SUMMARY

Using the IBM 1401 (8K) computer, a program was written for the numerical estimation of the eutectic temperature from an equation which could not be solved analytically.

A second program was written in a more general form to print tables of eutectic temperatures over a range of *Lf'* values from 100 to 6000 cal. and melting points from 10 to 300°.

The errors inherent in the eutectic expression and the program were elucidated.

This study demonstrates one of the several possible applications of computers in pharmaceutical research and development.

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Evaluation of the Physical Properties of Compressed Tablets I

Tablet Hardness and Friability

By JAMES A. SEITZ and GERALD M. FLESSLAND

Studies were conducted to evaluate what changes occurred in the physical properties of compressed tablets as the operation of a rotary tableting machine was varied. Thin large-diameter tablets showed a capping tendency that was not apparent in smaller-diameter or thicker tablets. The crushing strength of tablets stored at 71 per cent R.H. for 28 days was unchanged, but the tablets became more friable. Increasing the compressional speed reduced the crushing strength and increased the capping tendency, but did not affect the friability of compressed tablets. At the higher compressional rates, the tablets showed a greater elastic response than at the slower speeds. Compressing the tablets at various depths in the die had no affect on the physical properties of the compressed tablets.

In the evaluation of the physical properties of compressed tablets, many test procedures have been developed in an attempt to study the mechanical strength of compressed tablets (1–10). Tablet hardness is the nonspecific term routinely applied to several tablet parameters: (*a*) resistance to bending or breaking, (*b*) crushing strength (axial or radial), (*c*) impact strength, and (*d*) resistance to attrition or abrasion.

In addition to the above-indicated properties, it is desirable to have a testing procedure capable of assessing tablet flaws—capping, splitting, chipping—under controlled experimental conditions. The phenomenon of capping has been studied by several investigators (11–15), but the relationship between this tablet flaw and the mechanical strength of a tablet has received little attention.

In previous studies where tablet hardness was critically evaluated, single-punch tableting machines or rotary compressors operating at a slow rate were employed (16, 17). These studies revealed some valuable data, but additional information was needed to determine the influence of the various rotary tableting machine operations on the crushing strength, friability, and capping tendency of compressed tablets. The purpose of the present investigation was to elucidate the role played by rotary tableting machines on influencing the physical properties of the resulting compressed tablets.

In addition, the effect of storage conditions, tablet size, tablet density, and tablet thickness on the physical properties of compressed tablets was assessed.

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EXPERIMENTAL

The tablets were compressed on a Stokes B-2 rotary compressing machine. The tableting machine was run at 36 r.p.m. with $^{13}/_{32}$-in. standard concave punches unless otherwise indicated. The tablets were individually weighed on a Mettler balance to the nearest 0.1 mg., and the thickness was measured with a micrometer to the nearest 0.001 in. The crushing strength was determined on an air-pressure operated Strong-Cobb hardness tester to the nearest $^1/_4$ of a scale reading.

The friability assessment was conducted on 20 tablets in an apparatus similar to the Roche friabilator (9). The tablets were tumbled in the friabilator

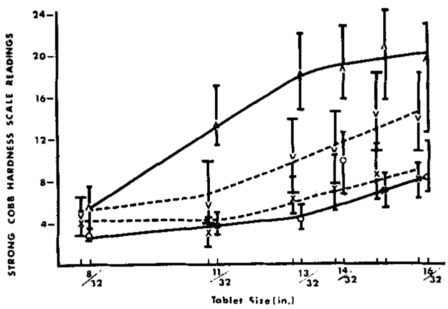

Fig. 1.—Key: Abscissa-sliding scale, vertical lines represent range of readings; —O—, dibasic calcium phosphate–lactose, low density; —Λ—, dibasic calcium phosphate–lactose, high density; – – X – – –, standard sugar granulation, low density, – – V– – –, standard sugar granulation, high density.

for 100 and 200 revolutions. These were then dusted and weighed; the results were expressed as per cent weight loss. If there were any capped tablets, their weight loss was not calculated into the friability results. A tablet was classified as capped when one-half or more of the convex face of a tablet had eroded away during the friability test.

