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ADHESION OF TABLETS IN A ROTARY TABLET PRESS II. EFFECTS OF BLENDING TIME, RUNNING TIME, AND LUBRICANT CONCENTRATION

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ABSTRACT

Of the three essential functions of tablet lubricants, only the true lubricant and glidant properties have been studied in detail by objective means. Only recently has instrumentation which permits the objective measurement of the antiadhesion activity in a rotary tablet press been developed. Using a rotary press instrumented to measure the adhesion of tablets to the lower punch face, this study focuses on the adhesion of tablets in two direct compression systems. At any given compression force, adhesion of microcrystalline cellulose tablets lubricated with magnesium stearate appeared to decrease with increases in blending time or intensity of blending. Over a three-hour running time, adhesion force was found to increase to peak values and then to decline with both microcrystalline cellulose and hydrous lactose lubricated with magnesium stearate. However, ejection forces decreased gradually to apparently limiting values in each case. The adhesion of tablets to the lower punch face appeared to be affected partly by the condition of the tablet - die wall interface. Studies comparing lubricated and unlubricated microcrystalline cellulose suggest two opposing effects on tablet adhesion: (1) enhancing adhesion due to an increased reaction at the lower punch resulting from reduced die wall friction; and, (2) reducing the adhesion of tablets via the "anti-adherent" effect. At the lubricant levels studied, stearic acid generally appeared to be less efficient than magnesium stearate in reducing both the adhesion and ejection forces in microcrystalline cellulose blends. However, with hydrous lactose blends, the true lubricant and antiadherent activities of stearic acid appeared to be greater than those of magnesium stearate at the 1.00% level of addition.

INTRODUCTION

The tablet lubricant is one of the most essential excipient components in tablet formulation. Three fundamental functions of lubricants in tableting have been recognized: (1) reducing friction at the tablet - die wall interface (true lubricant activity), (2) facilitating the flow of powders or granulations (glidant activity), and (3) preventing the adherence of powders to the punches and die (antiadherent activity). A vast number of studies focusing on the true lubricant and glidant activities of lubricants have been published. However, only recently has the instrumentation become available to measure the anti-adhesion activity of lubricant.

The details of the instrumentation for measuring tablet adhesion in a rotary press have been previously described (1). In this instrumentation, the adhesion of tablets to the lower punch face is measured by means of a strain gauged cantilever beam affixed to the feed frame in front of the sweep-off blade. Tablets are detached from the lower punch by striking the instrumented beam. The adhesion force is the total sweep-off force measured by the beam less that due to the momentum of the tablet. The effect of compression force, tablet dimensions, magnesium stearate concentration and grade of magnesium stearate on the adhesion force of tablets was investigated (1). Generally, increasing compression force, or decreasing magnesium stearate concentration caused increasing adhesion in compressible sugar, microcrystalline cellulose and hydrous lactose direct compression fillers. With microcrystalline cellulose lubricated with 0.10% magnesium stearate, adhesion forces decreased with increased tablet thickness at constant compression force. Increases in tablet diameter at constant thickness and compression pressure resulted in increased adhesion forces. Different grades of magnesium stearate were found to possess different degrees of antiadhesive activity, whereas their differences in true lubricant activity (based on the ejection forces) were almost indistinguishable.

The present study is intended to further explore tablet adhesion in direct compression systems. True lubricant efficiency has been shown to improve with prolonged blending time; therefore, one objective of this study was to determine whether antiadhesion activity is similarly affected. Since actual tableting in the industry generally involves continuous operation of the tablet press, it was of interest to determine the effect of prolonged tableting on the adhesion and ejection forces. It was also the intent of this study to evaluate and compare the antiadhesion oroperties of stearic acid and magnesium stearate in two representative direct compression tablet fillers.

EXPERIMENTAL

All tableting was performed on a Stokes RB-2 rotary tablet press (Stokes Engineering, Philadelphia, PA.) which had been instrumented to monitor compression, ejection and adhesion forces (1,2). The direct compression fillers used were microcrystalline cellulose, N.F.[1], and hydrous lactose, U.S.P.[2] The lubricants used were magnesium stearate U.S.P.[3] and stearic acid U.S.P.[4]

Preparation of Tablets

All lubricants were screened through an 80 mesh sieve prior to blending. Aside from the running time experiment, the batches were of 400 g. and 500 g. for microcrystalline cellulose blends and hydrous lactose blends, respectively. Except as noted, all powders, were blended in a 1.89 L twin shell blender (Liquid-Solids Blender, P-K # LB-3794, Patterson-Kelly Co., East Stroudsburg, PA.) for 15 minutes without use of an intensifier bar.

Only a single station was used to avoid errors due to slight differences in tooling length. The same set of flat-faced 1.111 cm. diameter punches and die was used in all studies to avoid possible errors

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1. Avicel[R] 102, FMC Corporation, American Viscose Division, Newark, DE 19711
2. Fast Flo[R], Foremost Dairies, Inc., San Francisco, CA 94104
3. Amend Drug and Chemical Company, Irvington, NJ 07111
4. J.T. Baker Chemical Company, Phillipsburg, NJ 08865

in adhesion measurements due to differences in the state of polish of the punch face. Press speed was held at 24 RPM in all studies as this is the speed at which the adhesion instrumentation was calibrated (1). All experiments were performed in a controlled humidity area (50 ± 10% relative humidity) where the temperature was maintained at 25° ± 2° Celsius. In all experiments, tablet thickness was kept constant since previous work had shown adhesion force to vary with thickness at a given compression force (1). Except in the running time experiments, thickness was held constant at 0.290 ± 0.003 cm. regardless of the compression force through the simultaneous adjustment of die-fill and compression settings.

During the experiment, approximately 10 tablets were compressed at each compression force before the ejection force and adhesion force readings were taken. Unless otherwise specified, adhesion and ejection forces were determined at at least five compression forces. Before beginning and after each experiment the punches and die were cleaned with soap water, rinsed with hot water, and dried with tissue paper soaked with acetone. After the tablets made had aged for 24 hours, tablet hardness was determined on a Schleuniger (Heberlein) Hardness Tester (Model 2E/106, Series 7203, Key Industries, Farmingdale, N.Y.). Except as noted, the values reported represent the means of 20 readings for both ejection forces and adhesion forces, and 10 readings for hardnesses.

Effect of Blending Time

Since true lubricant efficiency has been shown to improve with prolonged blending (3,4), it was of interest to determine whether antiadhesion activity would be similarly affected. Microcrystalline cellulose was blended with 0.10% magnesium stearate under four conditions: 5 minutes, 10 minutes, and 15 minutes all with intensifier bar off; 10 minutes with intensifier bar off plus two minutes with the intensifier bar on.

Effect of Running Time

This study was intended to determine what effect prolonged tableting would have on the adhesion and ejection forces of two direct compression fillers. Microcrystalline cellulose and hydrous lactose were lubricated with 0.10% and 0.50% magnesium stearate respectively. The batch size was 1.8 kg. in both cases. In this study, blending was carried out in the larger 7.56 L twin shell blender (Liquid-Solids Blender, P.K. # LB-5695, Patterson-Kelly Co., East Stroudsburg, PA.). The compression forces were 71 kg. for microcrystalline cellulose blend, and 472 kg. for lactose blend. These compression forces produced tablet hardnesses of 7 ± 1 kg. for both blends. The die fill was set to give the tablet weight of about

300 mg. for microcrystalline cellulose and 400 mg. for lactose. The selected weight and compression force settings were not changed throughout the runs. The time when the target weight and compression force were achieved was taken as time zero. Adhesion and ejection forces were recorded for about two minutes at each of at least six times during the three hour runs.

Effect of Lubricants

I. Effect of Stearic Acid and Magnesium Stearate Concentrations on the Adhesion and Ejection Forces of Microcrystalline Cellulose Tablets

Stearic acid and magnesium stearate were chosen as representative lubricants in this study because of their widespread use in tableting. The use of microcrystalline cellulose uniquely allows tableting without lubricant, thereby providing an unlubricated control for comparison. Four concentrations of stearic acid (0.10%, 0.25%, 0.50% and 1.00%) and five concentrations of magnesium stearate (0.05%, 0.10%, 0.25%, 0.50%, and 1.00%) were evaluated and compared with runs containing no lubricant. As previously noted, tablet thickness was kept constant and runs were made at five compression forces.

II. Effect of Prelubricated Die and Unlubricated Die on the Adhesion and Ejection Forces of Plain Microcrystalline Cellulose Tablets

This experiment was designed to compare the adhesion and ejection forces developed during the compression of unlubricated microcrystalline cellulose first in an unlubricated die and then in the same die after lubricating the die wall with stearic acid.

Due to the unavailability of the same lot of microcrystalline cellulose used in all other experiments, another lot of the same material was used in this experiment. The plain filler was compressed first in the unlubricated die. When a sufficient number of adhesion and ejection force readings had been obtained, the tablet press was stopped. The die was then removed, cleaned with hot water and dried with tissue paper soaked with acetone. A two percent solution of stearic acid in acetone was applied on the die wall until the surface was completely coated with a film of stearic acid. No lubricant was applied to the punch faces. The die was carefully placed back into position in the die table, and the tablet press started. When the target thickness and compression force had been obtained, the adhesion and ejection readings were taken until the stearic acid film started to wear off as indicated by a progressive increase in the ejection force readings. The tablet press was then stopped and the die removed and cleaned in the manner described. The plain filler was again compressed first in the unlubricated die and later in the prelubricated die, at each of the next four compression forces. The results reported represent means of 15 determinations.

III. Effect of Stearic Acid and Magnesium Stearate Concentrations on the Adhesion and Ejection Forces of Hydrous Lactose Tablets

Four concentrations of magnesium stearate (0.25%, 0.50%, 1.00%, and 1.50%) and stearic acid (0.25%, 0.50%, 1.00%, and 2.00%) were each evaluated and compared. In the same manner as the microcrystalline cellulose study, tablet thickness was held at the same constant value for either lubricant. Runs were made at six compression forces. Since this filler cannot be tableted without a lubricant, no unlubricated controls were possible.

RESULTS AND DISCUSSION

Effect of Blending Time

The effects of blending time on the adhesion force and the unit ejection force (ejection force per unit apparent area of tablet - die wall contact (2)) of microcrystalline cellulose tablets containing 0.10% magnesium stearate are summarized in Figures 1 and 2, respectively.

