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ADHESION OF TABLETS IN A ROTARY TABLET PRESS I. INSTRUMENTATION AND PRELIMINARY STUDY OF VARIABLES AFFECTING ADHESION

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ABSTRACT

This study describes instrumentation to measure the adhesion of tablets to the lower punch face by means of a strain gaged cantilever beam affixed to the feed frame in front of the sweep-off blade. The tablet is detached from the lower punch by striking this blade. The adhesion force is the total force measured by the beam less that due to the momentum of the tablet. Tableting was performed on a Stokes RB-2 press previously instrumented to monitor compression and ejection forces. Generally, the higher the compression force, or the lower the magnesium stearate concentration, the higher the adhesion in three direct compression fillers (compressible sugar, microcrystalline cellulose, lactose). With microcrystalline cellulose (0.1% magnesium stearate), adhesion decreased with increased tablet thickness or decreased tablet diameter (constant thickness) at constant compression pressure Simultaneous measurement of ejection forces revealed that differences in true lubricant efficiency did not necessarily

reflect differences in adhesion. The ability to distinquish differences in adhesion offers promise in assisting in the rational design of tablet formulations.

INTRODUCTION

Since the early days of tableting, lubricants have been included in tablet formulations. Added in small quantities, these agents serve in three ways to improve the processing characteristics of the formulation (1): (1) preventing sticking to punch faces and the die wall ("antiadherent" activity); (2) improving the flow properties of the formulation ("glidant" activity); and (3) reducing friction at the tablet-die wall interface during tablet formation and ejection ("true lubricant" activity). A given lubricant may possess one or more of these activities to varying degrees and formulators often combine such agents in an attempt to optimize these processing characteristics.

The application of instrumentation technology to tableting equipment has permitted the quantitative evaluation of the true lubricant efficiency of lubricants through the measurement of such parameters as ejection force (2), R-value (3), force lost to the die wall (4). Glidant activity has been quantitated by such means as rate of flow measurements (5), angle of repose measurements (6), rotational viscometry (7), and the analysis of tablet weight variation (8). However, antiadherent activity continues to be evaluated primarily by inspection of tooling, and few attempts at quantitation have been reported.

Naito *et al.* (9,10) reported a device designed to measure the "slipping force" between the tablet surface and the upper

punch face. The tablets were compressed on an instrumented single punch press fitted with a modified upper punch assembly and a split die. The upper punch was not retracted after compression. After each tablet compression, the intact upper punch-tablet die assembly was transferred to a device which measured the force required to rotate the upper punch while the tablet was held stationary in the die. Numerous direct compression formulations were evaluated and data were presented which showed that slipping force measurements could be used to predict the tendency of these formulations to stick.

Recently Ritter and coworkers (11) quantitated tablet strippability using an "instrumented strain gage measuring arm" of a rotary tablet machine. Four formulations were tested. Three of them employed mixtures of polyethylene glycol 4000 and lactose granulation in various proportions as base materials, and 0.5% silica-type glidant. The fourth formulation contained only lactose granulation and 1% magnesium stearate. The mixtures were compressed at different compression forces. They concluded that the stripping force of the tablets decreased with decreasing polyethylene glycol 4000 concentration in the mixtures, and increased with increasing the compression force or running time with some mixtures. No details were given of the design, placement or calibration of the measuring device.

The present study details the design and calibration of instrumentation to measure the adhesion of tablets to the lower punch face in a rotary tablet press. This instrumentation is used

to study several basic factors which might influence the adhesion of tablets prepared from representative direct compression fillers. These factors include compression force, lubricant level, tablet dimensions, and different grades of magnesium stearate. In addition, adhesion data are compared with ejection force data in certain cases.

EXPERIMENTAL

Description of Instrument and Rationale.

All tableting was performed on a Stokes RB-2 rotary tablet press (Stokes Engineering, Philadelphia, PA) which had been instrumented as previously described (12) with resistance strain gages to monitor compression and ejection forces.

After a tablet is ejected from the die it is swept off the lower punch by a blade attached to the front of the feed frame. In so doing, the sweep-off blade exerts a quantity of force sufficient to overcome both the adhesion of the tablet to the lower punch face as well as the momentum of the tablet. In this study, an instrumented cantilever beam was affixed to the feed frame in front of the sweep-off blade. Thus, the tablet is detached from the lower punch face by striking the instrumented beam, thereby allowing the magnitude of the sweep-off force to be measured.

A tempered stainless steel blade, as outlined in Figure 1, was chosen for the instrumented beam. The width of the beam was almost identical to that of the sweep-off blade.

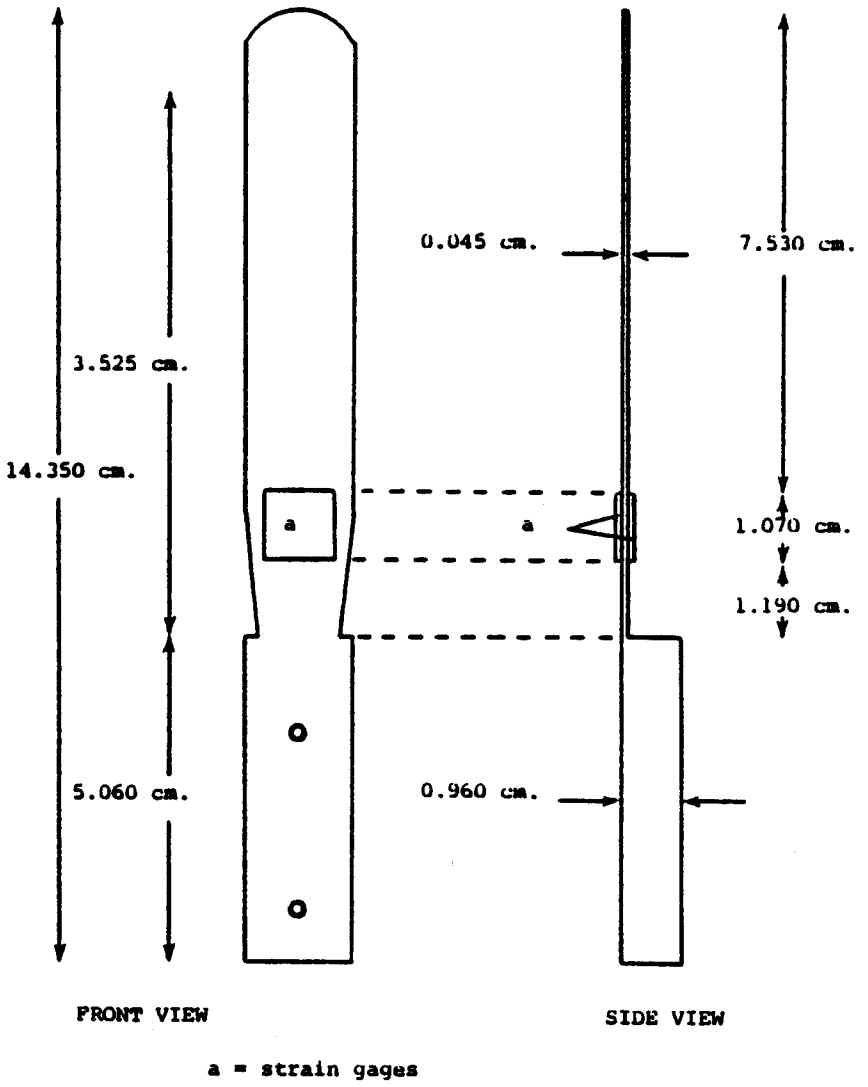

FIGURE 1
Outline Sketch of Instrumented Beam

Installation of Strain Gages and Circuitry.

A pair of metal foil resistance "self-temperature-compensated" strain gages (type CEA-06-125UT-120, Micro-Measurements, Romulus, MI 48174) were bonded to either side of the beam. Such gages allow close matching of the thermal expansion coefficient of gage elements with that of the structure to which they are bonded. The strain gage configuration chosen consisted of two grid elements, perpendicular to each other, mounted along the length of the gage backing. The gages were oriented so that one of each pair was parallel to the major strain axis. Bonding of the gages was carried out according to a standard procedure provided by the strain gage manufacturer (3). The gages were mounted such that the center alignment mark of one gage was perfectly matched with the center alignment of the gage on the opposite side of the beam. A similar procedure was used for bonding a four post terminal strip below one set of the gages.

The gage elements parallel to the axis of the beam were connected in adjacent arms of a Wheatstone bridge. The gage elements perpendicular to the beam axis served as "Poisson" gages and completed the Wheatstone bridge circuit. This four-gage bridge arrangement achieves both maximum sensitivity and linear output, and provides additional temperature compensation.

A shielded four conductor cable with a ground wire was used to connect the bridge to a carrier preamplifier (Hewlett Packard, Model 8805A, Palo Alto, CA 94306). The adhesion event, detected by the instrumented beam, was monitored by measuring the bridge

unbalance voltage using this carrier preamplifier and recorded on an oscillographic recorder (Hewlett Packard, Oscillographic Recording System 7702B, Palo Alto, CA 94306) or displayed on an oscilloscope (Tektronix 5103N Oscilloscope System, Beaverton, OR 97005).

Assembly of Feed Frame with Instrumented Beam.

The far end of the instrumented beam (away from the tablet sweep-off site) was rigidly fastened to the feed frame in front of the sweep-off blade by means of two bolts. An aluminum spacer provided a clearance of approximately 1 cm. between the instrumented beam and the sweep-off blade. The assembled modified feed frame was mounted on the rotary tablet press in the usual manner (Figure 2).

Calibration of the Instrumented Beam.

Calibration is necessary to convert the oscillographic signals to force readings. It is essential to know the position at which the tablet strikes the instrumented beam. To locate this position, the modified feed frame was mounted on the tablet press. A small batch of powder was compressed manually on the tablet press by turning the flywheel by hand. The position at which the tablets strike the instrumented beam was marked. Once this position was located, the instrumented beam was disassembled from the feed frame and clamped on a horizontal platform. The beam was calibrated statically by applying known loads to the beam at the located position. The deflections corresponding to the weights were recorded on the oscillograph. The calibration data are tabulated in Table 1; each value of the deflections

FIGURE 2
Overall View of Feed Frame with Instrumented Beam

reported is an average of three determinations. Linear regression analysis using data from the trial, revealed excellent linearity over the range of forces tested with a correlation coefficient of 0.999 and a slope of 0.769 g. force per mm. of recorder stylus deflection.

TABLE 1

Calibration of Instrumented Beam

Applied Force (g.)	Attenuation	Deflection on Recorder (mm) ± S.D.*
5.00	1	6.5 ± 0.06
10.00	1	12.9 ± 0.06
20.0	2	13.0 ± 0.10
50.0	5	13.0 ± 0.15
100	10	13.0 ± 0.00
200	20	13.0 ± 0.10

*Standard deviation

Correlation coefficient = 0.999
Slope: 0.769 g/mm.
Intercept: 0.0223 g.

