that energy consumption also could be one useful means for evaluating ejectability besides the maximum ejection force.

As shown in Fig. 2, there appears to be a good linear correlation between the energy consumption and the maximum ejection force under the same condition of the addition of one lubricant over the whole range of ejection force measured. However, as is evident from Fig. 3, even in the same maximum ejection force, the shape of the curves changes with a close relation with lubricity, depending on the kind of lubricant and the application condition. Figure 3 shows representative examples of the ejection force curves, among those obtained from the control and eight kinds of lubricated samples, in which the maximum ejection force fell within the range of 40–50 kg. For every chart, the peak was at around 500 μm (incorporation method) or 250 μm (mixing method) from the starting point of the upper punch. This finding demonstrates that the intimacy of a tablet and die wall is completed within 1 sec and that the maximum ejection force is produced just before it.

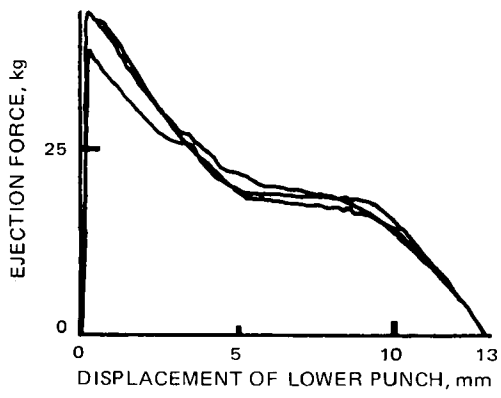

Figure 1—*Reproducibility of ejection force curves [lubricated by 0.2% stearic acid (incorporation method)]. Compression force = 1100 kg.*

In the control, the time lag until the tablet took to the die wall was longer than with the lubricated samples. For stearic acid, magnesium stearate, and calcium stearate, the peaks were sharp with both methods of application; they were rounded and somewhat irregular for the control. After passing the peak, the ejection force tended to decrease rapidly with the moving of the upper punch and then showed a plateau or a second peak inside the outlet for stearic acid, magnesium stearate, and calcium stearate; it decreased monotonously to the outlet for the control and talc.

The outlet of a die cavity is usually tapered due to the manufacturing technique and to prevent capping of the compressed tablets. Table II gives the geometric dimensions of the die cavity used in the present work. The position of a tablet moving in the die cavity, calculated from the paper speed and the position of the second peak on each chart, agreed with that of the diameter of the die wall shown in Table II. This finding suggests that the second peak shows the elastic recovery of a tablet inside the tapered outlet and is closely related to the lubricity of a tablet. Thus, it became clear that, even with the same maximum ejection force, differences in the shape of curves gave the different energy consumption. Therefore, the correct evaluation of ejectability should be made using energy consumption rather than ejection force.

The correlation between the compression force and energy consumption of tablets lubricated with 1% of calcium stearate is shown in Fig. 4 (mixing method). It appears that both parameters are directly and linearly related on the double-log scale over the whole range of compression forces used. The same result was also obtained for this lubricant with the incorporation method. The regression lines and the confidence limits of estimated values at the compression force of 1000 kg are summarized in Fig. 5 and Table III for the incorporation method using magnesium stearate. As shown in Fig. 5, these lines did not intersect. Therefore, the lubricant efficiency may be compared by the value of energy consumption interpolated into the compression force of, for example, 1000 kg.

Changes in energy consumption with the concentration of lubricant addition are shown in Fig. 6. With the incorporation method, the energy consumption (W_I) decreased rapidly at a very low lubricant concentration and then recovered immediately before decreasing again for three of the lubricants but not stearic acid. No minimum

