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ASPECTS OF THE LUBRICATION REQUIREMENTS FOR AN AUTOMATIC CAPSULE FILLING MACHINE

by L.E. Small and L.L. Augsburger
Pharmacy Department
University of Maryland School of Pharmacy
Baltimore, MD 21201

ABSTRACT

Aspects of the lubrication requirements for an automatic capsule filling machine, instrumented to monitor compression and ejection forces, were studied under various filling conditions. Three common capsule fillers (compressible starch, microcrystalline cellulose, and anhydrous lactose) were filled into No. 1 gelatin capsules. Two main sets of runs were made. The first set was designed to study the influence of powder bed height, piston height and compression force on the ejection forces generated during the filling process. The second set was aimed at comparing lubricant type and levels. It was shown that the ejection force is increased by increasing the powder bed height, piston height and compression force. Compressible starch and microcrystalline cellulose required relatively low levels

of magnesium stearate as compared to anhydrous lactose. The performance of stearic acid and especially magnesium lauryl sulfate compared favorably with magnesium stearate in compressible starch.

INTRODUCTION

Since the introduction of instrumentation techniques to the tablet press[1], considerable attention has been paid to the measurement of the compression and ejection forces generated during tableting operations[2,3]. These measurements have helped guide the formulator in the choice of tablet excipients and their concentrations to produce dosage forms that are bioavailable and conform to the requirements of high speed production.

Recently, instrumentation techniques have been applied to modern, fully automatic capsule filling equipment[4,5]. In this report these techniques have been employed to study the effects of lubricant type and level on the ejection forces generated during the filling cycle of an automatic capsule filling machine (Zanasi LZ-64, USM Corp., Machinery Division, Beverly, MA) using three common capsule fillers.

The filling principles of the equipment used in this study have similarities to those of a tablet press and a lubricant is needed in the formulation for successful operation. Articles in the literature dealing with capsule formulation report levels of magnesium stearate ranging from 0.06%[6] to 15%[7]. The capsule filling methods varied in these reports.

Reier, et al.,[8] developed a mathematical model relating selected physical powder properties and machine settings to the encapsulation process employing a semiautomatic machine. However, the lubricant type and level were not variables under consideration in their model. The level of magnesium stearate was maintained throughout their experiments at 1%. Samyn and Jung[9] incorporated up to 5% magnesium stearate in hand filled capsules. Newton, et al.,[10] also added up to 5% magnesium stearate in experimental formulations filled on a manual capsule filling machine. Caldwell and Westlake[6] used fully automatic filling equipment (Zanasi LZ-164) similar to that used in this report and incorporated 0.06% magnesium stearate in lithium carbonate capsules. Stoyle[11], also using similar equipment, mentioned lubricant requirements of up to 3% using plain lactose. Khalil, et al.,[7] studied lubricant levels of up to 15% magnesium stearate in chloramphenicol formulations filled on a semiautomatic machine.

Generally, the rationale for the determination of the lubricant level is not given. Newton and Razzo[12] stated that a lubricant is added to a capsule formulation to "ensure reproducible filling by a suitable machine." Weight variation data[6] has been used as a measure of lubricant requirement although this may be more of an indication of a glidant effect than true lubrication.[13]

The techniques used in this report allow direct measurement of ejection forces and therefore may give a better indication of the true lubricant requirements of fully automatic capsule filling machines of this type.

EXPERIMENTAL

Preparation of Powder Blends: The lubricants used in this study were magnesium stearate, U.S.P., powder (Amend Drug & Chem. Co., Irvington, NJ), stearic acid, food grade (Hystrene 9718, Humko Sheffield Chem., Memphis, Tenn.) and magnesium lauryl sulfate, pharmaceutical grade (Sipon MLS, Alcolac, Baltimore, MD). Magnesium stearate is generally accepted as the most efficient lubricant while stearic acid represents a non-metallic alternative. Magnesium lauryl sulfate has received some attention as a lubricant[2,6,14] not possessing the hydrophobic properties of magnesium stearate. Pregelatinized starch, U.S.P., compressible starch, (Sta-Rx 1500, Colorcon, Inc., West Point, PA), microcrystalline cellulose, NF, (Avicel PH 103, FMC Corp., Food & Pharmaceutical Prods., Phila., PA), and lactose, U.S.P., anhydrous (Direct Tableting Grade, Humko Sheffield Chem., Memphis, Tenn.) were used as the representative fillers. No model active ingredient was used.

There were two batch sizes: 2 kg and 500 g. Preblending of the required amount of prescreened lubricant (80 mesh) with a small amount of filler was done in a plastic bag and the remaining filler was then added. The 2 kg batches were mixed in a twin shell liquid-solids blender (7.6 l, Patterson-Kelly Co., East Stroudsburg, PA) for 10 minutes without the intensifier bar and then for three minutes with the intensifier bar running to ensure efficient distribution of the lubricant. The 500 g batches were mixed in a cantilever model liquid-solids blender (1.9 l, Patterson-Kelly Co., East Stroudsburg, PA) for the same ten and three minute periods, respectively.