Correction for Angle of Approach.

Due to the geometric configuration of the instrumented beam mounted on the feed frame, the path of the tablet moving in circular motion is not perpendicular to the beam. Figure 3 illustrates the geometry of tablet sweep-off. The recorded force (f) represents the vector component of the total sweep-off force (F) which is normal to the beam and at Θ degrees from the tangential path of the tablet; the other vector component acts along the plane of the beam. Figure 4, which shows the direction of the tablet after being swept off, illustrates that the recorded force is the reaction normal to the beam. The arbitrary dimensions

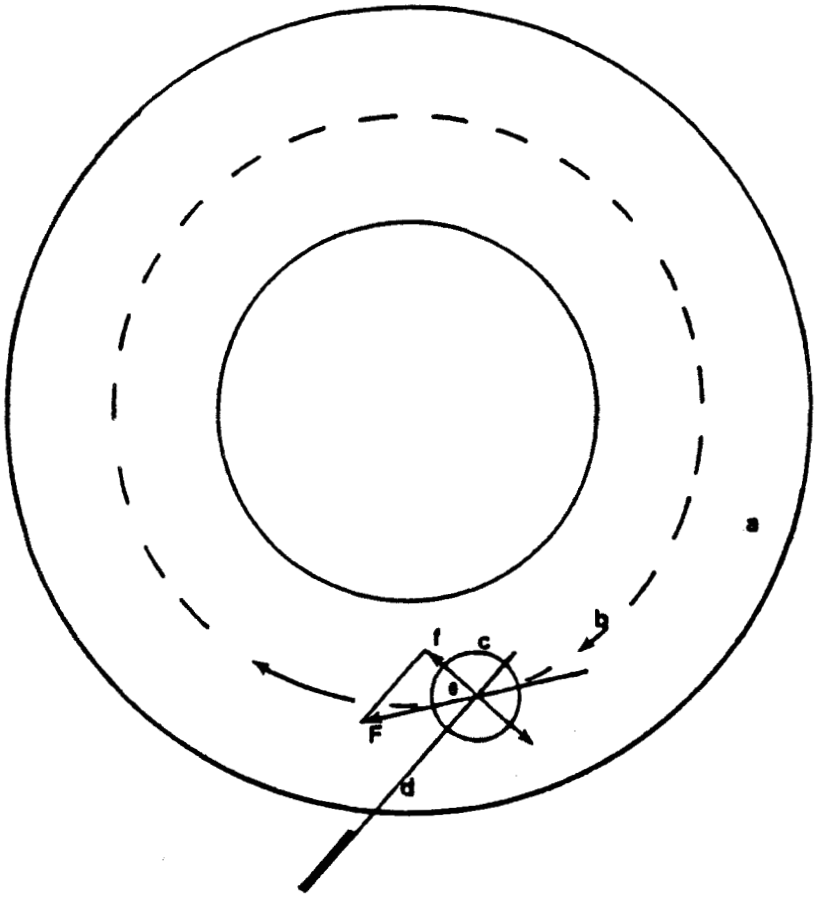

FIGURE 3
Geometry of Tablet Sweep-Off: (a) die table; (b) path of the tablet; (c) die; (d) instrumented beam; (f) force recorded at the instrumented beam; and (F) total sweep-off force = f/cos θ

of the vector components and path of the tablet were drawn and determined by the use of a vernier calliper. The angle, θ, between F and f was found to be 52 degrees. The relationship between F and f is given by the following equations:

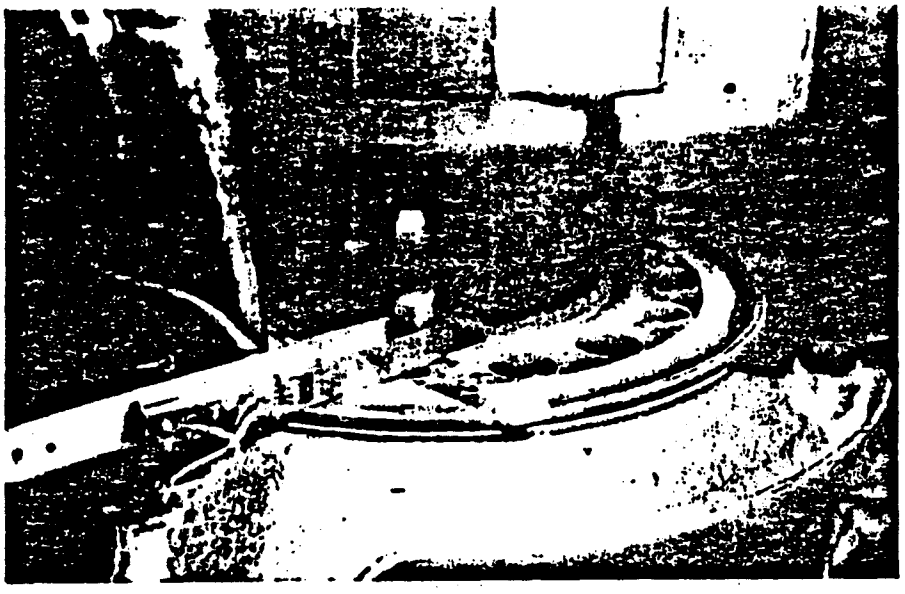

FIGURE 4
Photograph Showing the Direction of a Tablet After Being Swept Off.

$$F = f/\cos 52^{\circ} \quad (1)$$

or

$$F = 1.62\,(f) \quad (2)$$

where F is the total sweep-off or tangential force exerted by the tablet, and f is the recorded vector component which is normal to the beam.

Correction for Force Due to Tablet Momentum.

The signal detected during tableting actually represents two components of force applied to the instrumented beam. One component is due to the momentum of the tablet; the other component

is the actual force required to overcome the adhesion of the tablet to the lower punch force. To separate out the adhesion force, it was necessary to assess the contribution of tablet momentum. To this end, a series of known weights were suspended from an upper punch holder by a fine thread. The weights were arranged to strike the same position on the instrumented beam as a tablet being swept from the lower punch face. With the tablet press running at its operating speed of 24 RPM. (which was kept constant throughout this study), the force due to the momentum of these weights was recorded on the oscillograph. The suspended weights tended to sway slightly from the target position because of the centrifugal force. Only the signals obtained when the weights collided with the target position were taken into consideration. The data are tabulated in Table 2. Each value is a mean of ten determinations. From linear regression, this

TABLE 2

Correction for Force Due to Tablet Momentum

Suspended Weight (g.)	Recorded Force (g.) ± S.D.*
1.00	4.6 ± 0.10
2.00	9.2 ± 0.10
5.00	23.1 ± 0.55
10.00	46.2 ± 0.75

*Standard deviation

Correlation coefficient = 0.999
Slope: 4.62 g/g. suspended weight
Intercept: -0.0306

force was related to tablet weight as follows:

$$F_m = 4.62w-0.03 \quad (3)$$

where F_m is the force due to the momentum of the tablet in g. and w. is tablet weight in g. Thus, the adhesion force was given by:

$$F_A = F - 1.62\ F_m \quad (4)$$

or

$$F_A = 1.62\ (f-4.62w+0.03) \quad (5)$$

where F_A is the adhesion force in g., f is the force measured in g. at the instrumented beam, and w is tablet weight in g. The force exerted by 1 g. suspended weight was found to be slightly less than that obtained from a 1 g. weight sitting on the die tablet at the same position where the tablet should be (4.59 g. vs. 4.79 g.). This difference is likely due to friction between the weight and the die table.

The instrumented beam has a capability to measure a force (f) of up to 120 g. (equivalent to the total sweep-off force (F) of 194 g.) before the instrumented beam bends back enough to touch the sweep-off blade. The maximum measurable adhesion force (F_A) will be determined by tablet weight.

In all subsequent studies, compression, ejection, and adhesion events were simultaneously and continuously recorded on oscillographic recorders.

Preparation of Tablets.

The direct compression fillers used in these studies were microcrystalline cellulose, N.F.[1], lactose, U.S.P.[2], and compressible sugar, U.S.P.[3]

To promote good blending and uniform dispersion, magnesium stearate was passed through an 80 mesh screen before blending with direct compression fillers. All batches were of 500 grams except for the microcrystalline cellulose blends, which were 300 grams. In each case the lubricant and filler were blended in a 1.89L twin shell blender (Liquids-Solids Blender, P-K #LB-3794, Patterson-Kelly Co., East Stroudsburg, PA) for 15 minutes. The intensifier bar was run during the final three minutes to insure efficient distribution of the lubricant. Unless otherwise specified, the same lot of magnesium stearate, U.S.P.[4] was used in all studies.

Flat-faced circular 1.111 cm. punches were used in all cases except in the experiment where punch diameter was varied. Only a single station was used to avoid possible tooling errors. As previously mentioned, press speed was held at 24 RPM in all studies.

At the beginning of each experiment approximately 50 tablets were run at a high compression load in order to condition the die wall. During the experiment 10 tablets were compressed at each force range before 20 readings were taken. The tablet thickness was measured with a micrometer calliper immediately after ejection. After each experiment the punches and die were cleaned with hot water and dried with soft tissue paper soaked with acetone. The tablet hardness was determined on a Schleuniger (Heberlein) Hardness Tester (Model 2E/106, Series 7203, Key Industries, Farmingdale, NY.) 24 hours after the tablets had been

made. The reported values of each parameter (e.g. ejection force and adhesion force) represent the means of 20 readings except for tablet hardnesses which are the means of 10 determinations. The experiments were performed in a controlled humidity area (50 percent ± 10 percent relative humidity) where temperature was maintained at 25° ± 2° Celsius.

Effect of Compression Force.

Usually, ejection force and the tablet hardness increase with increased compression force. It was the purpose of this study to see if the compression force similarly affected the adhesion.

This study included three direct compression fillers: microcrystalline cellulose, lactose, and compressible sugar. Each sample was lubricated with 0.50% w/w magnesium stearate and compressed at six compression forces. The tablet target weight for all blends was 400 mg. With the microcrystalline cellulose blend, the tablets were compressed with forces up to 472 kg. at which lamination occurred. With lactose and compressible sugar, the compression forces were varied up to 944 kg.

Effect of Lubricant Concentration.

Increases in true lubricant concentration have been found to reduce the friction at tablet-die wall interface, thus, resulting in decreased ejection forces. It was the objective of this study to investigate the effect of increases in lubricant concentration on tablet adhesion. Even though one study (1) has reported magnesium stearate only to be a "fair" antiadherent, it was chosen in this study because of its widespread usage in tableting.