In all cases, increases in compression force resulted in increasing adhesion force. These results confirm previously reported findings (1). However, at any given compression force, adhesion force tended to decrease with increasing blending time or intensity of agitation. The apparent order of

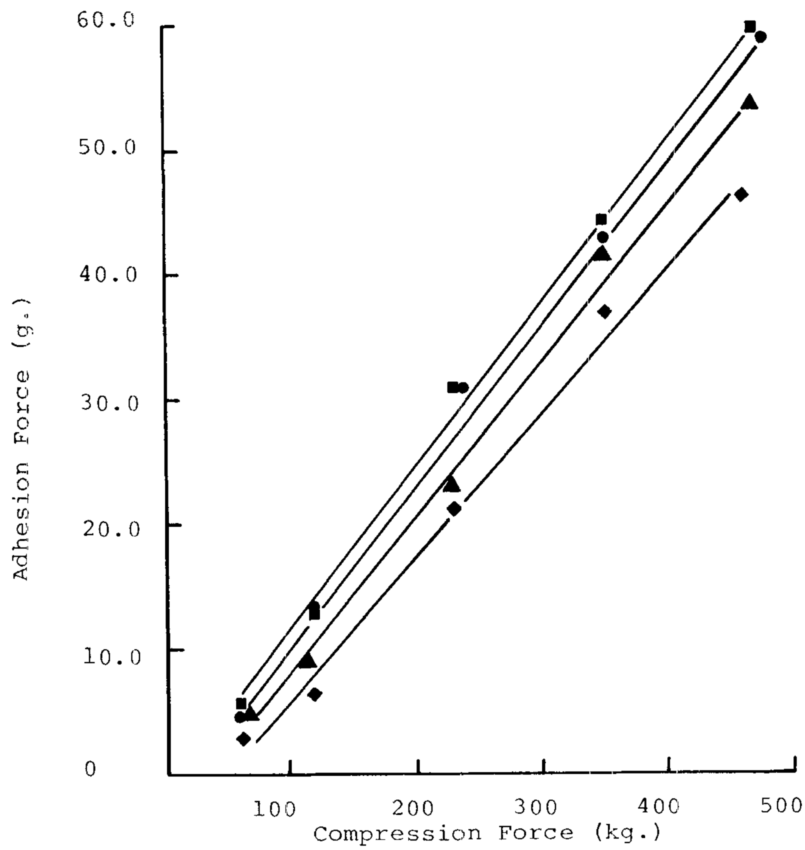

FIGURE 1
Effect of Blending Time or Intensity of Blending on the Adhesion Force of Microcrystalline Cellulose Tablets Containing 0.10% Magnesium Stearate. ■ 5 minutes; ● 10 minutes; ▲ 15 minutes; ◆ 10 minutes plus 2 minutes with intensifier bar on.

decreasing adhesion forces with blending time was: 5 minutes > 10 minutes > 15 minutes > 10 minutes plus 2 minutes with intensifier bar on. This effect is no doubt due to a greater surface coverage of the filler with lubricant at longer blending time (3,5), thus

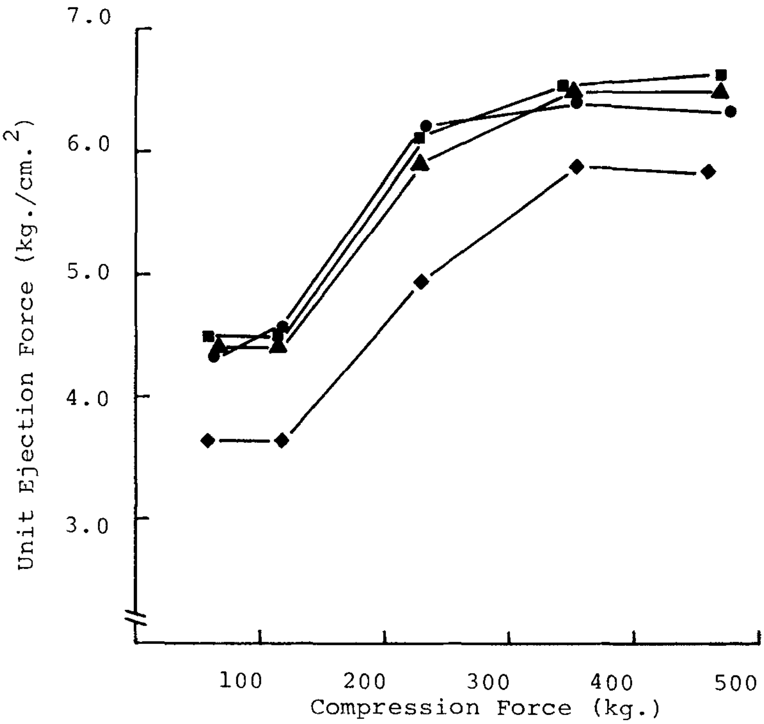

FIGURE 2
Effect of Blending Time or Intensity of Blending on the Unit Ejection Force of Microcrystalline Cellulose Tablets Containing 0.10% Magnesium Stearate. ■ 5 minutes; ● 10 minutes; ▲ 15 minutes; ● 10 minutes plus 2 minutes with intensifier bar on.

reducing the adhesion to the punch face. The unit ejection force - compression force profiles (Figure 2) were comparable at 5, 10 or 15 minutes blending times and all showed higher ejection forces than that obtained after blending 10 minutes plus 2 minutes with the intensifier bar on. This trend, i.e. the decreased ejection force with intensity of blending also confirms previously reported findings (3,5).

The effect of blending time on the compressibility of microcrystalline cellulose is shown in Figure 3. Tablet hardness generally decreased with blending time or intensity of blending. Decreasing compressibility with increased blending time or agitation in blending previously has been observed with other tableting materials, for instance, spray-dried lactose

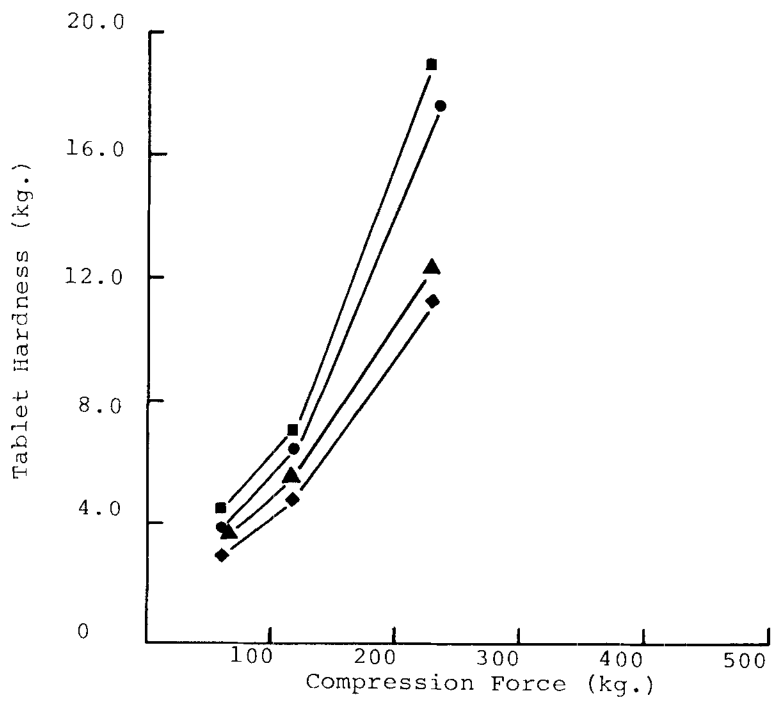

FIGURE 3
Effect of Blending Time or Intensity of Blending on the Unit Ejection Force of Microcrystalline Cellulose Tablets Containing 0.10% Magnesium Stearate. ■ 5 minutes; ● 10 minutes; ▲ 15 minutes; ◆ 10 minutes plus 2 minutes with intensifier bar on.

lubricated with 1% magnesium stearate (3), compressible starch lubricated with 0.1% magnesium stearate (6), and compressible sugar lubricated with 0.75% magnesium stearate (7).

Blending was standardized at 15 minutes (without use of intensifier bar) in all subsequent studies.

Effect of Running Time

The results of the running time experiment are summarized in Figures 4 and 5. As can be seen, adhesion forces generally increased with running time. In the case of microcrystalline cellulose (Figure 4), adhesion force seemed to increase gradually, reaching a maximum of about an 18% increase at 2.5 hours. A very slight decrease was observed at 3 hours; however, the adhesion force was still greater at 3 hours than the initial value. The unit ejection force was found to decrease to an apparently limiting value with running time.

With hydrous lactose (Figure 5), adhesion force also increased with running time, reaching a maximum of about a 39% increase after half an hour. This was followed by a progressive decrease to approximately the initial value after 2 hours of running. As with microcrystalline cellulose, the unit ejection force of the lactose tablets decreased with running time to an apparently limiting value. In no case was there any evidence of filming or picking in these runs.

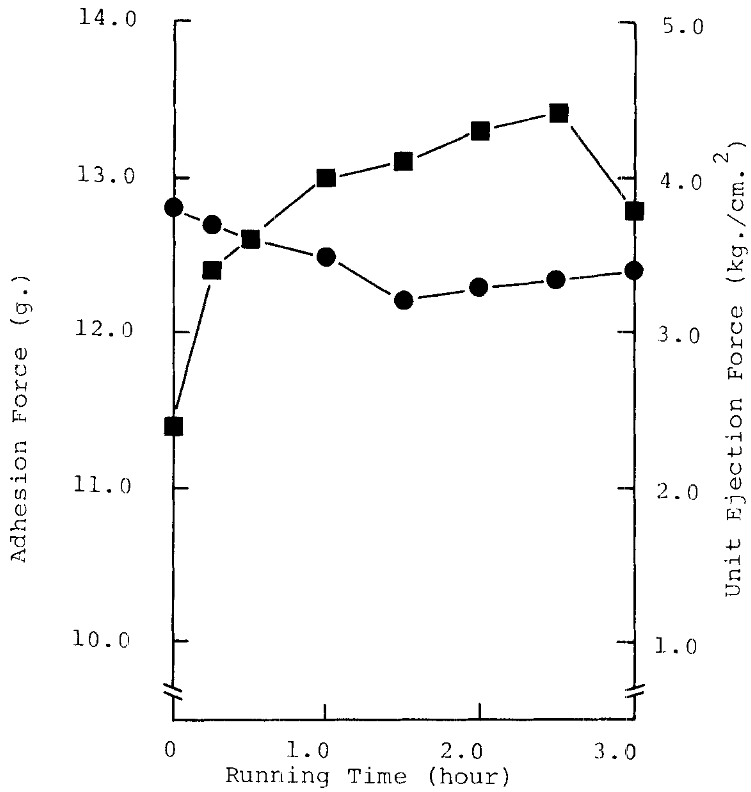

FIGURE 4
Effect of Running Time on the Adhesion and Unit Ejection Forces of Microcrystalline Cellulose Tablets Containing 0.10% Magnesium Stearate Compressed at 71 kg. Compression Force. ■ Adhesion Force; ● Unit Ejection Force.