Capsule Filling: The prepared blends were filled into No. 1 gelatin capsules (Gelatin Pre-Fit capsules, Parke-Davis & Co., Detroit, MI). Filling was accomplished on an instrumented, fully automatic capsule filling machine[4] (Zanasi LZ-64) using a specially designed dosator piston. The normally cylindrical middle shank of the piston was altered to a rectangular cross section and served as the bonding site for strain gauges that monitored compression and ejection forces generated during the filling cycle.

A more sensitive piston was used in this study than was previously reported. An original No. 1 piston was instrumented in a manner identical in all respects as previously described except that the entire middle shank was altered to a smaller (0.742 cm wide and 0.127 cm thick) cross sectional area.

When calibrated, this instrumented piston exhibited a linear response (r = 0.999) and the slope of the calibration curve was found to be 7.35 microstrains/kg. The maximum load applied in calibration was 40 kg.

Runs were conducted under different conditions of machine settings. The powder bed height in the hopper can be adjusted from 30 mm to a maximum of approximately 50 mm (actual 49.4 mm). This setting is the depth of powder into which the dosator dips. The piston height is the main factor in controlling weight fill. This adjustment determines the length of the slug deposited into the gelatin shell. The 2 kg batches were used in runs where the powder bed height and the piston height were varied. The 500 g batches were used for other runs in which the powder bed height was held at 50 mm and the piston height was held at 15 mm.

In all cases the powder blend was added gradually to the hopper while the machine was running and with the dosator in place. To prevent any possible change in powder bed bulk density due to changes in reservoir powder weight, care was taken to maintain the reservoir bed height to within approximately 25 mm ± 12 mm during all runs. Sufficient time was allowed for the powder bed to come to equilibrium conditions as evidenced by the recorded traces.

The reported data represent the means of 25 capsule fillings at each setting. Although this model normally operates with 2 dosators, the machine was run at slow speed with only the instrumented dosator in place (33 capsules/min.). A previously described solenoid switching system[4] provided capsule feed only as required for the instrumented dosator. Fill weight varied according to the bulk density of the material being filled and the powder bed height and the piston height settings.

Ejection Force Study: Two main sets of runs were made. The first set, employing the 2 kg batch size, was designed to study the influence of powder bed height, piston height and compression force on the resultant ejection force generated during the filling process. For these runs the initial powder bed height was 30 mm and the initial piston height was 15 mm.

These settings were then held constant and the compression force increased from the zero compaction level (setting where the compression knob does not depress or tamp the piston and a precompression force results[4]) up to four additional compression force levels. Where there are missing data points, the precompression force exceeded the lower compression force levels or no further compaction could be added to the piston.

After these compression force adjustments were completed, the piston height was lowered, in 1 mm decrements, to a minimum of 12 mm, and the process repeated for that powder bed height. To accomplish the powder bed height changes, the hopper was emptied, the powder bed height reset, the piston height adjusted to 15 mm and blend added to the hopper as described above.

The second set of runs was aimed at comparing lubricant type and levels. In order to reduce the number of experimental runs, a single powder bed height (50 mm) and piston height (15 mm) were chosen. The previous study showed that maximum ejection force values always resulted when this combination of powder bed height and piston height was used. The 500 g batches were used for these runs. Four levels of magnesium stearate were used in each filler, those levels being dependent on the requirements of the filler. In addition one appropriate level of stearic acid and of magnesium lauryl sulfate was run in each filler. Unlubricated compressible starch was also run under these conditions.

RESULTS AND DISCUSSION

The ejection force data for the unlubricated compressible starch are presented in Fig. 1. These data represent the clearest picture of the effects of piston height and compression force on the ejection force. In contrast to compressible starch, neither microcrystalline cellulose nor anhydrous lactose could be run unlubricated in a scheme such as that followed in Fig. 1 due to excessively high ejection forces and possible damage to the machine.

The first data point of each piston height is the result of the precompression force. When the compression force is increased to 3.6 kg, the ejection force decreased slightly or was changed only slightly at the four piston height settings. Why this occurs is not clear, but a possible explanation may be derived from a consideration of the dosing process. The filling head of the dosator captures a portion of the powder blend as it dips into the hopper. Since the powder bed height is greater than the piston