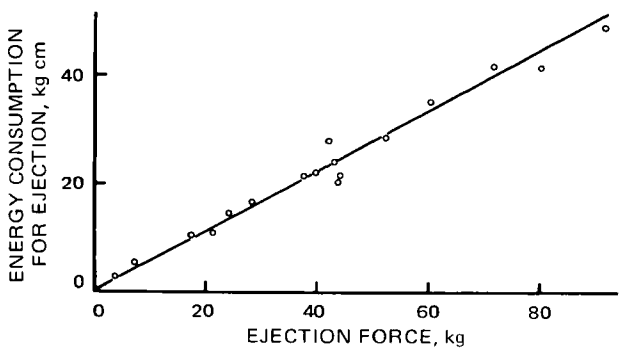

Figure 2—*Relationship between energy consumption for ejection and maximum ejection force [lubricated by 0.5% stearic acid (mixing method)].*

[9] Erweka model TBT/S, Erweka-Apparatebau, Offenbach/Main, West Germany.

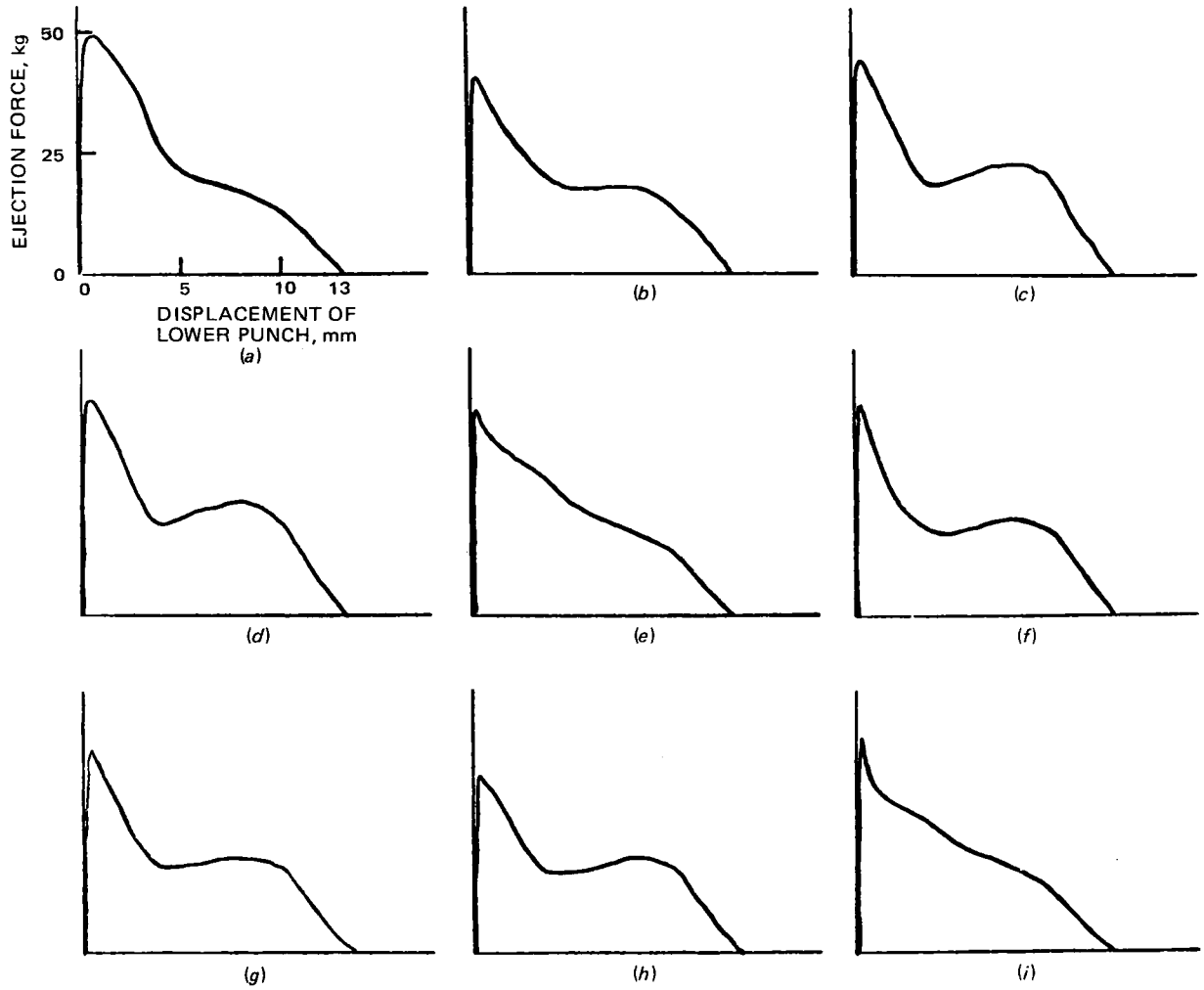

Figure 3—*Representative examples of ejection force curves lubricated by (a) nothing (compression force = 1020 kg), (b) 0.2% stearic acid (960 kg, incorporated), (c) 1% calcium stearate (1440 kg, incorporated), (d) 1% magnesium stearate (1410 kg, incorporated), (e) 1% talc (690 kg, incorporated), (f) 0.5% stearic acid (1140 kg, mixed), (g) 0.2% magnesium stearate (1430 kg, mixed), (h) 0.2% calcium stearate (1940 kg, mixed), and (i) 0.5% talc (410 kg, mixed).*

value was shown for stearic acid at the same region of concentration.

This result was probably due to the difference in the dispersion state of the ethanol-soluble stearic acid and of the ethanol-insoluble other lubricants in the binding agent. There were practically no significant differences in ejectability among stearic acid, magnesium stearate, and calcium stearate. With the mixing method, the energy consumption (W_M) decreased rapidly up to about 0.5% addition without showing either the minimum or the maximum, except for talc, and lubricity was saturated at the higher concentration.