The direct compression fillers employed in this study were microcrystalline cellulose, lactose, and compressible sugar. With microcrystalline cellulose, three levels of magnesium stearate were compared: 0.10%, 0.50%, and 1.00%. With lactose, 0.10% magnesium stearate was found to be insufficient to reduce the tablet-die wall friction; therefore, 0.50%, 0.75%, and 1.00% magnesium stearate levels were compared. With compressible sugar, 0.10% magnesium stearate was found to be too low, but 1.00% magnesium stearate was found to be too high since tablets exhibited a form of "chipping" at high compression force in which small sections of the tablet face appeared to break away near the tablet edges. Thus, only two levels of magnesium stearate were studied with compressible sugar: 0.50% and 0.75%. The compression force ranges for lactose and compressible sugar blends were 118 kg. up to 1180 kg. With microcrystalline cellulose blends, lamination was observed at all three lubricant levels; however the higher the lubricant concentration, the lower the compression force at which lamination was observed. Because of this problem the compression force ranges for microcrystalline cellulose blends were varied so that the highest compression force for each blend was the force at which lamination was observed.

Effect of Tablet Thickness.

Most parameters used to evaluate true lubricant efficiency are influenced by tablet dimensions (i.e. tablet thickness and tablet diameter). Increasing either tablet thickness or tablet diameter will result in increasing tablet-die wall friction. This

observation led to the next two studies: the effects of tablet thickness and tablet diameter on the adhesion force.

In this study, microcrystalline cellulose lubricated with 0.10% magnesium stearate was compressed at three compression forces. At each compression force, six thicknesses were evaluated. The thickness was varied by simultaneously changing die fill and compression setting. To maintain a given compression force while die fill is increased to increase tablet thickness, it is necessary to make a compensatory adjustment in compression setting.

Effect of Tablet Diameter.

As mentioned earlier, an increase in tablet dimensions will cause an increase in tablet-die wall friction due to the increased tablet-die wall area of contact. However, adhesion force is expected to depend on the area of contact with the punch face. The area of contact between the tablet and the lower punch face will depend on the size and shape of the tooling, but not the tablet thickness. Thus, this study is designed to investigate the influence of tablet diameter on the adhesion of flat faced tablets.

Only the microcrystalline cellulose blend containing 0.10% magnesium stearate was studied. Tablets were prepared using circular flat faced punches with diameter of 0.794 cm., 1.111 cm., and 1.588 cm. Tablet thickness was held constant at 0.264 cm. $\pm$ 0.003 cm. Adhesion forces were measured at at least five compression forces.

Comparison of Different Grades of Magnesium Stearate.

In a preliminary study, three grades of magnesium stearate were evaluated and compared in terms of adhesion force, ejection force

and compressibility in microcrystalline cellulose. These were magnesium stearate, regular[5]; magnesium stearate EA (food grade)[5]; and, magnesium stearate, dense[5]. Each grade was assayed for magnesium oxide equivalent and loss on drying using U.S.P. procedures. The results shown in Table 3 indicated that all three samples met U.S.P. requirements for both magnesium oxide equivalent and loss on drying.

Only one concentration (0.10% w/w) of magnesium stearate was studied. Tablet target weight was 400 mg. and the tablets were compressed at six different compression forces.

RESULTS AND DISCUSSION

In this study, the adhesion of tablets to the lower punch face was determined from measurements of tablet sweep-off force by attaching a force sensitive cantilever beam to the feed frame in front of and parallel to the sweep-off blade. This design permitted the direct measurement of the sweep-off force in a manner which required minimal modification to the machine and which did not interfere with normal machine operation.

A typical sweep-off tracing is shown in Figure 5. Tracing A, obtained from the oscillographic recorder at a chart speed of 2.5 mm./sec., was the result of multiple sweep-off events. In most cases in this study the relative standard deviation was within the range of 1.00% to 6.00%. Tracing B represents a single sweep-off event as displayed on an oscilloscope.

Effect of Compression Force.

The effect of compression force on adhesion force and unit ejection force are given in Figures 6 and 7, respectively.

TABLE 3

Magnesium Oxide Equivalent and Loss on Drying of Different Grades of Magnesium Stearate

Sample	Magnesium Oxide Equivalent (%)			Loss on Drying (%)		
	Trial 1	Trial 2	Average	Trail 1	Trial 2	Average
Magnesium Stearate, Regular	7.47	7.06	7.27	3.98	3.92	3.95
Magnesium Stearate, Dense	7.56	7.66	7.61	3.14	3.05	3.10
Magnesium Stearate, EA (Food Grade)	7.27	7.36	7.32	3.51	3.52	3.52

NOTE: Magnesium stearate U.S.P. contains the equivalent of not less than 6.8 percent and not more than 8.0 percent of magnesium oxide. Loss on drying is not more than 4 percent.

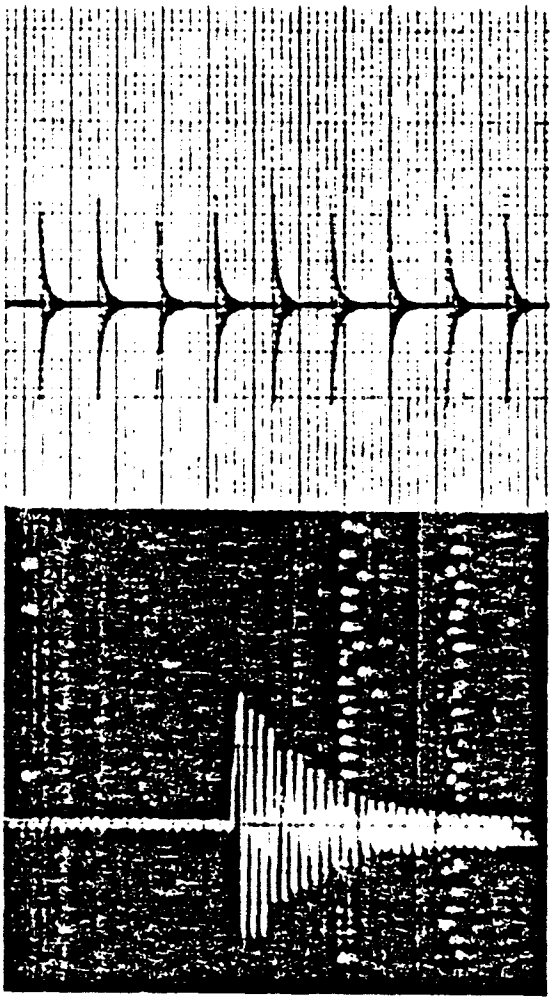

FIGURE 5
Sweep-Off Tracing From Instrumented Beam. A. From Oscillographic Recorder; B. From Oscilloscope.

Generally, the higher the compression force, the higher the adhesion force. This observation confirms the earlier findings of Ritter and coworkers (11). The increased adhesion is apparently due to a greater reaction at the lower punch. As the

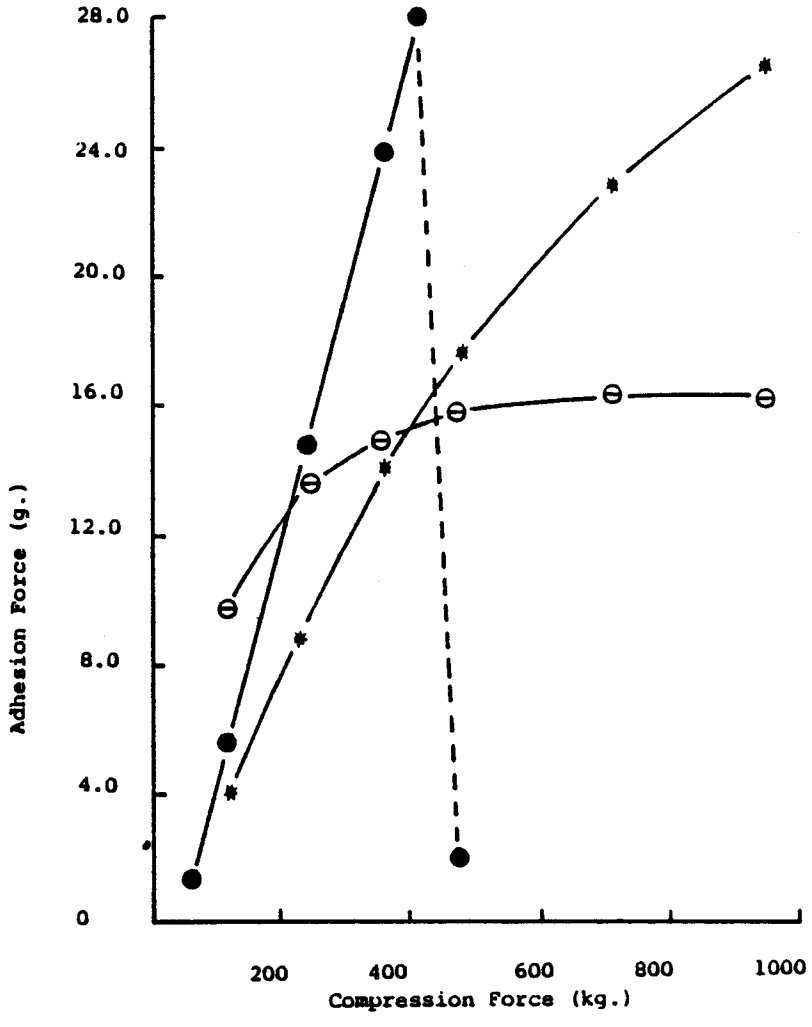

FIGURE 6
Effect of the Compression Force on the Adhesion Force of Tablets Containing 0.50% Magnesium Stearate. ● Microcrystalline Cellulose; ✱ Lactose; ⊖ Compressible Sugar. (The broken line links results obtained from laminated tablets.)