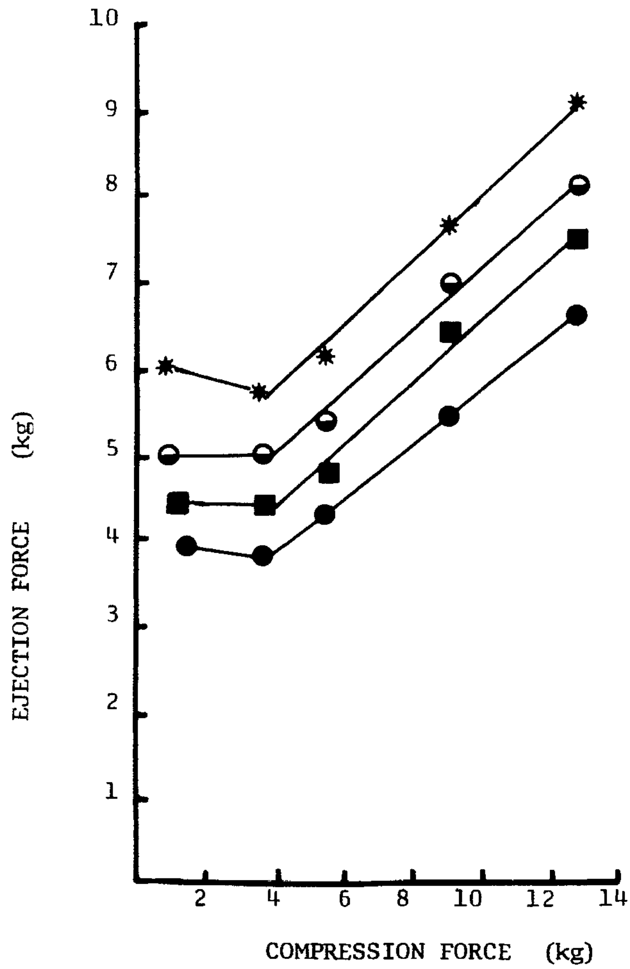

FIGURE 1

Effect of Compression Force on the Ejection Force of Unlubricated Compressible Starch at a Powder Bed Height of 50 mm. Key: Piston Height (mm): ✱ 15; ◒ 14; ■ 13; ● 12.

height, that portion of blend which is captured must be compacted to some degree. A measure of this compaction is the precompression force. The small increase in the compression force to 3.6 kg slightly tamps the piston and may initiate an ejection type of movement by the precompression powder slug, thereby causing a lower than expected ejection force when the slug is dispensed. However, ejection forces increased as the compression force was increased beyond this level. Presumably, any such effects on the precompression slug are negligible in relation to the larger residual radial forces developed with higher compression forces.

The effect of piston height (i.e., slug length) on the ejection force also is seen in Fig. 1. The ejection/compression force plots for the piston heights are spaced approximately equally apart. Therefore, the ejection force is also a function of slug length.

Figure 2 shows the dramatic effect of a very low level of lubricant on the ejection force of compressible starch. Magnesium stearate, at the 0.005% level, reduced the ejection force of this starch from a 4-9 kg range, as shown in Fig. 1, to a 1 to 1.8 kg range for the 50 mm powder bed height setting. Although the two plots resemble each other, the effect of piston height on ejection force is less pronounced at lower compression forces and becomes more distinct at higher compression forces for the lubricated material.

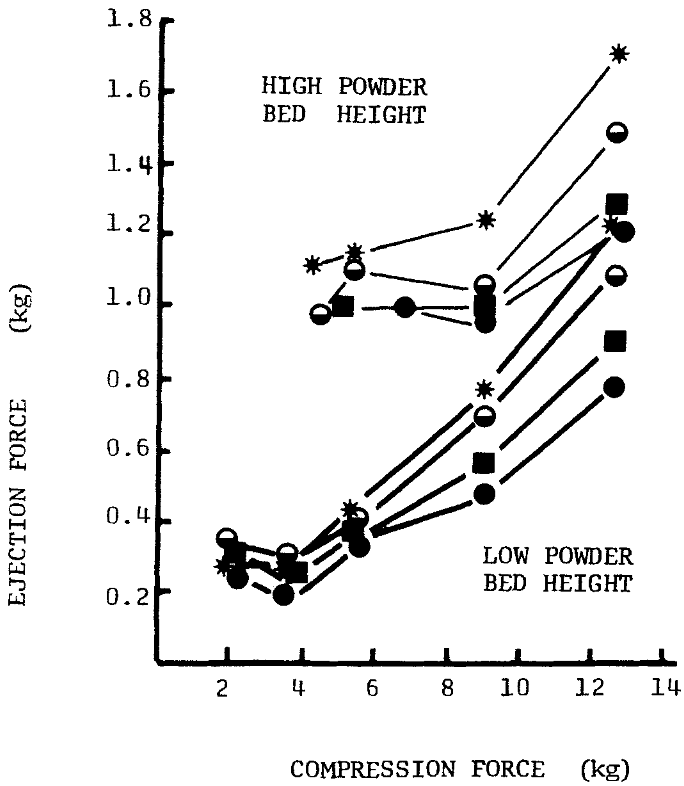

FIGURE 2

Effect of Compression Force on the Ejection Force of Compressible Starch Containing 0.005% Magnesium Stearate. Key: Piston Height (mm): ✱ 15; ⊖ 14; ■ 13; ● 12. Powder Bed Height (mm): ——— 30; ——— 50.

A large difference in ejection force levels is observed in Fig. 2 between the two powder bed height settings. Regardless of the powder bed height, the difference in fill weight between any two adjacent piston height settings for a given powder bed height is approximately 20 mg. However, when the fill weights of the same piston height settings are compared at the two powder bed height settings, again there is about a 20 mg. difference (Table I). This implies that the influence of powder bed height differences on ejection force is greater than the influence of the piston height settings used in this study.

Similar data, as that presented in Fig. 2 for compressible starch with magnesium stearate, are

TABLE I

Gross Capsule Fill Weights of Compressible Starch Containing 0.005% Magnesium Stearate According to Machine Setting.

