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Some Studies on Compression Properties of Tablet Matrices Using a Computerized Instrumented Press

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INTRODUCTION

The compression properties of eight tablet matrix materials have been investigated using an instrumented single punch tablet press interfaced with a digital computer. The matrices used included two sources of calcium phosphate, lactose, two grades of microcrystalline cellulose, a modified corn starch and two grades of a mixture of alfa-cellulose and calcium phosphate. These components were lubricated with one-half percent magnesium stearate and compressed at varying compaction forces. Properties measured on the uncompacted powders included bulk and tap density and particle size, as determined by sieve analysis. The following tablet properties were measured: weight, thickness, hardness,

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tablet properties were measured: weight, thickness, hardness, friability and disintegration time. It has been found that several properties of the compressional force:time curve (computer print-out) are apparently linearly related to the compressional force and the slopes and intercepts of may be characteristic of a given component. Differences between tablet matrices were detected in both computer parameters and finished tablet properties. It is suggested that the type of compressional force:time curve and the analyses reported in this paper may be of value for both raw material specifications and for advancing our knowledge of the fundamental physico-chemical functions governing the compaction process.

The pharmaceutical compressed tablet is probably the most important dosage form in both North America and Western Europe. There is an increasing realization that the properties of the so-called "inert components" of a tablet can significantly modify such important properties as the bioavailability of the pharmacologically active component. They can also have a profound effect on the processing characteristics of formulations, especially important in a direct compression process. There is, therefore, considerable interest in developing comprehensive raw material specifications for all tablet excipients and especially matrix materials. The Codex of Pharmaceutical Excipients being developed by an Anglo-American team led by Professor Jack Cooper exemplifies this interest. Further, there is substantial interest in elucidating further our understanding of the factors which control the compaction process.

Schwartz and his co-workers have recently developed an instrumented tablet press interfaced to a computer which allows rapid evaluation of a variety of compaction parameters (1, 2). It seems possible that this system will allow the definition of the "compression fingerprints" of tablet matrices, in addition to its use for total formulations.

The direct compression technique for the production of pharmaceutical tablets has several advantages (3). In particular, it

offers significant advantages in terms of cost - both for labor and equipment. Only a quite limited number of materials which can serve as the bulk or major component are available for use in direct compression and thus it is particularly important to define fully the properties of these substances which may be related to the compaction process.

In the present paper, a study of eight direct compression matrices is reported. Data obtained from the instrumented tablet press:computer system is related to other matrix properties.

EXPERIMENTAL

Materials

The following direct compression formulations were evaluated:

Formula IA - dicalcium phosphate dihydrate[1]

IB - dicalcium phosphate dihydrate[2]

IIA - a mixture of dicalcium phosphate dihydrate and α - cellulose[3]

IIB - a mixture of dicalcium phosphate and α-cellulose (coarse grade)[4]

IIIA - microcrystalline cellulose[5]

IIIB - microcrystalline cellulose (coarse grade)[6]

IV - modified, pregelatinized, starch[7]

V - anhydrous lactose[8]

All formulations contained one-half per cent magnesium stearate[9]

Methods

The following properties of the bulk, uncompressed powders were measured: bulk and tap density and particle size. Densities

[1]Emcompress, Edward Mendell Co., Inc., Carmel, NY 10512

[2]Unmilled, Stauffer Chemical Co., Westport, CT 06880

[3]Emcocel (fine), experimental grade, Edward Mendell Co., Inc., Carmel, NY 10512

[4]Emcocel (coarse), experimental grade, Edward Mendell Co., Inc. Carmel, NY 10512

[5]Avicel PH 101, FMC Corp. Philadelphia, PA 19103

[6]Avicel PH 102, FMC Corp., Philadelphia, PA 19103

[7]Sta-Rx 1500, A. E. Staley Co., Decatur, IL 62570

[8]Humko Sheffield, Lyndhurst, NJ 07071

[9]Mallinkrodt, Inc., St. Louis, MO 63147

were measured using a graduate cylinder and motorized tapping device set to operate for 2,000 cycles[10]. Sieve analysis was accomplished using a nest of sieves and fraction analyzer[11]. The powders were sieved for twenty minutes and the geometric mean particle size was calculated for each matrix.

The magnesium stearate was mixed with the tablet matrices using a twin-shell blender[12]. Tablets were made using a single punch press[13], monitored by a special computer system. The compressional force was varied up to a maximum 3.5 kilo Newtons (approximately 8,000 lbs) at a constant tablet weight and a machine speed of 60 tablets per minute. Punch diameter was approximately 0.95 cm (12/32") and target tablet weight was 300 mg, except for microcrystalline cellulose and the modified starch for which tablet weight was 200 mg (this produced tablets all of which were of essentially the same thickness).

On a single punch tablet press, it is possible to observe both the applied and transmitted compressional forces as well as the tablet ejection force. All these parameters were monitored by computer during the compressing operation, as well as by oscilloscope and recorded by photographs. For the applied and transmitted curves which are force versus time curves, the following parameters (illustrated in Figure 1 and defined in the Appendix) were obtained via computer print-out: peak height (maximum force), maximum slope, inflection point height, area under the curve and the time parameters of peak, width, inflection point and width at half-height.