These results suggest a gradual conditioning of the tooling with prolonged tableting. It may be significant that both fillers exhibited an initial pattern in which adhesion force increased while ejection force decreased. The reduction in ejection

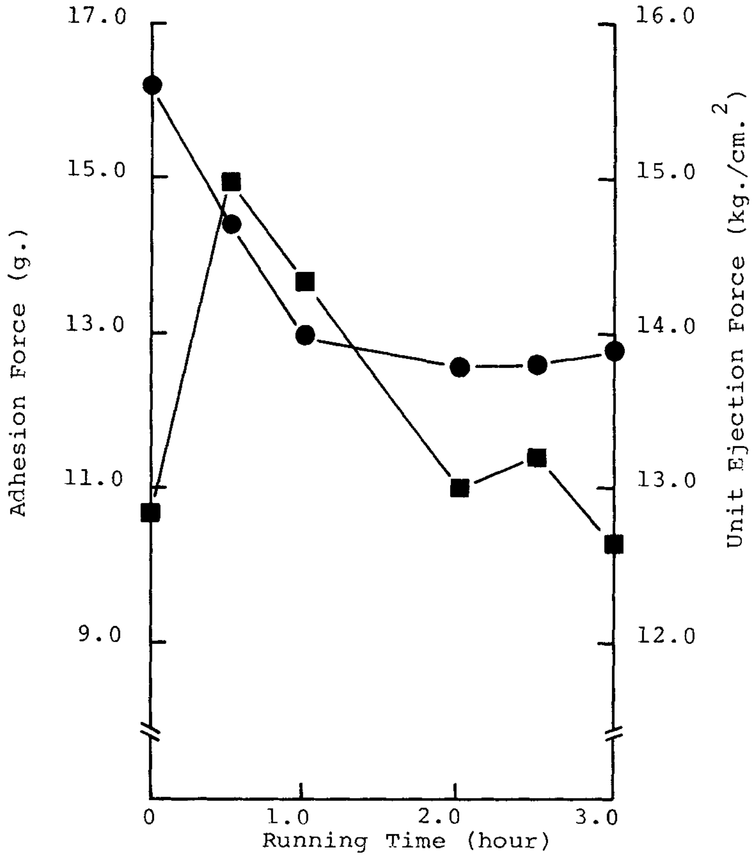

FIGURE 5
Effect of Running Time on the Adhesion and Unit Ejection Forces of Compressible Hydrous Lactose Tablets Containing 0.50% Magnesium Stearate Compressed at 472 kg. Compression Force. ■ Adhesion Force; ● Unit Ejection Force.

force with running time suggests a gradually improving force transmission through the compact due to reduced die wall friction. This, in turn, would be expected to result in increasing adhesion due to an increasing reaction at the tablet-lower punch interface.

Although this study was carried out at a relatively slow speed of 24 revolutions per minute, ejection forces did appear to reach a limiting value in each case during the three hour run. At least in the case of hydrous lactose, the adhesion force declined markedly from its maximum value, possibly indicating a conditioning effect at the punch face. It is likely that the effect of running time on ejection and adhesion forces will depend on the nature of the formulation and on such factors as compression force, machine speed, any segregration of components and/or particle size with time, and the state of polish of the tooling.

Although adhesion and ejection forces did appear to vary with extended running times, relatively constant readings at any compression force set were observed during the initial period of the run, which was usually within five minutes after the target tablet thickness and compression force were achieved. It was during this period, in which apparently constant readings were observed, that the adhesion and ejection readings were taken in all other experiments.

Effect of Lubricants

Although previously reported preliminary studies (1) had shown antiadhesion efficiency to increase with lubricant concentration, this study was

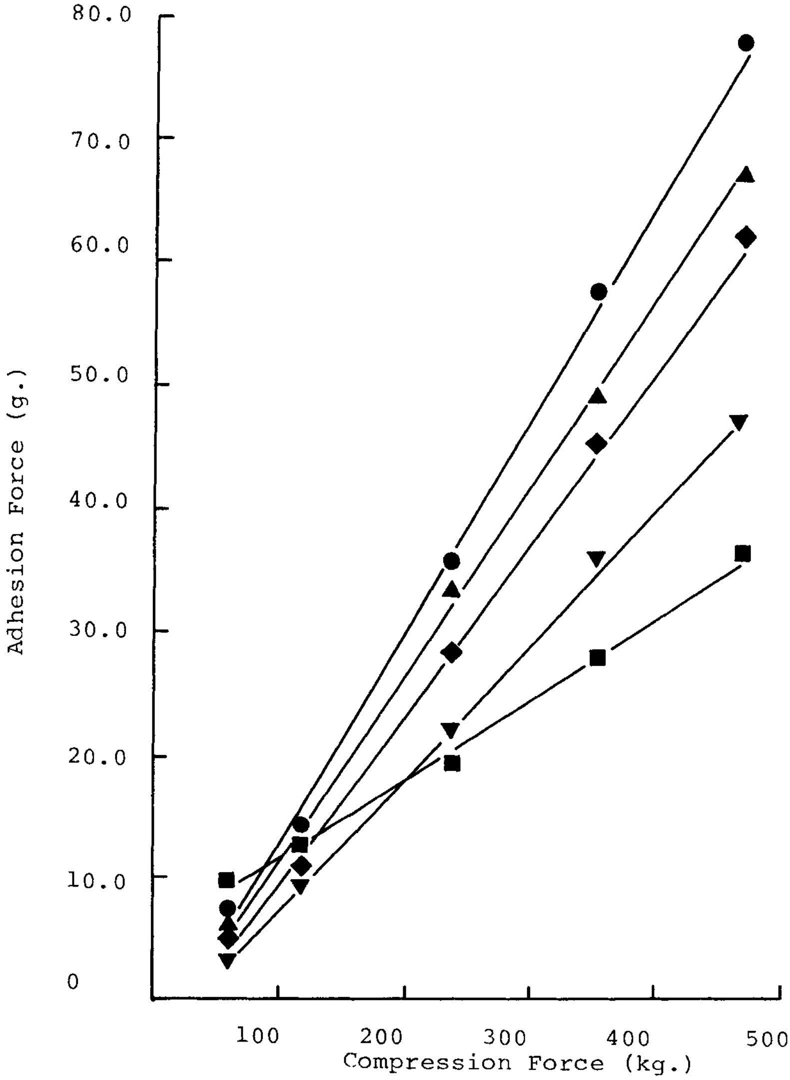

FIGURE 6
Effect of Compression Force on the Adhesion Force of Microcrystalline Cellulose Tablets Containing Stearic Acid. Percent Stearic Acid, ■ 0.00; ● 0.10; ▲ 0.25; ◆ 0.50; ▼ 1.00.

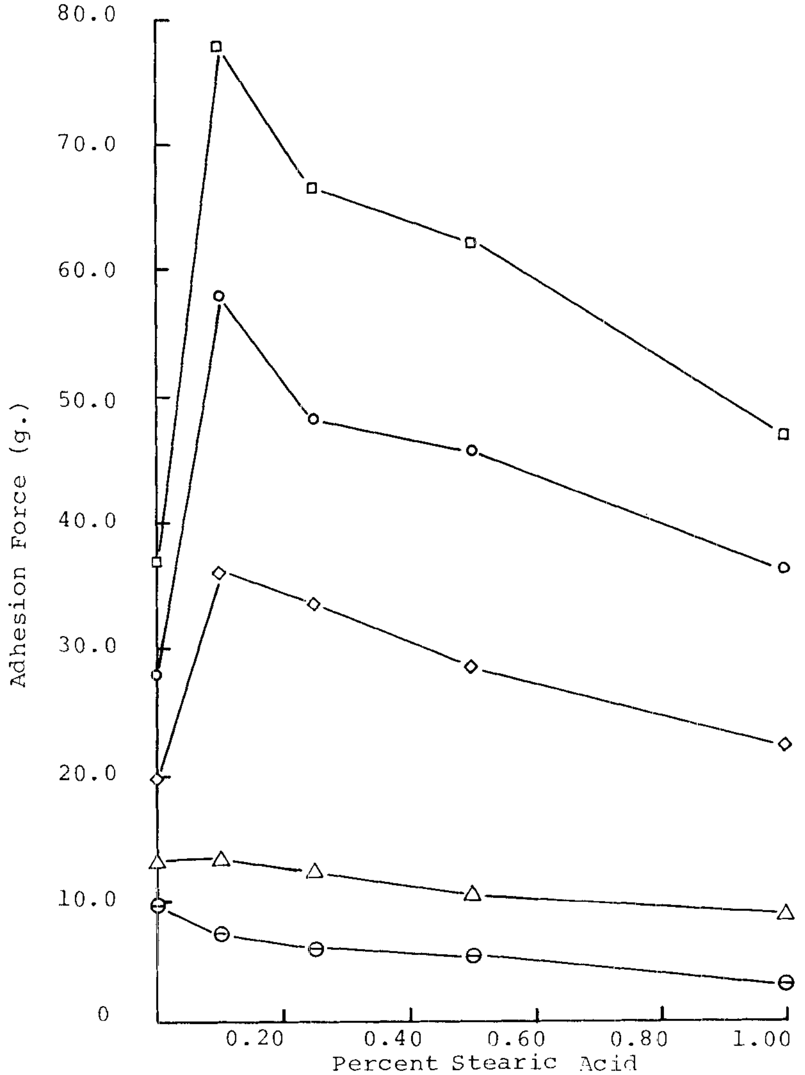

FIGURE 7
Effect of Stearic Acid Concentration on the Adhesion Force of Microcrystalline Cellulose Tablets. Compression Force, ⊖ 59 kg.; △ 118 kg.; ◇ 236 kg.; o 354 kg.; □ 472 kg.

designed to more thoroughly delineate this concentration dependency in specific systems.

I. Effect of Stearic Acid and Magnesium Stearate Concentrations on the Adhesion and Ejection Forces of Microcrystalline Cellulose Tablets.

The results of the study of the effect of stearic acid concentration on the adhesion and ejection forces of microcrystalline cellulose tablets are summarized in Figures 6-8. Although adhesion forces generally increased with compression force for both the lubricated and unlubricated batches (Figure 6), a somewhat different pattern emerged when the effects of stearic acid concentration were compared (Figure 7). Regardless of the concentration of stearic acid, adhesion forces at or lower than those of the unlubricated control were found only at the two lowest compression forces (59 kg. and 118 kg.). At all higher compression forces (236-472 kg.) the unlubricated filler exhibited lower adhesion forces than all lubricated blends. For the lubricated batches, adhesion forces were greatest at 0.10% stearic acid and progressively decreased with increasing lubricant concentration. The unit ejection forces (Figure 8) obtained with the unlubricated control were markedly higher than those obtained with the lubricated blends at any compression force; increasing lubricant concentrations caused decreasing ejection forces.