It is, therefore, evident that stearates exhibit sufficient effectiveness at a concentration of less than 1% addition. Both magnesium stearate and calcium stearate exhibited similarly shaped curves over the whole range of addition concentration and showed better ejection properties than stearic acid. Talc showed a complicated behavior of two maxima and minima, and the concentrations of addition giving these values were almost the same for both methods of application. Talc also required far greater energy consumption at any one concentration than the other three lubricants. Moreover, especially for the incorporation method, the effect of addition of talc was hardly recognized, while the lubricity was less than that of the control at a concentration of 0.5%.

Table II—Geometric Dimensions of Die Cavity

Depth from Outlet of Die Cavity, mm	Diameter of Die Cavity, mm
0	8.050
1	8.009
2	8.006
3	8.005
4	8.005
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20	8.005

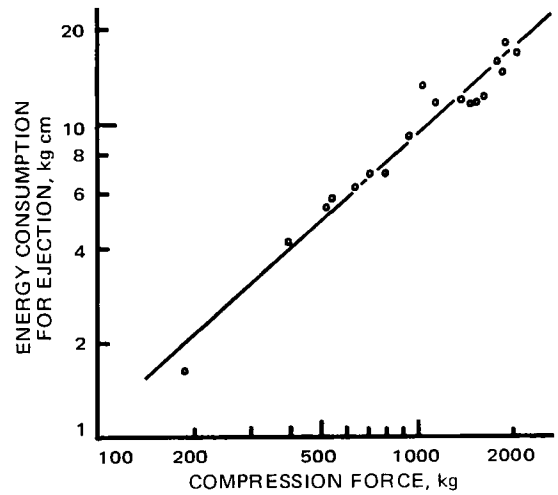

Figure 4—*Relationship between energy consumption and compression force [lubricated by 1% calcium stearate (mixing method)].*

