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INSTRUMENTED TABLET PRESS STUDIES ON THE EFFECT OF SOME FORMULATION AND PROCESSING VARIABLES ON THE COMPACTION PROCESS

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ABSTRACT

Using an instrumented tablet press, compression force-time measurements were used to evaluate the effects of formulation and processing variables on the compaction process. The effects of tablet press speed, punch size, depth of upper punch penetration (into the die), and the setting of the overload spring mechanism were studied. The effects of tablet weight, particle size and amount of lubrication were also studied. Several direct compression materials which are believed to compact by different mechanisms were used in the study. The results indicate the sensitivity of the area under the compression force-time curve and the Area/Height ratio. Some of the changes seen in the area and A/H ratio were those which would be expected from a relatively

simple model of compaction/compression. The results clearly show the usefulness of the instrumented tablet press as an analytical tool in the development of tablet formulations, the evaluation of processing requirements, and the remedy of tablet production problems.

INTRODUCTION

It is becoming common practice at several pharmaceutical companies to obtain compression profiles of formulations during the development stage. These profiles may act as formulation "fingerprints" and aid in troubleshooting problems that may occur during production [1-3]. Several characteristics of the compression profile have been suggested as formulation "fingerprints". These characteristics can be described as observed (e.g. maximum compression force) and derived parameters. Derived parameters, which can be calculated from direct measurements of the force-time curve, include area under the force-time curve, Area/Height ratio, maximum slope (on the upward portion of the curve), minimum slope (on the downward portion), and the width at half the height, along with several other parameters.

Several papers have reported on the value of a derived parameter called the Area/Height ratio [3-5]. This ratio is obtained by plotting the Area under the compression force-time curve as a function of the maximum compression force and performing linear regression on this relationship. The regression coefficient (or slope) is defined as the A/H (Area/Height) ratio. Chilamkurti et al., who used a single station eccentric tablet machine in their study suggested that data on the Area/Height ratio could possibly indicate the inherent compressibility of the material being compressed [3-5]. They concluded that the higher the A/H ratio, the less the inherent compressibility of the material. The A/H ratio was defined as a measure of the time required to transmit a given amount of energy to a pharmaceutical system [4].

The present authors, in a previous communication, reported on the possible value of using the A/H ratio as a calibration tool for the comparison of compaction data obtained from several tablet presses [6]. In a paper, describing the instrumentation of a Stokes B-2 rotary tablet press, it has been shown that data obtained from the computer interfaced machine possesses a high degree of precision and reproducibility [8]. This tablet compression monitoring device allows the determination of several observed and derived parameters.

This paper (together with a second communication) reports on an investigation of the utility of compression force-time data. The effects of formulation and processing factors on several observed and derived parameters are described. In the analysis of the experimental data, emphasis is placed on the derived parameter, the Area/Height ratio and how it is affected by these formulation and processing variables.

MATERIALS

Microcrystalline cellulose (Avicel PH-102, PH-101 and PH-105, FMC Corp.), dicalcium phosphate dihydrate (Emcompress, Edward Mendell Co.), anhydrous lactose (Sheffield Chemical Co.), pregelatinized starch (Starch-1500, Colorcon), acetaminophen (Ruger Chemical), and magnesium stearate (Fisher Chemical) were used in the study.

METHODS

The direct compression matrices were blended with magnesium stearate in a WAB Turbula type T2C shaker/mixer for five minutes prior to being compressed. In most cases, the blended materials were compressed with 3/8 inch standard concave punches on a Stokes B-2 rotary tablet press at a press speed of 30 revolutions per minute. The tablet press was instrumented with integral piezoelectric transducers in the eye bolt and ejection cam to measure compression and ejection forces [1]. The tablet press is interfaced with a microcomputer using an analog-to-digital converter to process the signals. An oscilloscope allows fine adjustment of the compression force while the press is operational.

The analysis of the experimental compression curves was performed on a microcomputer using a program written at the University of Rhode Island. The results of analysis of individual compression and ejection curves was uploaded to an IBM 4381-3 mainframe computer located at the University. The data was then analyzed using a statistical software package, SAS version 85.2, for various regression analysis models.

The effect of tablet press speed on compaction parameters was characterized using three materials: Avicel PH-102, Emcompress, and anhydrous lactose and varying the press speed, 25, 30, 37.5, 42.9, 50 and 60 revolutions per minute. These operating speeds were selected to allow an equal number of points to be collected for each compression and ejection curve by varying the sampling rate of the analog-to-digital converter. The actual sampling rates ranged from 833 Hz to 2000 Hz. The materials were then compressed at various compression forces upto a maximum of fifteen kilo-Newtons.

Tablet weight was investigated by designing a fractional factorial design with tablet weight and compression force as the independent factors. Two lubricated direct compression materials, Avicel PH-102 and Emcompress were compressed at various compression forces between two and twenty-five kilo-Newtons at several tablet weights. The tablet weights were varied for each of the materials. Only a limited range of weights could be used for Avicel PH-102 due to its low bulk density.

Emcompress was blended with an amount of magnesium stearate to give a 0.5% lubricant concentration and compressed to investigate the effect of the amount of upper punch penetration on the shape of the compression force-time curve. Tablets were compressed at various compression forces over a range of 0 to 25 kilo-Newtons at a weight of 600 milligrams per tablet. A series of compressions were performed at the following punch penetration depth settings: 1/8", 3/16", 1/4", 5/16" and 3/8 inches. The tablet press was operated at a speed of thirty revolutions per minute.

The effect of lubricant concentration was investigated using Avicel PH-101, Avicel PH-102 and Emcompress. The systems contained varying concentrations of magnesium stearate. The magnesium stearate and direct compression matrix were mixed for five minutes prior to compression. Blends were compressed at a press speed of thirty revolutions per minute. Tablets were compressed at various forces between zero and twenty kilo-Newtons. Table I details the material-magnesium stearate blends used in the study.

Particle size was studied using three grades of Avicel (PH-101, PH-102 and PH-105). These materials were mixed with 0.25% magnesium stearate in a WAB Turbula model T2C shaker/mixer for five minutes. These powder blends were then compressed. All materials were compressed using the same die fill volume. Bulk and tap densities were obtained for the three materials and the tablet weights, thicknesses, and hardnesses were measured. The tablet press was operated at a rotational speed of 30 revolutions per minutes. Tablets were compressed at six compressional forces between two and fifteen kilonewtons.

The direct compression matrices were blended with 0.5% magnesium stearate in a WAB Turbula type T2C shaker/mixer for five

TABLE I

Formulations Used To Study The Effect of Lubricant

On The A/H Ratio

Matrix	Magnesium Stearate Concentration					
	0 %	1/16 %	1/8 %	3/16 %	1/4%	1/2 %
Avicel PH-101	X	X	X	X	X	X
Avicel PH-102	X	X	X		X	X
Emcompress					X	X

TABLE II

Bulk and Tapped Densities of Several Materials Used in the Study

Material	Bulk Density (g/ml)	Tap Density (g/ml)
Anhydrous Lactose	0.544 (0.007)	0.796 (0.008)
Avicel PH-101	0.293 (0.003)	0.417 (0.009)
Avicel PH-102	0.285 (0.002)	0.408 (0.007)
Emcompress	0.780 (0.006)	0.910 (0.008)
Starch 1500	0.621 (0.008)	0.801 (0.013)

*Note: Values in parentheses are standard deviations of three determinations of the densities.

minutes. These blends were then compressed at various compression forces between zero and 30 kilonewtons.

