J. Pharm. Pharmac., 1970, **22**, *Suppl.*, 64 S–69 S *Received March* 17, 1970

The effect of rate of loading on the strength of tablets

J. E. REES, J. A. HERSEY AND E. T. COLE

Pharmaceutical Research & Development, Sandoz A.G., CH-4002 Basel, Switzerland

The breaking strength of tablets containing lactose and microcrystalline cellulose has been determined using an Instron Universal Testing Instrument at loading rates corresponding to cross-head movements of 0·05 to 5·0 cm min^{-1}. For tablets of 2 to 30 kg, nominal strength, an increase in the loading rate produced a significant increase in the breaking strength, although the absolute increase in the mean strength value was only 2 kg for the strongest tablets. The standard deviation of replicate values was apparently unaffected by loading rate. Results obtained using the motorized Heberlein and Erweka instruments to determine the strength of compressed tablets, indicated that discrepancies in the strength values may be partially attributed to differences in the rates of loading.

Several authors have compared the methods used to determine the mechanical strength of compressed tablets. However, few attempts have been made to isolate selected operational variables to rationalize discrepancies in the strength values obtained in these comparisons, although Brook & Marshall (1968) obtained accurate calibration figures for several instruments by using a load transducer in place of the tablet.

The strength of pharmaceutical tablets is usually determined by failure in diametrical compression. Rudnick, Hunter & Holden (1963) have shown that the tensile strength of a compact can be computed from the results of this test, provided shear failure is prevented by correct load distribution.

Smith (1949) and McCallum, Buchter & Albrecht (1955) concluded that variations between operators influence the reproducibility of results obtained in diametrical compression tests using the Monsanto (or "Stokes") and Strong Cobb instruments. Variability in the rate of loading may be a critical factor in the discrepancies observed.

A simple attempt to compare the effect of high and low rates of loading, using the Monsanto tester was described by Fairchild & Michel (1961). Neither the mean strengths nor the coefficients of variation differed appreciably.

Ritschel, Skinner & Schlumpf (1969), using eight different instruments found no significant differences in the reproducibility of strength values due to variation in the rate of loading but, for most instruments, there were significant differences between the results of operators.

Mahler & Mitchem (1964), using dental amalgam, found the rate of loading to have no effect on the tensile strength measured in an elongation test, or the transverse strength determined in a three-point loading, cross-breaking test. However, the axial crushing strength of cylindrical specimens increased with the rate of loading as reported by Taylor, Sweeney & others (1949). These results may explain the conclusions of Endicott, Lowenthal & Gross (1961) and Delonca, Puech & others (1967),

Table 1. *Particle size analysis of constituent powders*

Sieve size μm	Avicel % oversize	Lactose % oversize
250	—	18·0
177	0	35·2
149	1·3	49·3
125	3·9	58·2
105	7·4	65·0
74	22·1	78·5
53	34·7	84·5
37	53·0	—

Sifting time 5 min. Sift amplitude 8. Pulse amplitude 10.

that a three-point-loading, cross-breaking test provides a more reproducible measurement of tablet strength than a diametrical compression test.

We set out to determine whether the load required to fracture a compact in diametrical compression depends on the rate at which the load is applied. By the isolation of this operating variable, a more fundamental comparison can be made between the results of strength tests using different instruments, or between such tests made by different operators using the same instrument.

EXPERIMENTAL

Compacts of uniform strength were required to reduce the number of replicates examined, whilst maintaining the necessary statistical significance for interpretation of the results. A suitable tablet was made from: lactose, anhydrous (Sheffield Chemical) 49·5, microcrystalline cellulose (Avicel) 49·5, colloidal silica (Aerosil) 0·5, magnesium stearate 0·5. The particle size distribution of the two major constituents was determined using an Allen-Bradley Sonic Sifter (Table 1). The maximum particle size of the colloidal silica was 160 μm and of the magnesium stearate, 96 μm (determined by microscopic examination). This composition was dry mixed, and sufficient material (410 mg) was compressed to form a compact of approximately 4 mm thickness at zero porosity. An eccentric tablet press (Oerlikon), with plane-faced, bevel-edged punches of 10 mm diameter, was operated continuously at approximately 50 cycles/min with automatic die filling.

Tablets were prepared at five different pressures corresponding to nominal strengths of 2, 5, 10, 20 and 30 kg. The weight uniformity of tablets prepared at each pressure is shown in Table 2.