Powder Bed Height (mm)	Piston Height (mm)	Gross Fill Weight (mg) Compression Force (kg) P-C[a]	3.62	5.43	9.05	12.7
50	15	419(.4)[b]	-c	420(.5)	421(.5)	422(.5)
	14	400(.5)	-c	400(.5)	400(.4)	402(.9)
	13	377(.5)	-	-c	378(.5)	379(.5)
	12	360(.6)	-	-d	360(.4)	361(.6)
30	15	400(2.0)	399(.5)	402(.6)	402(.6)	402(.5)
	14	379(.7)	381(.6)	383(.6)	384(.5)	383(.6)
	13	359(.4)	361(.8)	363(.6)	364(.6)	362(.6)
	12	338(.7)	340(.6)	342(.6)	343(.8)	342(.5)

[a]Precompression; [b]% RSD, n = 25; [c]P-C force > 3.62 and < 5.43; [d]P-C force of 5.6 kg.

presented for microcrystalline cellulose containing 0.02% magnesium stearate and for anhydrous lactose containing 0.2% magensium stearate (Figs. 3 and 4, respectively). There is again a separation of ejection force values between powder bed heights for both microcrystalline cellulose and lactose. The

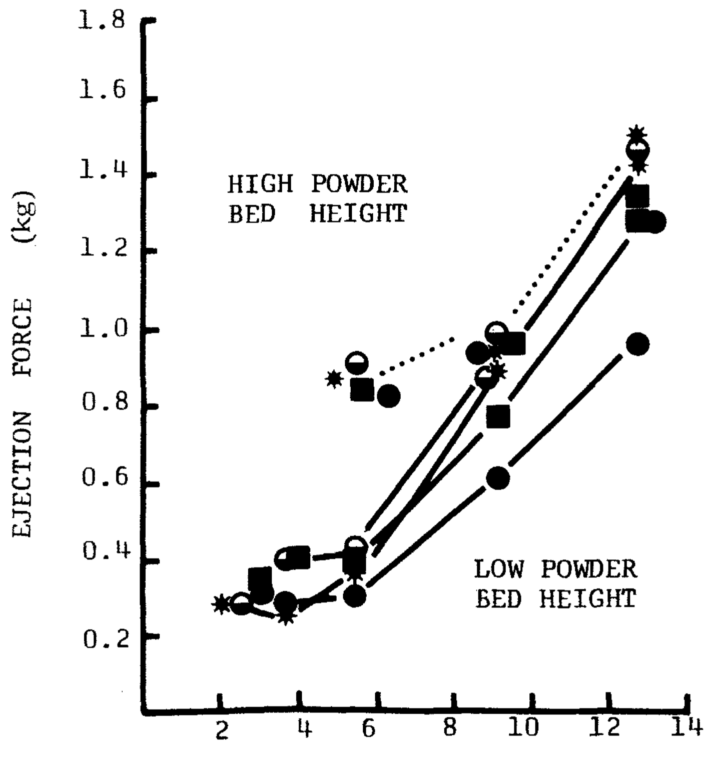

FIGURE 3

Effect of Compression Force on the Ejection Force of Microcrystalline Cellulose Containing 0.02% Magnesium Stearate. Key: Piston Height (mm): ✱ 15; ◒ 14; ■ 13; ● 12. Powder Bed Height (mm): ——— 30; ········ 50.