RESULTS

Material Effects

Characterization data, bulk and tapped densities, for the materials used in this study are given in Table II. The densities of these materials differ greatly, and thus substantial differences in compaction curves might be expected. In order to compare the areas under the compression force-time curves, the

TABLE III

Areas and Properties of Tablets Compressed According to Bulk Densities at Similar Compression Forces

Material	Force kN	Area N-sec	Weight mg	Thickness inches	Hardness kp
anhydrous lactose	6.81 (0.08)	370.12 (2.92)	548.5 (1.7)	0.2779	6.45 (1.08)
Avicel PH-101	6.77 (0.17)	393.30 (8.64)	302.5 (1.5)	0.1740	6.01 (0.46)
Avicel PH-102	6.82 (0.18)	393.10 (8.80)	300.7 (2.2)	0.1784	5.80 (0.33)
Emcompress	6.73 (0.09)	375.83 (3.76)	791.6 (0.8)	0.2850	6.30 (0.45)
Starch 1500	6.71 (0.10)	414.62 (7.78)	621.2 (1.6)	0.3357	4.30 (0.41)

*Note: values in parentheses are standard deviations of the parameters, standard deviations for thickness values were too small to report.

TABLE IV

Areas and Properties of Tablets Compressed According to Tap Densities at Similar Compression Forces

Material	Force kN	Area N-sec	Weight mg	Thickness inches	Hardness kp
anhydrous lactose	6.81 (0.07)	371.39 (3.01)	566.8 (1.5)	0.2856	6.75 (0.50)
Avicel PH-101	6.79 (0.15)	393.90 (6.75)	298.8 (1.6)	0.1789	6.01 (0.45)
Avicel PH-102	6.82 (0.18)	393.10 (8.80)	300.7 (2.2)	0.1784	5.80 (0.33)
Emcompress	6.80 (0.09)	359.78 (4.02)	658.8 (1.2)	0.2440	4.88 (0.30)
Starch 1500	6.70 (0.05)	402.53 (4.12)	584.4 (1.2)	.3158	4.00 (0.40

*Note: values in parentheses are standard deviations of the parameters, standard deviations for thickness values were too small to report.

TABLE V

Areas and Properties of Tablets Compressed to Yield Similar Thicknesses at Similar Compression Forces

Material	Force kN	Area N-sec	Weight mg	Thickness inches	Hardness kp
anhydrous lactose	6.50 (0.09)	320.23 (5.46)	361.0 (1.2)	0.1986	3.50 (0.40)
Avicel PH-101	6.52 (0.12)	389.12 (9.98)	361.2 (1.9)	0.1998	6.83 (0.71)
Avicel PH-102	6.49 (0.16)	385.75 (9.73)	349.1 (1.8)	0.2003	6.79 (0.68)
Emcompress	6.51 (0.07)	320.97 (4.92)	513.9 (1.2)	0.2000	3.43 (0.33)
Starch 1500	6.48 (0.08)	340.01 (3.96)	333.3 (1.5)	0.1995	2.15 (0.29)

*Note: values in parentheses are standard deviations of the parameters, standard deviations for thickness values were too small to report.

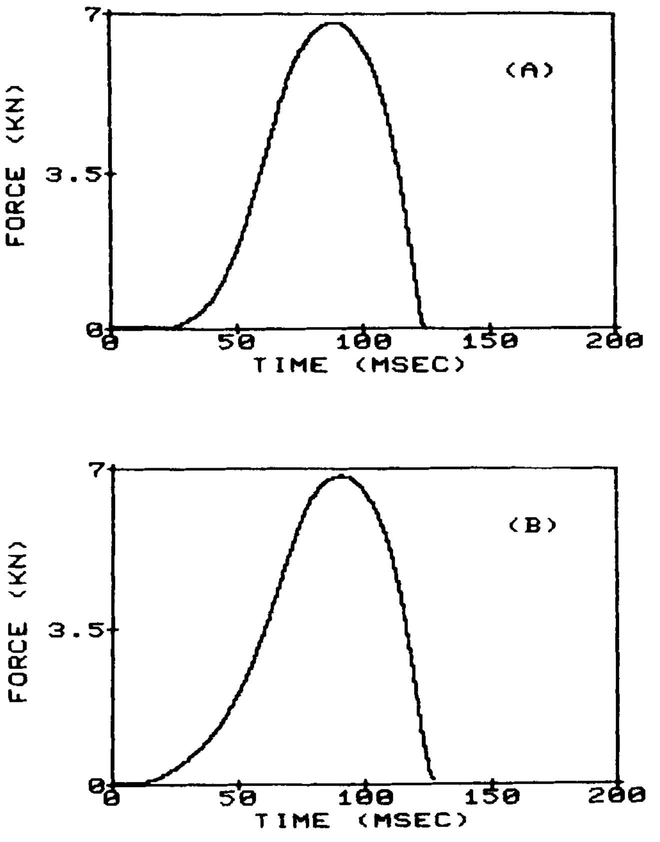


FIGURE 1

Compression curves for (a) anhydrous lactose, (b) Avicel, (c) Emcompress and (d) Starch 1500 when tablet weight adjusted for the bulk density of the material

materials were compressed using three different methods: (1) adjust the tablet weight for differences in bulk density, (2) adjust the tablet weight for differences in tap density, and (3) adjust the tablet weight to yield tablets being compressed with similar thicknesses. Tables III to V show the maximum compression

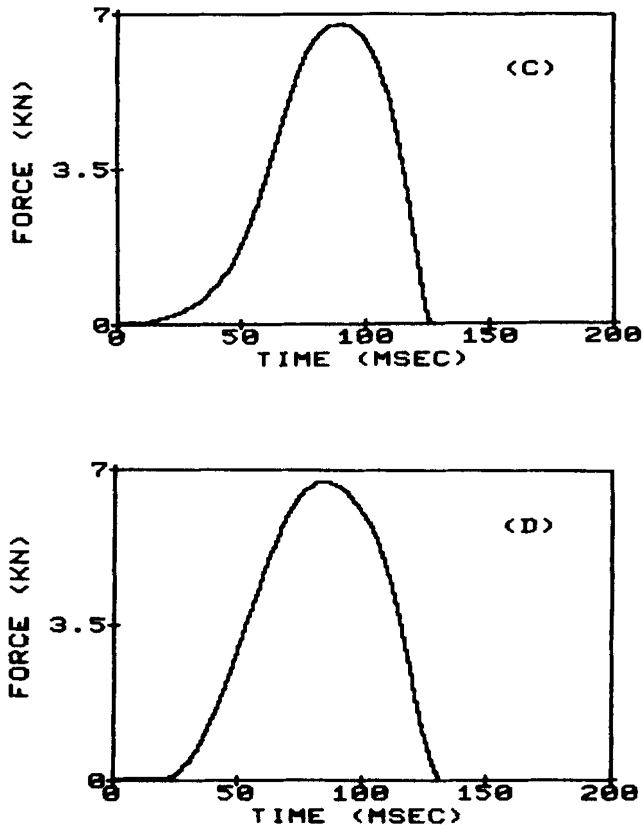


FIGURE 1 (continued)

force, the area under the curve, and the properties of the tablets produced. Figures 1 and 2 show compression force-time curves when these materials are compressed according to their bulk and tap denisities. The compression force-time curves from producing tablets of similar thicknesses are illustrated in Figure 3. A similar compression force was used for each compression. Apparent densities of each of the compactions was calculated using the volume and weight of the resultant tablets and are given in Table

