A TEST FOR THE MECHANICAL STRENGTH OF COMPRESSED TABLETS

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Compressed tablets should reach the user free from mechanical damage; they should exhibit the correct dosage in each product and present an elegant appearance. Normal conditions of transport and storage give rise to diverse forms of damage, especially to fracture, crushing and abrasion. Liability to damage from mechanical stresses varies according to the tablet manufacturing process employed; different formulations of the same active ingredients may show varying responses under apparently identical conditions of stress.

A reliable laboratory test for the susceptibility of tablets to mechanical damage would be of value in the comparative assessment of formulation techniques and for the routine control of production batches; several authors[1,3–5], have described tests designed for this purpose These measured resistance to fracture, crushing, indentation, or to agitation and abrasion. Abrasion and fracture are the principal stresses met in the normal transport and storage of tablets and a shaking-test might be expected to evaluate susceptibility to damage in "field" conditions in a reliable manner, the response being accelerated by magnification of these stresses.

Many laboratories are known to conduct shaking-tests by agitating the tablets in a closed vessel. The tablets break down to form a fine powder which is permitted to accumulate in the vessel, thereby progressively decreasing the mechanical action exerted on the remaining larger fragments. This effect is unusual in field conditions, where the amount of fine powder in relation to the number of tablets is seldom sufficient for this "cushioning" to occur. It was, therefore, decided to improve the shaking-test by removing the "fines" as they were formed, and also to devise an apparatus and procedure that could easily be reproduced.

The Shaking-Test Apparatus (Fig. 1)

The vessel in which the tablets were agitated, consisted of a 6 in. length of standard 1 in. diameter borosilicate glass pipe-line. This was connected to an identical piece by means of a normal joint, but was separated from it by a 12-mesh 22-gauge wire screen to form a diaphragm between the tubes. The open end of the upper tube was closed with a rubber-bung; the lower tube had a cotton plug in its far end. Two such shaking-tube assemblies were fitted by means of felt-lined clamps to a hard-wood panel, which was attached to the baseboard by a pivot arm and by means of a suitable casting, to an eccentric on a heavy flywheel. The flywheel was belt-driven from a constant-speed electric motor. The baseboard was bolted in a vertical position, to a brick wall so that at "rest" the long axes of the

shaking-tubes were vertical. Because of the method of attachment of the shaking-panel, the shaking-tubes traversed an eccentric path so that the tablets were agitated in a random fashion. The reproducibility of the apparatus is dependent upon the principal dimensions and the speed of the motor. To remove adherent dust from the tablet-remnants after shaking, the remnants were allowed to roll freely down an inclined half-cylinder of 18-mesh wire gauze onto the scale-pan of a balance.

Basic test procedure. (*a*) The apparatus, as constructed, was found to give 260 to 270 strokes per minute in tests over a period of 18 months. This agitation was found to be satisfactory since the tablets were shaken vigorously, but did not strike the rubber-bung (the resilience of which might be variable). (*b*) A fixed number of tablets was employed in each determination; after weighing, they were transferred to a clean and dry shaking-tube (a similar load being applied to the other tube on each occasion). (*c*) The apparatus was started by a switch on the motor and allowed to run for a period of time measured by stop-watch. (*d*) The powder accumulated in the cotton-plugged end of the lower tube was allowed to fall to waste and the tablet remnants in the upper tube were rolled down the inclined sieve on to the scale-pan. The final weight was then recorded.

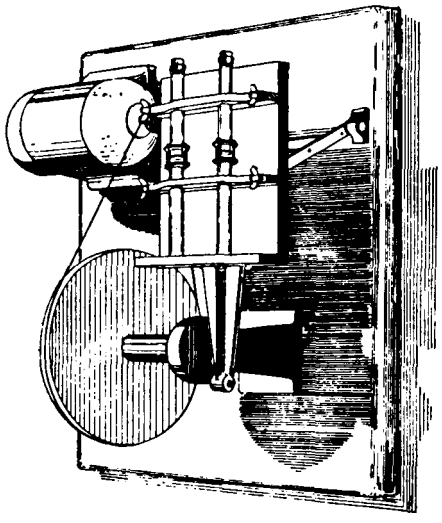

FIG. 1. Drawing of the apparatus for testing the mechanical strength of tablets. (Detailed drawings will be gladly supplied by the authors on request.)