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[10] Model JEL-ST2, Numec Instruments and Control Corp., Monroeville, PA 15146

[11] Geosince Instrument Corp., Mount Vernon, NY 10500

[12] Patterson-Kelley, East Stroudberg, PA 18301

[13] Model F, Stokes Compacting Equipment Division, Penwalt Corp., Warminster, PA 18974

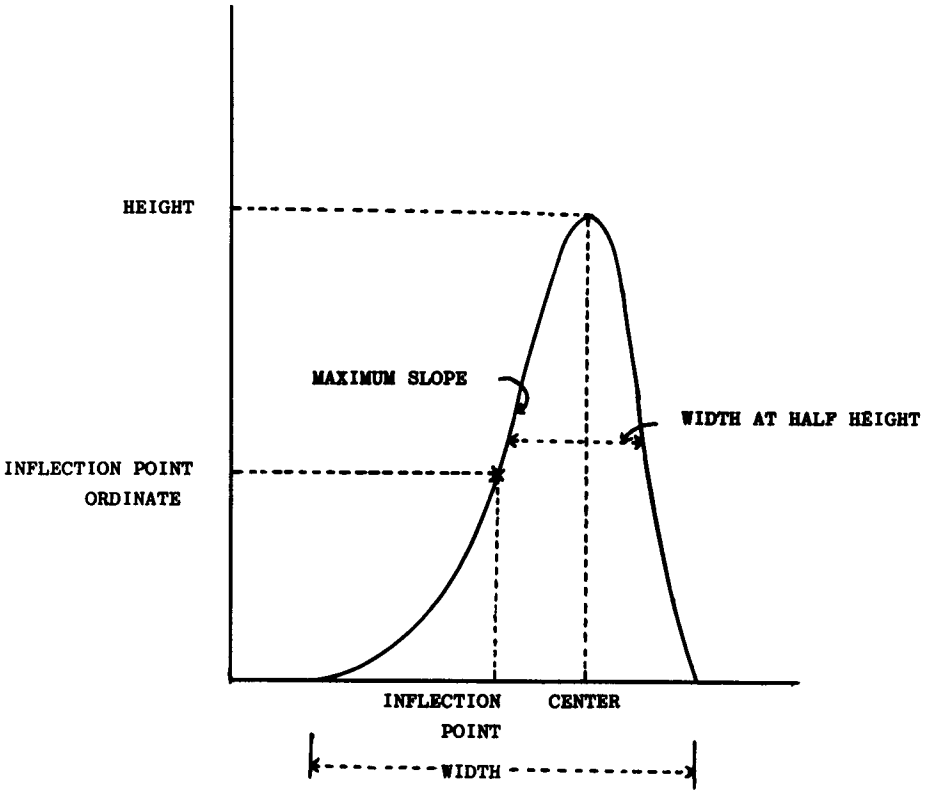

Fig. 1 Compression parameters of an applied force curve.

Labels to axes:
ordinate: Compressional Force (Newtons)
abscissa: Time (seconds)

The following tablet properties were measured: weight[14], thickness[15], hardness[16], friability[17], and disintegration time. A sample size of ten tablets was used for weight, thickness and hardness determinations. Friability was determined by using an

[14]Mettler H8 balance, Mettler Instrument Corp., Heightstown, NJ 08520

[15]Zeus micrometer

[16]Erweka hardness tester, Erweka G.m.b.H., Frankfurt, Germany

[17]Erweka abrasion tester, Erweka G.m.b.H., Frankfurt, Germany

Table I

Geometric mean particle size and bulk and tap density values for the eight matrices investigated

Matrix	Geometric Mean Diameter (in microns)	Density ($G\ cm^{-3}$) Bulk	Tap
dicalcium phosphate dihydrate (source 1)	160	0.82	1.03
dicalcium phosphate dihydrate (source 2)	163	0.85	1.07
alfa-cellulose & dicalcium phosphate dihydrate (grade 1)	102	0.54	0.71
alfa-cellulose & dicalcium phosphate dihydrate (grade 2)	205	0.59	0.75
microcrystalline cellulose (grade 1)	62	0.30	0.44
microcrystalline cellulose (grade 2)	100	0.29	0.43
pregelatinized starch	83	0.61	0.80
anhydrous lactose	125	0.55	0.81

abrasion tester[17] with 20 tablets for 20 minutes. Disintegration time was determined for six tablets (for each run) with a USP disintegration apparatus[18] (with discs) at 37°C, in water.

RESULTS AND DISCUSSION

Table I lists the geometric mean particle size and bulk and tap density values for the eight materials. Fig. 1 shows a typi-

[18]Scientific Glass Apparatus Co., Inc., Bloomfield, NJ 07003

cal compression curve, and the parameters analyzed to define the curve. A number of plots of these different compression force parameters against either other compression force parameters or against tablet properties were made and in many instances, good evidence of linear relationships was obtained. Two examples of such plots are shown in Figs. 2 and 3, for area under the curve vs.