A standardized sugar tablet formulation was used in most of the studies. It consisted of the following formula:

Powder sugar with 3% starch	59.5%
Lactose U.S.P.	25.5
Corn starch	10.6
10% w/w starch paste	0.9 (Dry weight)
Magnesium stearate U.S.P.	0.5
Talc	3.0

It was prepared by mixing the first three ingredients in a Stokes mixer, granulating the powder blend with a 10% w/w starch paste and then passing it through a No. 6 screen on a Fitzpatrick model D comminuting machine at 1500 r.p.m. After drying for 18 hr. in a hot-air tray drier at 60°, it was milled through a 2A screen on the Fitzmill at 750 r.p.m. The milled granulation was blended with the talc and magnesium stearate. The granule size distribution, as determined with U. S. Standard sieve screens, was 41–48% retained on No. 30 screen, 23–30% retained on No. 60 screen but passed through a No. 30 screen, and 25–33% passed through a No. 60 screen. Its moisture content was determined by a Karl Fischer analysis and a Cenco moisture balance. The moisture values varied from 1.1 to 2.0% as measured by the Karl Fischer technique. This particular formulation was selected because prior work in our laboratory and work conducted by others on the formula ingredients (18) showed this formulation yielded tablets which had low crushing strength and had a capping tendency under certain manufacturing conditions.

RESULTS AND DISCUSSION

As previously indicated, the crushing strength of a tablet is a function of the tablet formulation; but varying the size and density (thickness, weight) of the compressed tablet has a greater influence on some formulations than others. A series of tablets were compressed at two different but constant densities. At each tablet size a tablet thickness was selected, which represented a thickness commensurate with the tablet size. Therefore, at the larger tablet sizes, the thickness of the tablets remained relatively unchanged. Figure 1 illustrated the difference in crushing strength (CS) of tablets prepared with a dibasic calcium phosphate–lactose granulation and the standardized sugar formulation. The lower-density tablets were compressed with just enough pressure to obtain a satisfactory appearing tablet. The high-density tablets were compressed at the upper limits or maximum pressure. At the lower compressional pressure, only small differences were observed in the tablet CS values between the two formulations. As the compressional pressure was increased, the tablet porosity was decreased, greater intergranule surface contact was realized, and intergranule binding and granule strength assumed a greater role in the CS values of the compressed tablets. Tablet formulations, which possess good intergranule binding and granule strength, can exhibit great extremes in their CS values. In this case, the two curves for each formulation represent the range of crushing strength which can be attained.

In a normal tableting process, an operator may attempt to maintain the compressed tablet specifications with ±0.005 in. thickness and ±2–3% weight of the average values (11). With these standards,

Table I.—Physical Property Values[a] and Coefficients of Variation

Tablet Size, in.	Wt., mg. Mean	Wt., mg. CV[b]	Thickness, in. Mean	Thickness, in. CV[b]	Strong-Cobb Hardness Tester Scale Reading Mean	Strong-Cobb Hardness Tester Scale Reading CV[b]
16/32 low density	616.4	0.8	0.188	0.3	8.1	8.4
high density	617.6	1.1	0.181	0.5	15.1	12.0
15/32 low density	560.9	1.1	0.192	0.4	8.8	12.7
high density	563.1	1.2	0.185	0.6	14.7	11.9
14/32 low density	437.5	2.0	0.173	0.9	7.4	17.1
high density	439.4	3.3	0.170	0.8	11.1	16.5
13/32 low density	366.9	1.3	0.169	0.4	6.5	12.8
high density	365.4	1.8	0.164	0.6	10.6	14.9
11/32 low density	206.1	2.0	0.142	0.5	3.1	20.2
high density	204.7	2.4	0.135	0.9	5.9	23.3
8/3 low density	88.5	1.8	0.113	1.1	4.2	15.0
high density	88.1	2.5	0.111	1.1	4.9	21.3
4/32 low density	18.9	3.0	0.091	1.1	1.0	34.2
high density	18.9	2.8	0.084	1.3	1.7	21.3

[a] Fifty tablets evaluated individually. [b] Denotes coefficients of variation in per cent.

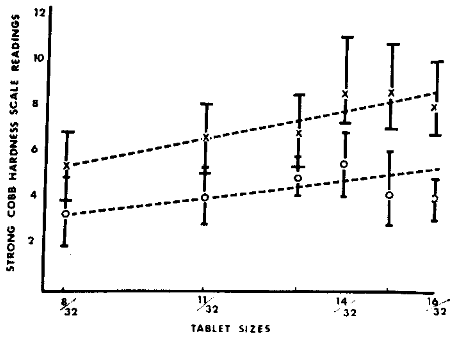

Fig. 2.—Key: Vertical lines represent range of readings; O, .150 in. thickness; X, .190 in. thickness.

a rather broad range of Strong-Cobb hardness test results can be obtained. For example, a ±2–3% weight variation can occur without an apparent change in the tablet thickness; conversely, if the operator of the tablet compressor controls the tableting operation by measuring the tablet thickness (±0.005 in.), much greater weight variations than the standards would be obtained. Table I shows the test results for the standardized sugar formulation, which were illustrated in Fig. 1.