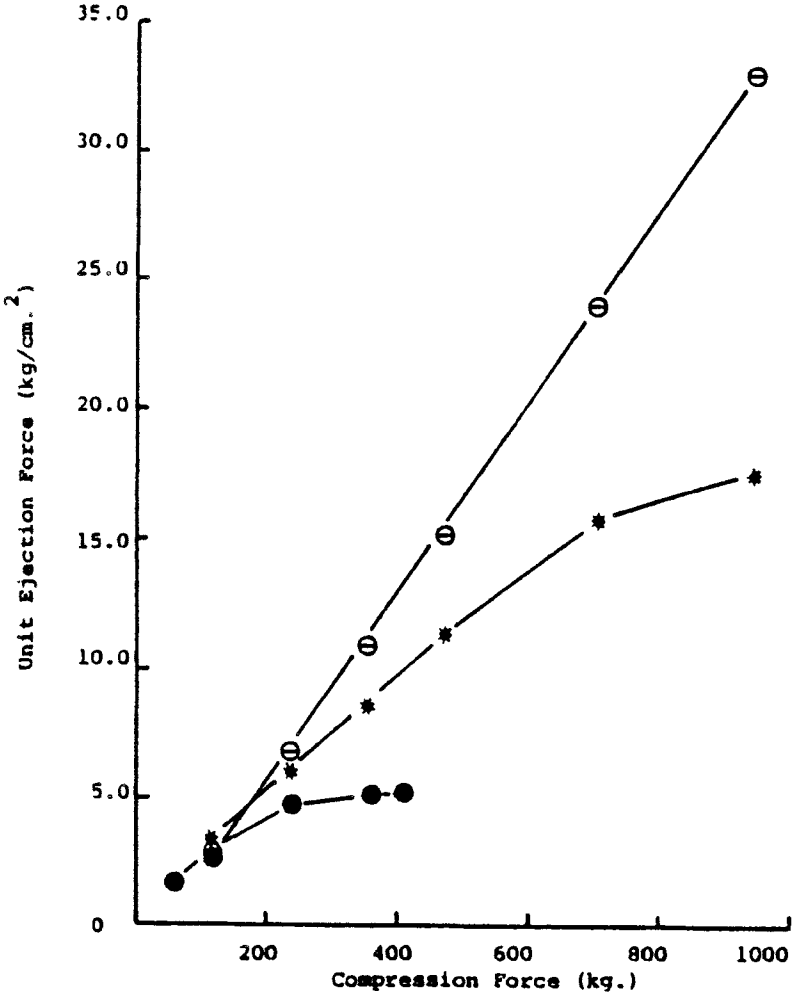

FIGURE 7
Effect of Compression Force on the Unit Ejection Force of Tablets Containing 0.50% Magnesium Stearate. ● Microcrystalline Cellulose; ✱ Lactose; ⊖ Compressible Sugar.

compression force was increased, the binding strength between the tablet and lower punch would be expected to increase as well.

At lower compression foces (< 200 kg.) compressible sugar exhibited greater adhesion than either lactose or microcrystalline cellulose; at higher compression forces, the order of adhesion was microcrystalline cellulose > lactose > compressible sugar. Because the lubricant level was the same in all batches (0.50%), the differences of adhesion between fillers must be due both to differences in specific filler interactions at the tablet-punch interface and to differences in the state of lubrication at the interface due to differences in filler specific surface area.

Lactose tablets showed a pattern of increased adhesion force with compression force similar to that of compressible sugar tablets. However, with lactose the adhesion force did not reach a maximal value within the range of compression force studied. With microcrystalline cellulose, the relationship of adhesion force and compression force was linear up to about 400 kg. Beyond this compression force, the adhesion force could not be properly measured because of tablet lamination. Holzer and Sjogren (14) reported that microcrystalline cellulose caused a larger remaining force on the lower punch (REF) at low compression forces than at higher compression forces. The lower REF at higher compression forces was attributed to elastic axial expansion with corresponding radial contraction which probably reduced the radial force. In addition, Shotton and Obiorah (15,16) also reported that materials which develop low die wall pressure were prone to

cap or laminate. Thus, the lamination of microcrystalline cellulose tablets at high compression forces may very well be due to axial elastic recovery and concomittant weakening or rupture of interparticulate bonds within the tablet. Because the degree of lamination in each tablet was not the same, the adhesion of laminated tablets tended to vary to a greater degree than in other runs, as shown by a relatively high relative standard deviation of 9.52%.

The increase in adhesion strength with compression force may be interpreted in terms of the classic model for adhesion (17, 18) and tableting physics. According to the model, the microstructure of even the smoothest surfaces consists of irregularities and jagged asperities. As a result, two surfaces brought into contact will touch only in isolated regions. Thus, the true area of contact is much less than the apparent area. As surfaces are brought together, the pressure is extremely large at the initial points of contact and deformation occurs. This deformation causes an increase in the true area of contact which continues until the local pressure falls to the yield pressure of the softer material. It is at the true area of contact where surface forces such as atomic, molecular or electrostatic forces can have sufficient influence to produce a stable structure such as tablet or cause adhesion of surfaces. Thus, the mechanical strength of the tablet and any bonds formed between the tablet and confining surfaces such as the punch faces will be dependent both on the quality of the attractive forces and the area over which they act.

These two properties are, in turn, clearly dependent upon both the nature of the materials involved and the compacting load.

This is true even though the opportunity exists for the lower punch to actually fall away from the tablet surface after compression. The potential area of contact which is re-established as the punch rides up the ejection cam is greater by virtue of the higher compressive load.

The ejection force data for these runs appear in Figure 7. The unit ejection force (ejection force per unit apparent area of tablet-die wall contact) increased with compression force, as expected. Of the three fillers, compressible sugar showed the highest unit ejection forces in these runs. As anticipated, microcrystalline cellulose exhibited the lowest unit ejection forces.

Effect of Lubricant Concentration.

An increase in lubricant concentration results in the increased number of lubricant particles not only throughout the tablet, but at the surface as well. Therefore, tablet adhesion should be expected to decrease with increasing lubricant concentration.

The effect of magnesium stearate on the adhesion forces of microcrystalline cellulose, lactose, and compressible sugar are summarized in Figures 8-10. As expected, the adhesion forces of all three direct compression fillers decreased with increases in magnesium stearate concentration.

With microcrystalline cellulose , tablet lamination was observed at all three lubricant levels (0.10%, 0.50%, and 1.0%

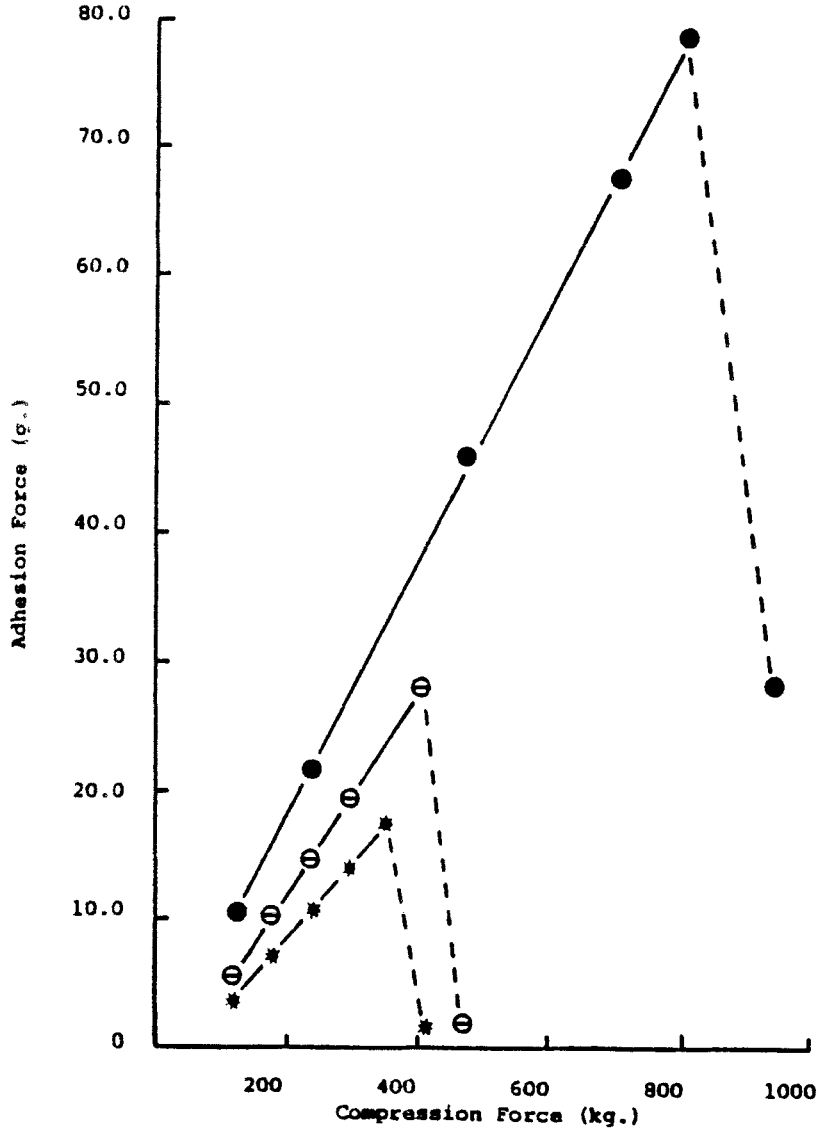

FIGURE 8
Effect of Magnesium Stearate Concentration on the Adhesion Force of Microcrystalline Cellulose Tablets. ● 0.10%; ⊖ 0.50%; ✱ 1.0%.

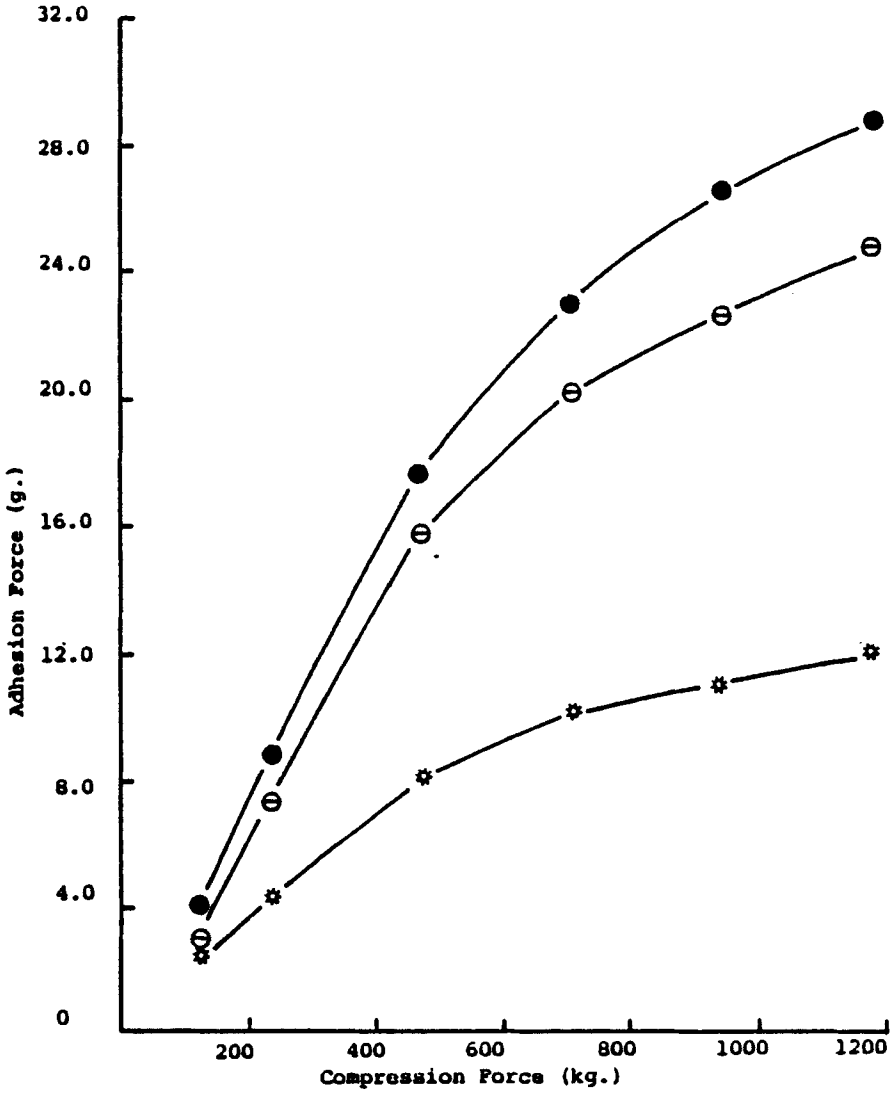

FIGURE 9
Effect of Magnesium Stearate Concentration on the Adhesion Force of Lactose Tablets. ● 0.50%; ⊖ 0.75%; ✲ 1.0%.