The results of the study of the effect of magnesium stearate concentration on the adhesion and ejection forces of microcrystalline cellulose tablets appear in Figures 9-11. As was found in the stearic acid study, adhesion force increased with compression

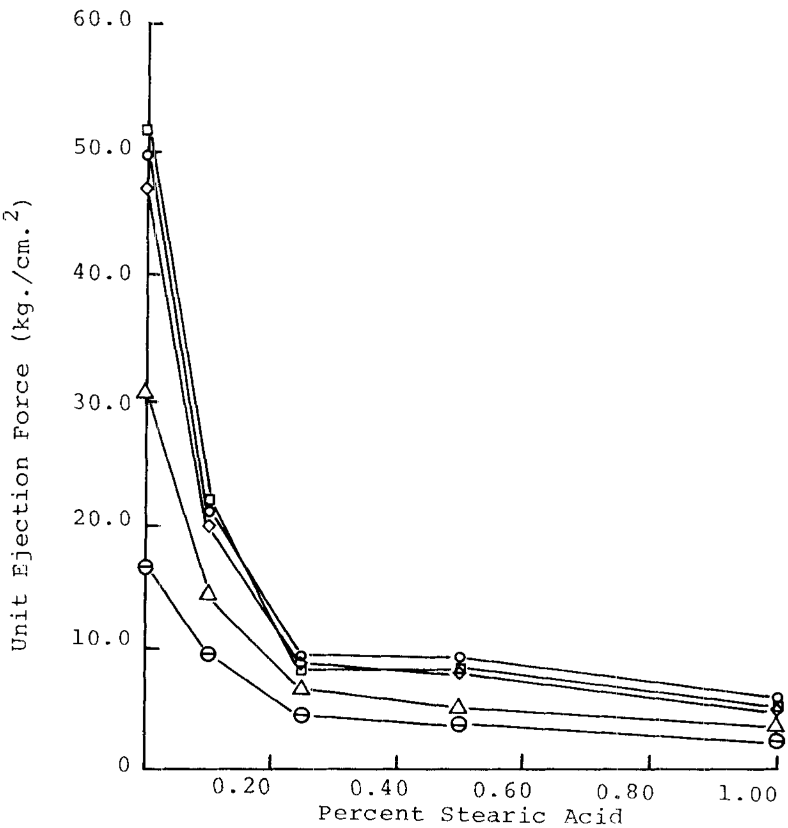

FIGURE 8
Effect of Stearic Acid Concentration on the Unit Ejection Force of Microcrystalline Cellulose Tablets. Compression Force, ⊖ 59 kg.; △ 118 kg.; ◇ 236 kg.; o 354 kg.; □ 472 kg.

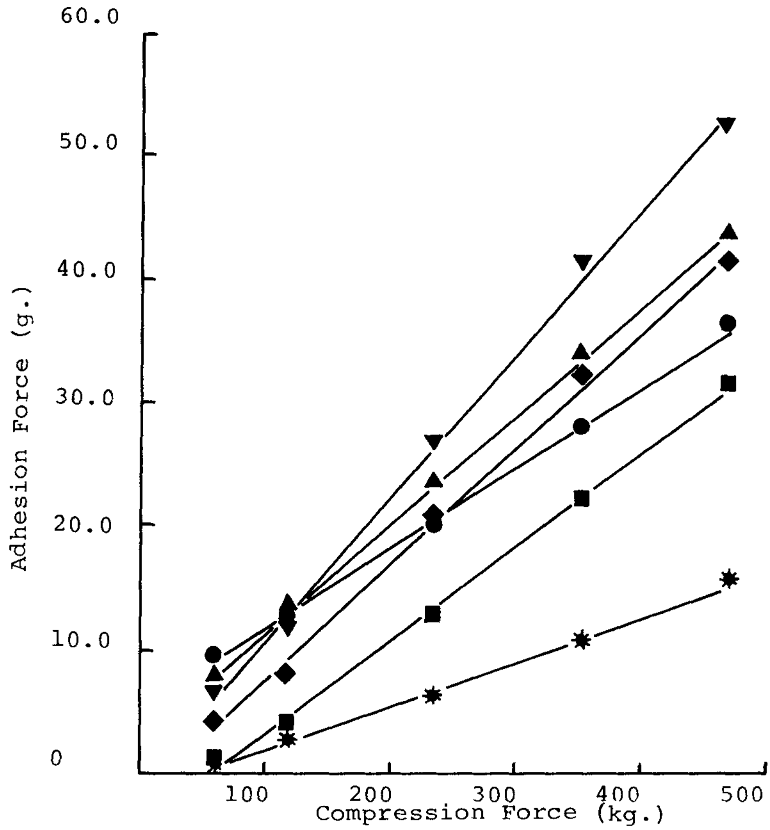

FIGURE 9
Effect of Compression Force on the Adhesion Force of Microcrystalline Cellulose Tablets Containing Magnesium Stearate. Percent Magnesium Stearate, ● 0.00; ▲ 0.05; ▼ 0.10; ◆ 0.25; ■ 0.50; ✱ 1.00.

force (Figure 9). Again, increasing magnesium stearate levels produced adhesion forces at or below those of the unlubricated filler only at the low compression forces (59 kg. and 118 kg., see Figure 10). At higher compression forces, adhesion forces rose to well above those of the unlubricated controls at 0.10%

magnesium stearate and then progressively declined with increased magnesium stearate levels. Unlike the stearic acid runs, however, adhesion forces were able to be lowered to below those of the unlubricated controls with increasing lubricant levels at these compression forces. This may be reflecting a greater antiadherent efficiency of magnesium stearate at the

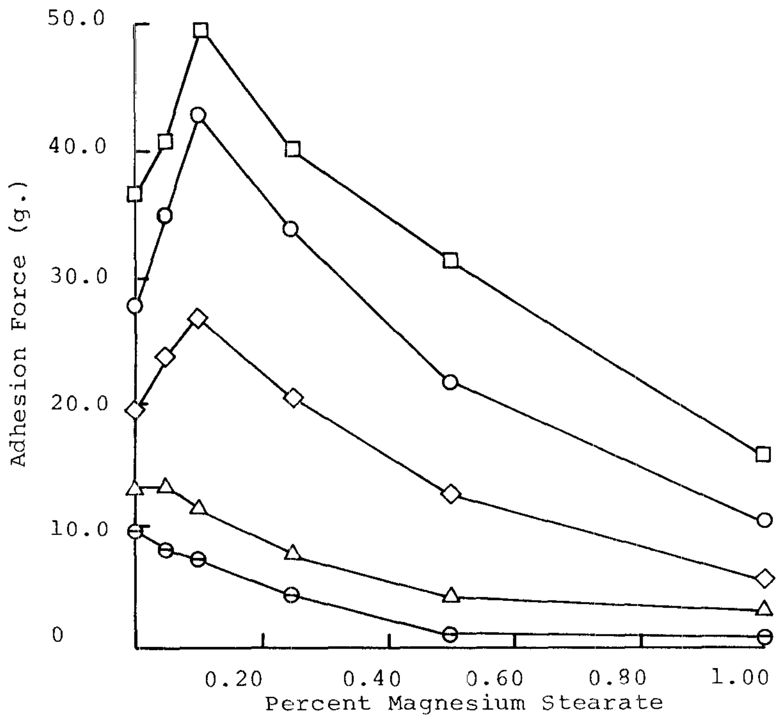

FIGURE 10
Effect of Magnesium Stearate Concentration on the Adhesion Force of Microcrystalline Cellulose Tablets. Compression Force, ⊖ 59 kg.; △ 118 kg.; ◇ 236 kg.; ○ 354 kg.; □ 472 kg.

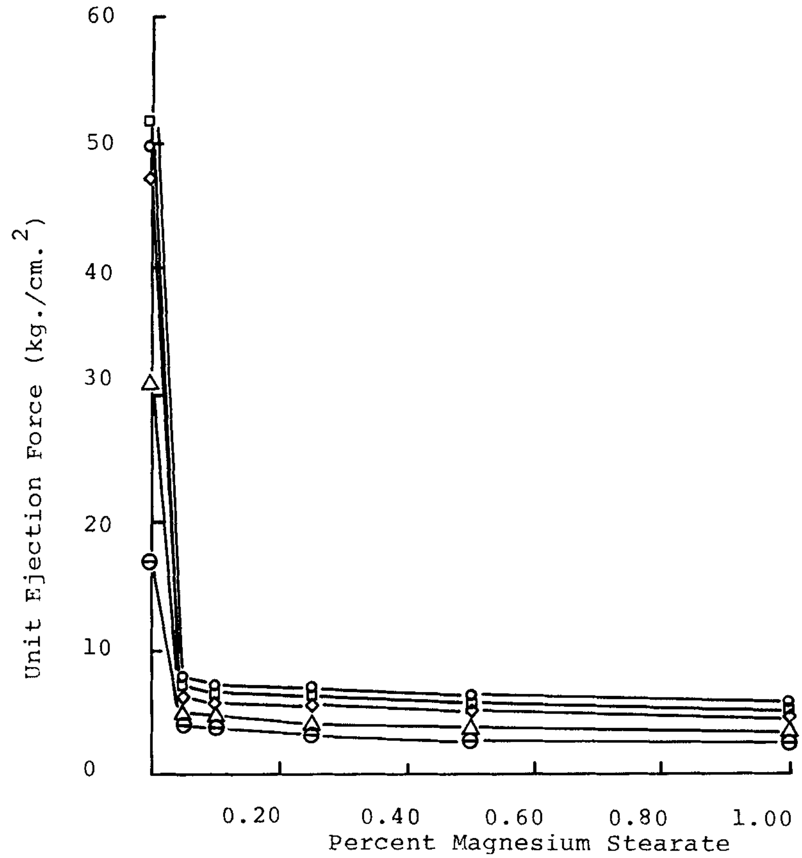

FIGURE 11
Effect of Magnesium Stearate Concentration on the Unit Ejection Force of Microcrystalline Cellulose Tablets. Compression Force, ⊖ 59 kg.; △ 118 kg.; ◇ 236 kg.; ○ 354 kg.; □ 472 kg.

tablet-lower punch interface. As was observed in the stearic acid study, the unit ejection forces (Figure 11) were found to decrease with increased magnesium stearate levels, and the ejection forces obtained with all lubricated blends were much lower than those obtained with the plain microcrystalline cellulose.