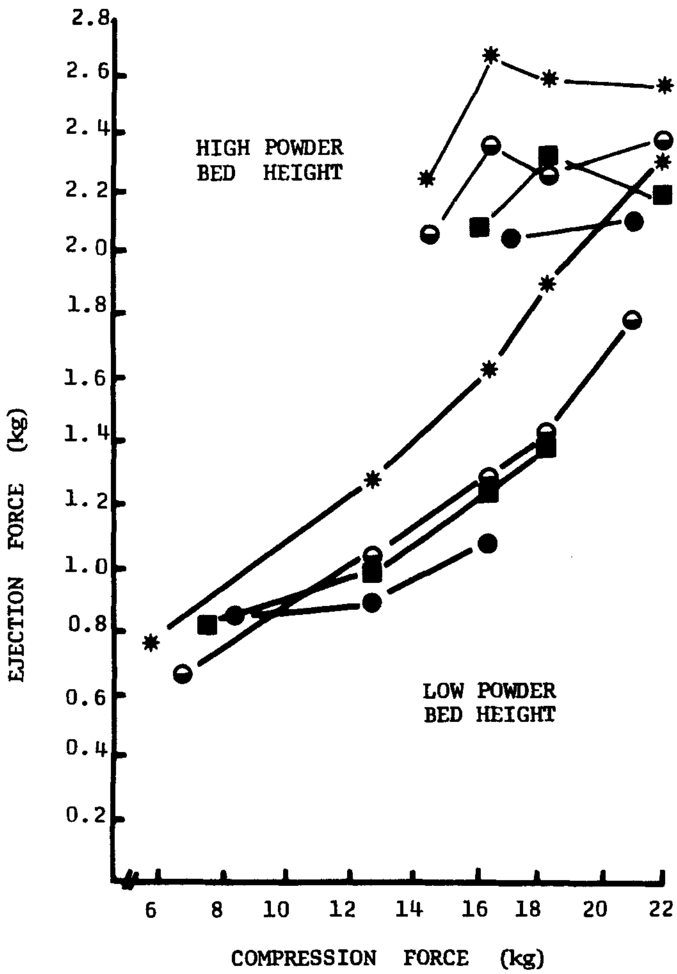

FIGURE 4

Effect of Compression Force on Ejection Force of Anhydrous Lactose Containing 0.2% Magnesium Stearate. Key: Piston Height (mm): ✱ 15; ⊖ 14; ■ 13; ● 12. Powder Bed Height (mm): ━━ 30; —— 50.

effect of piston height at the high powder bed setting for microcrystalline cellulose (Fig. 3) is less dramatic than is the effect for starch or lactose.

These results suggest that if uniform fill can be attained at a lower powder bed height and the necessary compensatory increase in piston height does not negate the effect, a decrease in powder bed height may provide a means of reducing ejection forces without an increase in the lubricant level of the formulation.

Although the compression force values for anhydrous lactose (Fig. 4) at the high powder bed setting are relatively high, the range is necessarily narrower than at the lower powder bed height due to the high precompression force values and an upper compression force limit of 21.7 kg imposed to prevent possible damage to the machine. The ejection forces at this setting tend to plateau, suggesting that the tamping of the piston at these compression forces does not appreciably alter the frictional forces generated by the precompression force. At the lower powder bed height, where the slug formed at precompression is comparatively less dense and in an earlier stage of compaction, tamping of the piston to increase the compression force does result in increased frictional resistance to ejection.

The effect of magnesium stearate levels in compressible starch is depicted in Fig. 5. Again the dramatic effect of the 0.005% level is remarkable

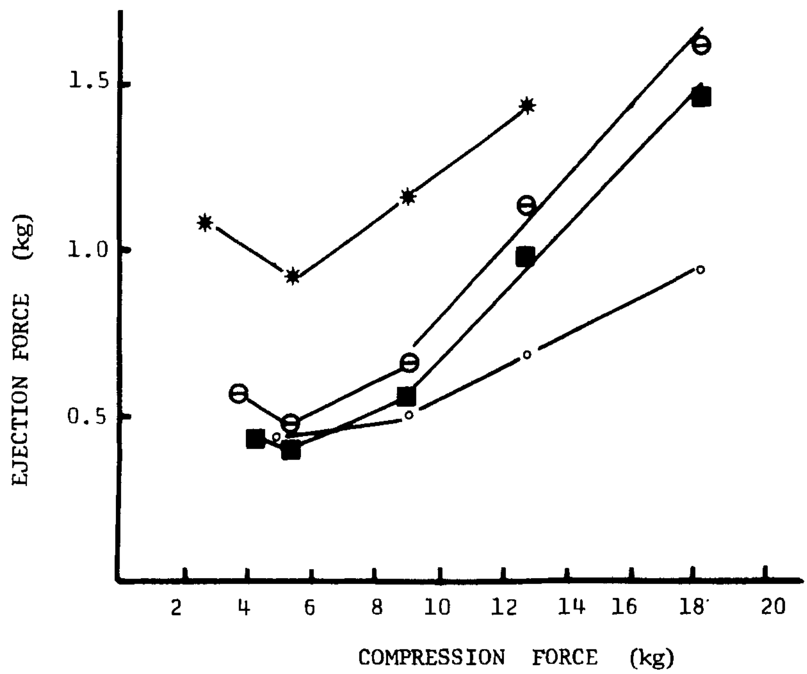

FIGURE 5

Effect of Magnesium Stearate Levels in Compressible Starch. Filling Conditions: Powder Bed Height = 50 mm and Piston Height = 15 mm. Key: Lubricant Level: ✱ 0.005%; ⊖ 0.01%; ■ 0.02%; ∘ 0.1%.

when compared to the unlubricated material (Fig. 1). Additional levels of lubricant, up to 0.1%, caused a further reduction in ejection forces of less than 1 kg.

Microcrystalline cellulose containing 0.5% magnesium stearate (Fig.6) exhibited ejection forces comparable to those of starch at the 0.1% magnesium stearate level. It is likely that the differences in the lubrication requirements of these two similar

