RESEARCH PAPERS

THE OPERATING CHARACTERISTICS OF SOME OFFICIAL WEIGHT VARIATION TESTS FOR TABLETS

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In his review of various current pharmacopœias, Smith[1] reported that several countries now include tests for controlling the variation in weight of compressed tablets. These tests differ in detail but follow a common principle. All limit the number of tablets which may deviate in weight by more than a specified amount from the mean of those examined, to 10 per cent. of the total number examined, while prohibiting any deviation of more than twice that amount. The pharmacopœias vary somewhat in the amount of deviation they allow but the main difference between them is in the number of tablets specified for the official sample. The British Pharmacopœia and the United States Pharmacopeia stipulate 20 tablets (the B.P. accepts as few as 10 if 20 are not available), the pharmacopœia of Finland 50, while the pharmacopœias of Denmark, Norway and Switzerland each require 100 tablets to be examined.

No attempt appears to have been made to determine the relation between the size of the sample and the ability of the test to reject batches of inferior material. It appeared to us that a comparison of the efficiencies of the various test criteria in official use would be of some value to the controlling authorities in deciding which test was most suitable for their needs.

The efficiency of a test may be judged by its ability to differentiate between batches of satisfactory material which it is desired to accept and batches of unsatisfactory material which it is desired to reject. When a test is based upon the examination of a random sample of small size it cannot be expected to be as discriminatory as the examination of a random sample of large size or of an analysis of the complete population of the batch. In the modern approach to the theory of acceptance sampling (see, for example[2]), of primary concern is the probability that a batch, having a specified quality, will be accepted by the test. For a test to be capable of distinguishing between the satisfactory and unsatisfactory batches it should have a high probability of accepting the satisfactory batches and a low probability of accepting the unsatisfactory batches.

The "operating characteristic" curve (OC curve) of a test shows the probability of acceptance plotted against some measure of the quality of a batch. From the OC curve, a manufacturer can determine the quality level at which his product must be maintained in order to guarantee him a high probability (for example, 95 per cent. or more) of acceptance.

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On the other hand, a consumer, or the controlling authority guarding the interests of the consuming public, can gauge the protection that the test affords by noting which quality levels have a low probability (for example, 10 per cent. or less) of acceptance.

The purpose of this paper is to present the OC curves of some official test criteria based on sample sizes of 10, 20, 50 and 100 tablets, respectively. The OC curves of two alternative unofficial tests are also presented for comparison. The relative advantages and disadvantages of these tests are discussed. As explained in Part I below, the OC curves were obtained by experimental sampling methods based on the assumption that the weights of individual tablets in the same batch follow a normal (bell-shaped) distribution. To investigate the validity of this assumption, a large number of tablets of various types were obtained and weighed.. The results of this investigation are reported in Part II below.

PART I. OC CURVES

Procedure

The official test criteria considered in this study were of the following form:—

Of n tablets examined, no more than 10 per cent. may deviate from the mean weight by more than x per cent. of the mean, and none may deviate by more than twice this amount.

All the pharmacopœias mentioned employ a test of this form, except the Danish which differs slightly in that the deviation allowed is a fixed quantity plus a percentage of the mean. For definiteness, the allowable deviation was taken as 5 per cent. of the mean; this is the official value used in these pharmacopœias for the heavier tablets. Our object was to determine the OC curves of this test criterion when 10, 20, 50 and 100 tablets, respectively, were stipulated for the sample size.

In order to define the OC curve, it is necessary to decide upon a suitable measure of the quality of a batch. For the weight variation test considered here, it seems reasonable to measure batch quality by the percentage of defective tablets in the batch, a defective tablet being defined as one which differs in weight from the batch mean by more than 5 per cent. of the batch mean. (It should be noted that, since the batch mean and sample mean do not in general coincide, a tablet which is defective in the batch may not be considered "defective" in the sample). For a normal distribution with mean m and standard deviation σ, the percentage defective is a function of the coefficient of variation σ/m, and can be determined with the aid of normal distribution tables[3]. We assumed that the distribution of tablet weights in a batch was satisfactorily representable by a normal distribution and formed artificial samples of tablet weights using the table of random normal deviates compiled by Wold[4]. Two hundred such artificial samples were assembled in each of the four sample sizes: 10, 20, 50 and 100. By applying the test criteria to them, we were able to obtain estimates of the desired OC curves.