In a rotary tablet press, although both the upper punch and lower punch participate in exerting force on the powder, the upper punch force has been reported to be greater than the lower punch force (8, 9). Shotton et al. (8) suggested that the system must be balanced by a force at the die wall acting in an upward direction and derived from the frictional reaction to a slight downward movement of the tablet during compression, since the upper roller is rigid and the lower roller is spring loaded through the overload mechanism. Therefore it is possible that the reduced die wall friction observed with the lubricated batches would cause more reaction at the lower punch, thereby resulting in an increase in adhesion. This effect seemed to be more pronounced at higher compression forces. A further supportive observation was that previously reported (1) with lubricated microcrystalline cellulose wherein an increase in tablet thickness (at constant compression force) was found to cause an increase in ejection force but a decrease in adhesion force.

II. Effect of Prelubricated Die and Unlubricated Die on the Adhesion and Ejection Forces of Plain Microcrystalline Cellulose Tablets

To further investigate the phenomenon observed in the preceding experiment wherein the unlubricated filler gave lower adhesion forces but higher ejection forces than the lubricated blends, an experiment was carried out comparing the adhesion and ejection forces obtained from unlubricated microcrystalline cellulose compressed in an unlubricated die to those obtained when the plain filler was compressed in the same die prelubricated with stearic acid. The results are shown in Figures 12 and 13.

With the unlubricated die, the ejection forces were markedly higher (Figure 12) but the adhesion forces (Figure 13) were lower than those obtained with the lubricated die, the difference being greatest at higher compression forces. This observation lends support to the previous observation that the greater adhesion force obtained with the lubricated microcrystalline cellulose runs (in comparison with the unlubricated controls) may be attributable to reduced die wall friction.

Although adhesion forces found with the lubricated blends (in both stearic acid and magnesium stearate studies) at the higher compression forces were greater at the low lubricant level than those found with the unlubricated controls, adhesion forces did decline when the lubricant concentration was increased (Figures 7 and 10). This appears to reflect the effect of an increasing concentration of lubricant at the tablet-lower punch interface.

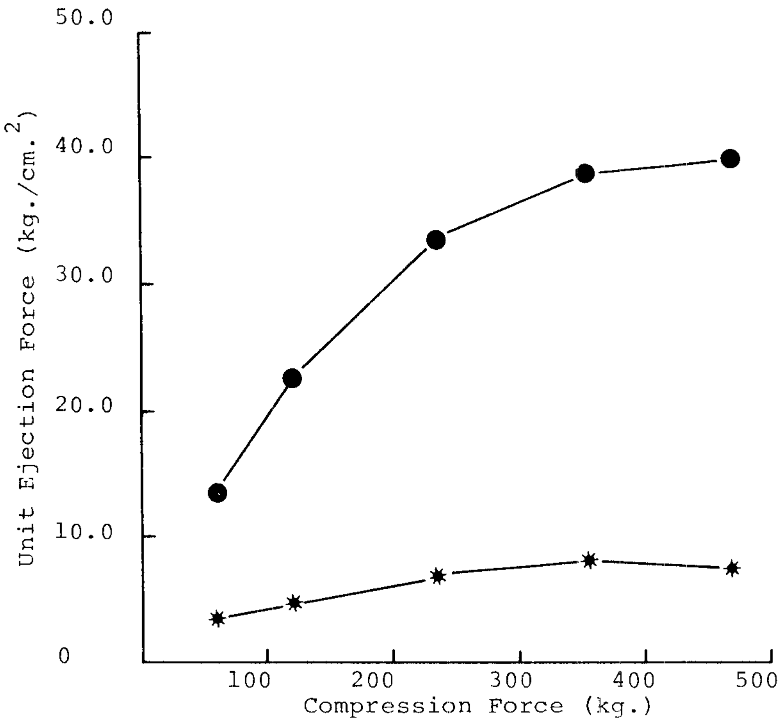

FIGURE 12
Effect of Die Wall Condition on the Unit Ejection Forces of Unlubricated Microcrystalline Cellulose Tablets. Die Wall Condition, ● Unlubricated; ✷ Prelubricated with Stearic Acid.

Thus, lubricants added to the powder mass would appear to have two opposing effects on tablet adhesion at the lower punch face: (1) enhancing adhesion due to an increased reaction at the lower punch which results from reduced die wall friction, (2) reducing adhesion via the "anti-adherent" function which is evident by a progressive decrease

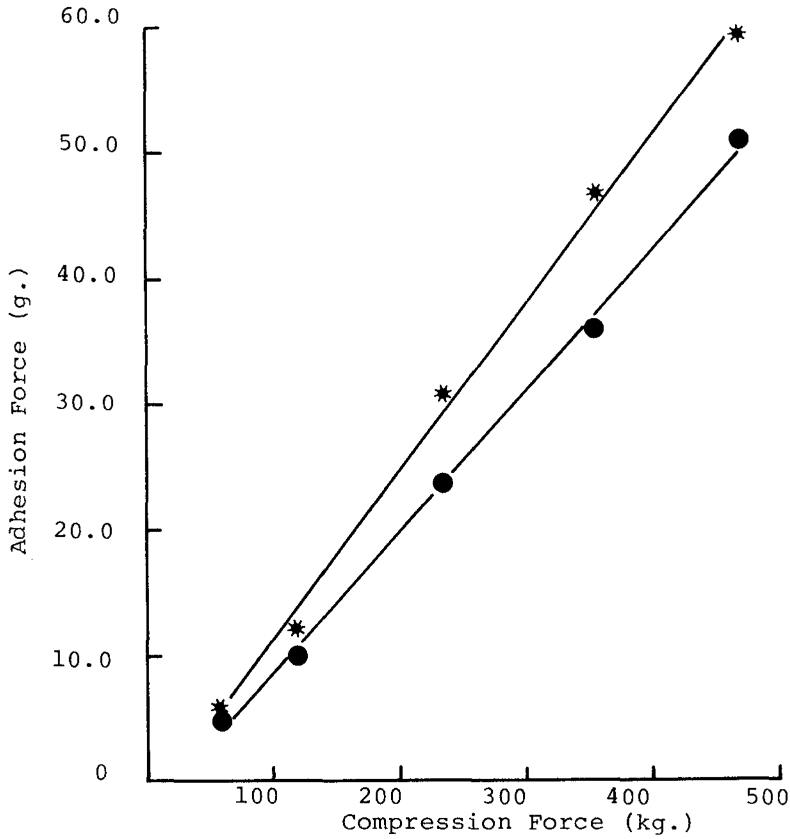

FIGURE 13
Effect of Die Wall Condition on the Adhesion Forces of Unlubricated Microcrystalline Cellulose Tablets. Die Wall Condition, ● Unlubricated; ✷ Prelubricated with Stearic Acid.

in adhesion force when the concentration of lubricant is increased. Thus, it would appear that the adhesion force measured at the lower punch face would represent the net result of these two competing effects.

III. Comparison of True Lubricant and Antiadherent Properties of Magnesium Stearate and Stearic Acid in Microcrystalline Cellulose

Within the range of lubricant concentrations studied, stearic acid generally appeared to be less efficient than magnesium stearate as judged by higher ejection forces and adhesion forces obtained at all corresponding concentrations. This observation may be attributable to a less complete spreading of stearic acid over the filler, as compared to magnesium stearate (5). However, there may also be differences in specific interactions at the tablet-tooling interface.

The comparative effects of the two lubricants at low concentration (0.10%) and at high concentration (1.00%) on the ejection force and adhesion force are illustrated in Figures 14 and 15 respectively. At the 0.10% level, the ejection forces (Figure 14) obtained with stearic acid were much higher than those obtained with magnesium stearate; however, at 1.00% the ejection forces obtained with stearic acid were only slightly higher than those obtained with magnesium stearate. As regards adhesion forces (Figure 15), although stearic acid generally gave higher adhesion readings than did magnesium stearate, the difference in the adhesion forces was less dramatic at 0.10% than at 1.00%. These results confirm previously

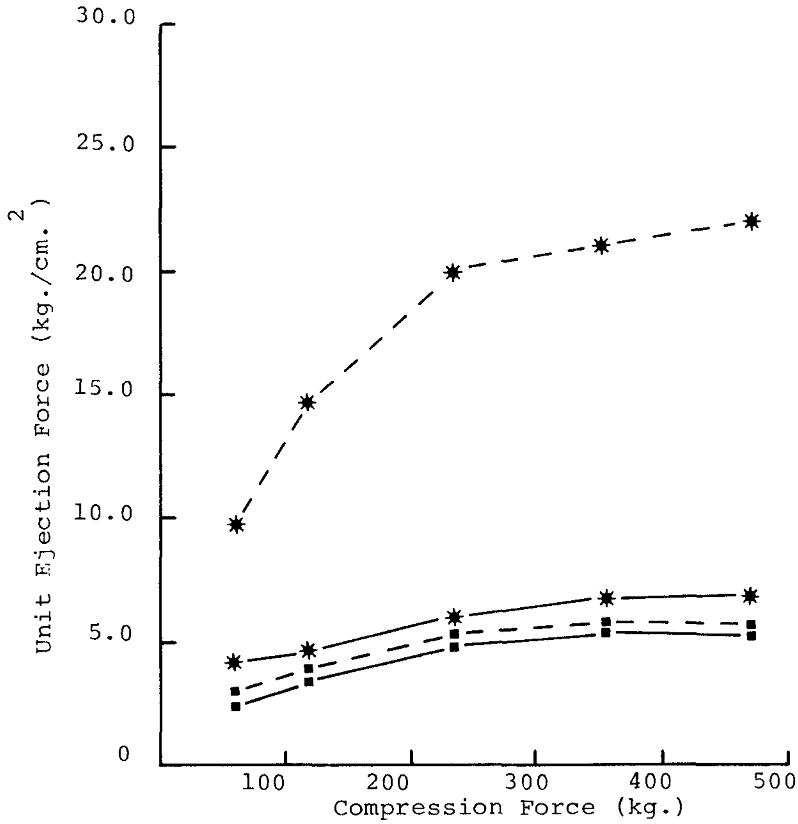

FIGURE 14
Comparative Effect of Stearic Acid and Magnesium Stearate on the Unit Ejection Force of Microcrystalline Cellulose Tablets. Lubricant, ---Stearic Acid; —— Magnesium Stearate. Percent Lubricant, ✱ 0.10; ■ 1.00.

reported findings that differences in true lubricant efficiency do not necessarily reflect differences in anti-adhesion efficiency (1).