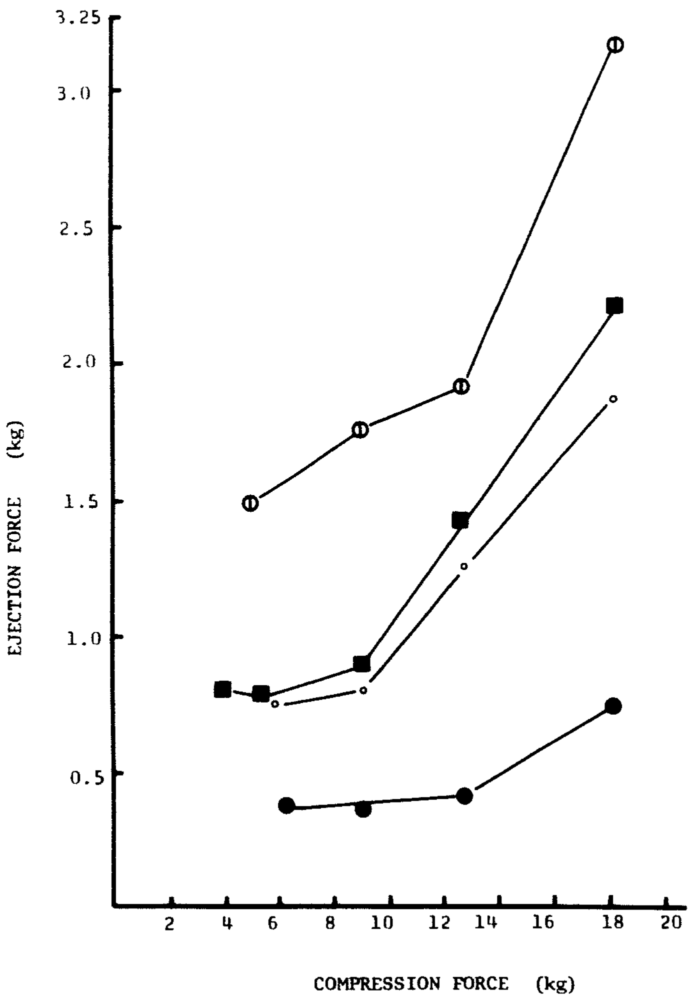

FIGURE 6

Effect of Magnesium Stearate Levels in Microcrystalline Cellulose. Filling Conditions: Powder Bed Height = 50 mm and Piston Height = 15 mm. Key: Lubricant Level: ⦶ 0.01%; ■ 0.02%; ∘ 0.1%; ● 0.5%.

materials are indicative of a higher specific surface area of microcrystalline cellulose which would require additional lubricant to achieve equivalent surface coverage. The one-half percent lubricant level was sufficient to maintain ejection forces below 1 kg as the compression force was increased. This contrasts with the other three blends (Fig. 6) prepared with lower levels of lubricant which exhibited greater increases in ejection forces with increasing compression forces.

Anhydrous lactose appears to have a higher lubricant requirement than either starch or microcrystalline cellulose. Lactose containing 3% magnesium stearate (Fig. 7) exhibited ejection forces of 2 kg and higher. When 1% or 0.5% magnesium stearate was used, ejection forces were only about 0.5 kg higher. Thus the 3% lubricant would seem to offer little advantage over the lower levels. Only the more extreme cases of the lubricated microcrystalline cellulose runs produced ejection force values greater than 2 kg. The 2 kg level was never reached in the lubricated starch runs.

Figure 7 also shows the results of lactose runs containing 3% magnesium lauryl sulfate and 1% stearic acid. Three percent magnesium lauryl sulfate was required to bring ejection forces within range of those forces produced by the magnesium stearate levels used. The relatively low ejection force values for the 1% stearic acid blend were surprising. However,

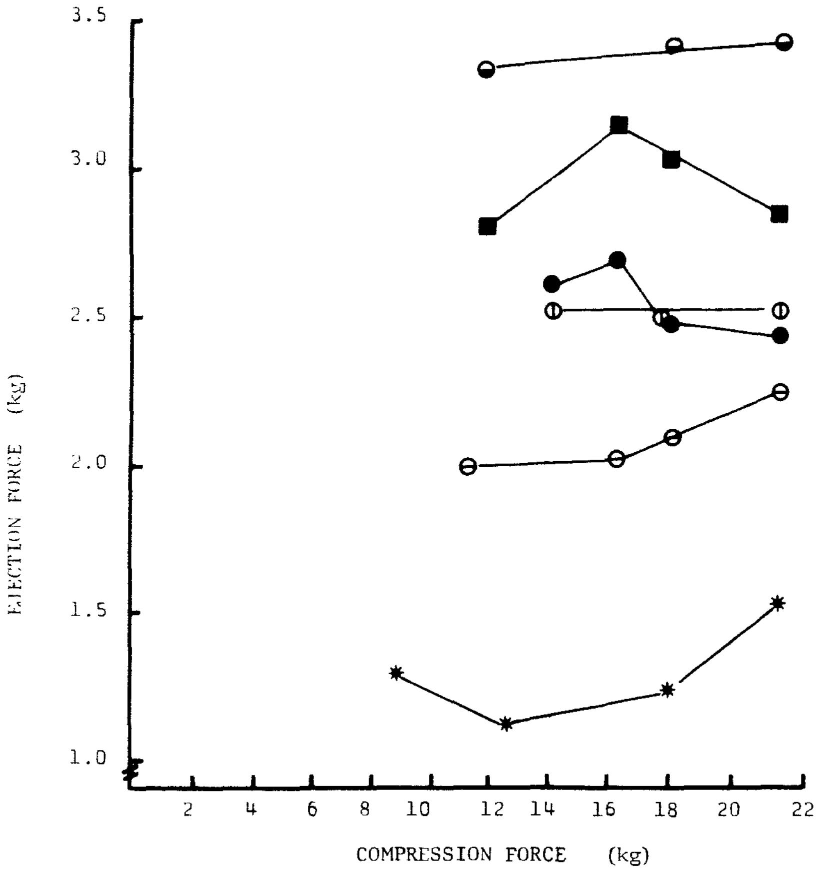

FIGURE 7

Effect of Lubricant Type on the Ejection Force of Anhydrous Lactose Blends. Filling Conditions: Powder Bed Height = 50 mm and Piston Height = 15 mm. Key: ◒ 3% Magnesium Lauryl Sulfate; ✱ 1% Stearic Acid; Magnesium Stearate: ■ 0.2%; ● 0.5%; ⦶ 1%; ⊖ 3%.