The strength of each series of tablets was measured on the same day, after 3 months storage to eliminate ageing effects (Rees & Shotton, 1970). The compacts were subjected to a conventional diametrical compression test, using an Instron Universal Testing Instrument, Model TTDM. A range of crosshead speeds was selected between 0·05 and 5·0 cm min^{-1}, and the force applied was measured using a type

Table 2. *Weight variation between tablets*

Nominal tablet strength kg	Mean tablet weight (g)	No. of determinations	Standard deviation of weight	Coefficient of variation
2	0·406	10	0·006	1·3
5	0·403	20	0·002	0·546
10	0·402	20	0·003	0·648
20	0·404	20	0·003	0·655
30	0·405	20	0·002	0·568

CCM load cell (maximum load 50 kg). It was necessary to replace the pen recorder by a recording ultraviolet oscillograph (SE Laboratories 3006) to achieve acceptable rates of response at high loading rates. At a cross head speed of 5·0 cm min^{-1} a 400 Hz galvanometer was needed to ensure adequate frequency response. The galvanometer was fitted with a pre-amplifier and a double-T filter which were enclosed in a Faraday cage to eliminate noise effects, whilst maintaining sufficiently high sensitivity. The sensitivity response, expressed as galvanometer trace deflection for 10 kg was 36·5, 18·1, 9·1, 3·7, 3·7 cm for the nominal tablet strengths of 2, 5, 10, 20, 30 kg respectively.

To relate our results to conventional tablet strength tests, and to compare them with those of Ritschel & others (1969), some measurements were made using an Erweka instrument and a motorized Heberlein testing instrument, under standard conditions of use.

RESULTS

The mean values of strength and the standard deviations were determined for each group of tablets at five rates of loading as shown in Table 3. For tablets of each nominal strength, the load required to cause fracture in diametrical compression increased with the rate of loading. This effect was more pronounced with tablets of high strength (Fig. 1).

For the tablets of 2 kg nominal strength, small differences in the mean strength values were observed at high and low rates of loading. Consequently, the statistical significance of the effect of loading rate was determined using the Student *t*-test (Table 4). For each group of tablets, the strength at a rate corresponding to 0·05 cm

Table 3. *The effect of loading rate on the diametrical crushing strength of tablets*

Nominal strength	Cross-head movement	Loading rate	Diametrical breaking strength Mean†	Standard deviation	Coefficient of variation
kg	cm min^{-1}	kg s^{-1}	kg	kg	%
2	0·05	0·096	1·92	0·07	3·6
	0·2	0·42	1·97	0·12	6·1
	0·5	1·09	2·09	0·16	7·7
	2·0	4·3	2·09	0·08	3·8
	5·0	10·1	2·13	0·09	4·2
5	0·05	0·33	5·66	0·28	4·9
	0·2	1·31	5·71	0·33	5·8
	0·5	3·34	5·98	0·41	6·9
	2·0	13·5	5·99	0·31	5·2
	5·0	28·5	6·33	0·34	5·4
10	0·05	0·59	10·3	0·7	6·8
	0·2	2·35	10·6	0·6	5·7
	0·5	6·38	11·3	0·6	5·3
	2·0	23·2	11·3	0·4	3·5
	5·0	57·8	11·8	1·0	8·5
20	0·05	1·1*	21·9	0·9	4·1
	0·2	4·29	22·5	0·9	4·0
	0·5	11·7	22·9	0·9	3·9
	2·0	39·6	23·5	1·2	5·1
	5·0	113·2	24·0	1·3	5·4
30	0·05	1·29	28·6	1·0	3·5
	0·2	5·16	29·6	1·3	4·4
	0·5	12·9	29·7	1·0	3·4
	2·0	52·4	30·8	1·1	3·6
	5·0	128·3	30·8	0·9	2·9

* No experimental data available—value determined by extrapolation.
† Mean of 10 replicate samples.