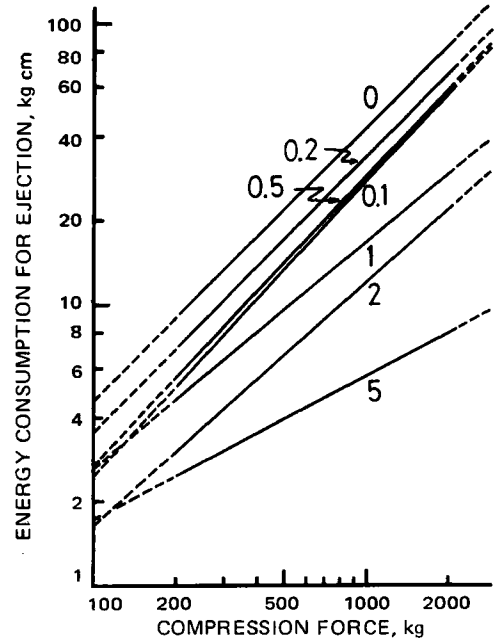

Figure 5—*Regression lines of energy consumption–compression force plots [lubricated by magnesium stearate (incorporation method)]. Numbers on curves are the lubricant concentrations in percent.*

The values of the transmission ratio (the ratio of the upper punch force to the lower punch force at the finished state of compression) interpolated into the compression force of 1000 kg on the transmission ratio–compression force curves (not presented in this paper) are given in Table IV. The tendency of energy consumption shown in Fig. 6 and that of the transmission ratio shown in Table IV are almost in agreement except for talc. This comparison makes the correlation between the lubricant properties during and after compression much clearer (2).

Energy consumption for the incorporation and mixing method is compared in Fig. 7, which indicates that the difference in lubricity according to the application method was most marked for magnesium stearate and calcium stearate; their ratio was about 2.6 times at 0.5% of lubricant present. This concentration agrees with those at which the lubricating effectiveness of magnesium stearate and calcium stearate almost reached the equilibrium state for the mixing method shown in Fig. 6. Above 0.5%, it decreased gradually with increasing

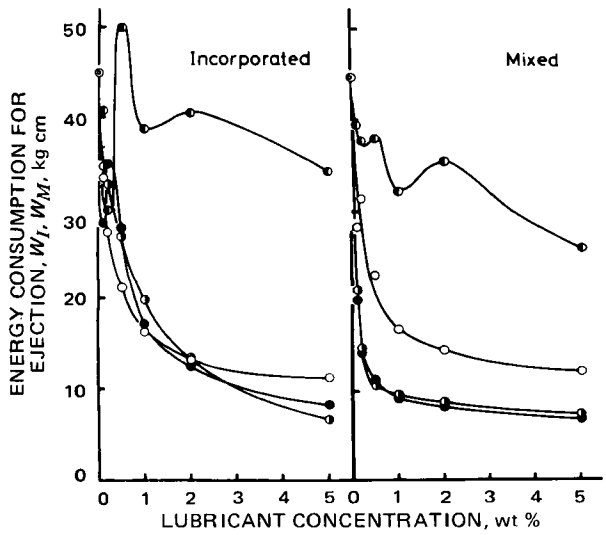

Figure 6—*Regressed energy consumption at compression force of 1000 kg. Key: ◎, control; ○, stearic acid; ●, magnesium stearate; ◑, calcium stearate; and ◐, talc.*

Table III—Estimated Values at the Compression Force of 1000 kg and Their Confidence Limits in Fig. 5

Lubricant Concentration, %	U.C.L., kg cm[a]	$\overline{W}$, kg cm[b]	L.C.L., kg cm[c]
0	54.0	44.6	37.2
0.1	38.6	28.2	21.1
0.2	49.6	34.7	24.1
0.5	35.7	28.7	23.4
1.0	22.0	17.2	14.5
2.0	16.9	12.4	9.1
5.0	13.3	8.3	5.4

[a] Upper confidence limit at 95% probability. [b] The estimated value interpolated in each regression line. [c] Lower confidence limit at 95% probability.

concentration, and no significant difference was obtained at a 5% concentration. On the other hand, the incorporation method gave somewhat better lubricity for stearic acid, but it did not show such a marked effectiveness as the other three. It may be concluded from these facts that the mixing method is better than the incorporation method in regard to ejectability at the common range of lubricant addition.

The lubricants applied in dry powder form (mixing method in the present work) were shown previously (4) to be present on the surface and extragranular regions of compressed tablets and not to mix intimately with the contents of granules. In the incorporation method, they would be captured at a lower concentration in the binding agent, which exists as the coating films in the intragranular region or over the surface of granulation. Consequently, the mobility of lubricant particles in the tablet and their frequency of contact with the die wall during compression would be lower than in the mixing method.