the tapped bulk density of this stearic acid blend was lower than any of the other lubricated lactose blends (Table II) and this may account in part for these low ejection forces. As a result the gross fill weight

TABLE II

Tapped Bulk Density of Lubricated Anhydrous Lactose Blends

Lubricant	Level (%)	Tapped Density (g/ml)[a]
SA[b]	1	0.805
MS[c]	0.2	0.835
MLS[d]	3	0.849
MS	0.5	0.858
MS	1	0.863
MS	3	0.878

[a]For method, see Ref. 15; drop height = 1.03 cm, 50 drops/2 min.; [b]Stearic acid; [c]Magnesium Stearate; [d]Magnesium Lauryl Sulfate.

of the 1% stearic acid blend (450 mg) was the lowest of the lactose blends studied (range of gross fill weights of the other lactose blends was 470-485 mg).

Figures 8 and 9 contrast the three lubricants at the 0.1% level in compressible starch and microcrystalline cellulose, respectively. The performance of stearic acid and especially magnesium lauryl sulfate compared favorably with magnesium stearate in compressible starch (Fig. 8). The favorable results of magnesium lauryl sulfate in starch tablets[2] and in capsule formulation[6,13] were previously reported. Magnesium lauryl sulfate produced higher ejection forces at equal levels in microcrystalline cellulose,

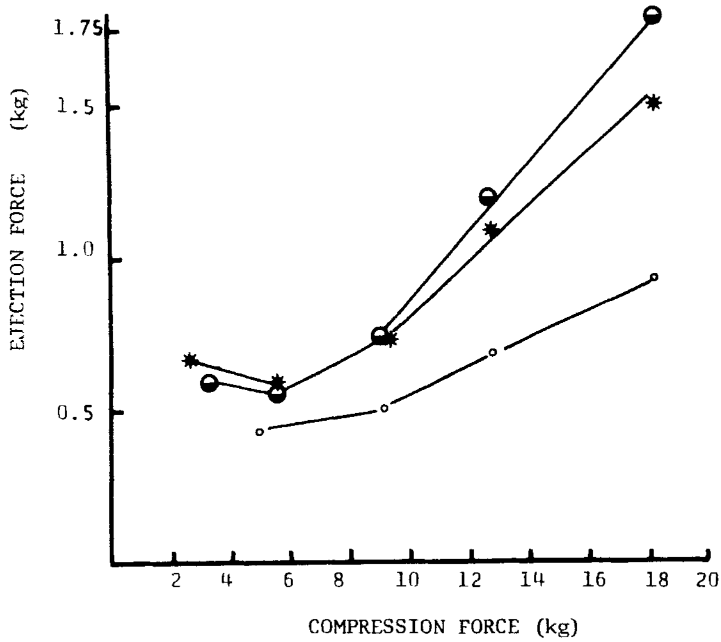

FIGURE 8

Effect of Lubricant Type on the Ejection Force of Compressible Starch Blends Containing 0.1% Lubricant. Filling Conditions: Powder Bed Height = 50 mm and Piston Height = 15 mm. Key: ✱ Stearic Acid; ∘ Magnesium Stearate; ◓ Magnesium Lauryl Sulfate.

again possibly reflecting a higher specific surface area of this filler.

For many encapsulated products the ratio of active drug to excipient is high. In such cases the type and level of lubricant used may well be determined more by the lubricant requirement of the active ingredient than by the filler. The results of the present study suggest that remarkably low levels of

