Chem. Pharm. Bull.
33(7)2924—2931(1985)

Comparison of Lubricant Efficiencies during Compaction of Lactose Powder

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(Received September 3, 1984)

Sodium, calcium, magnesium, zinc and aluminium stearates and behenic, stearic, palmitic, myristic and lauric acids were tested as lubricants during the compaction of lactose powder. Lactose powder, lactose mixtures with lubricants and lubricant powders were compressed in a cylindrical die with flat-surfaced punches. As the upper punch pressure required to compact a given lubricant to a certain porosity increased, the pressure required for the lactose mixture with that lubricant decreased. As regards the pressure–transmission ratio, the higher the value that the lubricant powder showed, the higher the value for the lactose mixture with that lubricant. The Heckel's constants were determined, and a larger k-value (the slope of Heckel's plot at high pressure) for lubricant powder resulted in a smaller value for the mixture. It is suggested that lubricants with higher melting points (metal stearates) provide more effective lubrication on the die wall and between lactose particles than lubricants with lower melting points (fatty acids).

Keywords——tablets; lactose powder; lubricant; metal stearate; fatty acid; compaction

Introduction

In our previous studies[2] on the effect of lubricants during the compaction of pharmaceutical powders, we took magnesium stearate as a lubricant. Comparisons of various lubricants during compaction of powders have been reported by many investigators, for example, Higuchi *et al.*,[3,4] Lewis and Shotton,[5] Maly,[6] Hölzer and Sjögren[7] and Paris *et al.*[8] They evaluated lubricant action by using the ratio of the lower punch force to the upper punch force, ejection force and so on. It is necessary to study lubrication phenomenon during the compaction of pharmaceutical powders from the standpoint of the control of powder bed/die wall friction.[9] It is also desirable to examine mechanically and chemically the mode of action of the lubricants. Such investigations require the systematic use of a number of lubricants over a wide range of content.

The effect of some metal stearates, which have often been used during compaction of metal powders, was investigated in relation to melting temperatures, vaporizing temperatures and viscosities at 250 °C.[10] Using fatty acids as a lubricant, Yarnton and Prosser[11] investigated the compacted density during compaction of copper powder as well as the flow properties at various temperatures. The effects were dependent on chain length. Pilpel *et al.*[12] investigated lactose mixtures with four fatty acids and lactose powder coated with the fatty acids. As the melting points of the fatty acids increased, the tensile strength of the lactose mixtures fell. When the tablets were prepared from powders coated at different temperatures, their compaction behavior was again dependent on the fatty acid chain length.

The present work was undertaken to evaluate the effect of lubricants quantitatively and systematically. The lubricants used were five kinds of metal stearates and five kinds of saturated fatty acids with carbon numbers from twelve to twenty. The pressure–transmission ratio and the density–pressure relationship were taken as measures of the lubricant efficiencies during the compaction of lactose powder.

Experimental

Preparation of Powders——Sample powders were lactose, sodium, calcium, magnesium, zinc and aluminium stearates, and behenic, stearic, palmitic, myristic and lauric acids. Sodium stearate and all of the fatty acids were crushed in a ball mill because sodium stearate was flaky and the fatty acids were granular. The fraction of magnesium stearate under 250 mesh and the fraction of the other lubricants that passed through a 100 mesh sieve were employed. Lactose powder was not sieved. The properties of the powders are listed in Table I. Lactose powder and a lubricant were mixed in a V-type mixer at a rotation speed of 50 rpm for 20 min. The lubricant content was 2.0%. Lactose powder, lactose mixtures and lubricant powders were left for at least a week in the room where temperature and relative humidity were maintained at 25 °C and 60% respectively, and then used.