Critical Examination of the Test

Effect of period of agitation on response. Two batches of a compound analgesic tablet were selected on the basis that Batch A consisted of firm tablets (by manual inspection) whilst Batch B was of poor to moderate mechanical strength. Mean initial weights of 20 tablets were, for Batch A, 10·67 g., and for Batch B, 10·61 g. Each point on the time-response curves (Fig. 2) represents the mean of 5 results for the loss in weight (in g.). From these results, it was decided to adopt a 2 minute period as the standard time of agitation for the following reasons. (*a*) The degree of agitation could be easily reproduced, (*b*) The losses in weight were readily measurable, (*c*) A clear distinction between the losses obtained with different batches of tablets was obtained, and (*d*) A reasonably short time-interval was desirable as a practical consideration.

Number of tablets per shaking-tube. It was necessary to determine the

effect of varying the number of tablets used in each test, and to decide upon the numbers to be used for different types of tablet. An indication of the spread of results obtained by varying the number of tablets per test, was derived from Table I; the results were most stable when 20 tablets were used in each test. A schedule to cover a wide range of average tablet weights was prepared, and is given in Table II.

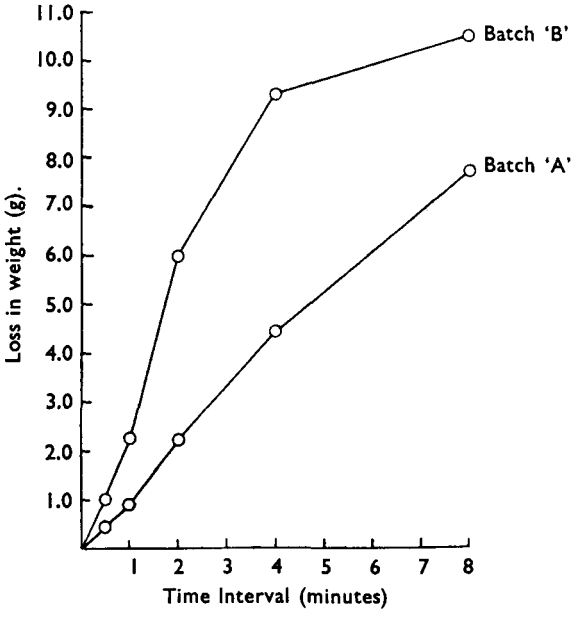

FIG. 2. Time response curves for an analgesic compound tablet. Each point represents the mean of 5 results.

Comparisons between samples in tests by one operator. The use of the test to discriminate between the mechanical strengths of different batches of tablets, was examined as shown in Tables III and IV. In Table III, two batches of tablets of the same formulation compressed on separate occasions were examined, 10 tests being conducted on each batch. The results showed a low standard deviation for each batch. Whether the difference between the 2 observed mean values was significant, was tested by a t-test: $t = \dfrac{\bar{x}_1 - \bar{x}_2}{\sqrt{\epsilon_1^2 + \epsilon_2^2}}$ where $\bar{x}_1$ and $\bar{x}_2$ were the mean values and ϵ_1 and ϵ_2 were the standard errors of the means. With 10 tests on each of batches X and Y, the value of t was 6·9, indicating a very high level of statistical significance for the difference between the means. For the first 4 tests on each batch, t is still 3·6 which is statistically significant. In Table IV, the results obtained by one operator on a single batch of tablets before and after a short period of storage are shown. In comparing the mean values obtained, the value of t was 3·5; this level of significance indicated that there was a true difference in mechanical strength between the samples which could be demonstrated by this method of testing. If the comparison was made for the first 4 readings on each sample, the value of t was 1·9; the difference between the mean values could not now be regarded as significant. The study of these results gave an indication of the lower limit of differences in mechanical strength that could be demonstrated in a reliable manner with only 4 readings.

TABLE I

RESULTS (LOSS IN WEIGHT IN G.) OBTAINED BY ONE OPERATOR ON A SINGLE DAY FOR ONE BATCH OF AN ANALGESIC COMPOUND TABLET, TO SHOW THE EFFECT OF THE NUMBER OF TABLETS PER SHAKING-TUBE ON THE NATURE AND REPRODUCIBILITY OF THE RESPONSE
(Mean tablet weight: 0·534 g.)