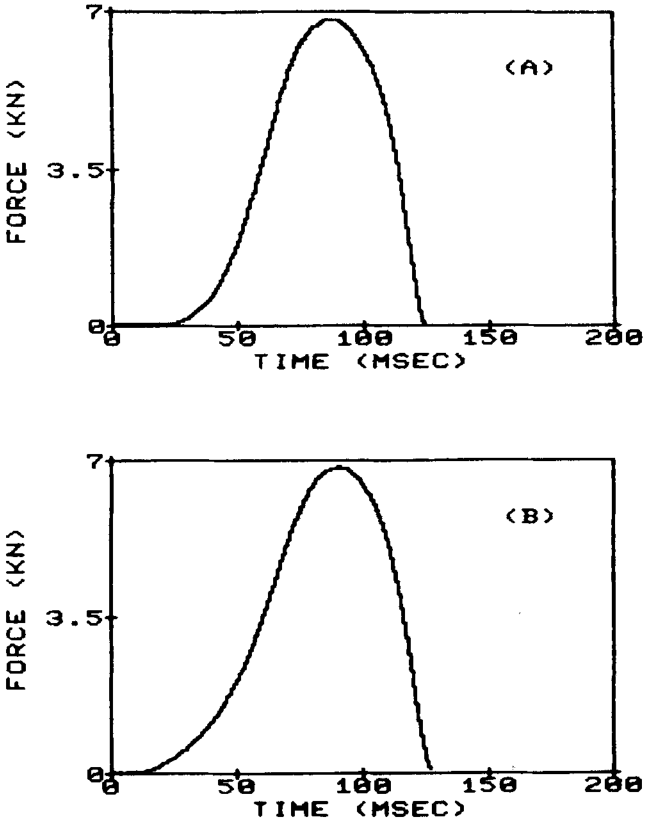
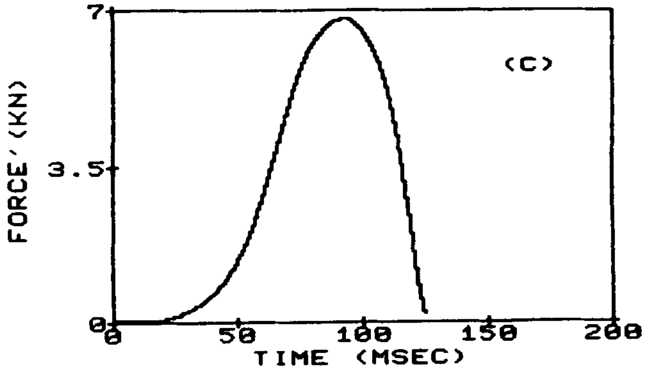


FIGURE 2

Compression curves for (a) anhydrous lactose, (b) Avicel, (c) Emcompress and (d) Starch 1500 when tablet weight adjusted for the tap density of the material

VI. The apparent density reported includes the interparticulate void spaces (between particles) as well as the intraparticulate void space (within the particles) of the compressed tablet.

As can be seen from these results, the shape of the compression force-time curve is determined by several factors,



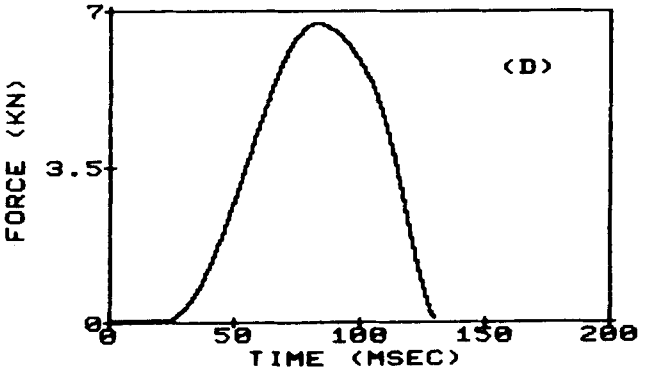


FIGURE 2 (continued)

including the behavior the material exhibits when put under stress. The results appear to indicate that the amount of material needed to compress tablets to similar thicknesses is largely dependent on the tap density of the material. This would agree with the general principle of compressibility (which is the inverse of the bulk modulus) where a material which undergoes the greatest change in volume during application of a stress is the most compressible material. From the results, a greater area

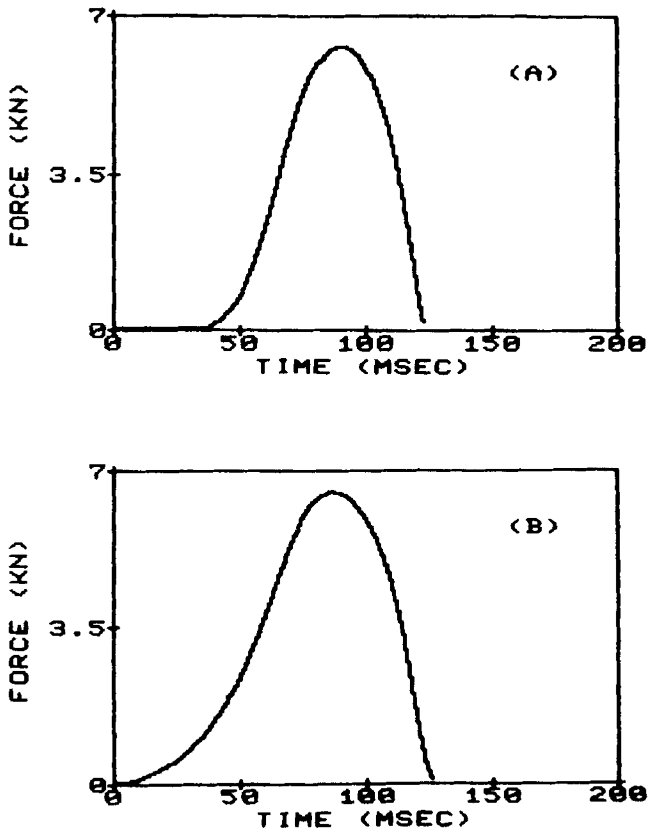


FIGURE 3

Compression curves for (a) anhydrous lactose, (b) Avicel, (c) Emcompress and (d) Starch 1500 when tablet weight adjusted for similar tablet thicknesses

resulted from compressing Avicel, which is generally regarded as the most compressible material used in this study. It is important to note that the term "compressibility" refers to the reduction in volume of a material, and not the consolidation of the material. The terms "compressibility" and "compactibility",

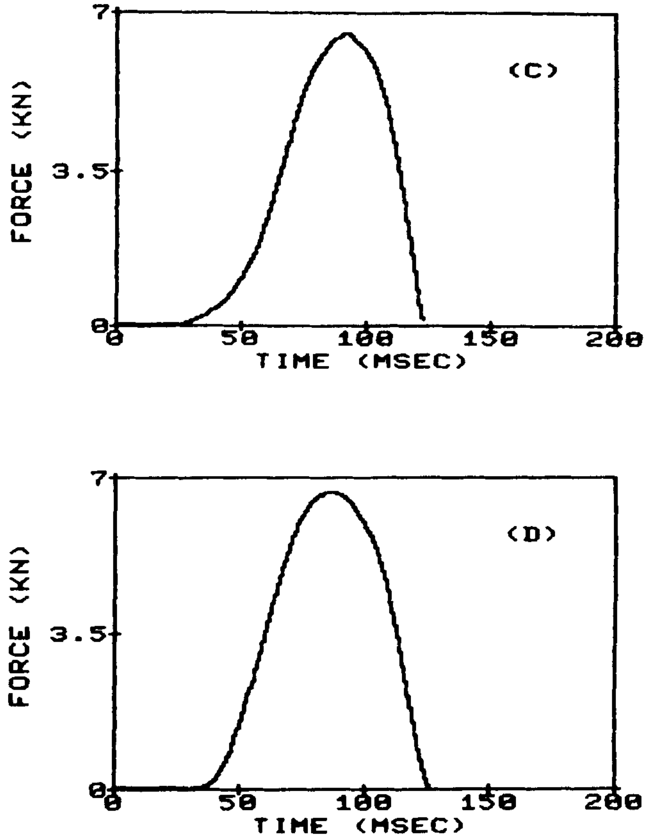


FIGURE 3 (continued)

are sometimes used interchangeably by many, but for purposes of clarification in this paper, compressibility is termed as the ability to reduce in volume and compactibility is the ability to form strong tablets.