In absolute numerical values, the smaller-diameter tablets exhibited much smaller variations; but in evaluating the results as a coefficient of variation (ratio of the standard deviation to the mean, which represents relative variability of a physical property of a given tablet size), the smaller tablets had a greater variability.

As shown in Table I, the standardized sugar granulation yielded tablets with relatively weak crushing strength; yet a difference of seven Strong-Cobb hardness units was obtained for the $^{16}/_{32}$-in. diam. tablet where the thickness difference was only 0.007 in. Although the compressing operation was closely controlled, an even greater spread in hardness values was obtained with the dibasic calcium phosphate–lactose granulation. This demonstrated the CS values were not only dependent on the particular tablet formulation, but the other tablet properties (size, density, etc.) were also important and should be enumerated when reporting Strong-Cobb hardness results.

Constant Tablet Density and Thickness with Varied Tablet Size.—The higher crushing strength (CS) values for the larger-diameter tablets could be attributed to their greater thickness and diameter. Tablets were therefore compressed at a constant tablet density and two thicknesses for tablet sizes from $^{8}/_{32}$ to $^{16}/_{32}$ in. It was observed that the differences in CS values were less between the smaller- and larger-diameter tablets (Fig. 2), and the thin large-diameter tablets exhibited a serious capping problem (Table II).

The evaluation of the capping tendency of tablet formulations normally has been assessed by empirical testing procedures. These techniques determined whether a formula capped when tablets were subjected to the shock and attrition of a particular test procedure. When a tablet is broken in half and internal stress lines are observed, tablet capping can be anticipated during normal handling, but it may not necessarily occur. The Strong-Cobb hardness tester provides no data on the capping tendency of a tablet formulation, but the friabilator subjects the tablets to reproducible test conditions where the capping tendency can be ascertained. Under these testing conditions, the thicker tablets did not exhibit a capping tendency, but the thinner larger-diameter tablets showed extensive capping. This would suggest that the thicker tablets had greater resiliency, so tablets with internal stresses were less likely to cap when subjected to the impact and attrition encountered in a friabilator.

Effect of Storage on the Physical Properties of Compressed Tablets.—It has been reported by several investigators that some tablets harden up on storage (19, 20). Therefore $^{13}/_{32}$-in. standard concave tablets of the same density were prepared at two thicknesses, 0.155 and 0.182 in., and stored in cabinets at 31 and 71% R.H., 25°. The relative humidity conditions were attained with saturated calcium chloride solutions for the 31% R.H. condition and a saturated ammonium chloride–potassium nitrate solution for the 71% R.H. environment (21). At periodic intervals, the friability, crushing strength, and capping tendency were evaluated.

In earlier moisture equilibrium studies, the rate of moisture absorption for the ingredients employed in this tablet formulation had been evaluated (22). When the tablet ingredients absorbed moisture and the compressed tablets expanded, it was felt that possibly the internal stresses observed in the newly compressed tablets might be relieved. After storage for 28 days at 71% R.H., 25°, the tablets picked up 1.5% mositure, and the tablet dimensions increased as illustrated in Fig. 3. There was no change in the crushing strength as determined by the Strong-Cobb hardness tester (Fig. 4), but the tablets appeared to be more friable. In addition, less capping was observed during the friability studies (Table III).

Influence of Compressing Speed on Tablet Properties.—Whenever the capping phenomenon was discussed in the literature (11, 23) the authors emphasized that increasing the compressing speed accentuated the tendency for a borderline formulation to cap. This event was normally attributed to the greater possibility for entrapment of air to occur at the faster compressional rates.