IV. Effect of Stearic Acid and Magnesium Stearate Concentrations on the Adhesion and Ejection Forces of Hydrous Lactose Tablets

Four concentrations of stearic acid were evaluated at six compression forces. The results

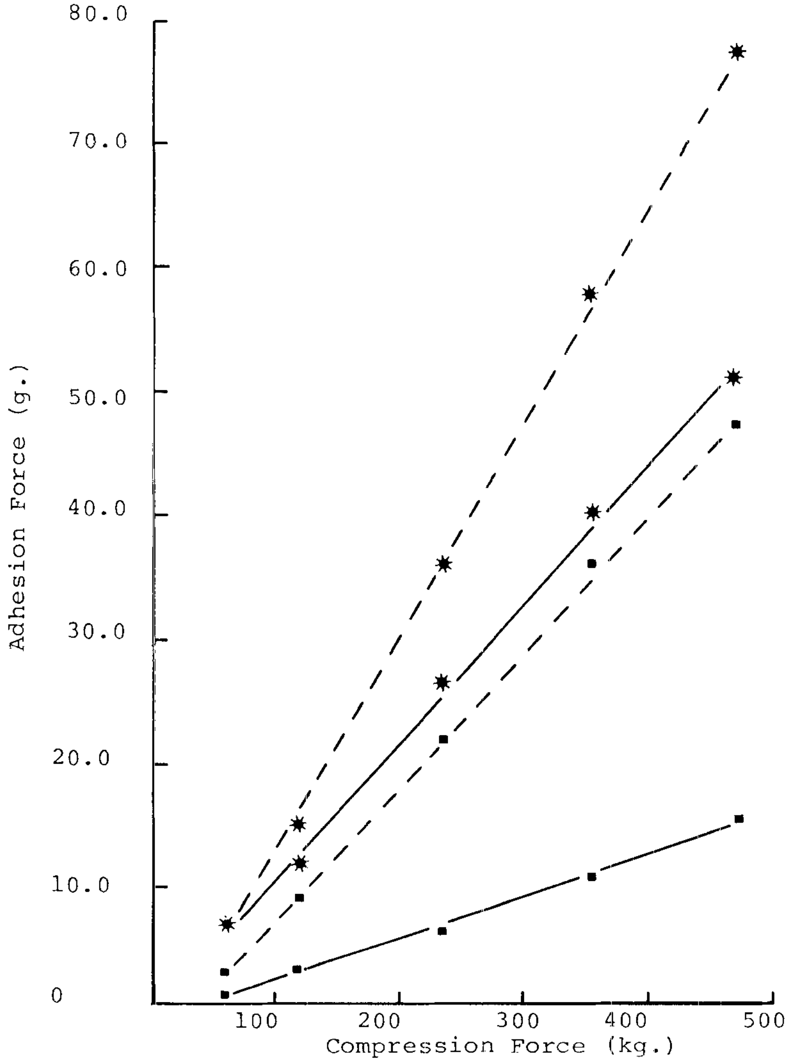

FIGURE 15
Comparative Effect of Stearic Acid and Magnesium Stearate on the Adhesion Force of Microcrystalline Cellulose Tablets. Lubricant, ---Stearic Acid; —— Magnesium Stearate. Percent Lubricant, ✱ 0.10; ■ 1.00.

are illustrated in Figures 16, 17, and 18. It was observed that adhesion forces generally increased with increasing compression force (Figure 16) up to a maximum value at 590 kg. compression force. At

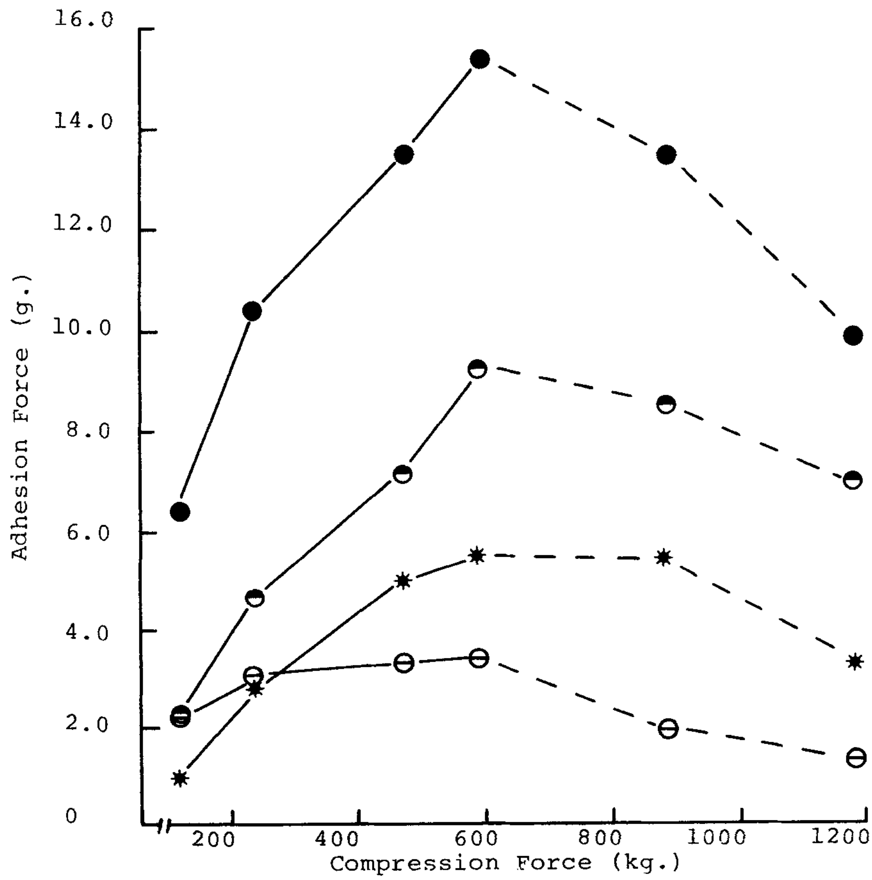

FIGURE 16
Effect of Compression Force on the Adhesion Force of Compressible Hydrous Lactose Tablets Containing Stearic Acid. Percent Stearic Acid, ● 0.25; ⊖ 0.50; ✱ 1.00; ◓ 2.00. (The broken lines link results obtained from chipped tablets)

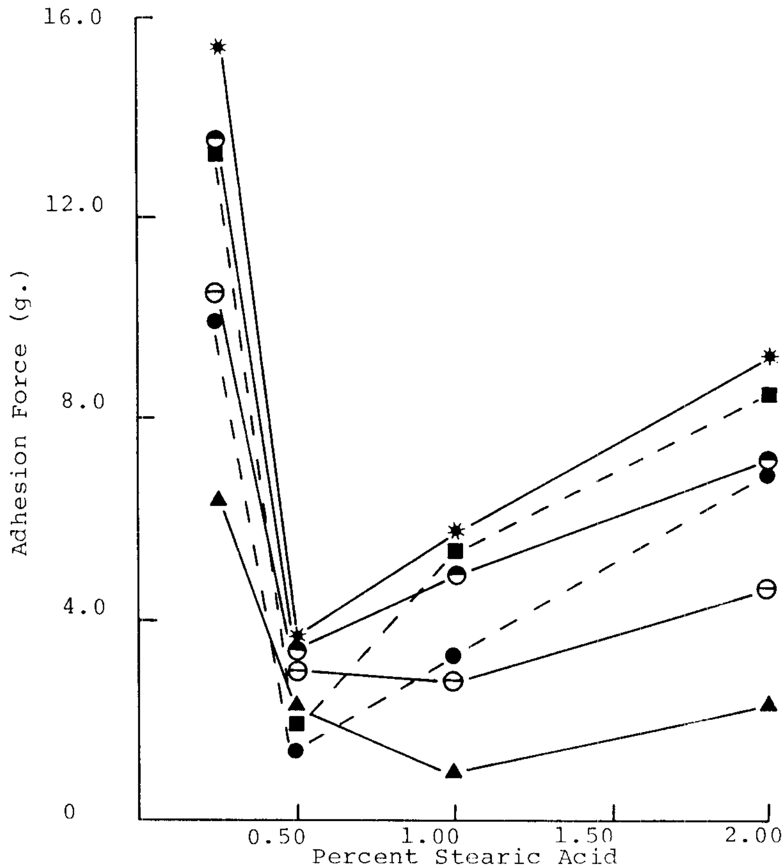

FIGURE 17
Effect of Stearic Acid Concentration on the Adhesion Force of Compressible Hydrous Lactose Tablets. Compression Force, ▲ 118 kg.; ⊖ 236 kg.; ◓ 472 kg.; ✷ 590 kg.; ■ 885 kg.; ● 1180 kg.. (The broken lines link results obtained from chipped tablets)

higher compression forces (885 kg. and 1180 kg.), the adhesion forces were found to decrease due to a surface chipping of tablet. This chipping causes a change in the tablet face characteristics and prevents the proper measurement of adhesion force (1).

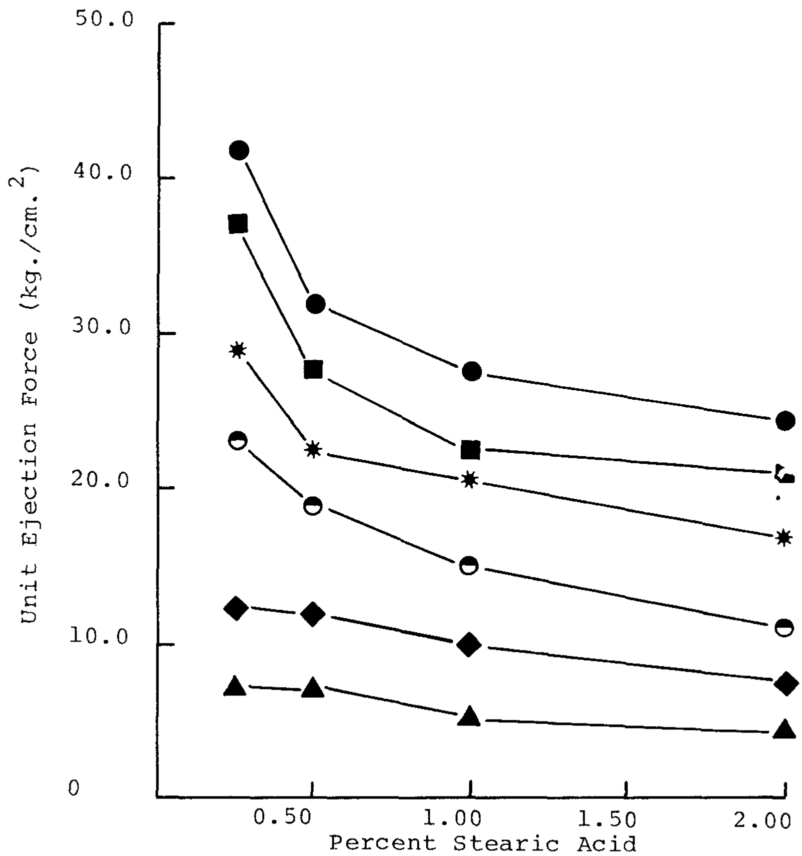

FIGURE 18
Effect of Stearic Acid Concentration on the Unit Ejection Force of Compressible Hydrous Lactose Tablets. Compression Force, ▲ 118 kg.; ◆ 236 kg.; ⊖ 472 kg.; ✱ 590 kg.; ■ 885 kg.; ● 1180 kg.