TABLE I. Properties of Materials

Material	Formula	mp[a] (°C)	Particle density[b] ($g \cdot cm^{-3}$)	Mean diameter[c] (μm)
Lactose	$C_{12}H_{22}O_{11} \cdot H_2O$	212	1.541	29.6
Sodium stearate	$CH_3(CH_2)_{16}COONa$	236	1.100	22.9
Calcium stearate	$[CH_3(CH_2)_{16}COO]_2Ca$	140	1.094	6.9
Magnesium stearate	$[CH_3(CH_2)_{16}COO]_2Mg$	140	1.106	8.0
Zinc stearate	$[CH_3(CH_2)_{16}COO]_2Zn$	121	1.156	7.2
Aluminium stearate	$[CH_3(CH_2)_{16}COO]_3Al$	110	1.051	10.2
Behenic acid	$CH_3(CH_2)_{20}COOH$	74	1.036	20.1
Stearic acid	$CH_3(CH_2)_{16}COOH$	66	1.011	28.7
Palmitic acid	$CH_3(CH_2)_{14}COOH$	60	1.009	27.9
Myristic acid	$CH_3(CH_2)_{12}COOH$	53	1.010	32.2
Lauric acid	$CH_3(CH_2)_{10}COOH$	42	1.019	25.7

a) The temperature at which the material began to melt, determined on a Yanagimoto micro melting point apparatus. *b*) Determined on a Beckman air comparison pycnometer. *c*) Determined by optical microscopy.

Compaction Apparatus and Procedures——The compaction apparatus and procedures were the same as in the previous paper.[2] The powders were compressed from the upper side with flat-surfaced upper and lower punches in a cylindrical die of 20.11 mm diameter. The compression speed was 0.046 mm/s. The powder weights were calculated to give 10.06 and 20.11 mm tablet thicknesses at zero porosity. The upper and lower punch pressures were measured with strain gauges, and the powder bed thickness with a differential transducer. The die and the upper and the lower punches were washed with 1 N potassium hydroxide–(water : ethanol) solution, dried in a current of dry air, and left for more than an hour in the air-conditioned room before use.

Results and Discussion

Pressure–Transmission Ratio

Based on Janssen's theory, the pressure–transmission ratio (the ratio of the lower punch pressure P_L to the upper punch pressure P_U) is given by

$$P_L/P_U = \exp(-4\mu_w K \cdot H/D) \qquad (1)$$

where μ_w is the coefficient of die wall friction, K is the ratio of the horizontal pressure to the normal pressure, H is the powder bed thickness and D is the diameter of the die. In Eq. 1 both μ_w and K are assumed to be constant.

The plots of the pressure–transmission ratio against the tablet thickness for lactose powder and lactose mixtures are shown in Fig. 1. The straight lines in Fig. 1 represent the cases where the products of μ_w and K were 0.05, 0.1, 0.2 and 0.4, respectively. The change of

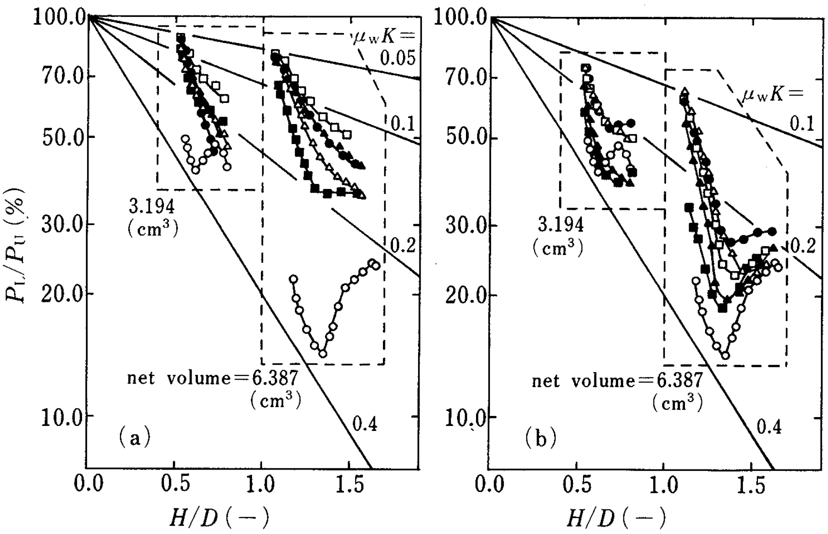

Fig. 1. Changes of Pressure–Transmission Ratio (P_L/P_U) with Thickness of Powder Bed (H)/Diameter of Die (D)

Lubricant content of each lactose mixture was 2.0%. Powder net volumes were 3.194 and 6.387 cm^3, corresponding to 10.06 and 20.11 mm tablet thicknesses at zero porosity, respectively.

(a): ○, lactose; △, lactose mixture with sodium stearate; □, lactose mixture with calcium stearate; ●, lactose mixture with magnesium stearate; ▲, lactose mixture with zinc stearate; ■, lactose mixture with aluminium stearate.