Several of these materials were compressed at several compression forces and the observed parameters, force and area were recorded. From these observations, the A/H ratio was calculated using least squares regression. The results of the linear regression coefficients indicate obvious differences between each of the materials compressed in any part of this study. A preliminary compression series appeared to confirm the findings of Chilamkurti et al. [3-5]. However the data reported in a later part of this paper indicates that the hypothesis advanced by Chilamkurti et al. may require modification.

Table VII shows the data obtained from this preliminary study, which indicates the precision of the data obtained and therefore it should be noted that standard deviation bars will be excluded from figures since they are very small.

Depth of Upper Punch Penetration

The amount of upper punch penetration was thought to be a possible cause for the differences in the Area/Height ratios between the similar tablet presses in an earlier reported study ["Preliminary Investigations On The Parity of Tablet Compression Data Obtained From Different Instrumented Tablet Presses"]. This study was conducted to see how much effect this machine adjustment would have on the shape of the compression curve.

Regression analysis was performed on the compression results obtained. The resultant parameters (A/H ratio and intercept), given in Table VIII, did not appear to be statistically significant. A heterogeneity of slope analysis was performed (using the general linear models procedure in SAS) to determine if the differences seen in the A/H ratios and intercepts calculated were actually of any statistical significance. The results of this procedure, shown in Table IX, indicate that the differences

TABLE VII

Area/Height Ratios and Intercepts of Several Materials

	Area/Height[2]	
Material	Ratio (E-03 sec)	Intercept (N-sec)
Avicel-101	58.39 (0.27)	-37.40 (2.92)
Avicel-102	57.66 (0.40)	-14.70 (4.14)
Emcompress	59.71 (0.51)	-73.75 (5.42)
Dicalcium Phos.Dihyd.[2]	60.68 (0.62)	-80.44 (6.51)
Anhydrous Lactose	63.77 (0.49)	-76.78 (5.02)

[1]Note: values in parentheses are standard errors of the estimates

[2]Note: from supplier of unbranded unmilled dicalcium phosphate dihydrate

observed in the A/H ratios and intercepts were not statistically significant ($p > 0.05$) and that the depth of upper punch penetration in the die did not appear to change the shape of the compression force-time curve.

The results indicate that it is the distance between the upper and lower compression rollers that determines the compression force for a given amount of material. If the amount of material being compressed is kept constant, then as the depth of upper punch penetration is adjusted, then the height of the lower pressure roll above the lower punch cam also must be

TABLE VIII

Effect of the depth of upper punch penetration on the Area/Height ratio and intercept values

Depth of Punch Penetration (inches)	Area/Height Parameters* Ratio E-03 sec	Intercept N-sec
1/8	58.07 (0.40)	-47.83 (3.67)
3/16	58.25 (0.39)	-43.17 (3.58)
1/4	56.92 (0.36)	-45.28 (3.40)
5/16	57.73 (0.38)	-45.81 (3.54)
3/8	58.47 (0.43)	-45.64 (4.00)

* Note: Standard errors of the parameter estimates are in parentheses, n=50

adjusted. It is the summation of the upper punch and lower punch travel that determines the resultant compression force.

It should be noted that theoretically, as the lower pressure roll is varied, the lower punch profile as it travels on the roller will be shifted in relation to the upper punch travel across the upper pressure roll. Yet, the shift in this lower profile was not significant to alter the area under the compression force-time curve.

TABLE IX

Results of a SAS Proc GLM using a heterogeneity of slope model* for the effect of depth of upper punch penetration

Dependent Variable: AREA

Source	DF	SUM OF SQUARES	F VALUE	PR > F
Punch Penetration	4	2846.56	5.52	0.0003
Height	1	13855354.74	99999.99	1E-70
Height*Punch Penetr.	4	1208.48	2.35	0.0553
Error	240	30914.93		
Corrected Total	249	13890324.71		

