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Computer analysis of the relation between tablet strength and compaction pressure

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The load necessary to fracture lactose monohydrate tablets under diametral compression has been determined using an Instron physical testing instrument, so that true tensile failure was obtained in all cases, leading to improved reproducibility. Four ranges of tablet thickness were examined at 12·7 mm diameter. All tablets gave a linear increase of breaking load with compaction pressure up to 310 MN/m². Expressing the tablet strength as the breaking load gave a separate regression line for each range of tablet thickness, whereas the use of tensile strength provided a common regression line, within given statistical limits, for all but the lowest range of tablet thickness. The fact that such a correlation is possible shows that the tensile strength is a property of the "as compacted" material and provides a new and useful parameter to maintain constancy of properties when tablet size is changed.

Pharmaceutical tablets, when compressed diametrically, as in any of the tablet crushing tests normally applied, may fracture in any of the five ways shown in the upper part of Fig. 1. Failure by any of the first four mechanisms (a–d) will lead to greater variability in the crushing strength measurements than will failure by mechanism 1 (e). This is purely tensile fracture, giving a straight crack dividing the tablet into two semi-circular parts. It occurs only when the force applied to break the tablet is carefully controlled: in such circumstances the stress distribution within the tablet is calculable (Frocht, 1948) and is as shown in the lower part of Fig. 1. The vertical stress component σ_y varies along the vertical diameter, as does the maximum shear stress τ. The horizontal stress component σ_x, however, is virtually constant along the vertical diameter and tends to split the tablet into two equal halves. The value of this uniform horizontal stress is, at failure, the ultimate tensile strength of the "as compacted" material forming the tablet, and is given by

$$\sigma_x = \frac{2P}{\pi Dt}$$

where P is the load necessary to cause fracture, D is the tablet diameter and t is its thickness.

The various versions of the crushing strength tests have been compared by Ridgway (1970). To ensure correct load application, it is sometimes necessary to have packing pieces between the tablet and the loading platens, and experiment appears to be the only method of assessing the nature and quantity of padding required. Recognition of tensile failure is, however, readily made by inspection of the tablets after fracture.

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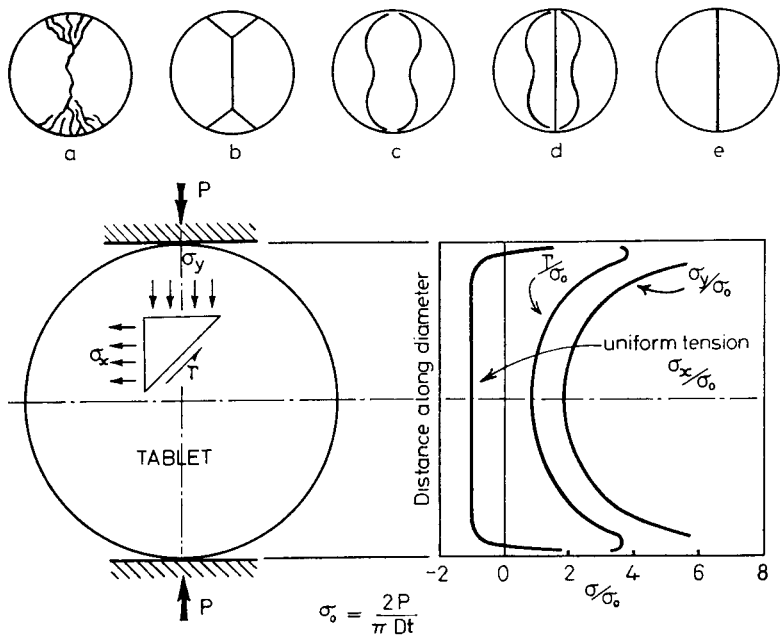

FIG. 1. Failure of tablets subjected to diametral compression:—(*a*) Compression failure locally at the loading points. (*b*) Failure under local shear at and near the loading points. (*c*) Failure along maximum shear loci when point loading applied. (*d*) "Triple-cleft" fracture due to transfer of load to each half-disc after breakage along the vertical diameter. (*e*) Ideal tensile failure.

The lower part of the figure illustrates the stress conditions in a tablet which are present when ideal tensile failure occurs.

The tensile stress (σ_x) on the vertical diameter is constant at $2P/\pi Dt$ over most of the graph. The compressive stress on the same diameter is σ_y. If ideal point loading was obtained this would tend to infinity. The shear stress is τ. The tablet material must be eight times stronger in compression and six times stronger in shear than it is in tension if the ideal tensile failure is to be obtained.