Test No.	No. of tablets per shaking-tube		
	10	20	30
1	1·77	1·96	2·29
2	2·08	1·88	1·94
3	1·77	1·95	2·40
4	1·43	1·98	2·25
5	2·07	1·82	2·34
Mean ($\bar{x}$)	1·82	1·92	2·24
Standard deviation (s)	0·27	0·07	0·18
Co-efficient of variation $\frac{(100s)}{\bar{x}}$	14·8	3·7	8·0

Results obtained by different operators testing various types of tablet. The results given in Table V indicated on inspection, that there would not be any significant difference between the results obtained by different operators using the new test. It was also seen that the test was applicable to different types of tablet and that there was little variation within the readings obtained for each batch of tablets; this suggested that there would generally be sufficient uniformity within batches of tablets for the test to be carried out on a minimal number of observations.

TABLE II

RECOMMENDED NUMBER OF TABLETS PER SHAKING-TUBE, IN RELATION TO THE AVERAGE TABLET WEIGHT OF THE SAMPLE

Average tablet weight (g.)		No. of tablets per shaking-tube
Exceeding	Up to	
—	0·05	150
0·05	0·1	100
0·1	0·2	75
0·2	0·3	40
0·3	0·4	30
0·4	0·6	20
0·6	0·8	15
0·8	1·0	12
1·0	1·1	10
1·1	1·3	8
1·3	1·5	7

TABLE III

RESULTS OBTAINED BY ONE OPERATOR ON 27.3.53, USING 20 TABLETS PER TEST (OF AN ANALGESIC COMPOUND TABLET) ON TWO DIFFERENT BATCHES, COMPRESSED ON THE SAME PRESS

Batch X			Batch Y		
Initial weight (g.)	Final weight (g.)	Loss (g.)	Initial weight (g.)	Final weight (g.)	Loss (g.)
10·43	5·54	4·89	10·11	6·00	4·11
10·37	5·08	5·29	10·70	5·88	4·82
10·39	4·53	5·86	10·71	7·14	3·57
10·41	4·93	5·48	10·71	7·26	3·45
10·44	5·25	5·19	10·67	6·21	4·46
10·38	5·08	5·30	10·61	6·11	4·50
10·44	5·32	5·12	10·68	6·44	4·24
10·49	4·45	6·04	10·69	7·09	3·60
10·39	4·78	5·61	10·70	7·13	3·57
10·44	4·55	5·89	10·67	6·09	4·58
Mean		5·47			4·10
Standard deviation		0·37			0·50
Standard error of the mean		0·12			0·16

TABLE IV

RESULTS OBTAINED BY ONE OPERATOR ON TWO DIFFERENT OCCASIONS, USING 20 TABLETS PER TEST (OF AN ANALGESIC COMPOUND TABLET) IN THE EXAMINATION OF A SINGLE BATCH; DURING THE PERIOD OF STORAGE, THE TABLETS WERE STORED IN LABORATORY CONDITIONS OF TEMPERATURE AND RELATIVE HUMIDITY

A. (Tests conducted on 27.3.53)			B. (Tests conducted on 2.4.53)		
Initial weight (g.)	Final weight (g.)	Loss (g.)	Initial weight (g.)	Final weight (g.)	Loss (g.)
10·69	8·75	1·94	10·66	8·48	2·18
10·70	8·60	2·10	10·71	8·55	2·16
10·66	8·57	2·09	10·69	8·23	2·46
10·64	8·54	2·10	10·67	8·56	2·11
10·64	8·78	1·86	10·58	8·02	2·56
10·79	8·89	1·90	10·69	8·31	2·38
10·67	8·93	1·74	10·71	8·50	2·21
10·65	9·00	1·65	10·69	8·50	2·19
10·65	8·58	2·07			
10·67	8·35	2·32			
Mean		1·98	.. ..		2·28
Standard deviation ..		0·20	.. ..		0·16
Standard error of the mean		0·06	.. ..		0·06