R-Square 0.9978 Root MSE 11.3495

*Statements of the GLM Procedure, including the model to determine the heterogeneity of slope. (PP = Punch Penetration)

```
PROC GLM;
  CLASS PP;
  MODEL AREA = PP HEIGHT HEIGHT*PP / SOLUTION;
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Pressure Overload Spring Setting

On the Stokes B-2 rotary tablet press (and also for many other rotary tablet presses) there is an overload tension spring to prevent damage occuring to the punches should a force be exerted beyond the maximum determined for that punch. An investigation as to whether the setting of this pressure overload

TABLE X

Effect of the Overload Pressure Setting

Setting of Spring (tons)	A/H Ratio ($x10^{-3}$ sec)
1.4	62.56 (0.56)
2.5	62.66 (0.61)
3.8	63.01 (0.63)
4.5	62.89 (0.49)

*Note: results obtained from compression of anhydrous lactose and 0.5% magnesium stearate. Values in parentheses are standard errors of the A/H Ratio estimates.

spring has any effect on the shape of the compression profile was conducted. It was felt that the setting of the overload mechanism might change area under the compression curve.

As can be seen in Table X, this variable did not change significantly the area under the compression force-time curve. It appears that this would only be a factor if one is compressing at loads relatively close to the overload setting of the tension spring and at that point a flattening of the compression curve would occur.

Tablet Press Speed

Tableting speed is defined here as the rotational speed of a rotary tableting machine. As the tableting speed is varied, the vertical punch velocity is also proportionately changed. It would be expected that tableting speed would significantly effect the area under the compression force-time curve since the time over which the compaction event is occuring is changed. It is not known as to what effect the tableting speed (or punch velocity) will have on the compaction behavior of the materials. Typical plots of area as a function of compression force are shown in Figure 4. The relationship of area to force with respect to tableting speed may be better understood in the three-dimensional plots illustrated in Figure 5. Using the A/H concept, the A/H ratios for the materials as a function of tableting speed are shown in Figure 6. This would suggest that Avicel PH-102 and Emcompress have similar A/H ratios, and hence behave similarly with respect to changes in tableting speed.

The differences in the compaction behavior of Emcompress and Avicel is well documented in the literature. When compacted, Avicel PH-102 undergoes a high amount of plastic deformation, which is dependent on time for the accommodation of stresses developed during compaction. On the other hand, Emcompress particles fracture when the elastic limit of the material is surpassed. Therefore, it would not be expected to see similar changes in the compaction of these materials with respect to tableting speed. Table X shows some of the area and force data that was obtained. The areas under the force-time curves of the two materials are significantly different, when compressed to similar compression forces. Yet, least squares linear regression