Failure in tension reduces the variability of the breaking load (Fell & Newton, 1970). The tensile strength is a fundamental property of the compressed tablet material and could, therefore, be a possible parameter for the characterization of tablets of different dimensions. Rees & Shotton (1969) showed that the strength of sodium chloride tablets of different dimensions could be compared by the expression $\left(\frac{P}{Dt_0}\right)$ where t_0 is the tablet thickness at zero porosity. They suggested that this expression could be considered as a "stress" (their inverted commas). It differs from the tensile strength defined above only by a multiplying constant, and by the use of the zero porosity thickness, which is constant, instead of the actual tablet thickness, which varies with the compaction pressure. Thus it neither represents the true stress that is acting, nor is it quite proportional to it, though it becomes more closely so as the compaction pressure increases. Thus, the use of the tensile strength proper (σ_x) appears likely to give an improved assessment of tablet strength. Derivation of the basic equation for tensile stress assumes that the compacted tablet is homogeneous throughout, whereas in fact tablets show an internal distribution of both density (Train, 1956) and hardness (Ridgway, Aulton & Rosser, 1971); these facts may limit the range of applicability of tensile strength methods.

MATERIALS AND METHODS

Materials

The powder used was lactose monohydrate B.P. supplied by Whey Products Ltd. (Crewe). The particle size distribution was Gaussian, with a median value of 67 μm s.d. 41 μm, as determined by an Alpine Air-Jet Sieve. The lactose was dried at 90° for 24 h and stored over silica gel.

Methods

Tablet preparation. Tablets were made on a Manesty F3 tablet machine instrumented by four foil strain gauges (Showa Sokki Kenkyusko, Japan, type 2b) connected as a bridge on the shank of a 12·7 mm diameter flat-faced upper punch. Another four strain gauges were similarly placed on the lower punch holder. The output from both bridges was fed into a signal conditioning unit, type MR701 (Data Acquisition Ltd., Stockport) and the amplified signal was recorded on a U.V. recorder, type 2005 (SE Laboratories (Engineering) Ltd., Feltham), fitted with type B160 moving coil galvanometers. The die walls and punch faces were thoroughly cleaned and then lubricated with a suspension of magnesium stearate in carbon tetrachloride. Tablets were prepared using a range of upper punch pressures at a machine speed setting of 42 tablets/min, for die fill weights of 0·4, 0·6, 0·8 and 1·0 g. The mean compaction pressure was calculated as the average of the upper and lower punch pressures. The weight of each tablet was determined to $\pm$0·0001 g. The diameter and thickness were determined to $\pm$0·005 mm.

Tablet strength. This was determined by diametral compression on an Instron physical testing instrument (Fell & Newton, 1968). The loading rate was 0·1 cm/min. No padding was used between the platens and the tablets, and all the tablets fractured in the fashion shown in Fig. 1 (e).

ANALYSIS OF RESULTS

For the large number of tablets examined the weight of fill and the compaction pressure could not be controlled exactly. The analysis was therefore designed to treat each tablet as an individual item. The calculations made enable the following tasks to be performed; regression lines are fitted to sets of data, associated in pairs, such as tablet breaking load and the corresponding mean compaction pressure P_m. The gradient, intercept and confidence ranges are calculated for each regression line. These linear regressions can then be compared, two at a time, and the significance level of the apparent differences between them determined. Such differences are examined in terms of the gradients and intercepts of the lines and of the quality of fit of the points to them. Comparison in pairs, although a little unorthodox (a more conventional approach would be a multiple regression analysis on all sets of data taken together), was preferred because the variations due to different tablet weights were expected to be substantial and not necessarily linear. Also this approach seemed to offer less difficulty in interpretation, whilst the computer programs* produced seemed likely to be of more general future value. The statistical methods are not generally presented in the standard textbooks in this form, but the underlying principles are well-documented (see, for example, Kendall & Stuart, 1951; Kenny & Keeping, 1951; Johnson and Leone, 1964).

* These are generally available through the University of London Descriptive Programme Index.

DISCUSSION

The compaction of 0·4, 0·6, 0·8 and 1·0 g quantities of lactose monohydrate at mean compaction pressures up to 310 MN/m² produced tablets with thickness: diameter ratios of 0·170–0·224, 0·250–0·330, 0·340–0·466 and 0·440–0·540 respectively. Analysis of the results for the relation between tablet breaking load and the mean compaction pressure resulted in the regression lines of Fig. 2. Statistical evaluation proved that each set of tablet weights yielded a significantly different relation (Table 1). Not unexpectedly, the results show that, as the quantity of lactose present increases, the breaking load of the tablets compacted with the same mean compaction pressure also increases.