TABLE V

RESULTS OBTAINED BY TWO DIFFERENT OPERATORS ON 3 BATCHES COMPRISING VARIOUS TYPES OF TABLET (ALL TESTS PERFORMED ON THE SAME DAY)

Product	Batch No.	No. of tablets per test	Operator A			Operator B		
			Initial weight (g.)	Final weight (g.)	Loss (g.)	Initial weight (g.)	Final weight (g.)	Loss (g.)
Tab. Codein Co. ..	320	15	9·78	8·52	1·26	9·81	8·50	1·31
			9·77	8·62	1·15	9·80	7·81	1·99
			9·80	7·92	1·88	9·74	7·91	1·83
			9·79	7·97	1·72	9·77	8·26	1·51
		Mean			1·50	..	.. ..	1·66
		Standard deviation			0·35	..	.. ..	0·30
		Standard error of the mean ..			0·18	..	.. ..	0·15
Tab. Dexamphet. Sulph. (5 mg. strength) ..	15	40	8·82	8·71	0·11	8·83	8·73	0·10
			8·83	8·72	0·11	8·84	8·74	0·10
			8·85	8·72	0·13	8·81	8·67	0·14
			8·81	8·67	0·14	8·86	8·73	0·13
		Mean			0·12	..	.. ..	0·12
		Standard deviation			<0·02	..	.. ..	<0·02
		Standard error of the mean ..			<0·01	..	.. ..	<0·01
Tab. Phenobarb. (½ gr. strength)	83	100	6·24	5·81	0·43	6·26	5·79	0·47
			6·26	5·77	0·49	6·26	5·80	0·46
			6·27	5·82	0·45	6·28	5·81	0·47
			6·26	5·79	0·47	6·25	5·80	0·45
		Mean			0·46	..	.. ..	0·46
		Standard deviation			0·02	..	.. ..	<0·01
		Standard error of the mean ..			0·01	..	.. ..	<0·01

DISCUSSION

The object of our experiments was to devise a reliable test for the susceptibility of compressed tablets to mechanical damage during transportation and storage, as this would help to prevent the issue of products that might otherwise reach the user in a damaged state. The reported test

seems suitable for the purpose and is relatively free from experimental error and sensitive to small differences between the mechanical strengths of various batches of tablets. The special feature of the test is that it removes fine powder, as it is formed, from the vicinity of the larger tablet remnants. The shaking vessel may be reproduced easily.

The test has been described as an assessment of "mechanical strength" in order to avoid confusion with factors such as "hardness" measured, for example, by indentation. Results were expressed in terms of "loss in weight" of a given number of tablets. The method of expression was preferred to a percentage calculation, as used in the "Friability Value" of Burlinson and Pickering[3] since this could yield an unduly favourable indication of the mechanical strength of overweight tablets.

A critical analysis of some results obtained in the test is reported. Similar results were recorded repeatedly over a period of 2 years, using various types of tablets in several hundred determinations. The test procedure was controlled by mechanical factors devoid of personal error and it was found that there was no significant variation in the agitation applied to the tablets in successive tests. The main source of error in the results for a given batch of tablets, was the variation between individual tablets in the samples taken.

Four readings were considered sufficient to yield a valid result on most occasions but the application of a *t*-test would be necessary to verify its significance in borderline cases.

A single mesh-size was chosen for the diaphragm of the shaking-vessel, since this allowed the apparatus to be used over the range from 6/32 to 20/32-in. tablet diameter, without alteration. No attempt was made to design the test as a means of comparison with a control tablet of standardised mechanical strength, since there was no likelihood that such a product could be prepared and stored satisfactorily.

The test was found to be most suitable for tablets prepared from materials of a crystalline, micro-crystalline or readily-pulverised amorphous nature. Results with coarsely fibrous and soft materials were unreliable. Readings obtained on those rare occasions on which the tablets became jammed together, were disregarded.

Results in the test have repeatedly demonstrated the following pattern. (*a*) Preparations involving the preliminary dry compression process appeared to show marked variation between the values of single observations, as well as high mean losses of weight. (e.g., Tab. Codein Co. see Table V). (*b*) Tablets prepared by moist granulation, gave moderate losses in weight in the test, but with small variations between observations, when a high proportion of starch was present. (e.g., Tab. Phenobarb.). (*c*) Tablets prepared by moist granulation and containing a high proportion of a sugar, showed the smallest losses in weight along with minimal variations between readings. (e.g., Tab. Dexamphet. Sulph.). These patterns agree with the general experience of the processes of tablet manufacture.