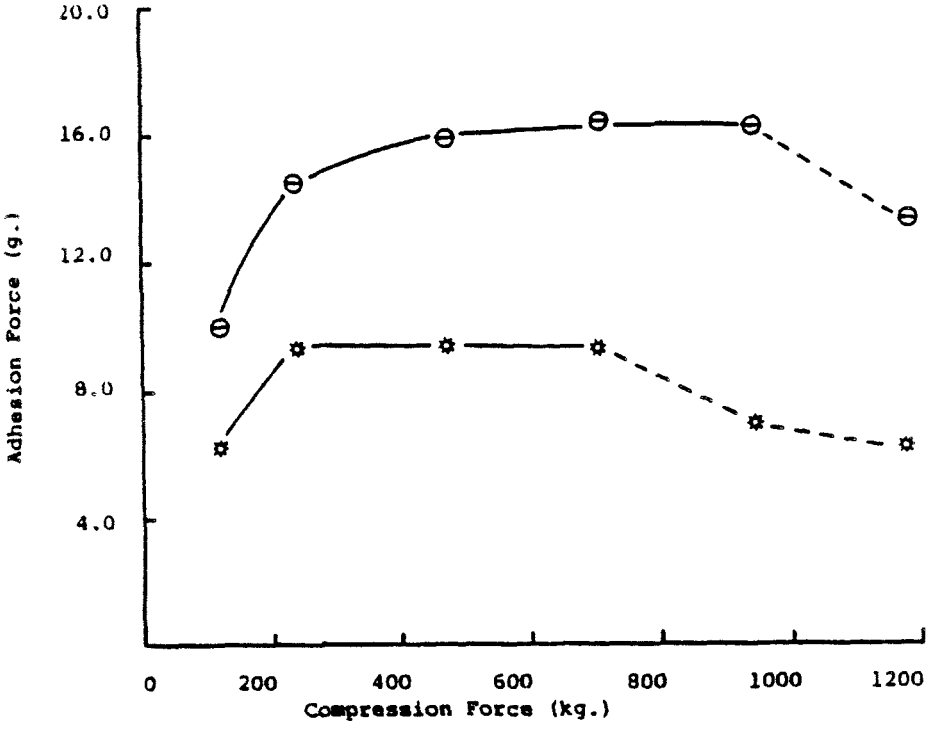

FIGURE 10
Effect of Magnesium Stearate Concentration on the Adhesion Force of Compressible Sugar Tablets. ⊖ 0.50%; ✡ 0.75%. (The broken lines link results obtained from chipped tablets.)

magnesium stearate); however, the higher the lubricant concentration, the lower the compression force at which lamination was observed. This is consistent with the fact that lubricants interfere with tablet bonding.

With lactose, the adhesion force tended to reach a limiting value at higher compression forces; however, the higher the magnesium stearate level, the sooner this limiting value was reached. With compressible sugar, the adhesion force increased

and reached equilibrium at relatively low compression forces, i.e., 236 kg. at 0.50% magnesium stearate and 472 kg. at 0.75% magnesium stearate. At both magnesium stearate concentrations, tablet chipping was observed at high compression forces. Tablet chipping causes a change in tablet face characteristic; thus, the adhesion force could not be properly measured at those compression forces.

More important, was the observation that differences in antiadhesion efficiency could not be inferred from differences in true lubricant activity, as reflected in unit ejection force, in these formulations. For instance, with microcrystalline cellulose, adhesion forces at 0.10% magnesium stearate were about double those at 0.50% magnesium stearate and more than twice as those at 1.0% magnesium stearate in the range of compression forces up to that at which lamination occurred. However, unit ejection forces (Figure 11) were about the same at 0.10% magnesium stearate and 0.50% magnesium stearate and only about 10% greater at 0.10% magnesium stearate than at 1.0% magnesium stearate. Similarly, large differences in adhesion force were observed in the lactose batches (0.50% and 1.0% magnesium stearate) and in the compressible sugar batches (0.50% and 0.75% magnesium stearate) whereas it was not possible to distinguish these lubricant levels on the basis of unit ejection force with these fillers (Figures 12 and 13).

Effect of Tablet Thickness.

For a given thickness, adhesion force increased, as expected, with each increase in compression force (Figure 14). However,

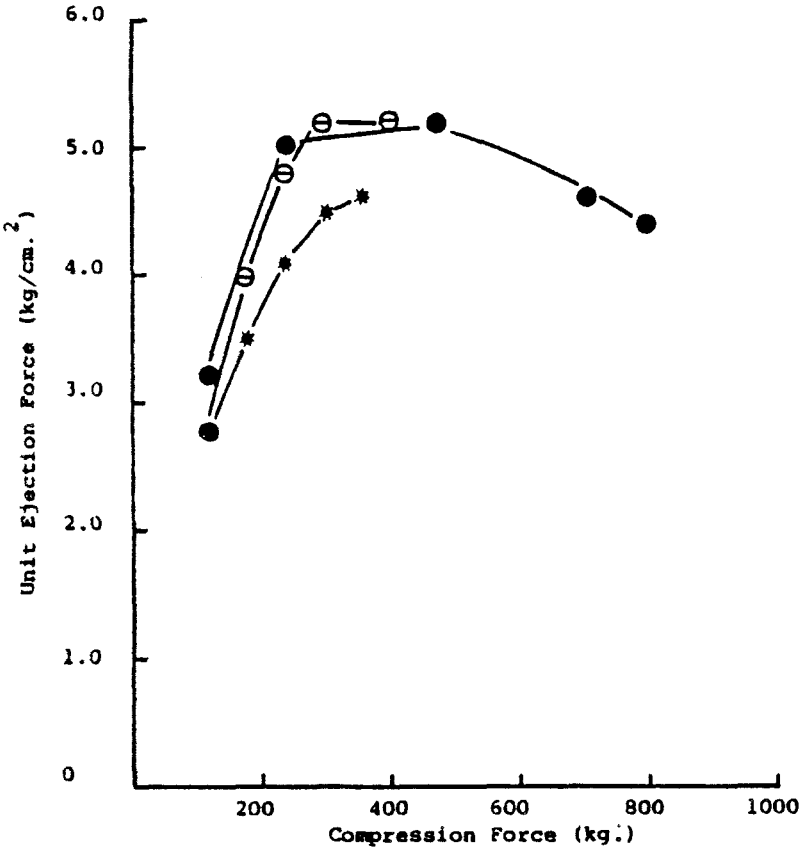

FIGURE 11
Effect of Magnesium Stearate Concentration on the Unit Ejection Force of Microcrystalline Cellulose Tablets.
● 0.10%; ⊖ 0.50%; * 1.0%.

at a given compression force, increases in thickness resulted in reduced adhesion. One contributing factor to these results may be derived from a consideration of punch travel in the rotary press. As die fill was increased to increase tablet thickness, it was necessary to make a compensatory adjustment in compression setting to maintain a given compression force. In this press,

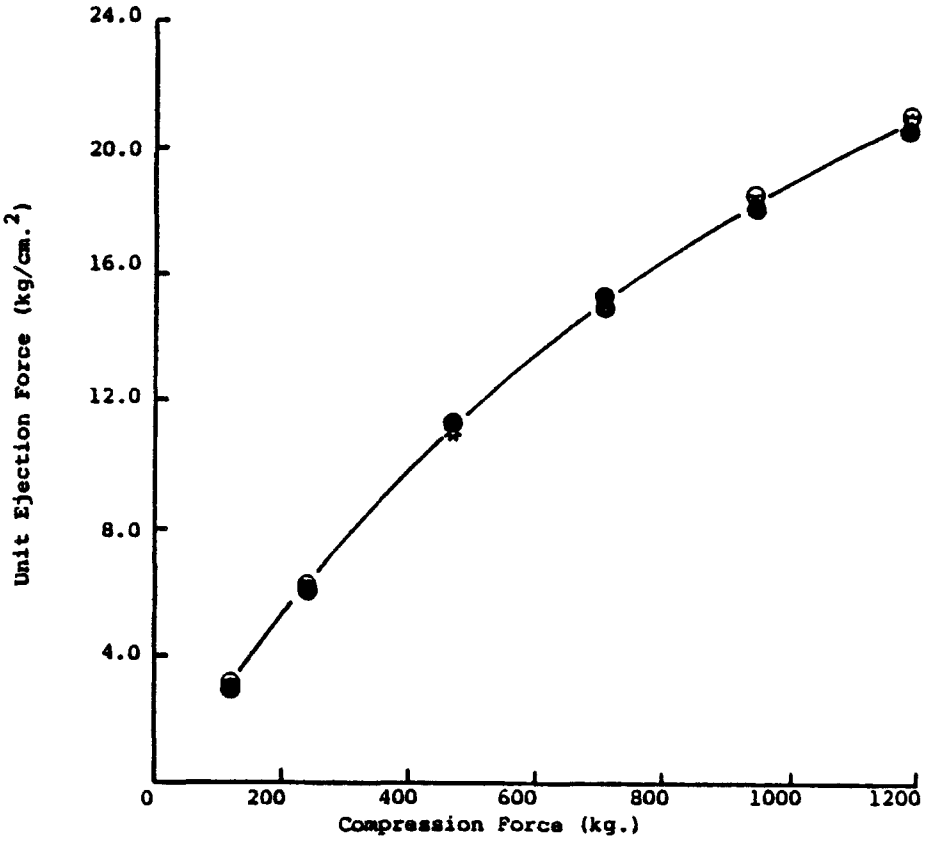

FIGURE 12
Effect of Magnesium Stearate Concentration on the Unit Ejection Force of Lactose Tablets. ● 0.50%; ⊖ 0.75%; ✲ 1.0%.