A definite difference in the ejectability of the two methods is likely to be due to the distribution state of the lubricant particles with newly exposed surface existing between the compressed tablet and die wall. From observations of direct compression tablets containing magnesium stearate, stearic acid, or talc, using the scanning electron microscope, it was confirmed that magnesium stearate was spread most completely. Stearic acid also was spread, but talc was not spread in spite of a partial crushing (24). The reason for the complicated phenomena shown in Fig. 6 is, however, unaccountable at present; work is in progress to clarify this point.

Tablet Hardness—The crushing strength of tablets has been reported in connection with compression force (6–8, 18, 19, 25–29). However, it is desirable that the relationship between hardness and porosity rather than that between hardness and compression force is presented to examine the mechanical strength of tablets, because the volume of tablets changes owing to the elastic recovery during the removal of compression.

A typical example of the relationship between the porosity of a

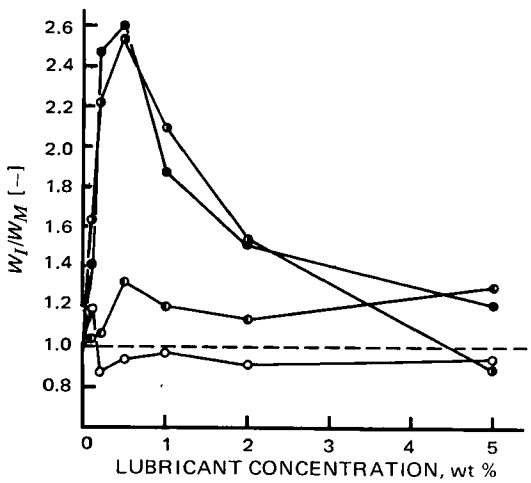

Figure 7—*Comparison of ejectability of two methods of application at compression force of 1000 kg. Key: ○, stearic acid; ●, magnesium stearate; ◑, calcium stearate; and ◐, talc.*

Table IV—Transmission Ratios under Compression Force of 1000 kg[a]

Lubricant Concentration, %	Stearic Acid		Magnesium Stearate		Calcium Stearate		Talc	
	I[b]	M[c]	I	M	I	M	I	M
0	0.678	0.678	0.678	0.678	0.678	0.678	0.678	0.678
0.1	0.685	0.692	0.726	0.750	0.689	0.741	0.687	0.695
0.2	0.710	0.700	0.690	0.801	0.677	0.787	0.687	0.693
0.5	0.736	0.727	0.705	0.860	0.713	0.859	0.685	0.714
1.0	0.778	0.776	0.750	0.883	0.743	0.881	0.706	0.733
2.0	0.802	0.801	0.814	0.904	0.802	0.897	0.709	0.746
5.0	0.846	0.869	0.860	0.916	0.867	0.914	0.741	0.778

[a] Each value was obtained by interpolating on the transmission ratio–compression force curves (not presented in this paper). [b] Incorporation method. [c] Mixing method.

finished tablet and hardness is shown in Fig. 8. The rate of decrease in hardness with increasing porosity was constant in semilogarithmic fashion, in the same manner as reported previously (30). This finding suggests that the following empirical equation by Duckworth (31) can be applied to the crushing of the compact containing such components as in this work:

$$H = H_0 \exp(-k\epsilon) \qquad \text{(Eq. 2)}$$

where H is the tablet hardness, H_0 is an imaginary maximum hardness of a tablet when completely compressed ($\epsilon = 0$), and k is the empirical constant. The values of H_0 and the slope, k, calculated from the regression lines of hardness–porosity data are plotted against the concentration of lubricant addition in Figs. 9 and 10. For a single method of application of one lubricant, these regression lines did not intersect each other within and below the range of porosity measured (ϵ = 0.07–0.20). Therefore, the tendency of H_0 in Figs. 9 and 10 corresponds with that of the hardness measured.