Using the standardized tablet formulation, $^{13}/_{32}$-in. standard concave tablets were compressed at a range of 1 to 41 r.p.m. The slower speeds were

Table II.—Friability Results

Thickness, in.	Tablet Size, in.	% Wt. Loss[a] 100 Revolutions	200 Revolutions
0.190	$^{8}/_{32}$	0.3	0.6
	$^{11}/_{32}$	0.4	0.8
	$^{13}/_{32}$	0.5	1.0
	$^{14}/_{32}$	0.4	0.8
	$^{15}/_{32}$	0.5 (*1*)	0.9 (*1*)
	$^{16}/_{32}$	0.4	0.9
0.150	$^{8}/_{32}$	0.8	1.4
	$^{11}/_{32}$	0.4	0.8
	$^{13}/_{32}$	0.5	0.8 (*1*)
	$^{14}/_{32}$	. . . (*3*)	. . . (*11*)
	$^{15}/_{32}$	. . . (*9*)	. . . (*20*)
	$^{16}/_{32}$	. . . (*15*)	. . . (*20*)

[a] Number of capped tablets are in parentheses. When the number of capped tablets became excessive, friability values were not calculated.

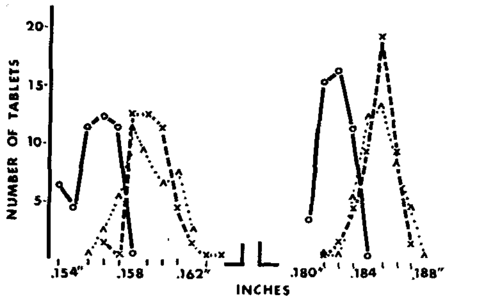

Fig. 3.—Change in tablet thickness after exposure at 71% R.H. and 25°C. Key: —O—, initial; ----Λ----, 9 days; ----X----, 28 days.

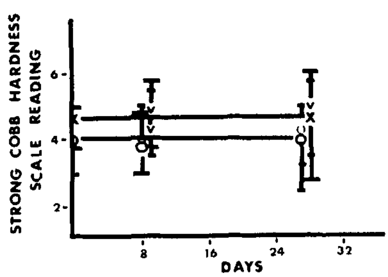

Fig. 4.—Key: Vertical lines represent range of readings; 31% R.H., O, .155 in.; X, .182 in.; 71% R.H., O, .155 in.; V, .182 in.

TABLE III.—FRIABILITY RESULTS

Thickness, in.	Time, Days	R.H., %	% Wt. Loss[a] 100 Revolutions	200 Revolutions
0.155	Initial		0.6 (*5*)	1.3 (*7*)
	8	31	0.6 (*1*)	1.1 (*6*)
	27		... (*2*)	... (*10*)
	8	71	1.2 (*3*)	2.0 (*8*)
	27		1.5	2.5
0.182	Initial		0.4	1.0
	9	31	0.7	1.2
	28		0.7	1.3
	9	71	0.9	1.7
	28		0.8	1.5

[a] Number of capped tablets are in parentheses. When the number of capped tablets became excessive, friability values had no importance.

accomplished by manually turning the flywheel at the indicated rates. As shown in Fig. 5, it was observed that the crushing strength improved at the slower compressing rates. However, there were practically no differences in the Strong-Cobb hardness results in the ranges (21–41 r.p.m.) normally employed with a Stokes B-2 rotary tableting machine.

Initial studies showed that the capping tendency was more apparent at the fastest compressing rate, but subsequent experiments failed to show any capping problem. This discrepancy was found to be related to minute quantities of moisture, for the initial granulation contained only 1.1% mositure while later formulations had 2.0% moisture (Karl Fischer analysis). These granulations were identical in their other physical properties. The crushing strength results were also higher for the formulations with the higher moisture content. No significant differences were obtained in the friability results when the rate of compression was changed (Table IV).

In an attempt to evaluate the influence of fines (60 mesh or finer) on the crushing strength and the capping phenomenon, studies were repeated with (*a*) 60 mesh fines, (*b*) all 40 mesh and finer material, and (*c*) all 30 mesh and finer material being removed prior to the addition of the talc and magnesium stearate. The tablets were compressed at 41, 26, and 1 r.p.m. with the same compressional setting. No differences were noted in the friability and crushing results; however, it was observed that at the same machine setting tablets compressed at the faster rates were thicker (Fig. 6). No capping was observed, but the results suggested that at 41 r.p.m. the granulation showed greater elastic response to compression; at the slowest compressional rate, the granulation had an opportunity to consolidate and less elastic response was observed. When only the 30 mesh or coarser granulation was studied, the thickness differences were more apparent (Fig. 7).