(b): ○, lactose; △, lactose mixture with behenic acid; □, lactose mixture with stearic acid; ●, lactose mixture with palmitic acid; ▲, lactose mixture with myristic acid; ■, lactose mixture with lauric acid.

P_L/P_U for each powder did not give a straight line, but increased linearly as the weight of the powder decreased. For unlubricated lactose powder and lactose mixture with magnesium stearate the changes of the pressure–transmission ratio in Fig. 1 were the same as reported in the previous paper[2]; in the case of lactose powder, P_L/P_U initially increased with a decrease of the thickness, followed by a decrease to a minimum and then a further increase, while in the case of lactose mixture with magnesium stearate P_L/P_U increased monotonously with decrease of the thickness. The plots for the lactose mixtures with the other stearates showed essentially the same profile of P_L/P_U against thickness as in the case of lactose mixture with magnesium stearate. On the other hand, P_L/P_U for lactose mixtures with fatty acids which were weighed to give 20.11 mm thickness at zero porosity showed a minimum, as found for lactose powder.

The pressure–transmission ratios for lactose mixtures with stearates were higher than those for the mixtures with fatty acids. In addition, the plots for the mixtures with stearates lay between the lines corresponding to $\mu_w K$ 0.05 and 0.2. On the other hand, the plots for the mixtures with fatty acids lay between the lines corresponding to $\mu_w K$ 0.1 and 0.4. These results show that the stearates are superior to the fatty acids as lubricants.[3,4]

Density–Pressure Relationship

Figure 2 shows the Heckel's plots[13] for lactose powder, lactose mixtures and lubricant powders, where the tablet thickness at zero porosity is 10.06 mm. In order to describe the compaction behavior of powder, Heckel has proposed the following equation:[13]

$$\ln(1/1-d)=k\cdot P+a \quad (2)$$

where d is the relative density of powder, P is the applied pressure and k and a are constants. As shown in Fig. 2, curved regions appeared in the plots at low pressure. Heckel has shown that the curved region is due to particle rearrangement processes before interparticle bonding becomes appreciable. In this region there was no appreciable difference between the plot for

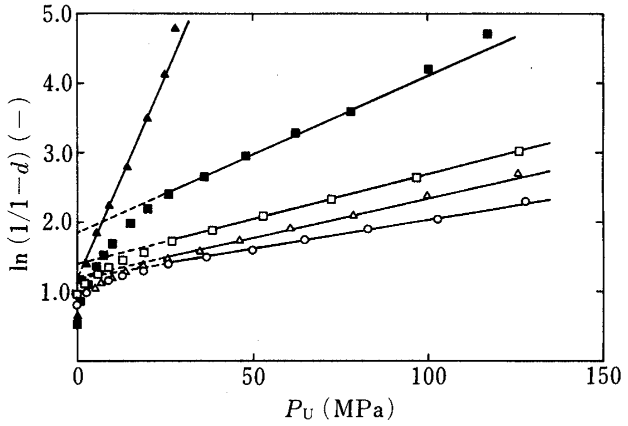

Fig. 2. Heckel's Plot

d is the relative density of powder and P_U is the applied pressure. Powder weight is calculated to give a tablet thickness at zero porosity of 10.06 mm.

○, lactose; ■, magnesium stearate; ▲, stearic acid; □, lactose mixture with magnesium stearate; △, lactose mixture with stearic acid.

Table II. Mean Values of Heckel's Plot Constants k and a

Lubricant concerned	Lactose mixtures			Lubricant powders		
	k (MPa^{-1})	a (−)	Number of data	k (MPa^{-1})	a (−)	Number of data
None	0.0085	1.19	2	—	—	—
Sodium stearate	0.0121	1.32	2	0.0523	1.38	3
Calcium stearate	0.0135	1.38	4	0.0348	1.49	2
Magnesium stearate	0.0143	1.35	4	0.0320	1.71	3
Zinc stearate	0.0133	1.35	3	0.0398	1.46	2
Aluminium stearate	0.0131	1.30	3	0.0314	2.98	2
Behenic acid	0.0108	1.22	2	0.0695	1.98	2
Stearic acid	0.0115	1.20	2	0.1422	1.11	2
Palmitic acid	0.0103	1.23	3	0.1745	1.18	2
Myristic acid	0.0111	1.19	2	0.1532	1.15	2
Lauric acid	0.0097	1.21	2	0.1296	0.85	2

lactose mixture with stearic acid and that for lactose powder. For lactose mixtures, the slope *k*s in the linear region of the plots were slightly larger than that for lactose powder. In addition, the plots for the two lubricant powders were markedly different from those for lactose powder and the mixtures. The plots for the lubricant powders showed a less-curved region at low pressure and larger values of *k* in the linear region as compared with those for lactose powder and the mixtures.