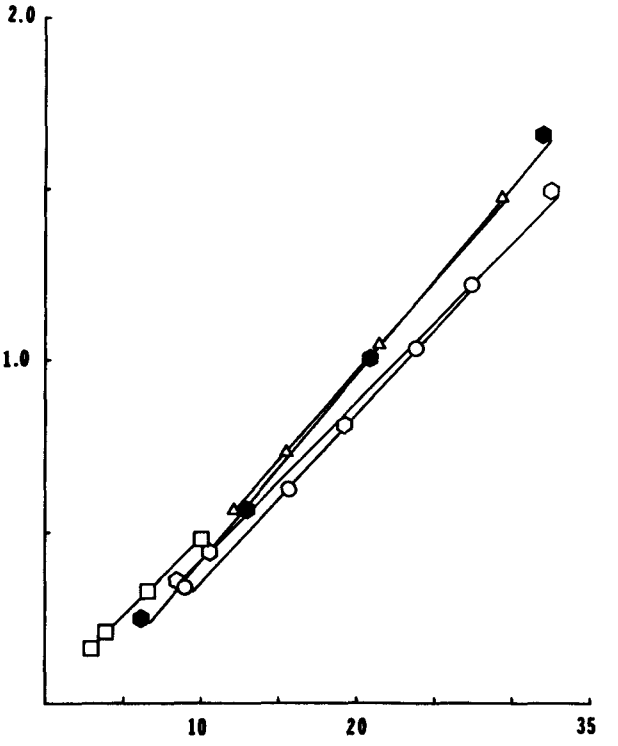

Fig. 2 Plot of area as a function of maximum compression force (Height)

Labels to axes:
ordinate: Area (Newtons seconds x 10^{-3})
abscissa: Height (Newtons x 10^{-3})

Key: ○ dicalcium phosphate dihydrate (source 1)
□ microcrystalline cellulose (grade 1)
△ alfa-cellulose and dicalcium phosphate dihydrate (grade 1)
⬡ pregelatinized starch
⬢ anhydrous lactose

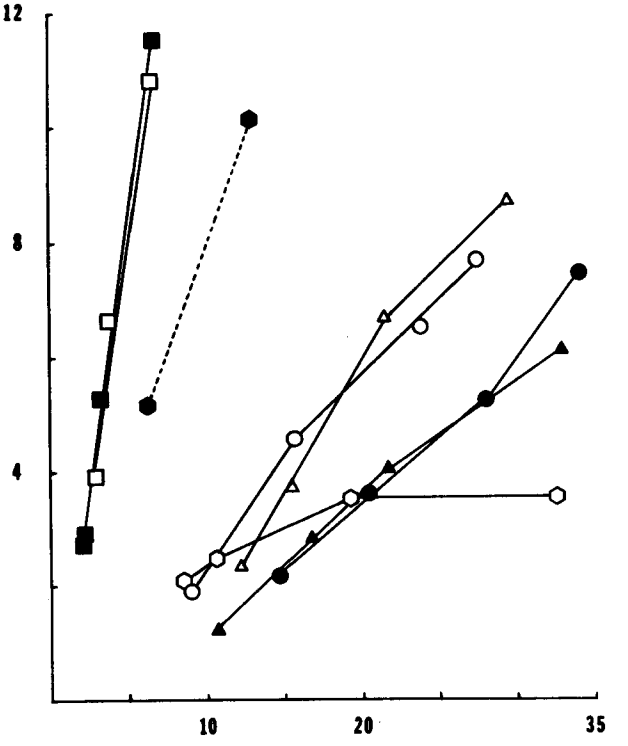

Fig. 3 Plot of hardness as a function of maximum compression force (Height)

Labels to axes:
ordinate: Hardness (Killograms)
abscissa: Height (Newtons x 10^{-3})

Key:
- ○ dicalcium phosphate dihydrate (source 1)
- ● dicalcium phosphate dihydrate (source 2)
- △ alfa-cellulose and dicalcium phosphate dihydrate (grade 1)
- ▲ alfa-cellulose and dicalcium phosphate dihydrate (grade 2)
- □ microcrystalline cellulose (grade 1)
- ■ microcrystalline cellulose (grade 2)
- ⬡ pregelatinized starch
- ⬢ anhydrous lactose

compression force and for tablet hardness vs. compressional force respectively.

The equipment used in this study allows determination of more information about the change of compressional force with time than has previously been possible with other systems. In general, the uses of instrumented tablet presses have been separated for production and for research and development. Rotary tablet machines have been utilized for production purposes, and the application has been primarily involved with the uniformity of the compressional force signal (and therefore tablet weight uniformity) and with ejection force measurement and uniformity. Instrumented single punch machines have had primary usage in research/development applications. In addition to compressional force and ejection force measurements, they have been utilized for measurement of die-wall pressure (4, 5) and punch displacement (6, 7). These types of measurements have enabled investigators to determine more detail in the physics of tablet compression (8).