Compression of Tablets at Various Depths in the Die.—If air entrapment played a major role in the capping tendency, presumably compressing the tablet deeper in the die would accentuate this tendency and possibly alter the crushing strength and friability results. The tableting machine was adjusted so the upper punch penetrated the die for $^2/_{16}$, $^3/_{16}$, $^4/_{16}$, $^5/_{16}$, and $^6/_{16}$ in.; thus, the tablets were compressed lower in the die. No differences were observed in any of the physical properties of the compressed tablets.

CONCLUSIONS

Air entrapment may still be a factor in contributing to the capping tendency of some granulations, but greater consideration should be given to the pos-

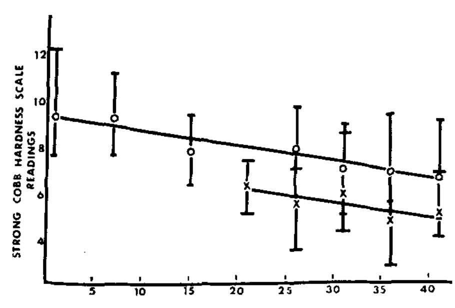

Fig. 5.—Key: Vertical lines represent range of readings; X, granulation *A*; O, granulation *B*.

TABLE IV.—FRIABILITY RESULTS FOR GRANULATIONS *A* AND *B*

Rate of Compression, r.p.m.	% Wt. Loss[a] Granulation *A* 100 r.p.m.	200 r.p.m.	Granulation *B* 100 r.p.m.	200 r.p.m.
21	0.5	1.2 (*2*)		
26	0.8 (*3*)	1.7 (*4*)	0.3	0.5
31	0.8 (*2*)	2.2 (*6*)	0.3	0.5
36	... (*4*)	... (*9*)	0.3	0.6
41	... (*7*)	... (*13*)	0.3	0.6

[a] Number of capped tablets are in parentheses. When the number of capped tablets became excessive, friability values had no importance.

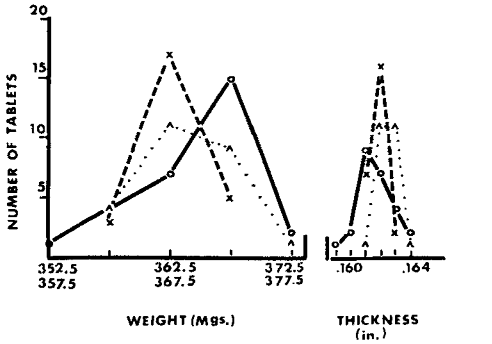

Fig. 6.—Key: —O—, 1 r.p.m.; - -X- -, 26 r.p.m.; - - -Λ- - -, 41 r.p.m.

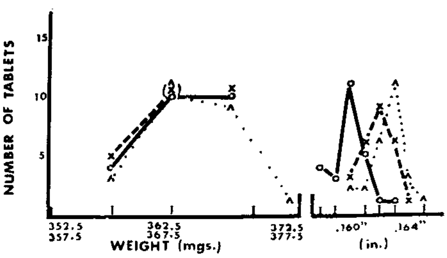

Fig. 7.—Key: —O—, 1 r.p.m.; - - -X- - -, 26 r.p.m.; - - - -Λ- - - -, 41 r.p.m.

sibility that the capping encountered at high compressional rates is associated with the elastic response of the granulation. This confirmed results previously reported on different materials by Shlanta (15) and Shotton and Ganderton (17).

Presumably, the compression of a thicker tablet or compressing the tablet deeper in the die would permit greater air entrapment and a greater tendency for capping, but this was not observed.

The role of moisture in some granulations is to improve intergranule binding, and relatively small quantities showed a profound influence on the physical properties of tablets.

Thin large-diameter tablets were more friable and exhibited a greater capping tendency than thin small-diameter tablets. There was no apparent relationship between the crushing strength and the friability of a compressed tablet. Actually, it was observed that the crushing strength values could be altered without observing any difference in tablet friability. Conversely, it was seen that tablets exposed to 71% R.H., 25°, for 28 days became more friable; but no significant change in the crushing strength was noted.

Because the physical properties of compressed tablets are dependent on so many factors, it is apparent that reporting tablet hardness values without citing the compressing conditions, moisture content, granule distribution, etc., should be seriously questioned. In describing the physical properties of compressed tablets, the test results should be stated in terms of what they specifically measure.

The test results obtained with the friabilator afford an opportunity to determine the friability and relative capping tendency of compressed tablets.

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