The value of *k* shows a positive correlation with the reciprocal of yield strength of the material particles.[13] Hence, it is assumed that the larger the value of *k* is, the easier it is to deform the material. The values of *k* and *a* for each powder, having a thickness at zero porosity of 10.06 mm, were calculated from the linear region of the Heckel's plot. The mean values of sample powders are listed in Table II. In the case of lactose mixtures, the values of *k* did not show any significant difference among mixtures with stearates or among mixtures with fatty acids, though the *k*-values of mixtures with stearates were larger than those of mixtures with fatty acids. The value of lactose powder was significantly smaller than those of the mixtures. It seems that stearates and fatty acids as lubricants make lactose powder easy to compact and that stearates do so more effectively than fatty acids.

With lubricant powders the fluctuation of the *k*- and *a*-data were large because of loss of fine particles or because of the extrusion of powder from the clearance between the die and the punches. The *k*-values did not show any significant difference among stearate powders or among fatty acid powders. On the other hand, the *k*-values for fatty acid powders were significantly larger than those for stearate powders. This indicates that fatty acids are easier to

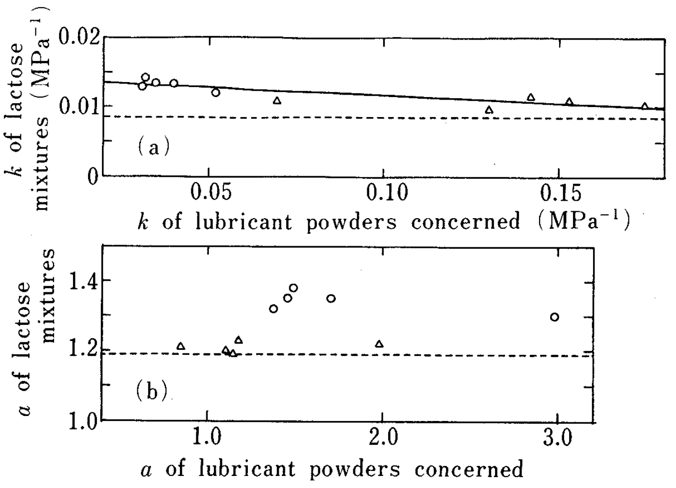

Fig. 3. Relationships of Heckel's Plot Constants for Lubricant Powders and Lactose Mixtures

(a) The slope of Heckel's plot, *k*, of lactose mixtures *vs.* *k* of the lubricant powders concerned.
(b) The intercept of Heckel's plot, *a*, of lactose mixtures *vs.* a of the lubricant powders concerned.
----, lactose; ○, stearates; △, fatty acids.

deform than stearates.

According to Heckel$^{13)}$ the value of *a* must be discussed in relation to the relative apparent density of the powder. However, this could not be measured exactly with our apparatus, so we can say nothing about the value of *a*.

The effects of compaction behavior of lubricant powders on that of lactose mixtures with the lubricants were evaluated. The data in Table II are plotted in Figs. 3(a) and (b) with the *k*- and *a*-values for lactose mixtures as the ordinate and those for the lubricant powders concerned as the abscissa. There was a negative correlation between *k* of lactose mixtures and *k* of the lubricant powders concerned (Fig. 3(a)), whereas in the case of *a* no correlation was recognized (Fig. 3(b)). This negative correlation indicates that a lubricant which is easier to deform shows lower efficiency during compaction of lactose powder at high applied pressures, that is, the range of pressures over which the Heckel's plot is linear. For lactose mixtures, the difference between the maximum value of *k* and the minimum was much smaller than that for lubricant powders. At high applied pressures the compaction behavior of lactose powder seems to be dominant rather than that of the lubricant in the mixture.