(A)

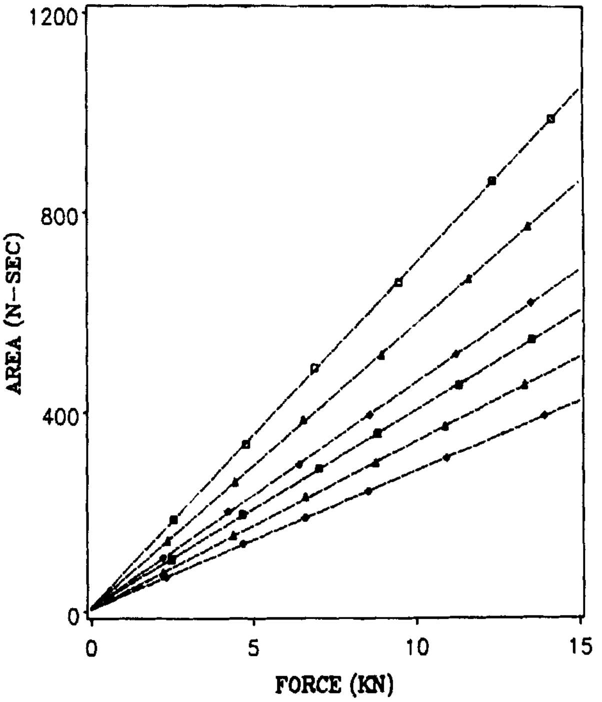
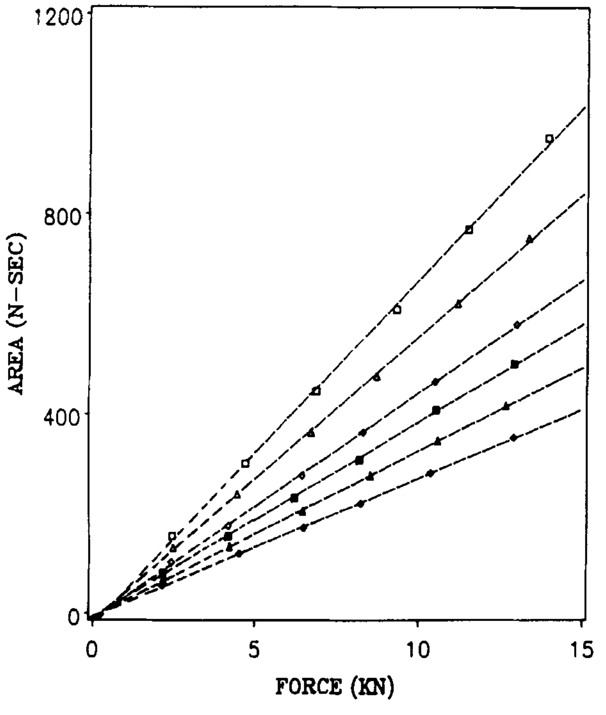


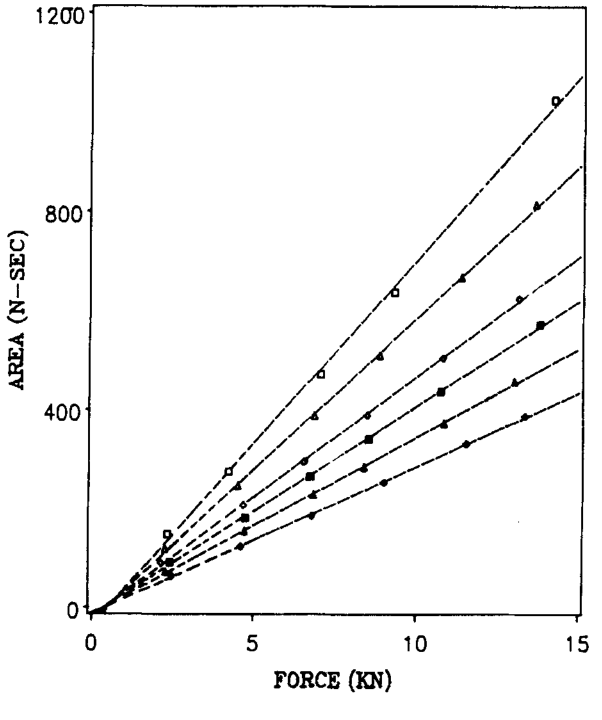
FIGURE 4

Plots of Area as a function of Force at several tablet press speeds for (A) Avicel PH-102, (B) Emcompress and (C) anhydrous lactose. Speed: (□) 25 rpm, (△) 30 rpm, (◇) 37.5 rpm, (■) 42.9 rpm, (▲) 50 rpm, and (◆) 60 rpm.

(B)


1200
800
400
0
AREA (N-SEC)
0
5
10
15
FORCE (KN)

(C)


1200
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AREA (N-SEC)
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FORCE (KN)

(A)

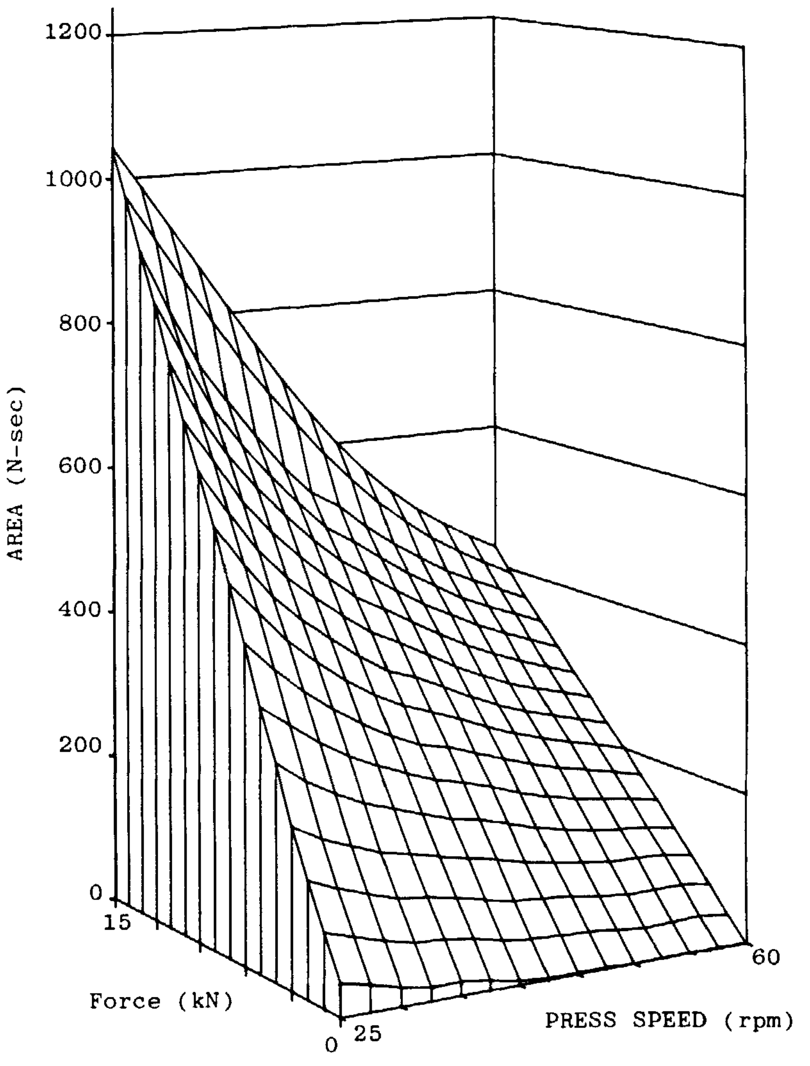

FIGURE 5

Three dimensional plots of Area as a function of force and tableting speed for (a) Avicel PH-102, (b) Emcompress and (c) anhydrous lactose

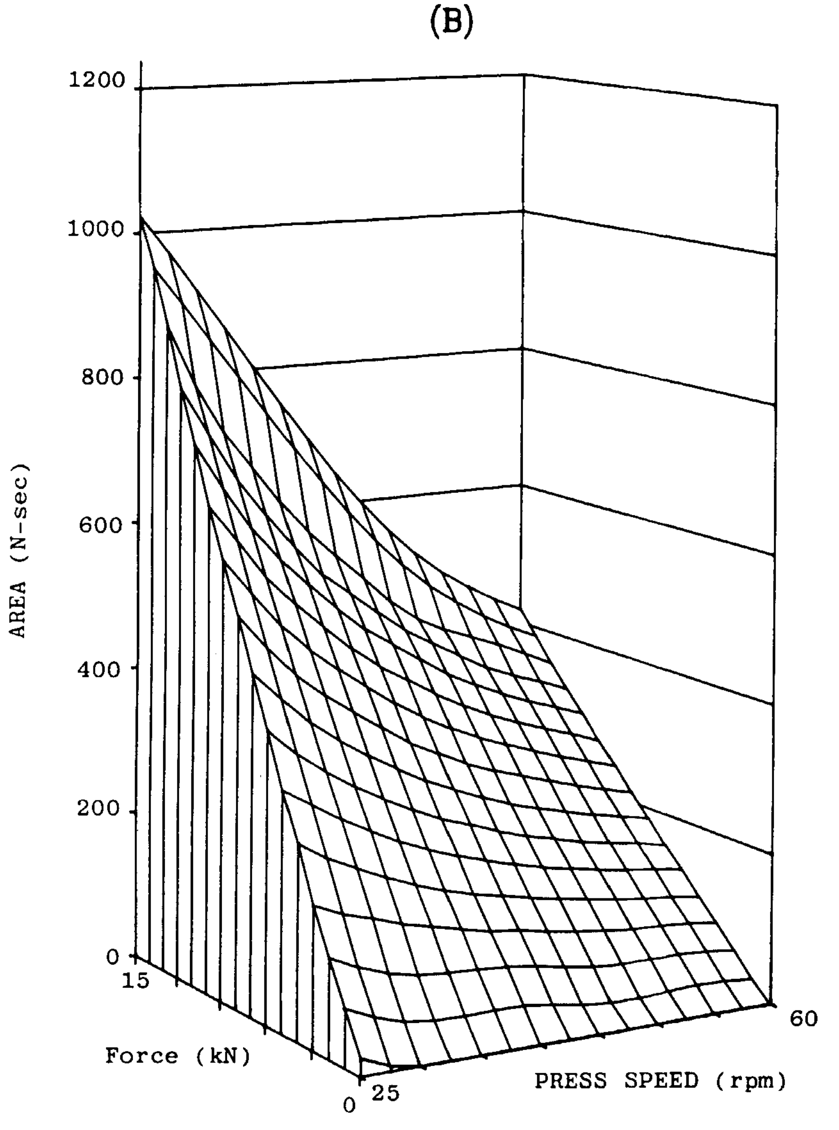

FIGURE 5 (continued)

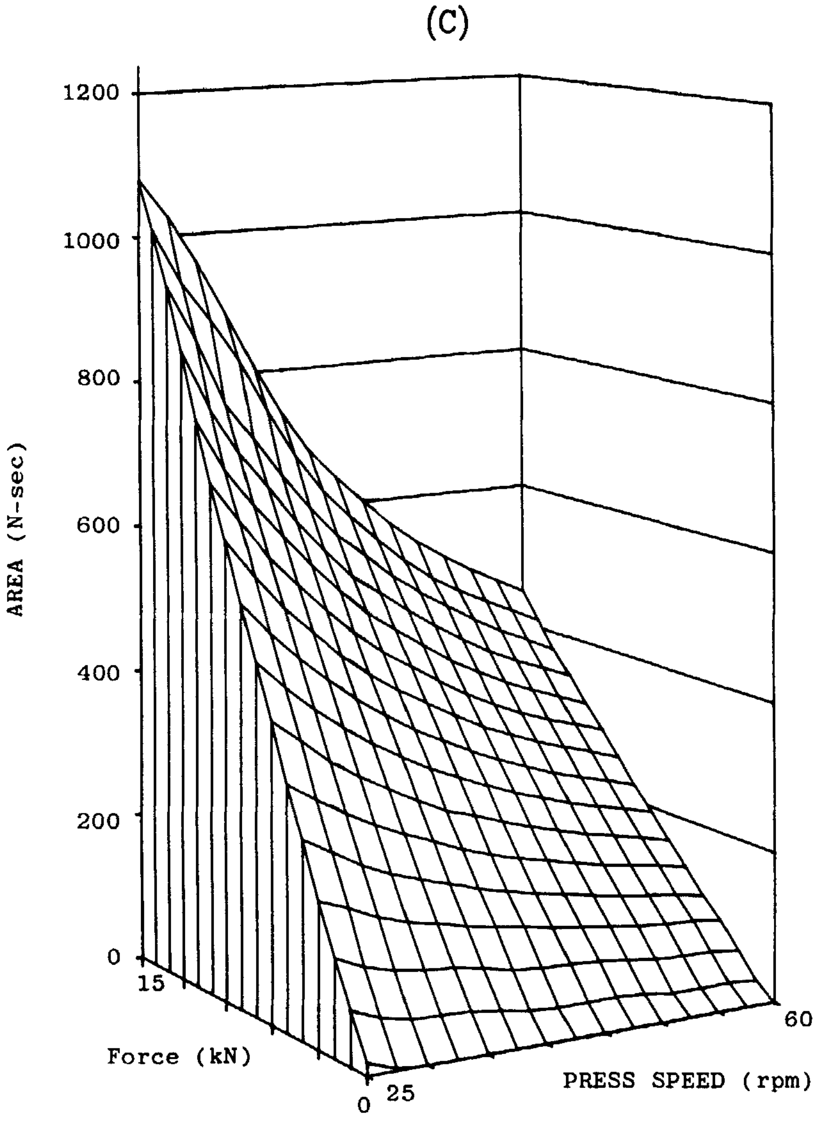

FIGURE 5 (continued)

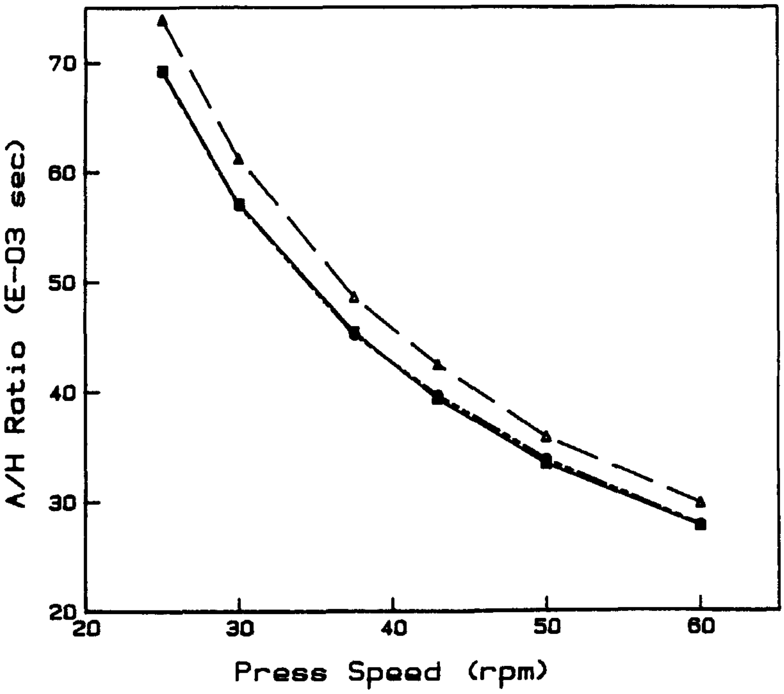

FIGURE 6

Plot of Area/Height Ratio (slope) as it relates to tableting speed for (O) Avicel PH-102, (□) Emcompress, and (Δ) anhydrous lactose

of area as a function of force shows no significant difference in the A/H ratios ($p > 0.05$). Figure 7 illustrates the changes that occur to the intercept value of the A/H relationship. These plots show that even though the A/H ratios of Avicel PH-102 and Emcompress are similar, the change in their A/H intercepts differ drastically when the tableting speed is changed. The A/H intercept of Emcompress converges on zero as the tableting speed

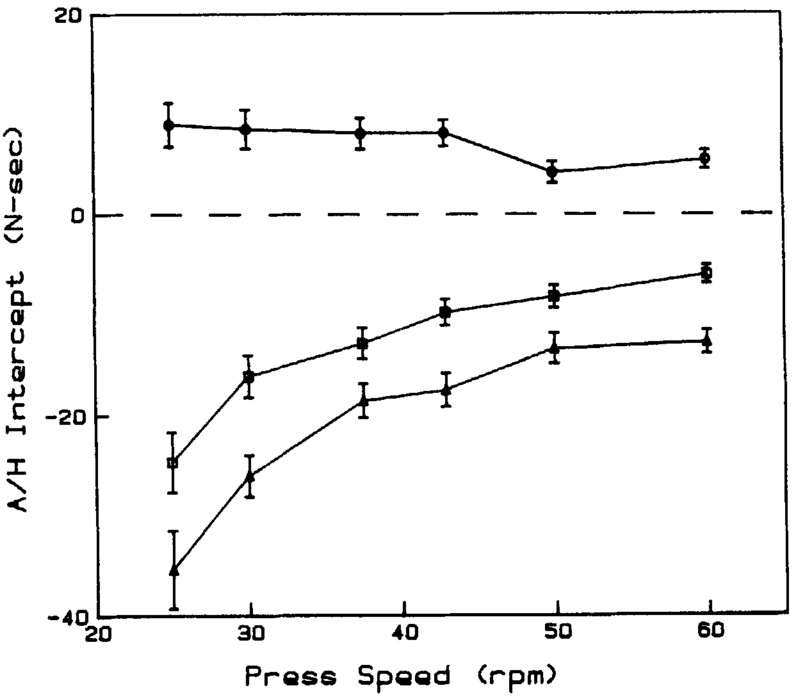

FIGURE 7

Plot of Area/Height Intercept as it relates to tablet speed for (○) Avicel PH-102, (□) Emcompress, and (△) anhydrous lactose

is increased, but that for Avicel PH-102 does not change significantly. An inverse linear relationship was found to exist between the intercept and the tableting speed for the Emcompress and anhydrous lactose ($R^2 > 0.9$). Conversely, a plot of the A/H ratio against the inverse tableting speed shows a linear relationship for all the materials compressed including the Avicel PH-102.

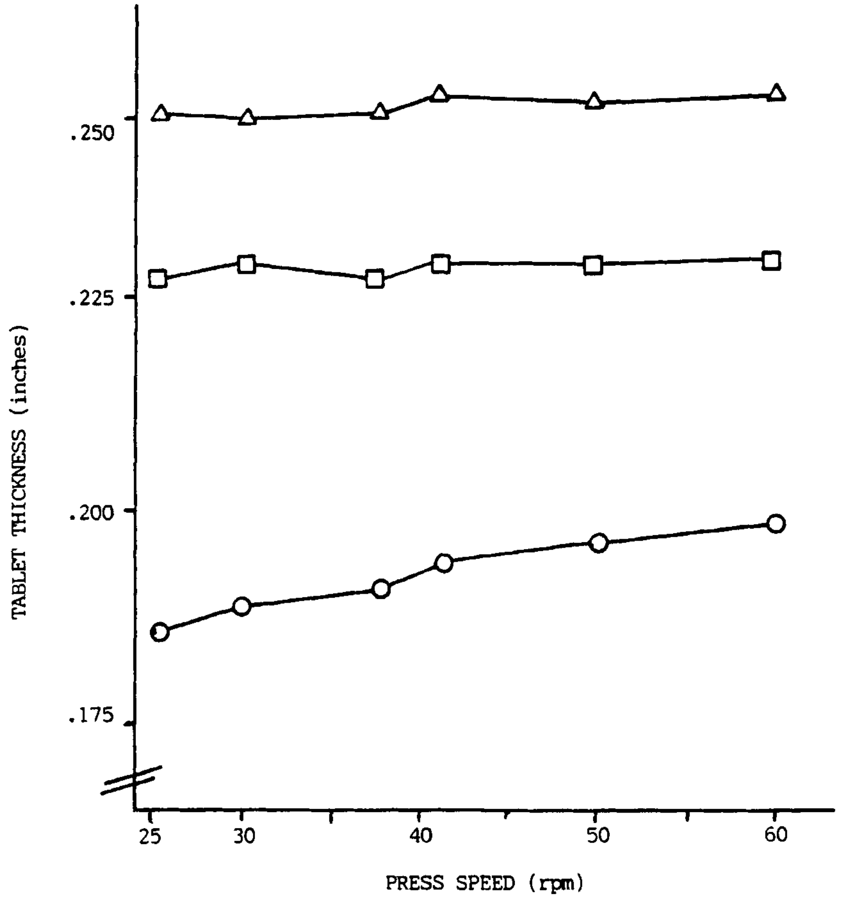

FIGURE 8

The relationship of tablet thickness versus tableting speed for (○) Avicel PH-102, (□) Emcompress, and (△) anhydrous lactose tablets compressed at 6.8 kN

Figure 8 shows the effect of tableting speed on tablet thickness. Tablet thickness decreased (or tablet density increased) with an increase in the "contact" time due to the prolongation of the time available for plastic deformation to occur for the Avicel PH-102. Emcompress and anhydrous lactose (brittle materials) showed no significant changes in tablet thickness (or tablet density) as a result of changes in the "contact" time during compression. The effect of "dwell" time can also be seen as a decrease in the tablet strength for Avicel PH-102 as the tableting speed was increased. This effect was not significantly seen in either the Emcompress or anhydrous lactose materials. The relationship of the A/H ratio to tableting speed was best determined to be that of an inverse proportionality.