The partial objective of this instrumented press system (1, 2) was to bridge the gap between basic research and the manufacturing area by analyzing the compressional force curves in more detail and by generating these curves as 'fingerprints' for formulations from the manufacturing area. These fingerprints could then serve as baseline data in a trouble-shooting function (e.g., raw material change, equipment change, etc.). It is also obvious that from a development perspective, these fingerprints and their subsequent analysis could be useful in evaluating and classifying various excipients, in formulating, and possibly in setting material specifications.

Towards that end, Fig. 2 shows that for all the systems studied, the area of the force:time curve, is a linear function of maximum compression force. This area is related to the work of compression, although the actual determination requires punch displacement measurements. Thus, for materials which have roughly the same change in volume (initial and final thickness) during the compressing operation, either of these measurements may be used as a first

approximation to rank the work or energy required to form a tablet of that excipient.

As shown in Table II, the slope values for the type of plot shown in Fig. 2 do show subtle differences. We are not presently able to state categorically that such differences are significant - this point is presently the subject of further investigation - however, if indeed such differences, although small, are found to be

Table II

Slope values of area:maximum compression force

(See Fig. 2)

Formula	Matrix	Slope (X 10^3) (sec)	Correlation Coefficient (number of points)
IA	dicalcium phosphate dihydrate (source 1)	48.34	0.9992 (4)
IB	dicalcium phosphate dihydrate (source 2)	53.71	0.9992 (4)
IIA	alfa-cellulose & dicalcium phosphate dihydrate (grade 1)	53.34	0.9999 (4)
IIB	alfa-cellulose & dicalcium phosphate dihydrate (grade 2)	53.37	0.9993 (4)
IIIA	microcrystalline cellulose (grade 1)	45.30	0.9998 (4)
IIIB	microcrystalline cellulose (grade 2)	46.62	0.9997 (5)
IV	pregelatinized starch	47.86	0.9989 (4)
V	anhydrous lactose	55.19	0.9990 (4)

Note: All the intercept values are very small, less than 0.25 Newton second.

real, these slope values may be of value in characterizing tablet matrices and in further elaborating compaction theory.

Tables II, III and IV show the results of other curve parameter vs. compressional force plots. In all cases, very good evidence of linearity was obtained for all matrices, but each matrix appears to be characterized by an individual slope (and in several cases, intercept) values. These results further support the hypothesis advanced above that the values shown in Tables II through IV reflect the nature of the compaction process as it occurs for any given matrix. A similar type of relationship was determined from transmitted force data (Tables V-VII).

The time to peak and peak width increased with increasing compressional force as expected, due to the machine mechanics. Differ-

Table III

Slope values of maximum slope:maximum compression force

Formula	Slope (sec^{-1})	Intercept (N. sec^{-1})	Correlation Coefficient (number of points)
IA	29.93	8.82	0.9996 (4)
IB	29.23	27.75	0.9991 (4)
IIA	24.96	-1.76	0.9994 (4)
IIB	26.50	8.96	1.0000 (4)
IIIA	24.98	-18.01	0.9997 (4)
IIIB	23.69	-9.51	0.9989 (5)
IV	35.27	-92.29	0.9991 (4)
V	22.63	54.18	0.9987 (4)

Table IV

Slope values of inflection point ordinate:maximum compression force

Formula	Slope ($\times 10^2$)	Correlation Coefficient (number of points)
IA	51.59	0.9986 (4)
IB	50.56	0.9989 (4)
IIA	60.63	0.9996 (4)
IIB	57.56	1.0000 (4)
IIIA	64.99	0.9993 (4)
IIIB	67.36	0.9999 (4)
IV	59.59	0.9803 (4)
V	60.61	0.9997 (4)

Note: Intercepts values are very small, less than 0.76 Newtons.

ences between materials, however, are apparent from the time parameter ratios. In order to further characterize the compression curves, the following time parameter ratios were calculated: 'Center/Width' (C/W) -- the ratio of peak time to compression time (the fraction of compression event before the peak); 'Inflection Point/Width' (I/W) -- the ratio of inflection point time to compression time (the fraction of compression event before the inflection point); 'Half-width/width' (H W/W) -- the ratio of the peak width at half-height to the total peak width (an indication of the shape of the curve); Inflection point/Center' (I/C) -- the ratio of inflection point time to peak time (the fraction of peak time before the inflection point). In addition to these time parameter ratios, one ratio was calculated involving the force measurements: 'Inflection Point Ordinate/Height'

Table V

Slope values of area:maximum transmitted force

Formula	Slope ($X 10^3$) (sec)	Correlation Coefficient (number of points)
IA	48.71	0.9994 (4)
IB	54.21	0.9990 (4)
IIA	55.01	0.9992 (4)
IIB	54.17	0.9990 (4)
IIIA	45.23	0.9999 (4)
IIIB	42.87	0.9999 (3)
IV	48.07	0.9988 (4)
V	55.89	0.9988 (4)

Note: All the intercept values are very small, less than 0.2 Newton second.