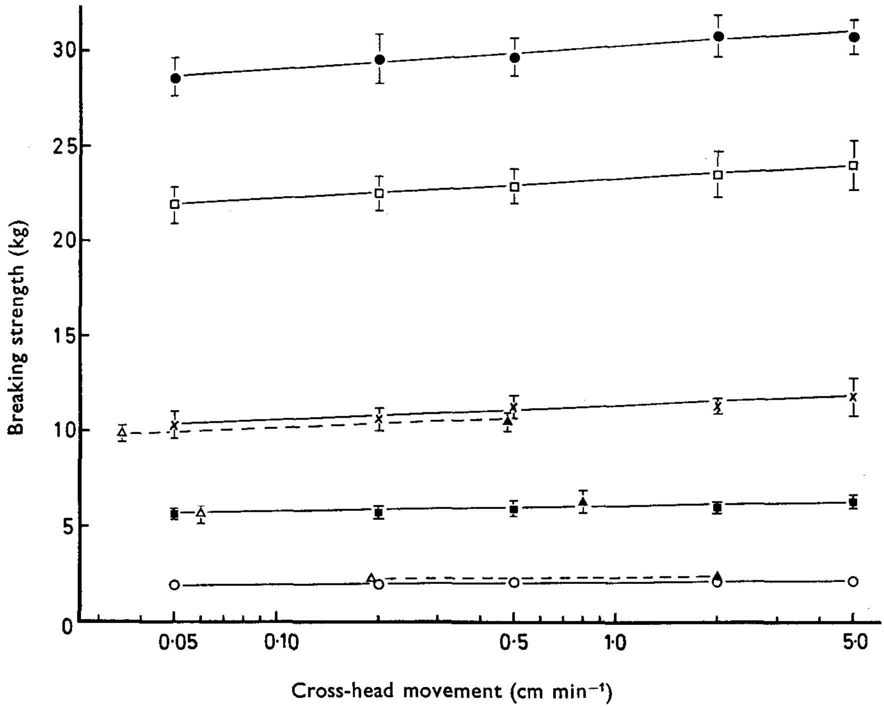

FIG. 1. The effect of rate of loading on the breaking strength of tablets. The range for each co-ordinate represents the standard deviation. Nominal strength: ○, 2 kg; ■, 5 kg; ×, 10 kg; □, 20 kg; ●, 30 kg; ▲, motorized Heberlein; △ Erweka.

min^{-1} cross-head movement was compared with the strength at the higher rates of loading. In most cases, there was 95% probability of a significant difference between the breaking strength at 0·05 cm min^{-1} and at 0·5 cm min^{-1}. In all cases, the value at 2·0 cm min^{-1} was significantly greater than at 0·05 cm min^{-1}.

A change in the rate of loading had no apparent effect on the standard deviation of replicate values of strength (Table 3).

Results from the Erweka instrument and the motorized Heberlein tester, for tablets of nominal strength 2, 5 and 10 kg, are recorded in Fig. 1 along with the results obtained using the Instron machine.

Table 4. *Comparison of the mean strength values at different loading rates, using the Student* t*-distribution*

Nominal strength	Comparison of mean strengths at different loading rates							
	0·05–0·2 cm min^{-1}		0·05–0·5 cm min^{-1}		0·05–2·0 cm min^{-1}		0·05–5·0 cm min^{-1}	
kg	*t*	(1–P)*	*t*	(1–P)*	*t*	(1–P)*	*t*	(1–P)*
2	1·19	70%	3·28	99·5%	5·69	99·9%	6·65	99·9%
5	0·36	20%	2·04	90%	2·48	97·5%	4·79	99·9%
10	1·02	60%	3·53	99·5%	3·84	99·5%	3·89	99.5%
20	1·72	80%	2·44	95%	3·48	99·5%	4·19	99·9%
30	1·88	90%	2·41	95%	4·60	99·9%	5·26	99·9%

* Minimum % probability of a significant difference between the mean values of strength at the two different rates of loading.

DISCUSSION

Statistical evaluation of the results for tablets of high and low strength has shown that there is a significant increase in the diametrical crushing strength as the rate of loading is increased from 0·02 to 5·0 cm min^{-1} cross-head movement.

The negative conclusions of Ritschel & others (1969) about the effect of loading rate may be attributed to the low strength of the tablets evaluated (1·8 and 4·7 kg) and also to the relatively large standard deviation of strength determinations compared with the present values for tablets of similar mean strength. The present results show that, for tablets of 2 and 5 kg nominal strength the dependency of strength on the loading rate is not large. Accordingly, only a small increase in the standard deviation of replicate strength values may be necessary to reduce to an insignificant level the differences between mean values of strength at different loading rates.

Although Ritschel & others (1969) did not quote values for the actual time between the onset of loading and the failure of a tablet, the mean times required to test ten tablets using each instrument were specified. Assuming that this arbitrary time period was related to the loading time for each tablet, it is interesting that the results of Ritschel & others show an increase in the strength values with a decrease in the time required for measurement, using those instruments for which the loading rate is approximately constant (Fig. 2). By contrast, for those instruments which do not apply the load at a regular rate, there was no apparent correlation. For the motorized Heberlein and Erweka instruments the rate of operation cannot be altered, and the data in Fig. 2 for these instruments correspond to a reliable and constant rate of loading.