Effect of Lubricant

There was a noticeable decrease in the A/H ratio as the amount of lubricant was increased in the formulation. The results are shown in Table XII. A contrast of the effects as determined by a heterogeneity of slope GLM model, indicated that only Avicel PH-101 without lubricant, was significantly different ($p < 0.05$) from the other concentrations of that material. The increase in the A/H ratio can be contributed to the increase in the amount of friction occurring during compaction. The difference seen between the two grades of Avicel may best be explained as a result of the two materials having different mean particle sizes and thus different amounts of surface area available for frictional contact during compaction. Since Avicel PH-101 has a smaller particle size, it would therefore have a greater A/H ratio.

(Emcompress blends with lubricant concentrations less than 0.25% could not be tableted satisfactorily without sticking and adhesion of material (and tablets) to the punches.)

TABLE XI

A/H Ratios of Different Levels of Lubricant

For Several Direct Compression Matrices

Matrix	Magnesium Stearate Concentration					
	0 %	1/16 %	1/8 %	3/16 %	1/4 %	1/2 %
Avicel PH-101	55.95	54.47	54.22	54.53	54.79	54.26
	(0.29)	(0.31)	(0.30)	(0.30)	(0.31)	(0.29)
Avicel PH-102	54.73	54.34	54.27	-	54.23	53.76
	(0.42)	(0.33)	(0.31)		(0.35)	(0.27)
Emcompress	-	-	-	-	59.43	58.89
					(0.34)	(0.22)

*Note: values in parentheses are standard deviations of the A/H Ratio estimates (DF of regression = 59).

TABLE XII

Results of Multiple Regression Analysis[1] for the Effect of Tablet Weight on the Area/Height Relationship

Coefficient	Parameter Estimate[2]	
Emcompress:		
b_1 (compression force)	56.608	(0.197)
b_2 (tablet weight)	0.132	(0.005)
intercept	-118.146	(3.636)
Avicel PH-102:		
b_1 (compression force)	53.069	(0.251)
b_2 (tablet weight)	0.227	(0.037)
Intercept	-74.552	(10.887)

[1]The multiple regression model used in these analyses was:

$$\text{Area} = b_1\text{Force} + b_2\text{Weight} + \text{Intercept}$$

[2]The units for the estimates are as follows: b_1, E-03 sec; b_2, N-sec/mg; and intercept, N-sec.

Tablet Weight

Tablet weight, or the amount of material being compressed was seen during the study of material characteristics, to affect the area under the force-time curve. Its affect on the A/H ratio was not known, and a study was designed to study this. Figure 9 shows three dimensional diagrams which indicate the effect of tablet weight on the area under the force-time curve for Avicel PH-102 and Emcompress. Both systems were lubricated with 0.5% magnesium stearate.

Analysis of the data shows that an increase in the amount of material being compressed will cause an increase in the value of the Area/Height ratio which will be obtained. An increase in the A/H ratio would be expected since a larger amount of die-wall friction is occurring during the compaction of the larger mass or amount of material. If both systems are adequately lubricated, then the increase in the A/H ratio can be considered a result of the increased resistance of the material to compression. The amount of interparticular friction occurring during compaction is considered to be neglible, and in a well lubricated system the amount of die-wall friction occurring should be minimal.