Compactability

To discuss the effect of the behavior of lubricants on the compactability of lactose mixtures, we measured the upper punch pressure P_U required to compact the sample to porosity 0.13 and P_L/P_U at the same porosity. The porosity of lactose powder was 0.13 when an upper punch pressure of 100 MPa was applied to the powder. The mean values of sample powders are listed in Table III.

During the compaction of pharmaceutical powders, the powder and the apparatus are exposed to high temperature due to frictional force on the die wall.$^{12)}$ This suggests that it is important to examine the behavior of lubricants at high temperature. The melting points of fatty acids varied with their chain length. Metal stearates showed much higher melting points than stearic acid (as shown in Table I). In Figs. 4(a) and (b) the above parameters are plotted as a function of the melting points of the lubricant powders concerned. In the case of lactose mixtures with fatty acids, as the melting point increased, the P_U required was smaller and the

TABLE III. Upper Punch Pressure Required to Achieve a Porosity of 0.13, P_U, and Pressure–Transmission Ratio at Porosity 0.13, P_L/P_U

Lubricant concerned	Lactose mixtures		Lubricant powders	
	P_U (MPa)	P_L/P_U (%)	P_U (MPa)	P_L/P_U (%)
None	100.0	45.4	—	—
Sodium stearate	59.1	71.7	13.5	76.9
Calcium stearate	49.0	78.1	17.0	71.9
Magnesium stearate	48.6	76.7	15.0	73.4
Zinc stearate	51.7	75.3	16.2	81.5
Aluminium stearate	56.2	66.8	11.9	76.5
Behenic acid	76.0	63.8	7.9	70.9
Stearic acid	73.7	64.4	6.7	61.3
Palmitic acid	78.9	64.5	5.1	65.7
Myristic acid	76.6	54.8	6.0	54.2
Lauric acid	85.9	49.9	10.1	57.2

Powder weight was calculated to give a tablet thickness at zero porosity of 10.06 mm.

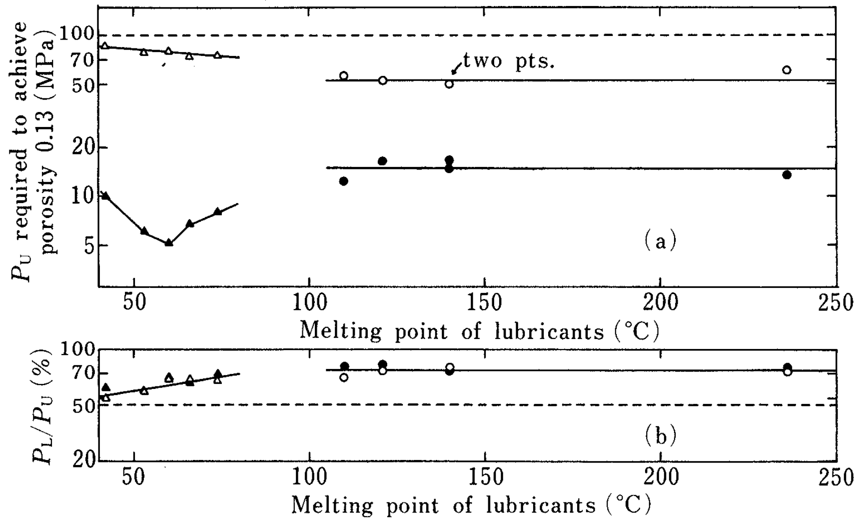

Fig. 4. Effect of the Melting Point of Lubricant on the Compaction Behavior of the Lactose Mixture

(a) Logarithm of applied pressure (P_U) required to achieve a porosity of 0.13 *vs.* melting point of the lubricants concerned.
(b) Logarithm of pressure–transmission ratio (P_L/P_U) at a porosity of 0.13 *vs.* melting point of the lubricants concerned.
----, lactose; ●, stearates; ▲, fatty acids; ○, lactose mixtures with stearates; △, lactose mixtures with fatty acids.