Some laboratories employ the Monsanto Hardness Test in which an individual tablet is crushed between a spring-loaded spindle and an anvil

(the test usually being carried out on each of 10 tablets from a batch). In comparing this method with our shaking-test, it is observed that, (*a*) the new test provides a closer assessment of susceptibility to the normal stresses encountered in field conditions, and (*b*) The Monsanto Test has the larger factor of personal error (in the positioning of the tablet, in setting the zero and in determination of the end-point). The Monsanto Test is useful, however, for checking the adjustment of a tablet press during operation and it may also give an estimate of variations in mechanical strength between individual tablets.

In the preparation of compressed tablets, it is desirable to adopt a compromise between optimal mechanical strength and disintegration time, as noted by Berry and Ridout[2]. Whilst there is a pharmacopœial method for the control of disintegration of tablets in water, it is noteworthy that the British Pharmacopœia has not yet adopted a procedure for the estimation of mechanical strength. It is suggested that the new test, perhaps modified by simplification of the apparatus and in the light of wider experience, could be the basis for an official procedure. Although the results quoted in this paper refer only to the comparison of batches of tablets of identical formula, it has been our experience that the test may be applied satisfactorily to compare different formulations provided that the active ingredient(s), average weight and diameter are standardised.

Summary

1. The need for a reproducible test for the mechanical strength of compressed tablets is considered.

2. A Shaking Test is described, which involves the separation from the larger tablet remnants of fine powder as it forms; the result is expressed in terms of the loss in weight of a specified number of tablets.

3. An apparatus is described and illustrated; the principal feature is an easily reproduced shaking vessel.

4. Consideration is given to the errors of the test and the significance of the results.

5. Comparisons are drawn between the Monsanto hardness test and the new shaking test.

6. It is suggested that the new test might form the basis for a Pharmacopœial procedure to standardise the mechanical strength of compressed tablets.

The authors wish to acknowledge the technical assistance of Mr. K. R. Bramley in carrying out much of the experimental work, the co-operation of Mr. R. Ganday, B.Sc., F.R.I.C., in whose analytical department the routine application of the test has been observed and the help of Mr. T. G. Desborough in preparing this paper.

APPENDIX*

FURTHER APPLICATION OF THE *t*-TEST TO TIME-RESPONSE PHENOMENA

(1) CODEINE COMPOUND TABLETS

Theoretical Tablet Weight 0·650 g.

Period of shaking (minutes) ..	2		3		4	
Batch	A	B	A	B	A	B
Individual readings for loss in weight in G.:						
1.	1·25	2·40	2·30	3·62	3·02	5·61
2.	1·42	2·48	2·60	3·77	3·27	6·28
3.	1·42	2·19	2·65	4·41	3·71	6·00
4.	1·41	2·78	2·48	3·77	3·69	5·79
Mean in g. ($\bar{x}$)	1·38	2·46	2·51	3·89	3·42	5·92
Standard deviation (s)	0·08	0·24	0·16	0·35	0·34	0·29
Coefficient of variation $\left(\frac{100\ s}{\bar{x}}\right)$	5·8	9·8	6·2	9·0	9·9	4·9
Standard error (ϵ)	0·04	0·12	0·08	0·18	0·17	0·15
$t\left(=\frac{\bar{x}_1-\bar{x}_2}{\sqrt{\epsilon_1^2+\epsilon_2^2}}\right)$	8·3		7·0		11·0	

(2) EPHEDRINE HYDROCHLORIDE TABLETS

Theoretical Tablet Weight 0·065 g.