This was observed at all concentrations of lubricant studied.

Figure 17 summarizes the effect of stearic acid concentration on the adhesion force. It can be seen that adhesion force decreased markedly at 0.50%

lubricant and generally increased with further increases in stearic acid concentration at all but the two lowest compression forces (118 kg. and 236 kg.). At these two compression forces there was a further reduction in adhesion force at 1.00% lubricant, followed by an increase at 2.00%. The increase in adhesion forces with increasing stearic acid concentrations beyond 0.50% was more pronounced at high compression forces (472 - 1180 kg.). This effect may possibly be attributable to a softening of stearic acid, which has a low melting point of 54°, particularly at the higher compression forces. Hanus and King (10) reported increases in temperature on compression of sodium chloride tablets which increased with increased speed of compression or applied pressure. Increases in the temperature on the upper and lateral surfaces of tablets during compression of a lubricated or unlubricated standard granulation were also reported (11).

It has been noted that low melting materials such as stearic acid and high molecular weight polyethylene glycols may soften sufficiently from the heat of compression to cause sticking (12,13). That this phenomenon was not observed in the stearic acid-microcrystalline cellulose runs may be attributable to the comparatively low compression forces required to produce tablets with that filler.

Although measurable increases in adhesion were observed in this study, it should be pointed out that no actual picking or filming was observed during these relatively short runs. In spite of the general increases in adhesion forces beyond 0.50% stearic acid, the adhesion forces measured at 1.00% or 2.00% lubricant were still lower than those obtained at 0.25%. Ejection forces were observed to decrease with increasing stearic acid concentrations at all compression forces tested (Figure 18).

In a similar manner as in the stearic acid experiment, four concentrations of magnesium stearate also were evaluated in hydrous lactose. The results are depicted in Figures 19, 20, and 21. As found in the previous experiment, adhesion force generally increased with increasing compression force (Figure 19) reaching a maximum value at 590 kg. compression force, and decreased at higher compression forces due to chipping of tablet surfaces. Unlike the previous stearic acid experiment, adhesion forces were found to decrease with increasing concentration of magnesium stearate at any compression force (Figure 20). The pattern resembled that of the lubricated micro-crystalline cellulose runs noted previously.

The effect of magnesium stearate concentration on the ejection force is shown in Figure 21. In general, the ejection forces were not affected by

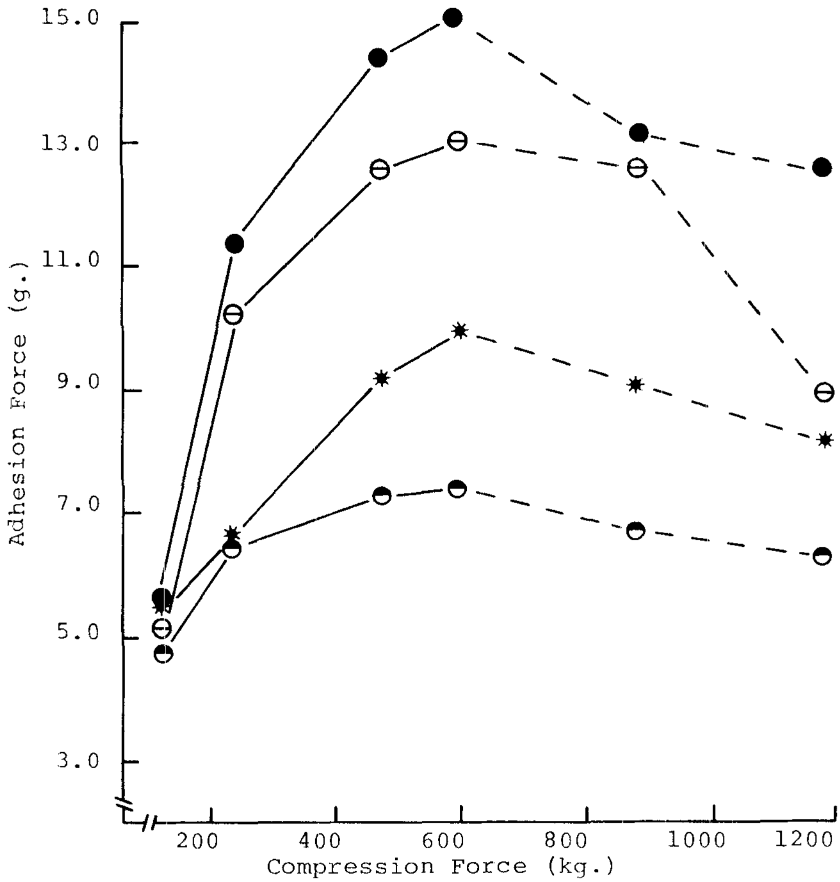

FIGURE 19
Effect of Compression Force on the Adhesion Force of Compressible Hydrous Lactose Tablets Containing Magnesium Stearate. Percent Magnesium Stearate, ● 0.25; ⊖ 0.50; ✷ 1.00; ◓ 1.50. (The broken lines link results obtained from chipped tablets).

lubricant concentration to any great extent; a slight decrease was observed at the 0.50% level at any compression force. However, at relatively high compression forces (590 - 1180 kg.), ejection forces were found to increase beyond the 0.50% lubricant level. This finding is not inconsistent with previously reported work (4, 14) concerning lactose - magnesium stearate blends compressed at similar ranges of compression forces and lubricant levels. Up to this point, no satisfactory explanation has been available.

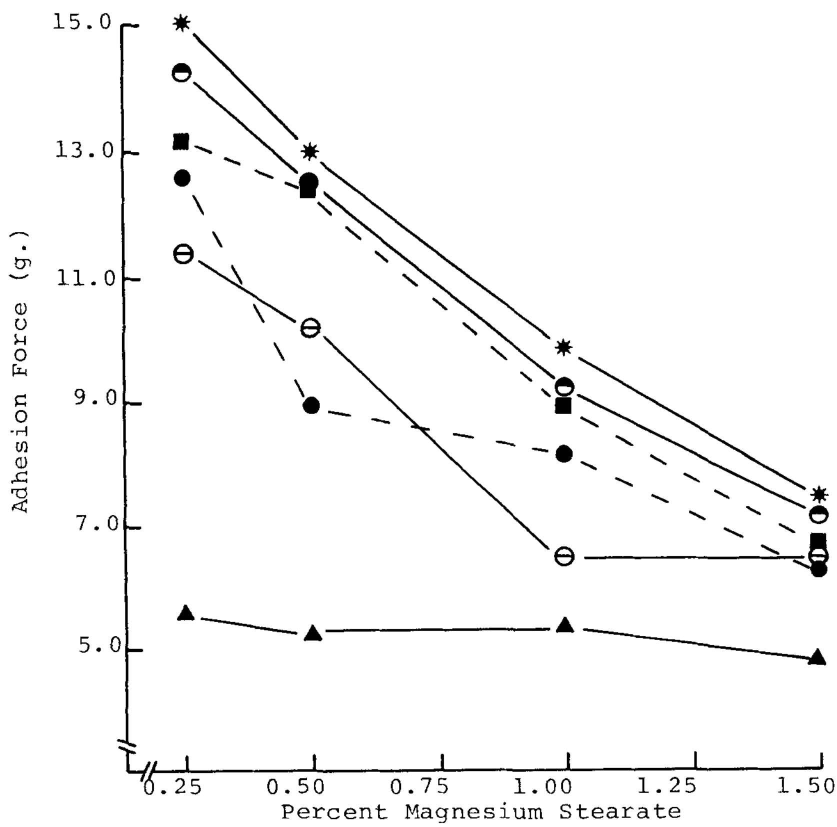

FIGURE 20
Effect of Magnesium Stearate Concentration on the Adhesion Force of Compressible Hydrous Lactose Tablets. Compression Force, ▲ 118 kg.; ⊖ 236 kg.; ◓ 472 kg.; ✱ 590 kg.; ■ 885 kg.; ● 1180 kg. (The broken lines link results obtained from chipped tablets).

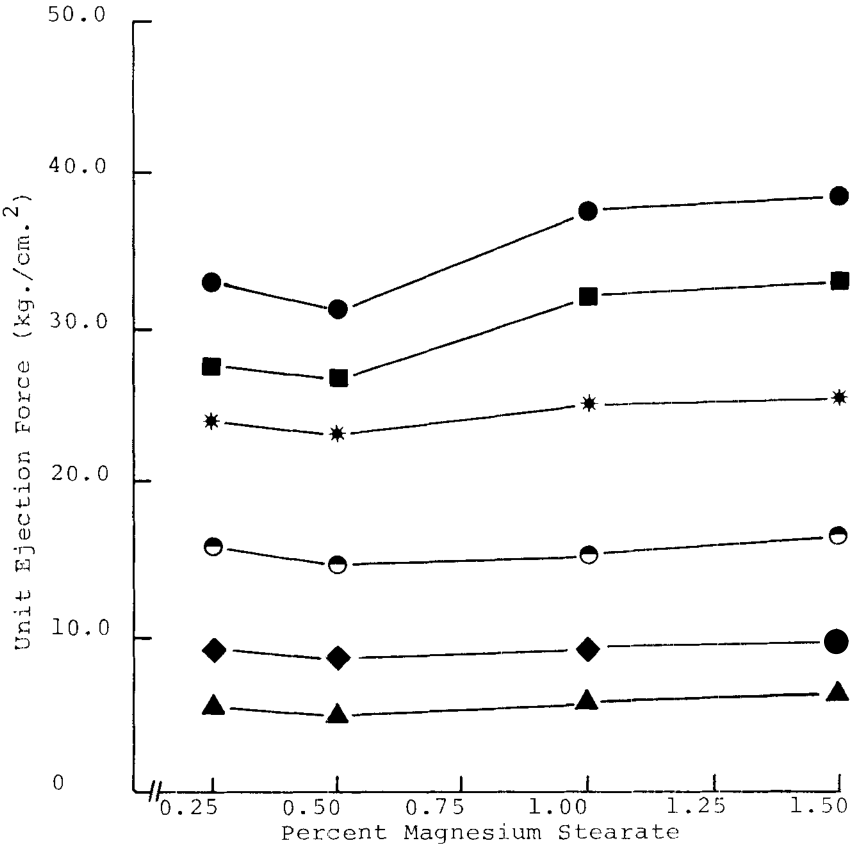

FIGURE 21
Effect of Magnesium Stearate Concentration on the Unit Ejection Force of Compressible Hydrous Lactose Tablets. Compression Force, ▲ 118 kg.; ◆ 236 kg.; ◓ 472 kg.; ✷ 590 kg.; ■ 885 kg.; ● 1180 kg.