Table VI

Slope values of maximum slope:maximum transmitted force

Formula	Slope (Sec^{-1})	Intercept (N. sec^{-1})	Correlation Coefficient (number of points)
IA	30.33	8.93	0.9998 (4)
IB	29.34	31.10	0.9996 (4)
IIA	24.99	-2.15	0.9987 (4)
IIB	26.76	13.43	1.0000 (4)
IIIA	25.71	-12.03	0.9992 (4)
IIIB	25.28	-6.51	0.9990 (3)
IV	35.82	-76.97	0.9994 (4)
V	23.15	45.27	0.9992 (4)

Table VII

Slope values of inflection point ordinate:transmitted force

Formula	Slope (X 10^2)	Correlation Coefficient (number of points)
IA	48.43	0.9998 (4)
IB	49.23	0.9995 (4)
IIA	62.83	0.9986 (4)
IIB	56.13	0.9998 (4)
IIIA	64.52	1.0000 (4)
IIIB	64.53	0.9995 (3)
IV	57.57	0.9832 (4)
V	59.66	0.9993 (4)

Note: Intercept values are all very small, less than 0.8 Newtons.

(I.O/H) -- the ratio of inflection point ordinate to peak height (the fraction of the compressional force applied before the inflection point).

The values, for any given ratio, for all the matrices fall within a narrow range. However, the effect of increasing compressional force on these ratios is clearly evident even though the changes in ratio values are relatively small. The parameter ratios for the matrix materials at approximately equivalent compressional force are shown in Table VIII. For the applied force (upper punch) curve, the ratio C/W showed an increasing trend with increase in compressional force for the formulations IIIA and B, however a reverse trend (usually) was followed for other formulations. An increasing trend was followed for the formulas IA and B for the H W/W. Formulas IIA and B did not appear to follow any trend for this ratio while the rest of the formulations showed a decreasing trend.

Table VIII

Compression curve parameter ratios at approximately equivalent compressional force

Formula	Maximum Compressional Force (Newtons)	Center / Width	Half-Width / Width	Infl. Point / Width	Infl. Point / Center	Infl. Point Ordinate / Height
IA	8936	.765	.421	.530	.692	.566
IB	14647	.726	.443	.496	.682	.560
IIA	12192	.707	.470	.466	.589	.584
IIB	10662	.708	.472	.468	.601	.568
IIIA	10124	.764	.416	.576	.753	.654
IIIB	9385	.777	.401	.599	.771	.662
IV	10653	.690	.512	.443	.643	.608
V	12975	.701	.513	.428	.611	.559

For the ratio I/W, formulations IA and B showed a decreasing trend while formulations IIIA and B exhibited an increasing trend. Formulations IIIA and B and IV showed an increasing trend for the ratio I/C and other formulations did not show any particular trend for this ratio. For the ratio I.O/H formulations IA and B exhibited a decreasing trend while other formulations showed opposite trends.

For transmitted force (lower punch) curves, formulations IA and B followed similar trends mostly to the ratios found in the applied force curve analysis. No such similarities were observed with formulations IIA and B. Both applied force curves and transmitted force curves showed similar trends for formulations IIIA and B for the ratio HW/W, I/W and I/C. Formulation IV showed similar trends for both applied and transmitted force curves for the ratios I/W,

I/C and I.O/H while formulation V exhibited similar trends for the ratios C/W, I/W and I/C.

In general, both sources of dicalcium phosphate dihydrate showed similar trends in parameter ratios with increasing compressional force. Both grades of microcrystalline cellulose were also similar in exhibiting parameter ratio trends (except I.O/H) with increasing compressional force. However, no such similarities, for the most part, were followed for the two grades of mixtures of alfacellulose and dicalcium phosphate dihydrate. Microcrystalline cellulose and dicalcium phosphate dihydrate showed opposite trends in their parameter ratios with increase in compressional force. Pregelatinized starch and anhydrous lactose followed trends similar to the microcrystalline celluloses, with the exception of the C/W ratio.

No relationship was apparent between ejection force and applied compressional force. The shape of the ejection curve (Fig. 3), however, does differ between the types of the matrix. Five distinct shapes of ejection force curve were obtained. Recently Matsuda and coworkers suggested that even at the same maximum ejection force, the shape of the curve changes with a close relation with lubricity depending on the formulation (9). Fig. 3 indicates the shape of five types of ejection force curves obtained. Formulations IA and B showed more than one peak in their ejection curves and the curve ends below the base line. For formulations IIA and B more than one peak was obtained, however, the end of ejection curve did not end below base line. Formulations IIIA and B usually showed a single peak. The shape of ejection curve for formulation IV was also similar to formulations IIIA and B, but often, after the curve reached the base line, a wavy line was obtained. Formulation V showed a very distinct shape of ejection curve than other formulations. Perhaps this formulation has the least lubricity of all the formulations.