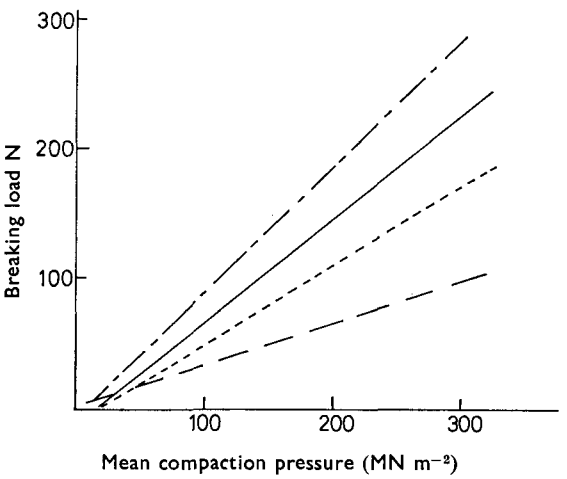

FIG. 2. Regression lines for the relation between the breaking load P, of the tablets and the mean compaction pressure P_m. The equations of the lines, with the residual variance of the P values given in parentheses are: 0·4 g tablets — — $P = 3{\cdot}29 \times 10^{-7} P_m + 2{\cdot}75$ (2·00) 49 points. 0·6 g tablets ------- $P = 6{\cdot}33 \times 10^{-7} P_m - 11{\cdot}57$ (0·80) 48 points. 0·8 g tablets —— $P = 8{\cdot}49 \times 10^{-7} P_m - 19{\cdot}61$ (1·50) 87 points. 1·0 g tablets — · — $P = 10{\cdot}01 \times 10^{-7} P_m - 13{\cdot}73$ (2·86) 70 points.

When the breaking loads are converted to tensile strengths, however, a different picture (Fig. 3) is obtained. Here the line for 0·4 g tablets is quite distinct from those for 0·6, 0·8 and 1·0 g tablets which are closely similar. Two of the differences within this set are only significant statistically at the 0·01% level despite the 48–87 points represented by each line; the third difference is totally insignificant (cf. Table 1). A common regression line was calculated for all 205 points from the 0·6 to 1·0 g experiments, yielding:

$$\sigma_x = 0{\cdot}0098\ P_m - 0{\cdot}33$$

with residual variance 2·58. It appears from the analysis that over the range of tablet weights 0·6 to 1·0 g the tensile strengths of 12·7 mm diameter lactose tablets are well correlated with compaction pressure by this common regression. Thus, in spite of the possible variation in the distribution of hardness within the tablet, the resultant tensile strength for the 0·6, 0·8 and 1·0 g tablets is the same, and the tensile strength is a linear function of the compaction pressure for all the tablets of these quantities studied. One allowance that can be made for the non-correlation of the

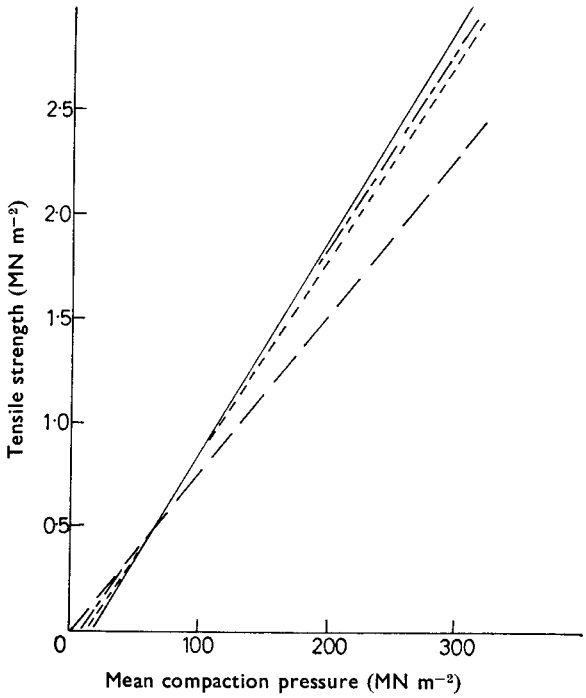

FIG. 3. Regression lines for the relation between the tensile strength σ_x, of the tablets and the mean compaction pressure P_m. The equations of the lines with the residual variance of the σ_x values given in parentheses are: 0·4 g tablets —— $\sigma_x = 0{\cdot}0075\ P_m - 0{\cdot}067$ (7·57) 49 points. 0·6 g tablets ------- $\sigma_x = 0{\cdot}0096\ P_m - 0{\cdot}221$ (1·30) 48 points. 0·8 g tablets —— $\sigma_x = 0{\cdot}0101\ P_m - 0{\cdot}267$ (3·42) 87 points. 1·0 g tablets — - — $\sigma_x = 0{\cdot}0096\ P_m - 0{\cdot}192$ (2·29) 70 points.