P_L/P_U larger. In the case of lactose mixtures with stearates, little difference in the P_Us required or in the P_L/P_U values was recognized. The reason for this may be that the melting points of stearates are all markedly high compared to the room temperature of 25 °C. The mixtures with stearates showed lower P_Us required and higher P_L/P_U values than the mixtures with fatty acids. A higher melting point lubricant more effectively improved the compactability of lactose powder. This agrees with the trend of Heckel's constants. Thus a softer lubricant, which has a higher *k*-value and lower melting point, shows less efficiency during the compaction of lactose powder. The plots for lubricant powders showed that stearates had higher P_Us required and higher P_L/P_U values than fatty acids (Figs. 4(a) and (b)).

The P_Us required to achieve porosity 0.13 were 5—17 MPa for lubricant powders, while

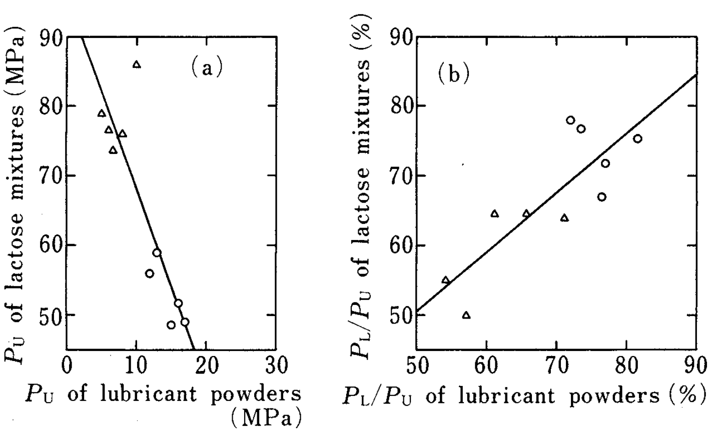

Fig. 5. Effect of the Compaction Behavior of Lubricant Powder on That of the Lactose Mixture

(a) Applied pressure (P_U) required to achieve a porosity of 0.13 of lactose mixtures *vs.* that of the lubricant powders concerned.
(b) Pressure–transmission ratio (P_L/P_U) at a porosity of 0.13 of lactose mixtures *vs.* that of the lubricant powders concerned.
○, stearates; △, fatty acids.

they were 49—86 MPa for lactose mixtures (Table III). Apparently there is a remarkable difference in compaction behavior between lactose powder, which is the chief ingredient of lactose mixtures, and lubricant powders. The fact that with lactose mixtures a porosity of 0.13 was achieved at lower P_Us than P_U with lactose powder (100 MPa) indicates an improvement in the compactability of lactose powder by lubricant powders. It is shown in Fig. 5(a) that the P_Us required for lactose mixtures correlate negatively with those for the lubricant powders concerned. It may be concluded that the addition of lubricant powder does improve the compactability of lactose powder, but that the high compactability of lubricant powder does not contribute to this effect.

On the other hand, it was demonstrated in the previous paper[14)] that when lubricant powder was admixed with sample powder, the decrease in the coefficient of die wall friction was greater than the decrease in the coefficient of internal friction during powder compaction in a die, and that the increase in P_L/P_U was chiefly due to the remarkable decrease in the coefficient of die wall friction. In this study the P_L/P_U values at porosity 0.13 for lactose mixtures were higher than that for lactose powder, 45.4% (Table III). Further, the P_L/P_U values for lubricant powders were 54—82%, while those for lactose mixtures were 50—78% (Table III). There is little difference between these values. Moreover, the P_L/P_U values for lactose mixtures increased with those for the lubricant powders, as shown in Fig. 5(b). Hence, it is suggested that the lubricant particles in lactose mixtures could behave on the die wall in the same way as they do in the lubricant powder and thus decrease the die wall friction.

Conclusions

During compaction of lactose powder the addition of stearates and fatty acids was found to have the following effects.

(1) The lactose mixtures with all the stearate salts used as lubricants in this study showed essentially the same changes of the pressure–transmission ratio with bed thickness as the mixture with magnesium stearate.

(2) The lactose mixtures with the stearates showed higher pressure–transmission ratios than the mixtures with the fatty acids.

(3) When a lubricant powder showed a smaller *k*-value (the slope of Heckel's plot at

high pressure), the lactose mixture with that lubricant showed a larger k.

(4) A lubricant powder which required higher applied pressure to achieve a certain porosity more effectively lowered the pressure required for the lactose mixture.

(5) The higher the pressure–transmission ratio at a certain porosity of lubricant powder, the higher the ratio for the lactose mixture with that lubricant.

References and Notes

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