The curves of H_0 and k were similar in shape and closely related. From this fact, it may be said that the harder the tablet, the more dependent the hardness is on the compression state, ϵ, and, therefore, the more structure sensitive is the tablet. The values of k fell within the range of 4–9 calculated by Knudsen (32) for porous materials like ceramics. This finding suggests that the mechanism of crushing of tablets does not differ from those of the above-mentioned compacts. As shown in Fig. 9, hardness decreased once remarkably at a very low concentration of every lubricant and then increased again with an increasing concentration of the addition. The occurrence of such a minimum in hardness values is in qualitative agreement with the behavior of energy consumption (Fig. 6).

In the case of the mixing method, the hardness curves were more complicated than those of the incorporation method; they gave two maxima for stearic acid and calcium stearate. For calcium stearate, an erratic result, showing H_0 = 96.0 kg at a 0.2% concentration, was obtained. This result was not accidental, and its confidence is supported by the fact that the hardness value at a 0.1% concentration did not give such a marked drop off as in the other three cases.

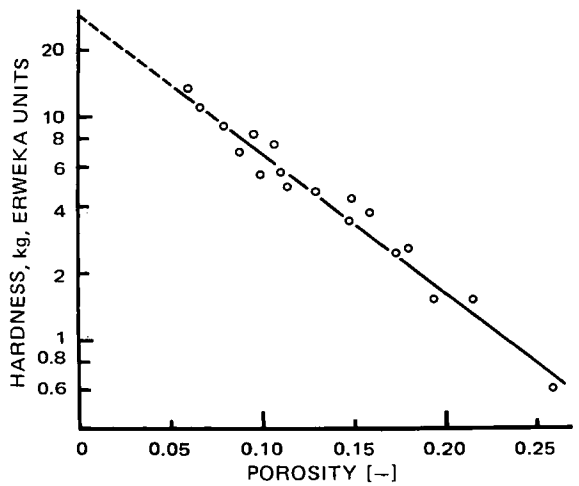

Figure 8—*Semilog plots of hardness and porosity [lubricated by 0.5% talc (incorporation method)].*

Strickland *et al.* (4) explained the effect of the concentration of addition of stearic acid and magnesium stearate as the smoothed curves (dotted lines in Fig. 10) in the hardness tests (Strong-Cobb unit) of sulfathiazole tablets. They stated that the addition of lubricants did not appear to have significant effects at concentrations less than 1%, which were effective for lubricant purposes. The shapes of curves connecting the plots of measured values were similar to the results of Shotton and Lewis (8) and the present work, and the complicated behavior of the addition was increased at lower concentrations.

The relation between good ejectability and a decrease in hardness may be accounted for as follows. For tablets containing magnesium stearate or calcium stearate, the film of lubricant particles over the lactose granulation decreases the area of actual binding and causes elastic recovery along with partial separation of the surface in contact when compression is removed. A more detailed explanation is not obvious at present, and additional information is necessary before any conclusion can be drawn.

The mixing method produced harder tablets than the incorporation method for all of the lubricants. In this respect, it is concluded that the mixing method is better than the incorporation method. However, the incorporation method gave a higher coefficient of correlation in the relationship between hardness and porosity than did the mixing method, and this result fulfilled some of the expectations described earlier.