The ratios of transmitted force to the applied force were calculated for all the formulations. These ratios represent the

'R' values as reported by Nelson and coworkers (10, 8). These values ranged from 0.70 to 0.91 at various compressional forces. At same compressional force, no siginificant difference in R values were found between the formulations. (Microcrystalline cellulose formulations could not be compared with rest since the microcrystalline celluloses required relatively low compressional forces.)

Tables IX and X show the physical properties weight, thickness, hardness, friability and disintegration time measured on the tablets. As expected, the weight uniformity for all formulations was excellent. Thickness decreased with an increase in compressional force for all the matrices. The change in thickness for a unit change in applied compressional force is relatively high for microcrystalline cellulose formulations in comparison with other matrices. Dicalcium phosphate dihydrate formulations (IA and B) produced tablets with highest apparent tablet densities while microcrystalline cellulose formulations (IIIA and B) had lowest apparent tablet densities. Difference in apparent tablet densities between two grades of microcrystalline celluloses was relatively small. Apparent tablet densities increased with increase in applied compressional force. This increase was rapid for microcrystalline cellulose formulations.

The individual tablet matrices can be characterized by the relationship between hardness and applied force. Such hardness-compaction force profiles are presented in Fig. 3 for the matrices investigated. Hardness increased with increasing applied force for all the matrices with the exception of pregelatinized starch for which a plateau was reached after certain force. It can be seen that the two types of calcium phosphate show significant differences in hardness values at any given compressional force. At equivalent pressures, formulations IIIA and B produced hardest tablets and the pregelatinized starch produced the softest. For formulations IIIA and B rapid changes in hardness with increasing applied force was also observed. Formulations IIIA and B produced the least friable

Table IX

Tablet Properties

Formula	Compressional Force, Newtons ($\times 10^{-3}$)	Weight (mg) Mean	Weight (mg) R.S.D.[a]	Thickness (mm) Mean	Thickness (mm) R.S.D.[a]
IA	8.936	303.3	0.31	2.42	0.34
	15.661	307.5	1.16	2.30	1.28
	23.823	304.2	0.40	2.19	0.50
	27.435	303.3	0.54	2.16	0.47
IB	14.647	305.2	0.69	2.28	0.51
	20.394	305.4	0.49	2.22	0.50
	27.965	306.3	0.38	2.15	0.47
	34.063	307.1	0.47	2.12	0.40
IIA	12.192	303.5	0.68	3.16	0.25
	15.528	309.7	1.00	3.09	0.73
	21.511	304.0	1.11	2.93	0.45
	29.472	304.0	0.73	2.83	0.74
IIB	10.662	305.0	0.60	2.99	0.25
	16.720	303.7	0.52	2.84	0.43
	21.684	303.6	0.54	2.76	0.28
	32.884	302.9	0.83	2.66	0.66
IIIA	3.020	199.9	1.71	3.01	0.96
	3.963	203.3	0.81	2.79	0.58
	6.650	205.2	1.30	2.43	0.51
	10.124	204.2	0.60	2.22	0.46
IIIB	2.211	197.5	1.25	3.20	0.27
	2.264	200.2	1.39	3.22	0.26
	3.367	199.1	0.37	2.83	0.32
	6.810	200.9	0.64	2.36	0.28
	9.385	200.4	0.54	2.19	0.29
IV	8.554	197.1	0.16	2.36	0.29
	10.653	197.2	0.32	2.29	0.31
	19.318	197.0	0.24	2.20	0.25
	32.631	197.2	0.22	2.20	0.24
V	6.227	298.4	0.75	3.52	0.31
	12.975	297.6	0.66	3.16	0.58
	20.990	304.9	1.09	3.05	0.63
	32.097	299.8	1.20	2.88	0.89