Multiple regression analyses were conducted on the experimental data of each of the materials. A simple multiple regression model was going to be used:

$$\text{Area} = b_0 + b_1\text{Force} + b_2\text{Weight} + e$$

From Figure 9, it would appear that the intercept term is not affected by the weight of material being compressed. In order to contrast the results of the analysis between the two materials, this simple multiple regression model need terms for the material effects to be added:

$$\text{Area} = b_0 + b'_0M + b_1F + b'_1FM + b_2W + b'_2WM + e$$

where M = Material

F = Force

W = Weight

and e = error

(A)

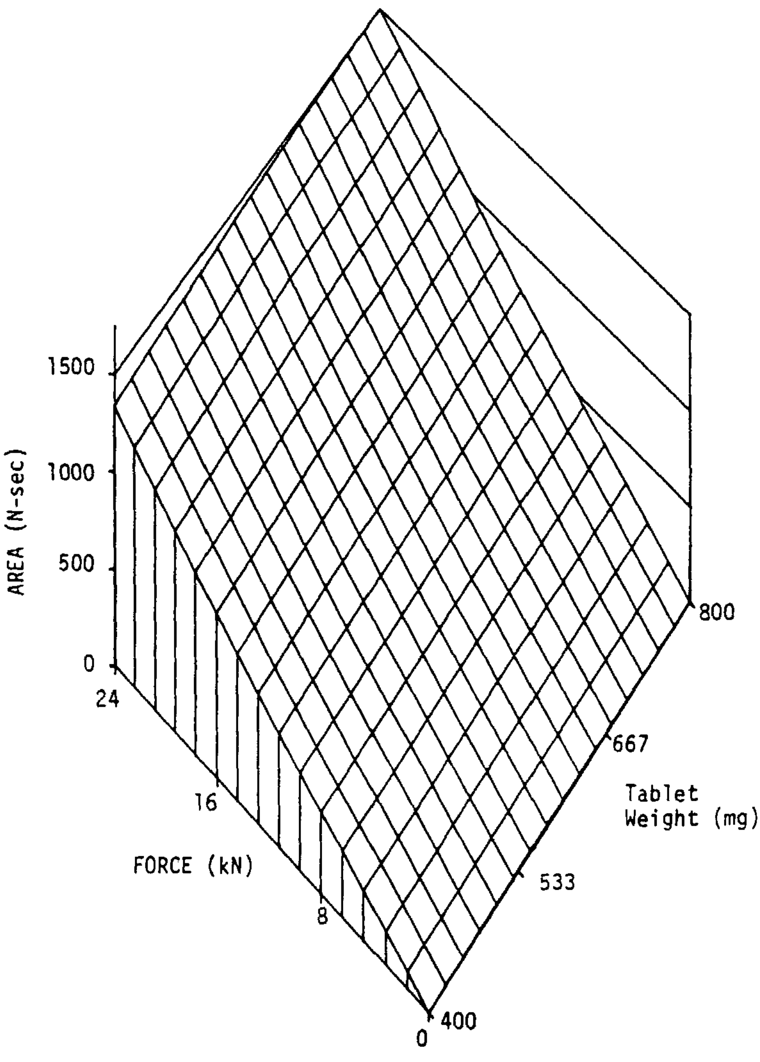

FIGURE 9

Three dimension plots illustrating the effect of tablet speed and force on the area under the compression force-time curve for (A) Avicel PH-102 and (B) Emcompress

(B)

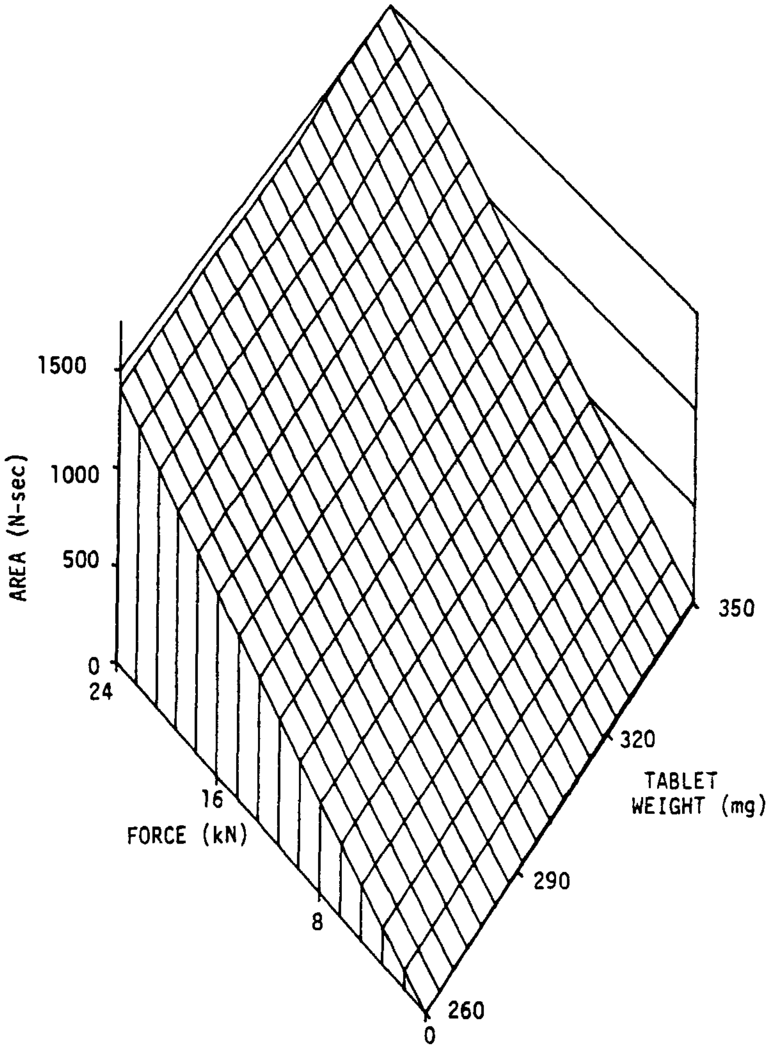

FIGURE 9 (continued)

The SAS output results of this analysis is given in Table XII. The analyses of the two materials were done separately so as not to biase the results of each material. As can be seen from the SAS GLM contrast results, the values for the regression coefficients are statistically significant (for force: $p < .0001$; weight: $p = .0109$). The estimates of the coefficients are very good with very small standard errors.

Particle Size:

Particle size cuts that would result in drastically different mean particle sizes could not be obtained in sufficient quantity to conduct an experiment on the rotary tablet machine. Thus, several brands of Avicel (PH-101, 102, and 105) were used. The A/H ratios and intercept obtained for all three brands were not significantly different (at a level of $p = 0.05$).

Other Derived Parameters

A regression analysis of the width of the compression curve at 50% of the maximum compression force as a function of the force, yields what is a linear relationship in all cases except for Avicel PH-102 and Avicel PH-101. The regression coefficient of this relationship is small but the intercept term appears to have some significance. It appears that it may be the inherent width of the compression curve and dependent on the material or formulation being compressed.

CONCLUSIONS

The results described in this paper clearly show the sensitivity of the area under the compression force-time curve and the derived parameter, Area/Height ratio, to formulation and processing factors. Clearly, the area under the force-time curve is not as simple a function as was first suggested by Chilamkurti et al., and further investigation is needed to fully characterize all the factors which can influence the area under the compression force-time curve, and hence the A/H ratio. In many cases, the changes in the A/H ratio are indeed those which would be expected from a relatively simple model of compaction/ compression. The significance of the negative intercept term is not known at this time.

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