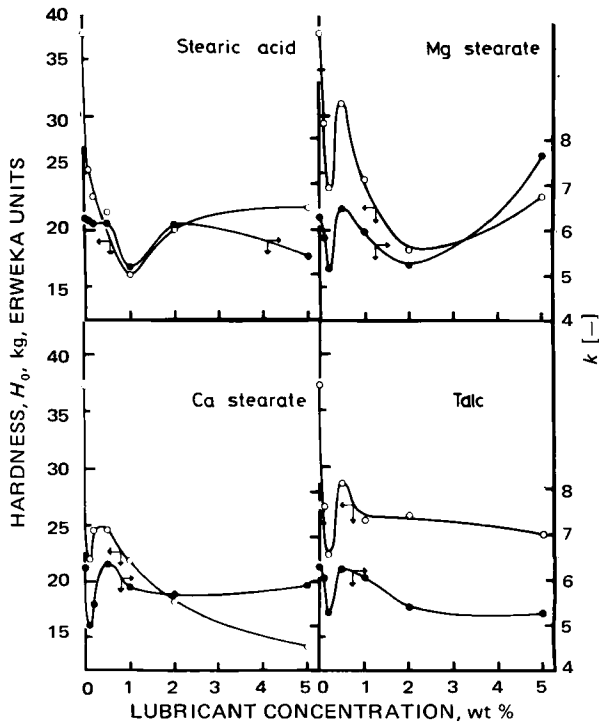

Figure 9—*Effect of lubricant concentrations on hardness (incorporation method). Key: ○, imaginary maximum hardness extrapolated to $\epsilon = 0$ on hardness–porosity plots; and ●, constant, k, in Eq. 2.*

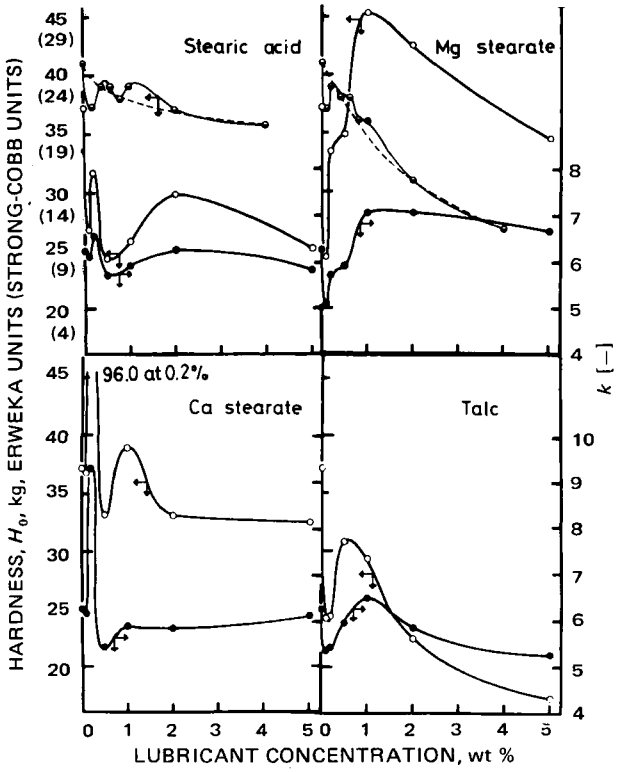

Figure 10—*Effect of lubricant concentrations on hardness (mixing method). Key:* ○, *imaginary maximum hardness extrapolated to* $\epsilon = 0$ *on hardness–porosity plots;* ●, *constant,* k, *in Eq. 2; and* ⊖, *hardness (Strong-Cobb units) measured by Strickland* et al. *(4).*

SUMMARY

The effect of lubricants on the ejectability and crushing strength of tablets of lactose granulation made by static compression was investigated. Formulations were prepared by incorporating such lubricants as stearic acid, magnesium stearate, calcium stearate, or talc into the granulation or by mixing each of them with it.

The ejection force curves of tablets compressed under the same condition showed good reproducibility but had different shapes for different lubricants and methods of application. The ejectability was evaluated by the energy consumption for ejection. In the incorporation method, ejectability was generally improved once at a very low additive concentration of lubricants and became worse again with increasing concentrations; ejectability generally improved progressively in the mixing method. The mixing method was better than the incorporation method for ejectability at any concentration of any lubricant.

Hardness was evaluated by the imaginary maximum value extrapolated to $\epsilon = 0$ on hardness–porosity curves. Hardness curves also decreased markedly at the same concentration as in ejectability, and hardness apparently was closely related to the lubricity of tablets. The mixing method was more useful with regard to hardness than was the incorporation method.

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* Present address: Rohto Pharmaceuticals Co., Osaka, Japan.

ˣ To whom inquiries should be directed.