[a] relative standard deviation

Table X

Tablet Properties

Formula	Compressional Force, Newtons ($x10^{-3}$)	Hardness (Kg) Mean	Hardness (Kg) R.S.D.[a]	Friability (percent)	Disintegration Time (Sec) Mean	Disintegration Time (Sec) Range
IA	8.936	1.9	15.45	4.80	No disint. in 1 hr.	
	15.661	4.6	7.34	2.61	No disint. in 1 hr.	
	23.823	6.6	14.37	1.51	No disint. in 1 hr.	
	27.435	7.7	7.85	1.38	No disint. in 1 hr.	
IB	14.647	2.2	20.31	4.15	No disint. in 1 hr.	
	20.394	3.6	10.90	2.58	No disint. in 1 hr.	
	27.965	5.3	12.73	1.83	No disint. in 1 hr.	
	34.063	7.5	22.77	1.47	No disint. in 1 hr.	
IIA	12.192	2.3	12.47	2.15	5	3 - 7
	15.528	3.7	9.20	1.24	7	5 - 10
	21.511	6.7	8.58	0.48	10	7 - 12
	29.472	8.8	5.04	0.33	13	10 - 18
IIB	10.662	1.2	13.18	4.81	7	5 - 10
	16.720	2.8	9.38	1.96	12	10 - 15
	21.684	4.1	6.38	1.22	21	18 - 25
	32.884	6.1	6.16	0.64	36	30 - 45
IIIA	3.020	3.9	6.75	0.68	17	12 - 25
	3.963	6.7	6.91	0.40	40	35 - 45
	6.650	10.8	9.92	0.44	66	55 - 80
	10.124	$>$15.0		0.29	138	115 - 170
IIIB	2.211	2.7	8.03	1.06	14	10 - 18
	2.264	2.9	9.91	0.93	20	18 - 23
	3.367	5.3	4.15	0.48	18	15 - 23
	6.810	11.6	5.28	0.25	52	45 - 55
	9.385	$>$15.0		0.05	116	90 - 155
IV	8.554	2.1	8.32	4.10	277	190-405
	10.635	2.5	13.33	2.92	275	220 - 455
	19.318	3.6	6.47	1.41	294	265 - 325
	32.631	3.6	10.96	1.26	305	297 - 310
V	6.227	5.2	12.48	2.36	223	197 - 252
	12.975	10.2	9.27	0.81	411	390 - 445
	20.990	$>$15.0		0.70	439	410 - 460
	32.097	$>$15.0		0.78	373	295 - 417

[a]relative standard deviation

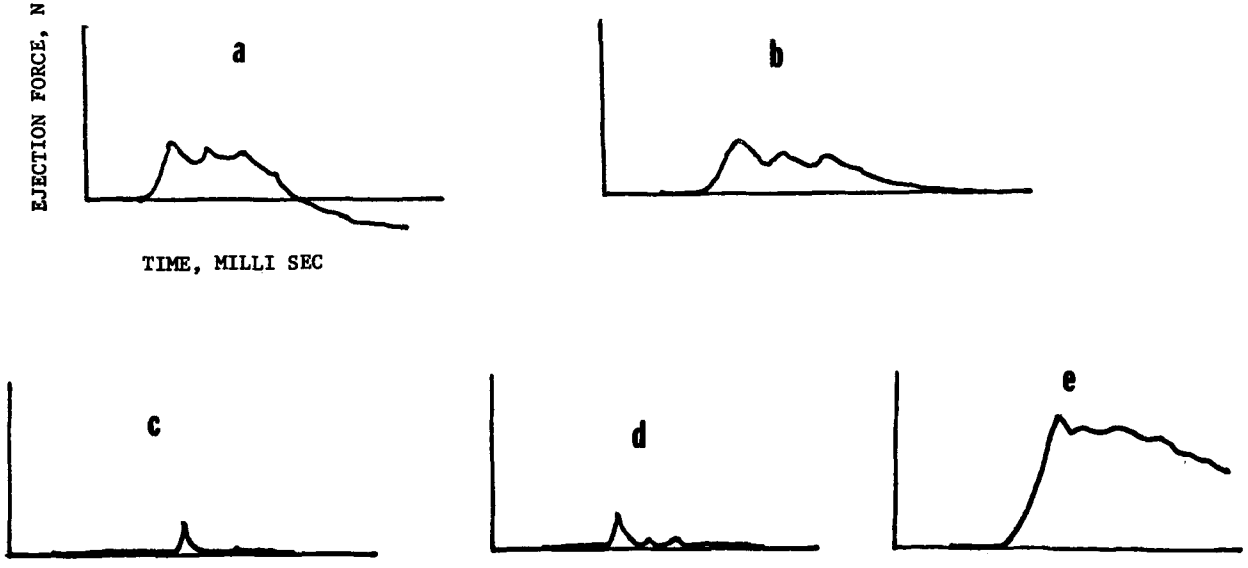

Fig 4. Ejection force:time curves

Key:
a. dicalcium phosphate dihydrate (source 1 and 2)
b. alfa-cellulose and dicalcium phosphate dihydrate (grade 1 and 2)
c. microcrystalline cellulose (grade 1 and 2)
d. pregelatinized starch
e. anhydrous lactose

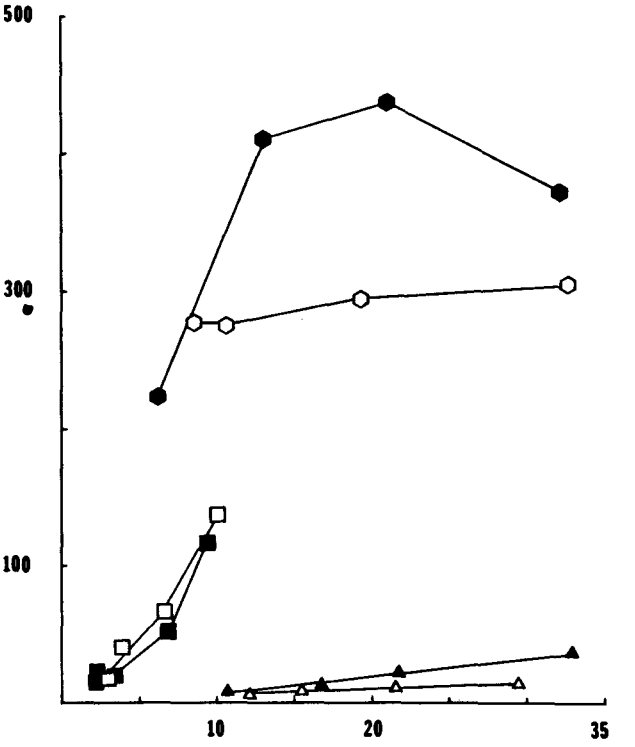

Fig. 5 Plot of disintegration time as a function of maximum compression force

Labels to axes:
ordinate: Disintegration time (seconds)
abscissa: Height (Newtons x 10^{-3})