this was accomplished by lowering the lower compression roller each time the tablet thickness was increased. This means that at each increase in thickness, the lower punch traveled over a shorter segment of the roller circumference, thereby resulting in shorter penetration times. With a relatively plastic material such as microcrystalline cellulose (19), this may well lead to

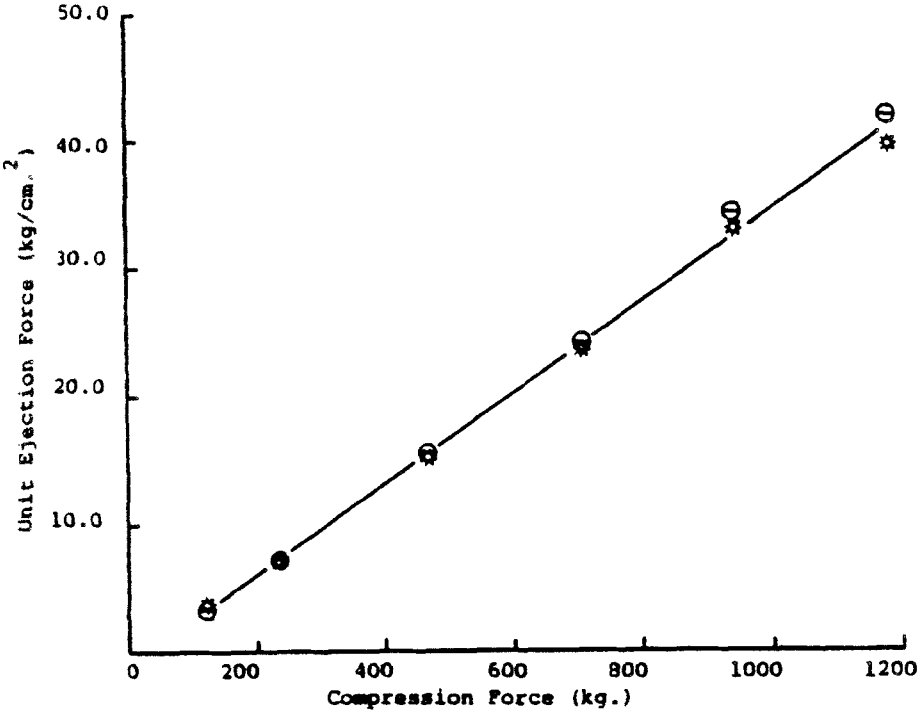

FIGURE 13
Effect of Magnesium Stearate Concentration on the Unit Ejection Force of Compressible Sugar Tablets. ⊖ 0.50%; ✡ 0.75%.

reduced true areas of contact and correspondingly weaker bonding at the punch face. Another possible contributing factor is suggested by the work of Shotton et al. (20). These investigators reported lower punch forces to be about 90% of the upper punch forces over a wide range of mean compression forces for two materials (sodium chloride and aspirin) in a similar rotary press. Die fill was maintained constant in this study. These investigators argued that the system must be balanced by a force at the die wall acting in an upward direction and derived from the

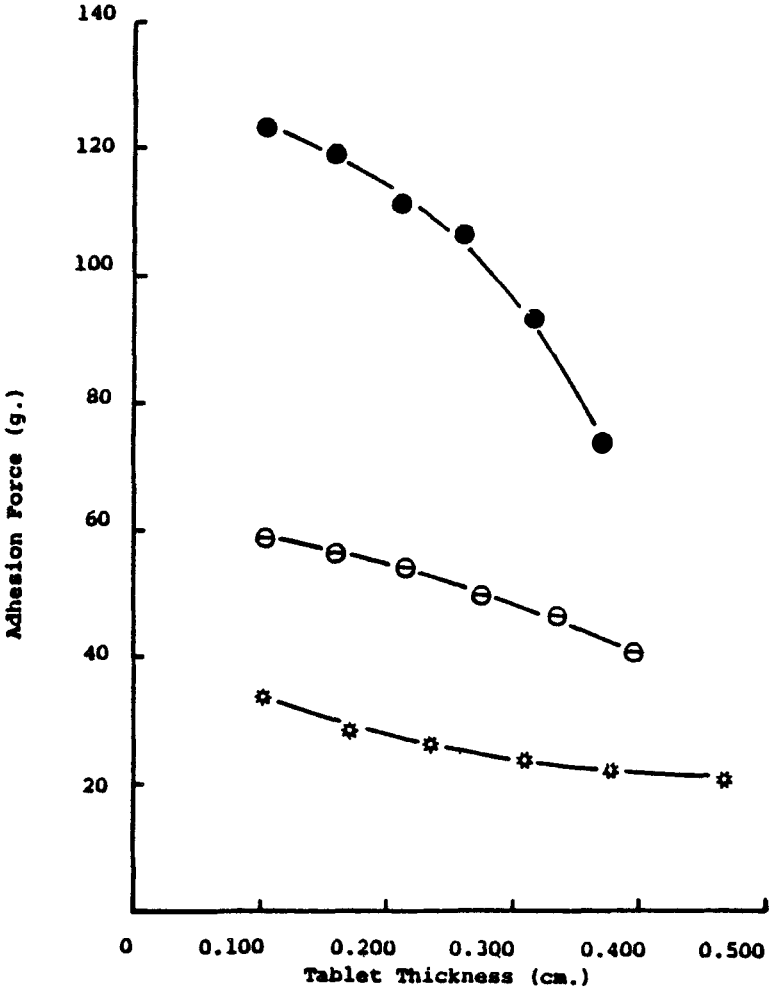

FIGURE 14
Effect of Tablet Thickness on the Adhesion Force of Microcrystalline Cellulose Tablets Containing 0.10% Magnesium Stearate. Compression Force, ✲ 236 kg.; ⊖ 472 kg.; ● 885 kg.

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. It is likely that increases in tablet thickness would result in increases in this frictional reaction of the die wall. Since in the present study the compression force was found to be constant at the upper punch face over the entire range of tablet thickness tested, there may well be a reduced reaction at the lower punch face with each increase in tablet thickness.

The effect of tablet thickness on ejection force (Figure 15) was opposite to that on adhesion force. The ejection force increased with increases in tablet thickness at all three compression forces tested. This is simply due to the increased friction at tablet-die wall interface. However, ejection forces obtained at the compression forces of 236 kg. and 472 kg. were similar and higher than those obtained at the compression force of 885 kg. The decreased ejection force at high compression force may be due to microcrystalline cellulose undergoing elastic axial expansion with corresponding radial contraction which probably reduces friction between the tablet and die wall, as reported by Holzer and Sjogren (14). Plots of unit ejection force vs. tablet thickness (Figure 16) clearly show that unit ejection force (ejection force/unit apparent area of tablet-die wall interface) is independent of tablet thickness.

Effect of Tablet Diameter

Adhesion forces were measured at six compression pressures except in the case of the 1.588 cm. tablets which were measured

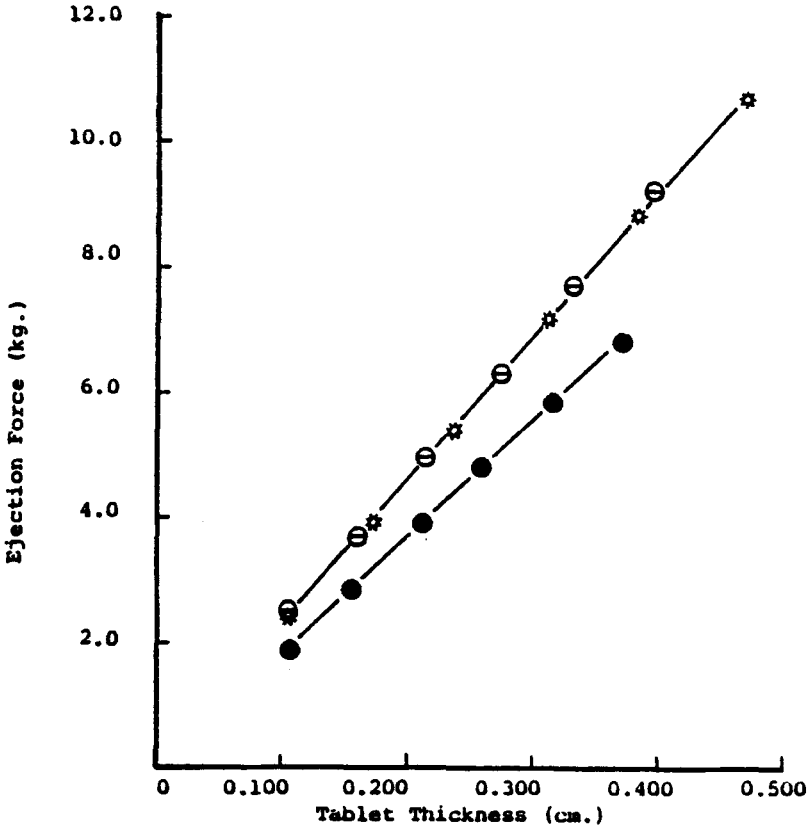

FIGURE 15
Effect of Tablet Thickness on the Ejection Force of Microcrystalline Cellulose Tablets Containing 0.10% Magnesium Stearate. Compression Force, ✲ 236 kg.; ⊖ 472 kg.; ● 885 kg.

at five compression pressures. The adhesion force of the 1.588 cm. tablets exceeded the capacity of the measuring device at high compression pressure. The results are shown in Figure 17. The adhesion forces obtained with 1.588 cm. diameter tooling were the highest, while those obtained with 0.794 cm. diameter tooling were the lowest for the range of compression pressures