Our findings have confirmed that the rate of loading, for tablets of 2, 5 and 10 kg nominal strength, is approximately ten times greater with the motorized Heberlein than with the Erweka (Table 5). There were significant differences between the strength values for the same tablets using these two instruments, and the results

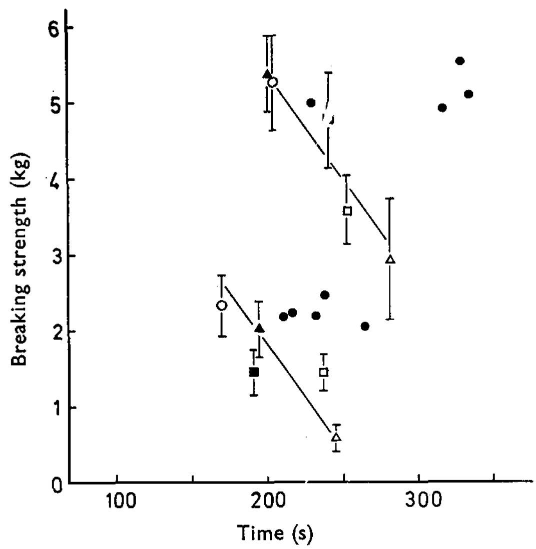

FIG. 2. The strength of tablets, and the standard deviation, determined by Ritschel & others (1969) using several instruments. The abscissa represents the time required to test the strength of ten tablets. ▲, motorized Heberlein; △, Erweka; ■, Strong-Cobb; □, DBT ("Siegfried"); ○, Pfizer; ●, other instruments.

Table 5. *Comparison of the results for diametrical crushing strength obtained using the motorized Heberlein and Erweka instruments*

	Erweka			Comparison of the mean strength values Erweka–Heberlein		Heberlein		
Nominal strength	Mean loading rate	Mean rate of platten movement	Mean strength† and standard deviation			Mean loading rate	Mean rate of platten movement	Mean strength† and standard deviation
kg	kg s^{-1}	cm min^{-1}	kg	*t*	(1–P)*	kg s^{-1}	cm min^{-1}	kg
2	0·4	0·19	2·25 ± 0·04	4·10	99·9%	4·2	2·0	2·49 ± 0·18
5	0·4	0·06	5·61 ± 0·47	3·40	99·5%	5·3	0·8	6·37 ± 0·59
10	0·4	0·035	9·84 ± 0·44	3·73	99·5%	5·7	0·48	10·56 ± 0·53

* Probability of a significant difference between the mean values of strength, using the two different instruments.
† Mean of 10 replicates.

obtained agree with the Instron data (Fig. 1) for the same rates of loading. This indicates that the calibration figure quoted by Brook & Marshall (1968), to convert the Erweka scale reading to a breaking load in kg, is not appropriate to the particular instrument we used. Thus, it is not certain that identical values for breaking strength will be obtained using different models of the Erweka instrument.

In addition, the effect of loading rate on the strength of different tablet formulations may not be identical. It is therefore interesting that the results of Ritschel & others (1969), for two appreciably different tablet compositions, show similar relations between strength and loading rate (Fig. 2), although the differences between the Heberlein and Erweka values were much greater than for the present tablet formulation. It is possible that the differences recorded by Ritschel & others may be due in part to calibration discrepancies between the two testing instruments used.

Even for the tablets of 20 kg nominal strength, studied in the present investigation, an increase in the loading rate by a factor of one hundred increased the mean strength value by only 2 kg. However, for manually-operated instruments it is possible that variation in the rate of loading at the instant of tablet failure may be sufficient to increase the deviation of replicate strength determinations, and to alter the mean value obtained.

Acknowledgements

We wish to express our gratitude to Mr. R. Best for advice and technical assistance with respect to the frequency response of recording instruments.

REFERENCES

BROOK, D. B. & MARSHALL, K. (1968). *J. pharm. Sci.*, **57**, 481–484.
DELONCA, H., PUECH, A., YOUAKIM, J., JACOB, M. (1967). *J. pharm. Belg.*, **22**, 21–30.
ENDICOTT, C. J., LOWENTHAL, W. & GROSS, H. M. (1961). *J. pharm. Sci.*, **50**, 343–346.
FAIRCHILD, H. J. & MICHEL, F. (1961). *Ibid.*, **50**, 966–969.
MAHLER, D. B. & MITCHEM, J. C. (1964). *J. dent. Res.*, **43**, 121–130.
MCCALLUM, A., BUCHTER, J. & ALBRECHT, R. (1955). *J. Am. pharm. Assoc. (Sci. Edn)*, **44**, 83–85.
REES, J. E. & SHOTTON, E. (1970). *J. Pharm. Pharmac.*, **22**, *Suppl.*, 17S–23S.
RITSCHEL, W. A., SKINNER, F. S. & SCHLUMPF, R. (1969). *Pharm. Acta Helv.*, **44**, 547–569.
RUDNICK, A., HUNTER, A. R. & HOLDEN, F. C. (1963). *Matl. Res. Stand.*, **3**, 283–289.
SMITH, A. N. (1949). *Pharm. J.*, **163**, 227–228.
TAYLOR, N. O., SWEENEY, W. T., MAHLER, D. B. & DINGER, E. J. (1949). *J. dent. Res.*, **28**, 228–241.