Key:
△ alfa-cellulose and dicalcium phosphate dihydrate (grade 1)
▲ alfa-cellulose and dicalcium phosphate dihydrate (grade 2)
□ microcrystalline cellulose (grade 1)
■ microcrystalline cellulose (grade 2)
⬡ pregelatinized starch
● anhydrous lactose

tablets. The formulations IA, B and IV produced the most friable. In all cases, friability decreased with increasing applied compressional force.

All matrices except dicalcium phosphate dihydrate, disintegrated rapidly (i.e., in less than eight minutes) at all hardness

values. Within this narrow range differences were still noted, although the practical significance may be negligible. Disintegration time:compaction force profiles are shown in Fig. 4. The mixtures of alfa-cellulose and dicalcium phosphate dihydrate exhibited the least change in disintegration time with pressure. Average disintegration times varied from 5-36 seconds for the mixtures of alfa-cellulose and dicalcium phosphate dihydrate, from 14 to 138 seconds for microcrystalline cellulose, from 275 to 305 for pregelatinized starch and from 223 to 439 seconds for anhydrous lactose. The calcium phosphate systems did not disintegrate in one hour. With the exception of anhydrous lactose, disintegration times increased with increasing compressional force. For anhydrous lactose, a drop in disintegration time was observed after certain pressure.

CONCLUSION

The observations listed above represent an initial tabulation of compressional force curve parameters and tablet properties for several tablet matrix materials. The pharmaceutical literature shows that there are many ways of making comparisons to evaluate materials; each formulator must select points of comparison which are meaningful to him.

It is obvious that the type of instrumented tablet press interfaced with a computer used in this study has considerable potential for both theoretical and practical studies of compaction and tablet matrices. Further work is obviously needed before the full significance of some of the values recorded in this paper can be ascertained.

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REFERENCES

1. A. S. Rosenberg, G. J. Faini, J. E. Allegretti, and J. B. Schwartz, paper presented at the A.Ph.A. Academy of Pharmaceutical Sciences meeting, San Antonio, Texas, November, 1980.
2. J. B. Schwartz, E. J. Dehner and J. E. Allegretti, Paper presented at the A.Ph.A. Academy of Pharmaceutical Sciences meeting, San Antonio, Texas, November, 1980.
3. K. A. Khan and C. T. Rhodes, Canad. J. Pharm. Sci., 8, 1 (1973).
4. E. Nelson, J. Am. Pharm. Assoc., Sci. Ed., 44, 494 (1955).
5. J. E. Carless and S. Leigh, J. Pharm. Pharmacol., 26, 289(1974)
6. E. Nelosn, L. Busse, and T. Higuchi, J. Am. Pharm. Assoc., Sci. Ed., 44, 223 (1955).
7. C. J. deBlaey and J. Polderman, Pharm. Weekblad, 105, 241 (1970).
8. K. Marshall in "Modern Pharmaceutics," Banker and Rhodes, ed., Chap. 10, Marcel Dekker, New York, 1979.
9. Y. Matsuda, Y. Minamide, and S. Hayashi, J. Pharm. Sci., 65, 1155 (1976).
10. E. Nelson, S. M. Naqvi, L. W. Busse and T. Higuchi, J. Am. Pharm. Assoc., Sci. Ed., 43, 596 (1954).

APPENDIX

The following parameters are calculated by computer to characterize the compression curve. This curve shows force (F) as a function of time, t. (See Fig. 1)

Symbol		
C	Center:	The time to reach the peak in the compression curve (in seconds).
H	Height:	The peak height or compressional force (in Newtons). For the upper punch, this represents applied force. For lower punch this represents transmitted force.
W	Width:	Peak width (in seconds) i.e., the duration of the compression event. The compression event is defined as the time during which the measured force (either applied or transmitted) has a finite value.
HW	Half-Width:	The peak width at half-height (in seconds).
MS	Maximum Slope:	The maximum slope on the ascending curve or the maximum positive finite value of dF/dt (in Newtons seconds^{-1}).

I	Inflection Point:	The time between the start of the compression event and the time when +dF/dt is maximal (in seconds).
I.O	Inflection Point Ordinate:	The value of force, F, at the inflection point (in Newtons).
A	Area:	Total area under the compression curve (in Newtons seconds).