Period of shaking (minutes) ..	2		3		4	
Batch	A	B	A	B	A	B
Individual readings for loss in weight in g.:						
1.	0·14	0·03	0·15	0·07	0·17	0·08
2.	0·16	0·03	0·15	0·06	0·23	0·09
3.	0·12	0·05	0·18	0·09	0·19	0·10
4.	0·21	0·04	0·14	0·08	0·24	0·10
Mean in g. ($\bar{x}$)	0·16	0·04	0·16	0·08	0·21	0·09
Standard deviation (s)	0·04	0·01	0·02	0·01	0·03	0·01
Coefficient of variation $\left(\frac{100\ s}{\bar{x}}\right)$	24·4	25·0	11·2	17·5	15·7	8·4
Standard error (ϵ)	0·02	0·01	0·01	0·01	0·02	0·01
$t\left(=\frac{\bar{x}_1-\bar{x}_2}{\sqrt{\epsilon_1^2+\epsilon_2^2}}\right)$	5·4		5·7		5·4	

(3) DEXAMPHETAMINE SULPHATE TABLETS

Theoretical Tablet Weight 0·225 g.

Period of shaking (minutes) ..	2		3		4	
Batch	A	B	A	B	A	B
Individual readings for loss in weight in g.:						
1.	0·24	0·26	0·53	0·15	0·67	1·26
2.	0·25	0·49	0·52	0·57	0·66	1·04
3.	0·33	0·17	0·49	0·47	0·64	1·10
4.	0·22	0·91	0·48	0·79	0·60	0·98
Mean in g. ($\bar{x}$)	0·26	0·46	0·51	0·50	0·64	1·09
Standard deviation (s)	0·05	0·33	0·02	0·27	0·03	0·12
Coefficient of variation $\left(\frac{100\ s}{\bar{x}}\right)$	19·2	71·6	4·7	54·0	4·9	11·2
Standard error (ϵ)	0·03	0·17	0·01	0·14	0·02	0·06
$t\left(=\frac{\bar{x}_1-\bar{x}_2}{\sqrt{\epsilon_1^2+\epsilon_2^2}}\right)$	1·2		0·07		7·4	

* Added after the paper was presented.

Discussion

The results quoted in this Appendix illustrate the time-response phenomena in batches, each consisting of tablets of relatively uniform mechanical strength, of widely differing theoretical tablet weight. In addition, the dexamphetamine sulphate tablets, Batch B is evidently composed of tablets of variable mechanical strength. The application of the *t*-test to a comparison of the mean losses in weight shows that the significance of the difference between the means can be seriously affected by the choice of an uneven batch.

When comparing uniform batches, it is seen that 4 readings at the 2-minute period of shaking, yield a result that (in comparisons of batches differing to a degree similar to those examined) is of acceptable significance. As the period increases, the coefficient of variation tends to fall; this presumably indicates that the more fragile tablets have been reduced to fragments passing No. 12 mesh during the first 2 minutes and that the later stage represents slower break-up of the more durable material.

If this is applied as a limit test for the mechanical strength of tablets, it is desirable to state:—

(*a*) An upper limit for the mean loss in weight.
(*b*) An upper limit for the coefficient of variation

all with reference to a 2-minute period of shaking and 4 readings.

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DISCUSSION

The paper was presented by MR. N. J. VAN ABBÉ.

MR. E. W. RICHARD (Upminster) referred to the statement in the paper that "The object of our experiments was to devise a reliable test for the susceptibility of compressed tablets to mechanical damage during transportation and storage," and pointed out that tablets were generally sent out from manufacturers in fairly well filled and stuffed containers. During the test it would seem that the tablets were quite free to move up and down in the vessel. Did the authors consider that the conditions obtaining when tablets loosely held in a container were shaken, were comparable with those of a well packed container sent through the post?

DR. B. K. MARTIN (Slough) suggested that the term "friability value" adopted by Burlinson and Pickering was a more apt description of the degradation of the tablet than the author's term "mechanical strength." He was concerned to know by what factor the normal stresses which were encountered by the tablet in its every day life had been magnified in the author's test.

MR. D. STEPHENSON (Dartford) referred to the suggestion that the test should be included in the Pharmacopœia and said that the patient was already adequately protected by the present tests and no advantage would be gained by including a test for hardness.

MR. N. J. VAN ABBÉ, in reply, said that difficulty had been encountered in correlating the small amount of normal damage with the great amount of damage in an accelerated test. The effect of dropping a bottle of tablets was different from the abrasion effect. He was unable to state to what extent normal conditions of usage were magnified in his test but it was valuable for comparing different batches of the same tablets.