Table 1. *Statistical comparison of the gradients and intercepts of the regression lines of tablet strength and mean compaction force.*

Tablets weight compared	Significance level (as a %) of the hypothesis that the parameters of the regression lines differ					
	Regression lines for breaking load		Regression lines for tensile strength		Regression lines for tensile strength corrected for voidage	
	Gradient	Intercept	Gradient	Intercept	Gradient	Intercept
0·4 : 0·6	<0·01	—	0·01	—	0·01	—
0·4 : 0·8	<0·01	—	<0·01	—	0·01	—
0·4 : 1·0	<0·01	—	<0·01	—	0·01	—
0·6 : 0·8	<0·01	—	8·5	35	5*	34*
0·6 : 1·0	<0·01	—	97	22–25	99	26
0·8 : 1·0	0·2	—	10·8	84–86	7	93–94

* Thus for example the gradients of the estimated regression lines for the tensile strengths, corrected for voidage, of 0·6 and 0·8 g tablets differ marginally, the difference being statistically significant at the 5% level. On the hypothesis that the true gradients are identical, the intercepts differ only at a 34% significance level, i.e. negligibly.

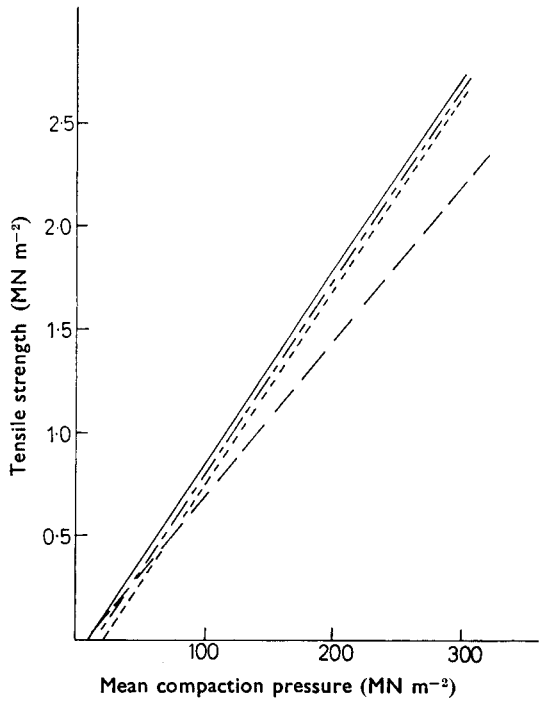

FIG. 4. Regression lines for the relation between the tensile strength, corrected for voidage $(\sigma_x)_c$, of the tablets, and the mean compaction pressure P_m. The equations of the lines, with the residual variance of the $(\sigma_x)_c$ values given in parentheses are: 0·4 g tablets —— $(\sigma_x)_c = 0{\cdot}0077\ P_m + 0{\cdot}0018$ (8·89) 49 points. 0·6 g tablets ------- $(\sigma_x)_c = 0{\cdot}0100\ P_m - 0{\cdot}159$ (1·28) 48 points. 0·8 g tablets —— $(\sigma_x)_c = 0{\cdot}0106\ P_m - 0{\cdot}218$ (3·90) 85 points. 1·0 g tablets — · — $(\sigma_x)_c = 0{\cdot}0100\ P_m - 0{\cdot}13$ (2·75) 70 points.

0·4 g tablets is to correct for the voidage. Since the fraction of the cross-sectional area occupied by solid is $(1 - e)$, where e is the fractional voidage, the tensile strength corrected for voidage will be $\frac{2P}{\pi Dt(1-e)}$. The regression lines of this quantity upon the mean compaction pressure are given in Fig. 4 where the line for the 0·4 g tablets is still distinct from that for the other three weights. This is confirmed by calculation (Table 1). However, the above correction for a voidage effect is only an average correction that cannot allow for local differences in voidage. The 0·4 g tablets have the highest surface to volume ratio and hence are subjected to greater surface friction and shearing during compaction. Rees & Shotton (1969) reported that for short compacts, relatively large deviations from the relation between compaction pressure and breaking "stress" occurred, particularly at higher pressures. The deviations, as in the present case, resulted in lower values of tablet strength than would have been expected by comparison with the thicker tablets. It is also noteworthy that the residual variance in the correlation on a tensile strength basis for 0·4 g tablets is greater than it is on a breaking load basis (7·57 as compared with 2·00). The thinner tablets are thus intrinsically more variable: this may be due to maldistribution of powder within the die, which is more likely to occur where the amount of powder fill is small.

The practical significance of the present work is in the preparation of tablets of different dimensions from the same formulation. If the tablets are compacted to give the same crushing force, in kg, on the testing machine, different compaction pressures will be required and their true strengths will be different, as will their friability resistance and disintegration time. Compaction to the same tensile strength will provide tablets of more nearly identical properties. Because of the common regression line, tablets of the same tensile strength can be prepared by ensuring that the same mean compaction pressure is applied, provided that the frictional effects are not so great that deviations from the common regression line occur. Linking the present findings with the correlation of the tensile strength of mixed component tablets reported by Fell & Newton (1970), the manufacture of tablets of known strengths containing different ingredients and of different dimensions becomes a feasible proposition.

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