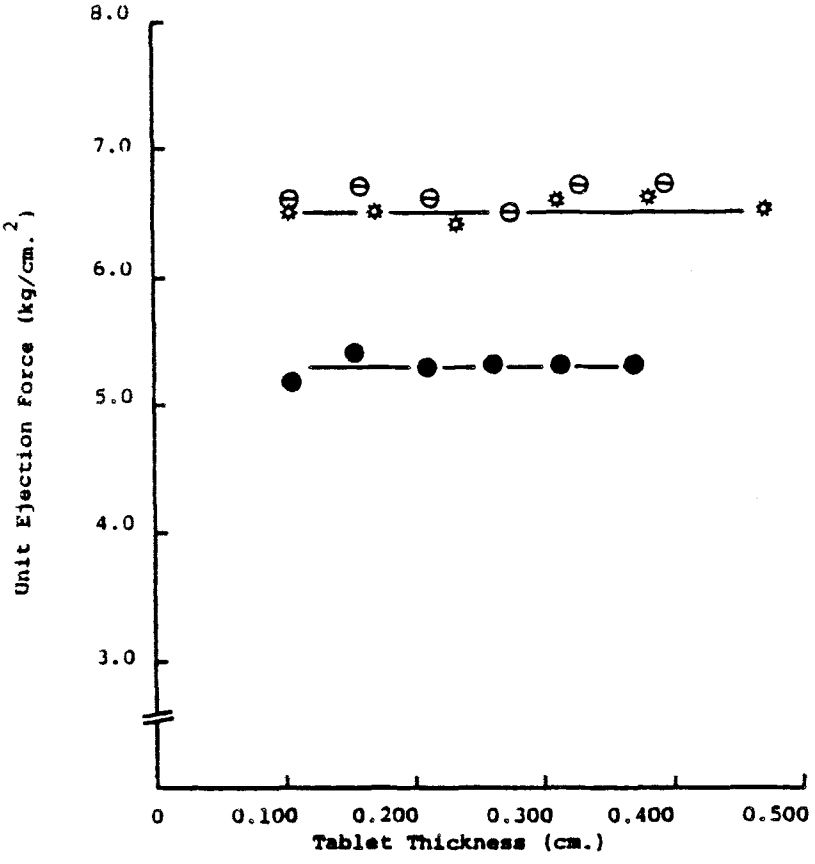

FIGURE 16
Effect of Tablet Thickness on the Unit Ejection Force of Microcrystalline Cellulose Tablets Containing 0.10% Magnesium Stearate. Compression Force, ✡ 236 kg.; ⊖ 472 kg.; ● 885 kg.

tested. Adhesion, as expected, appeared to be a function of apparent area of contact with the punch face since for a given compression pressure, the larger the diameter, the greater the adhesion. However, when unit adhesion force (adhesion force/unit area of punch face) was plotted against compression pressure

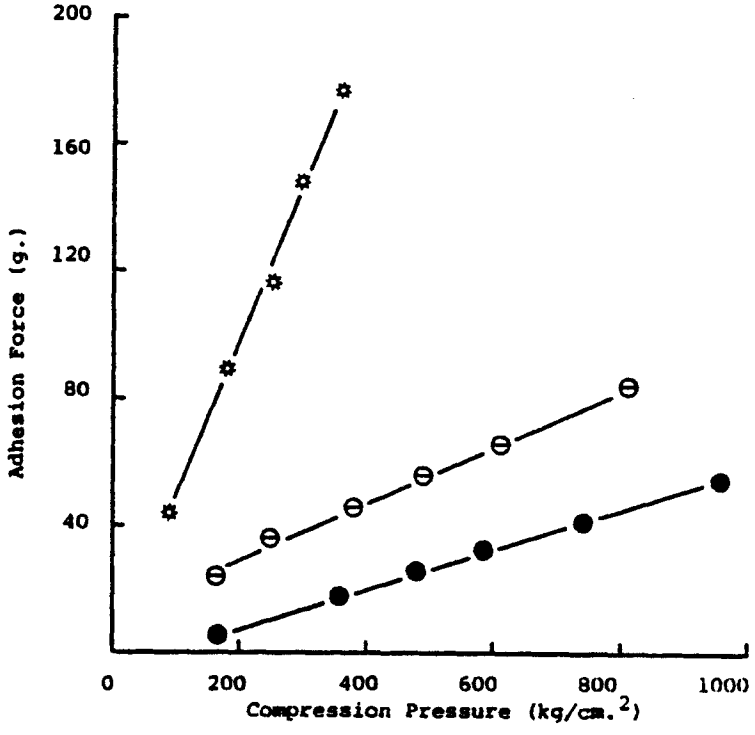

FIGURE 17
Effect of Tablet Diameter on the Adhesion Force of Microcrystalline Cellulose Tablets Containing 0.10% Magnesium Stearate. Tablet Diameter, ● 0.794 cm.; ⊖ 1.111 cm.; ✡ 1.588 cm.

(Figure 18), the same order of adhesion emerged, but there were some changes in the relative slopes and there was less distinction between the 1.111 cm. and 0.794 cm. tablets. Possibly the differences between the unit adhesion force plots and the total adhesion plots are due to the fact that stress is not uniformly distributed over the face of a tablet during compression (21).

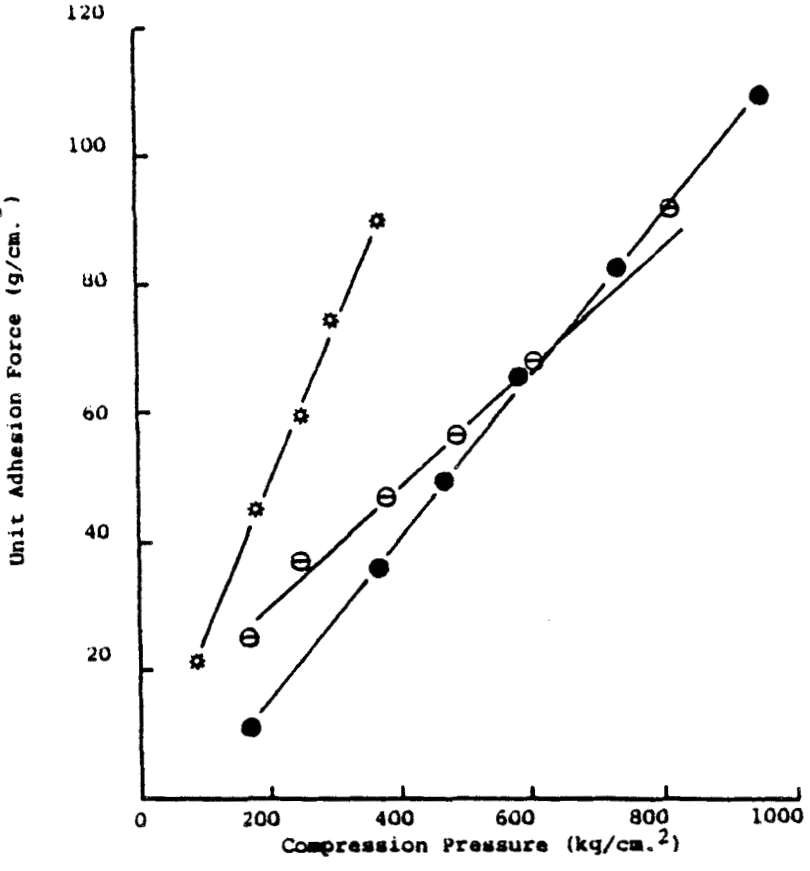

FIGURE 18
Effect of Tablet Diameter on the Unit Adhesion Force of Microcrystalline Cellulose Tablets Containing 0.10% Magnesium Stearate. Tablet Diameter, ● 0.794 cm.; ⊖ 1.111 cm.; ✡ 1.588 cm.

Corresponding plots of unit ejection force vs. compression pressure (Figure 19) were similar although not identical for the three tablet diameters.

Comparison of Different Grades of Magnesium Stearate.

The three grades of magnesium stearate compared were produced by the same manufacturer and claimed (22) to have the same specific

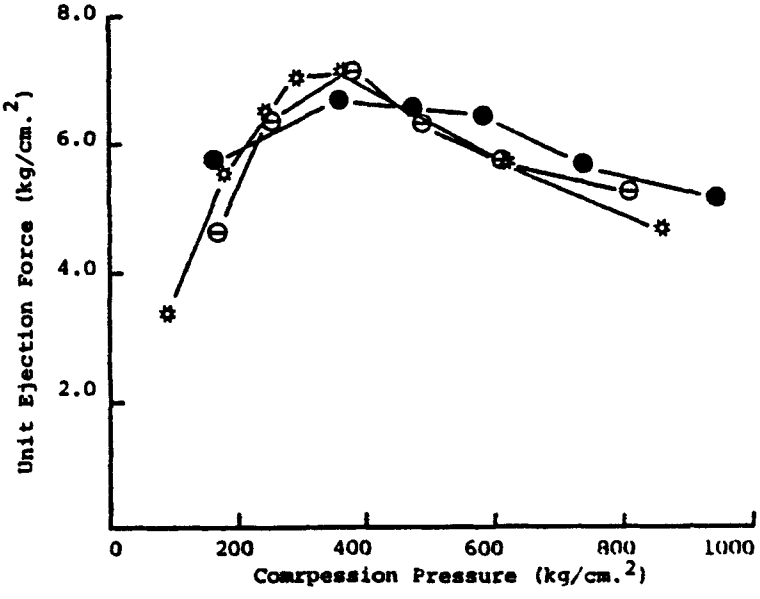

FIGURE 19
Effect of Tablet Diameter on the Unit Ejection Force of Microcrystalline Cellulose Tablets Containing 0.10% Magnesium Stearate. Tablet Diameter, ● 0.794 cm.; ⊖ 1.111 cm.; ✡ 1.588 cm.

gravity (1.03) and particle size specification of 99.9% through 325 mesh U.S. standard sieve except magnesium stearate, dense which was claimed 100% through 200 mesh U.S. standard sieve. Although these samples were not claimed to meet U.S.P. specifications, they were found to meet the U.S.P. loss on drying and magnesium oxide equivalent requirements.

The results are illustrated in Figures 20-22. Also included in these figures are similar data obtained in the foregoing experiments using a U.S.P. magnesium stearate obtained from a different supplier. The magnesium stearate, regular and magnesium stearate,

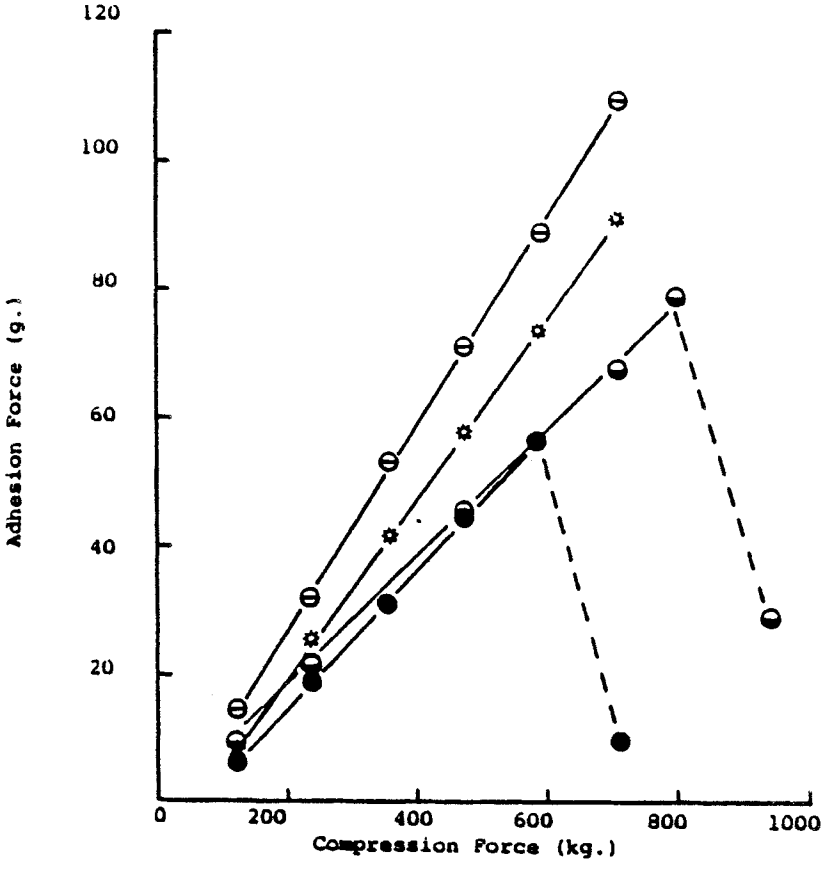

FIGURE 20
Effect of Different Grades of Magnesium Stearate on the Adhesion Force of Microcrystalline Cellulose Tablets Containing 0.10% Lubricant. ● Magnesium Stearate, Regular; ⊖ Magnesium Stearate, Dense; ✡ Magnesium Stearate, EA (Food Grade); ◒ Magnesium Stearate, U.S.P. (The broken lines link results obtained from laminated tablets.)