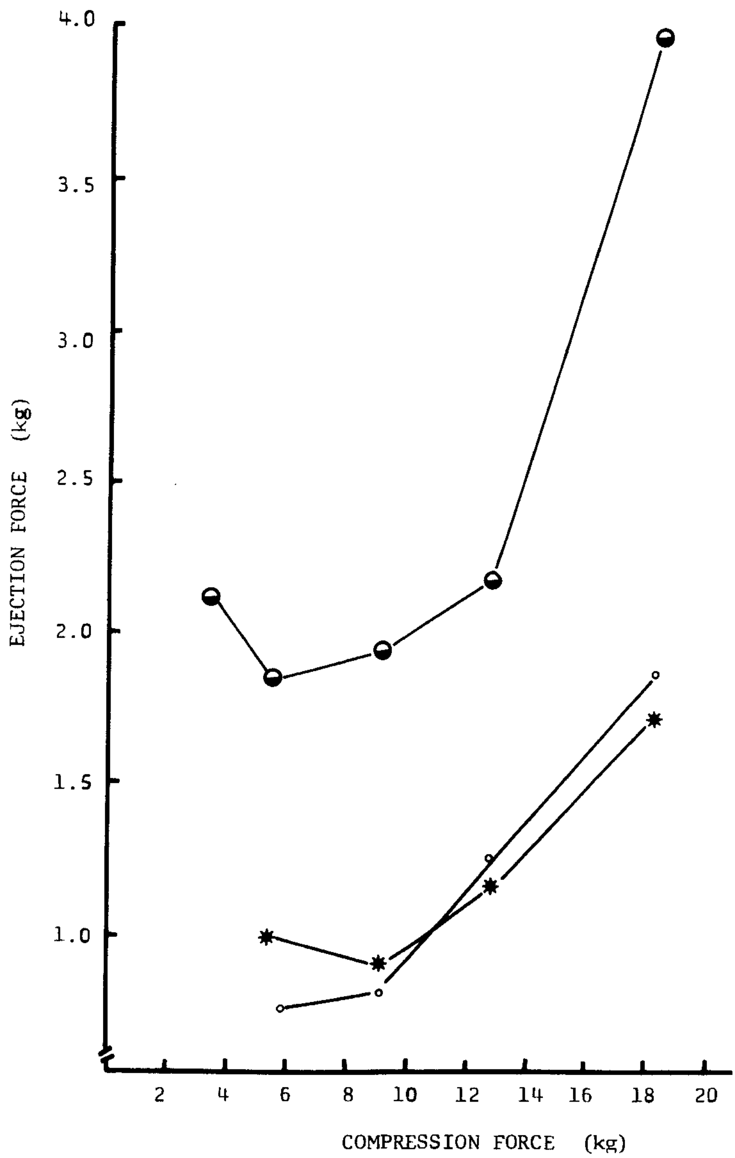

FIGURE 9

Effect of Lubricant Type on the Ejection Force of Microcrystalline Cellulose Blends Containing 0.1% Lubricant. Filling Conditions: Powder Bed Height = 50 mm and Piston Height = 15 mm. Key: ✱ Stearic Acid; ∘ Magnesium Stearate; ◒ *Magnesium* Lauryl Sulfate.

magnesium stearate (0.005% to 0.5%) may be sufficient to reduce ejection forces to an acceptable range in formulations where the relative amount of excipient is high. This is especially true for compressible starch and microcrystalline cellulose. However, studies such as these should prove of value in helping to establish the optimum lubricant requirement of any formulation. Recently, Murthy and Samyn[14] reported inhibition of *in vitro* dissolution rates from capsule formulations subjected to lengthy, high shear mixing (up to 30 minutes) using magnesium stearate levels of 0.5% and 2%. These results point up the potential of hydrophobic lubricants to interfere with drug release and, in particular, the need to give careful consideration to blending time and intensity. Thus selection of optimum lubricant concentrations and blending times on the basis of ejection force measurements may help improve drug release.

SUMMARY AND CONCLUSIONS

The magnitude of ejection forces produced in a fully automatic capsule filling machine are given for limited experimental runs using magnesium stearate, stearic acid and magnesium lauryl sulfate as lubricants in three common capsule fillers: compressible starch, microcrystalline cellulose and anhydrous lactose. Ejection forces are also given for a run completed using unlubricated compressible starch. No active ingredient was included.

It was shown that the magnitude of the ejection forces are affected by two important machine settings: 1) powder bed height and 2) piston height. An increase in either of these settings resulted in increased ejection forces for a given material.

Increasing the compression force or the force given to tamp the dosator piston also increased the ejection forces. The extent to which the ejection force is increased is dependent upon the powder bed height, piston height and the bulk density of the material being filled. These factors are important in determining the extent of the consolidation process at precompression. The influence of the tamping mechanism on ejection force is diminished the greater the compaction of the powder slug at precompression.

The addition of a relatively small percentage of magnesium stearate dramatically reduced the ejection forces of compressible starch as compared to the unlubricated material.

Results are given for the effect of varying magnesium stearate levels in the three fillers used and are compared with one level each of stearic acid and magnesium lauryl sulfate. Lactose generally exhibited greater ejection forces than either starch or microcrystalline cellulose at all of the magnesium stearate levels studied. Only the more extreme cases of the lubricated microcyrstalline cellulose runs produced ejection forces greater than those exhibited by the lactose blend containing the highest level of lubricant studied.

The performance of stearic acid and especially magnesium lauryl sulfate compared favorably with magnesium stearate in compressible starch. Magnesium lauryl sulfate produced higher ejection forces than did magnesium stearate or stearic acid at equal levels in microcrystalline cellulose. A high level of magnesium lauryl sulfate in lactose was required to bring ejection forces within range of those forces produced by the magnesium stearate levels studied.

Although the batch sizes used in this study were small compared to production runs and contained no active ingredient, the results of this report may serve as an indication of the lubrication requirements of capsule formulations and help clarify the interrelationships between machine variables and their effects on lubrication requirements.

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