V. Comparison of True Lubricant and Antiadherent Properties of Magnesium Stearate and Stearic Acid in Compressible Hydrous Lactose

In spite of the fact that magnesium stearate appears to delaminate more completely than stearic acid (5), batches containing magnesium stearate

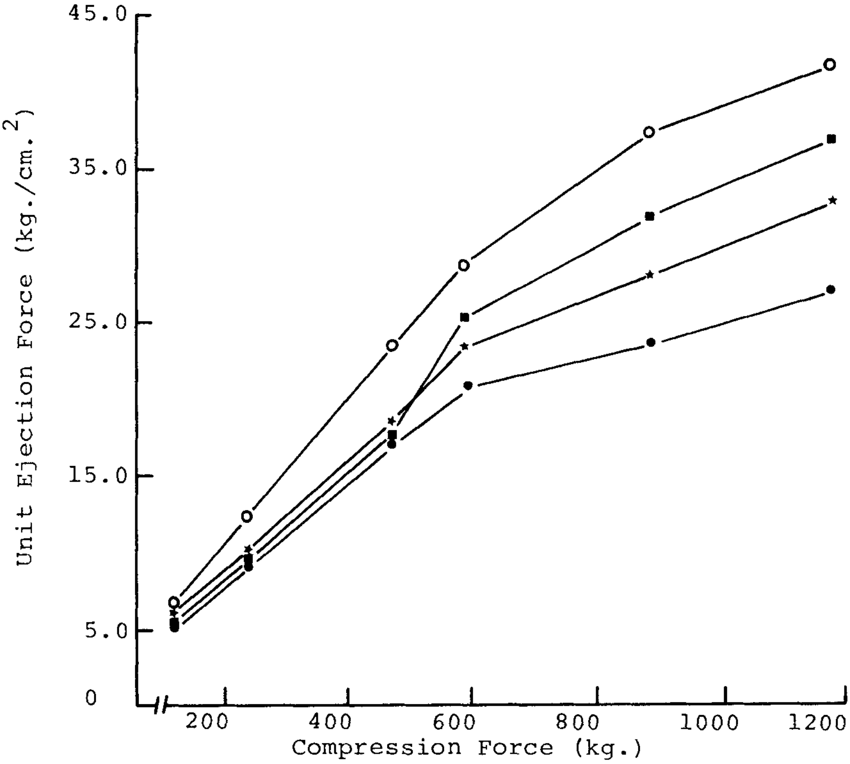

FIGURE 22
Comparative Effect of Stearic Acid and Magnesium Stearate on the Unit Ejection Force of Compressible Hydrous Lactose Tablets. Percent Stearic Acid, ○ 0.25; ● 1.00. Percent Magnesium Stearate, ★ 0.25; ■ 1.00.

exhibited lower ejection forces than those containing stearic acid only at the low lubricant level (Figure 22). At high concentration (1.00%) the ejection forces obtained with both lubricants were comparable at low compression forces; at higher compression forces, stearic acid exhibited appreciably lower

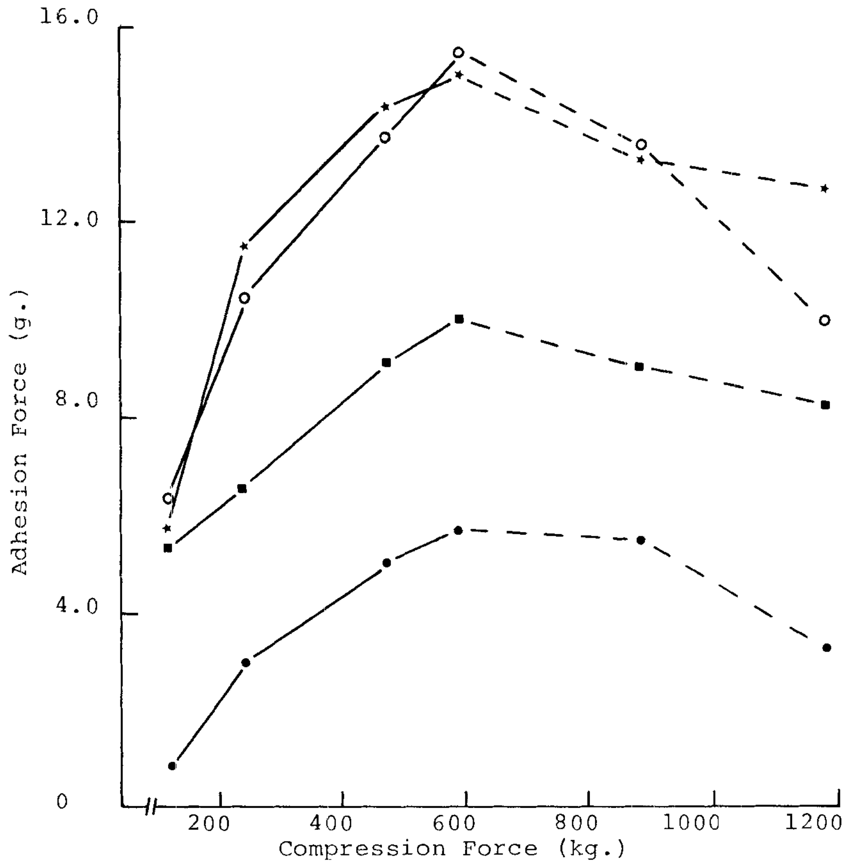

FIGURE 23
Comparative Effect of Stearic Acid and Magnesium Stearate on the Adhesion Force of Compressible Hydrous Lactose Tablets. Percent Stearic Acid, ○ 0.25; ● 1.00. Percent Magnesium Stearate, ★ 0.25; ■ 1.00. (The broken lines link results obtained from chipped tablets)

ejection forces than did magnesium stearate. Again, this would appear attributable to the softening of stearic acid, thereby facilitating the shearing off of lubricant film at the die wall upon the ejection of tablets. Similarly, Lewis and Shotton (15) in an evaluation of several lubricants at the 2% level in a sucrose granulation found that stearic acid (melting point = 54°C) exhibited much lower ejection force than did magnesium stearate (melting point = 186°C). The authors (15) suggested that lower melting points probably facilitate the formation of lubricant films on the die wall.

The adhesion forces obtained with stearic acid were comparable to those obtained with magnesium stearate at the 0.25% levels (Figure 23), but much lower than those observed with magnesium stearate at 1.00% lubricant. It appeared that at 1.00% level, stearic acid was more efficient than magnesium stearate in reducing both the ejection force and adhesion force in hydrous lactose.

SUMMARY AND CONCLUSIONS

The effects of blending time, running time and lubricant concentrations on the adhesion of directly compressed tablets to the lower punch face in a rotary press were studied. With microcrystalline cellulose - magnesium stearate blends, adhesion force tended to decrease with increased blending time or intensity of agitation. This observation was attributed to a greater surface coverage of the filler with lubricant at longer blending times.

During three-hour runs with lubricated batches, both microcrystalline cellulose and lactose fillers exhibited an initial pattern in which adhesion force increased while ejection force decreased. The reduction of ejection force in both cases suggested improved force transmission through the compact due to reduced die wall friction which may account for the initial increase in adhesion. The progressive decrease in adhesion following the attainment of the peak value (especially evident with lactose) may indicate progressive conditioning of the punch face.

Further studies comparing lubricated and unlubricated microcrystalline cellulose suggest that the adhesion of tablets to the lower punch may be the net result of two competing effects: (1) increasing adhesion due to an increased reaction at the lower punch face resulting from reduced die wall friction, and (2), reducing adhesion of the tablet by virtue of the specific "anti-adherent" effect.

Within the range of concentrations studied, stearic acid generally appeared to be less efficient than magnesium stearate in microcrystalline cellulose blends; higher adhesion and ejection forces were obtained with stearic acid at all corresponding concentrations.

With hydrous lactose lubricated with varying levels of stearic acid, adhesion forces decreased markedly at 0.50% lubricant and generally increased with further increases in lubricant concentrations. Such increased adhesion beyond 0.50% level was more pronounced at relatively high compression forces. This observations may possibly be attributable to a softening of stearic acid (melting point = 54°), particularly at the higher compression forces. With hydrous lactose - magnesium stearate blends, adhesion forces were found to decrease generally with increasing concentration of magnesium stearate.

The antiadhesion function of stearic acid in hydrous lactose was comparable to that of magnesium stearate at low lubricant level (0.25%), however, at high lubricant level (1.00%) stearic acid appeared to be more efficient than magnesium stearate. Stearic acid, at the high concentration, generally produced lower ejection forces than did magnesium stearate, whereas at the low concentration, higher ejection forces were obtained.

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REFERENCES

1. A. Mitrevej and L.L. Augsburger, Drug Dev. Ind. Pharm., 6 (4), 331-377 (1980).
2. A.M. Salpekar and L.L. Augsburger, J. Pharm. Sci., 63, 289-293 (1974).
3. A.C. Shah and A.R. Mlodozeniec, J. Pharm. Sci., 66, 1377-1382 (1977).
4. A.M. Salpekar, Ph.D. Dissertation, University of Maryland, Baltimore, MD, 1975.
5. Y. Matsuda, Y. Minamida, and S. Hayashi, J. Pharm. Sci., 65, 1155-1160 (1976).
6. C.F. Lerk, G.K. Bolhuis, and S.S. Smedema, Pharm. Acta Helv., 52, 33-39 (1977).
7. D.R. Savello, Ph.D. Dissertation, University of Maryland, Baltimore, MD, 1972.
8. E. Shotton, J.J. Deer, and D. Ganderton, J. Pharm. Pharmacol., 15, 106T-114T (1963).
9. P.E. Wray, J.G. Vincent, F.W. Moller, and G.J. Jackson, Paper Presented at A.Ph.A. Annual Meeting, Industrial Pharmacy Section, Dallas, TX (1966).
10. E.J. Hanus and L.D. King, J. Pharm. Sci., 57, 677-684 (1968).

11. M.J. Juslin, Farm. Aikak., 78 (9), 201-210 (1969), from Chem. Abstr., 73, 7170w (1970).

12. R.W. Mendes and S.B. Roy, Pharm. Tech., 3 (3) 69-75 (1979).

13. W.C. Gunsel and J.L. Kanig, in The Theory and Practice of Industrial Pharmacy, L. Lachman, H.A. Lieberman, and J.L. Kanig (Eds.), Lea & Febiger, Philadelphia, PA, 1976, Chapter 11.

14. A. Mitrevej, M.S. Thesis, University of Maryland, Baltimore, MD, 1979.

15. C.J. Lewis and E. Shotton, J. Pharm. Pharmacol., 17 suppl, 82s-86s (1965).