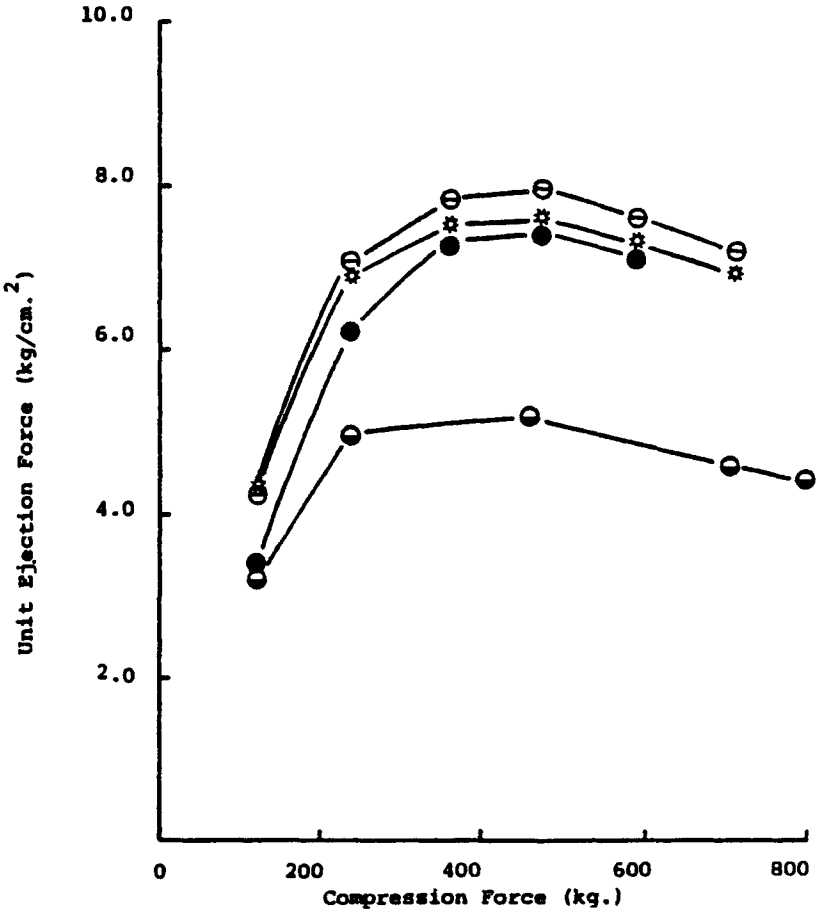

FIGURE 21
Effect of Different Grades of Magnesium Stearate on the Unit Ejection Force on Microcrystalline Cellulose Tablets Containing 0.10% Lubricant. ● Magnesium Stearate, Regular; ⊖ Magnesium Stearate, Dense; ✡ Magnesium Stearate, EA (Food Grade); ⊖ Magnesium Stearate, U.S.P.

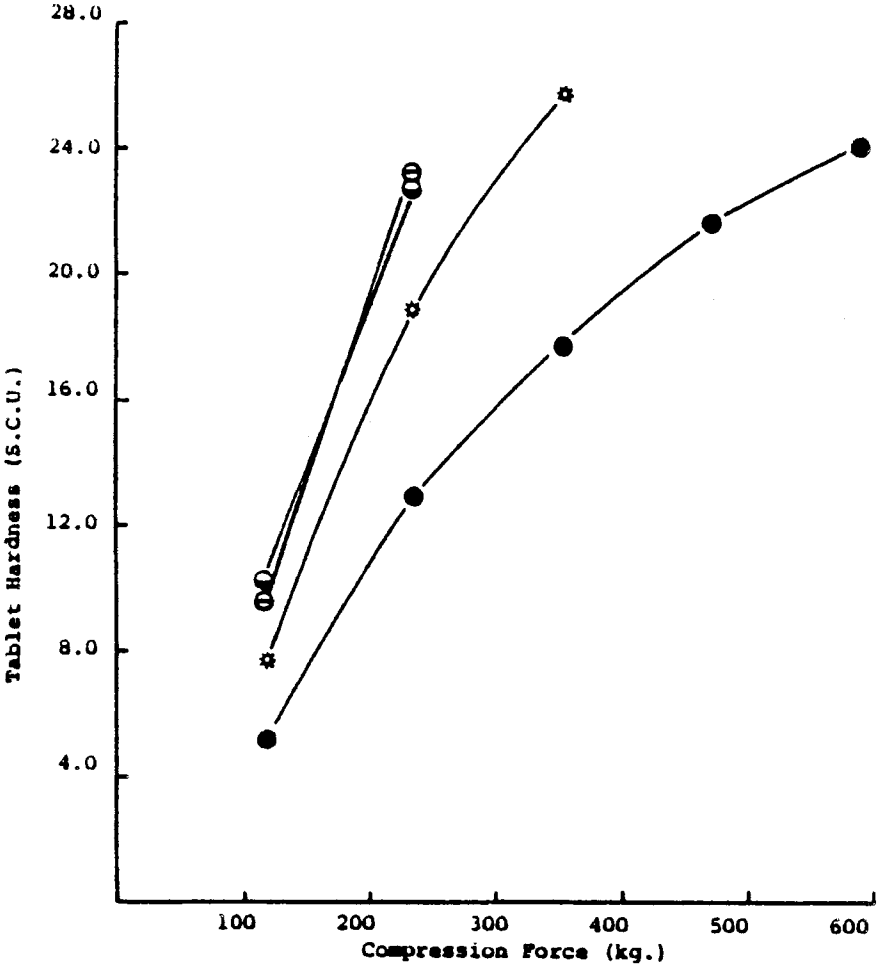

FIGURE 22

Effect of Different Grades of Magnesium Stearate on the Compressibility of Microcrystalline Cellulose Tablets Containing 0.10% Lubricant. ● Magnesium Stearate, Regular; ⊖ Magnesium Stearate, Dense; ✡ Magnesium Stearate, EA (Food Grade); ◒ Magnesium Stearate, U.S.P.

U.S.P. batches showed tablet lamination at about 600 kg. and 800 kg. compression forces respectively. The batch containing magnesium stearate, U.S.P. showed greater adhesion than either magnesium stearate EA (food grade) or magnesium stearate, regular at low compression force. However, the adhesion forces at higher compressio forces of magnesium stearate, U.S.P. and magnesium stearate, regular were not significantly different prior to lamination. At higher compression forces, the order of adhesion was magnesium stearate, dense > magnesium stearate EA (food grade) > magnesium stearate, regular and magnesium stearate, U.S.P.

Figure 21 shows the plots of unit ejection force vs compression force. Despite the similar adhesion, magnesium stearate, U.S.P. resulted in much lower unit ejection forces than those of magnesium stearate, regular at any given compression force tested except the first one which was less different. The order of unit ejection force was magnesium stearate, dense > magnesium stearate EA (food grade) > magnesium stearate, regular > magnesium stearate, U.S.P. Although significant differences were found in unit ejection force in the range of compression forces tested the differences were quite small for all three samples. However, the differences in adhesion were quite distinctive.

The compressibility results are shown in Figure 22. Although the magnesium stearate, U.S.P. batch exhibited the lowest unit ejection forces among the four samples tested, it also exhibited the highest compressibility, along with the magnesium stearate, dense batch. The tablets from both of these batches had hardnesses

greater than 28 S.C.U. at about the compression force of 300 kg. The order of compressibility was magnesium stearate, U.S.P. and magnesium stearate, dense > magnesium stearate EA (food grade) > magnesium stearate, regular. It is not possible to separate out exactly why these four samples of magnesium stearate perform as they do without more detailed information on the differences in their physicochemical properties.

SUMMARY AND CONCLUSIONS

The adhesion of tablets to the lower punch face was determined from measurements of tablet sweep-off force. This force was measured by means of a force sensitive cantilever beam attached to the feed frame in front of the sweep-off blade. This arrangement required minimal modification to the press and did not interfere with normal machine operation. Calibration took into account the momentum of the tablets and their striking angle.

Generally, the higher the compression force or the lower the magnesium stearate concentration, the higher was the adhesion force in three direct compression fillers: microcrystalline cellulose, lactose and compressible sugar. However, changes in adhesion force were not consistent with the change in unit ejection force with increased lubrication. Therefore, antiadherent activity could not be inferred from true lubricant activity. In studies with microcrystalline cellulose, increases in tablet thickness at a given compression force resulted in reduced adhesion, possibly due to differences in dwell time under compaction and/or differences in reaction at the lower punch. In addition, it was found

that increases in diameter at constant thickness resulted in increased adhesion at any given compression pressure.

Different grades of magnesium stearate were found to possess different antiadherent activity when evaluated in microcrystalline cellulose. However, it was difficult to distinguish their differences in true lubricant activity as measured by ejection force.

In summary, the instrumented cantilever beam described appears to be a sensitive tool for distinguishing differences in adhesion and shows promise in assisting in the rational design of tablet formulations.

ACKNOWLEDGEMENTS

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Presented to the IPT Section, A.Ph.A. Academy of Pharmaceutical Sciences, 26th National Meeting, Anaheim, California, April, 1979.

FOOTNOTES

1. Avicel^{R} PH 102, FMC Corporation, American Viscose Division, Newark, DE 19711
2. Fast-Flo^{R}, Foremost Dairies, Inc., San Francisco, CA 94104
3. Dipac^{R}, Amstar Corporation, Corporate Research and Development Labs., Brooklyn, N.Y. 11211
4. Amend Drug and Chemical Company, Irvington, J.J. 07111
5. Witco Chem. Co., Organics Div., New York, N.Y. 10017

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