Such an experimental sampling procedure is often used by statisticians. In the present instance it has several advantages over the alternative of

actually weighing a large number of tablets from a batch. Since it is far easier to select a number from a table than to weigh a tablet, the handling of 20,000 random numbers is a much more simple task than the weighing of a like number of tablets. With the use of random numbers, the form of the population distribution, together with its mean, standard deviation and other characteristics, are known whereas for a sample of actual tablets these characteristics can only be estimated from the information provided by the sample. Furthermore, the population mean and standard deviation of the random number samples can be altered at will, thus permitting the adjustment of the percentage defective in the population (i.e., the batch) to any desired level; this is a necessity in estimating the OC curve of a test. The main disadvantage of this procedure is that one is restricted to a distribution of known form, in this case the normal distribution, which at best can be only a good approximation to the distribution of the weights of an actual batch of tablets.

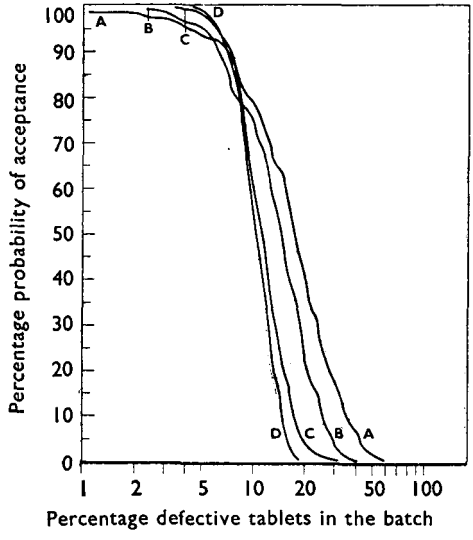

FIG. 1. OC curves for official weight variation tests based on samples of A = 10, B = 20, C = 50 and D = 100 tablets.

The random numbers in Wold's table represent a normal distribution with mean zero and standard deviation unity. By applying the transformation $X \rightarrow \sigma X + m$ to each random number X, they can represent the weights of a batch of tablets with coefficient of variation σ/m. The OC curves were estimated as follows. For each random number sample taken from Wold's table, the "critical" value of σ/m was determined such that, after applying the transformation $X \rightarrow \sigma X + m$ to each sample member, the sample led to acceptance of the batch for values of σ/m smaller than the critical value and to rejection of the batch for values of σ/m greater than the critical value. The critical value of σ/m was then converted to its corresponding value of the percentage defective by the use of tables of the normal distribution[3]. Thus, associated with each random number sample was a critical value of the percentage defective in the batch. For any specified value of the percentage defective, the probability of acceptance could then be estimated by counting the number of samples which had critical values of the percentage defective greater than that specified and expressing it as a percentage of the total number of samples. In this way, the OC curves of the test criteria were estimated. The results are illustrated in Figure 1.

Discussion

Figure 1 shows the operating characteristic curves of the official weight variation tests using 10, 20, 50 and 100 tablets, respectively. From these curves, it may be seen that a batch of tablets which contains a total of 5 per cent. underweight and overweight tablets (defined as falling short of and exceeding, respectively, the batch mean by 5 per cent. or more) will have a probability of being passed equal to 93, 95, 98 or 99 per cent. depending on whether a sample of size 10, 20, 50 or 100 is used for the test. Thus, providing the tablet manufacturer is maintaining a suitably low percentage of defective tablets in his batches, an increase in the size of the sample used for the weight variation test increases the chances of a batch being passed. On the other hand, a batch containing 20 per cent. defective tablets will have a probability of 0, 4, 23 or 40 per cent. of passing for 100, 50, 20 and 10 tablets, respectively, in the official sample. Thus, a batch which is so heterogeneous as to have 20 per cent. of its items outside the stipulated range has a 40 per cent. chance of passing the test when only 10 tablets are examined, compared with almost no chance of passing when a sample of 100 tablets is used. It is apparent, then, that the size of the sample has a considerable effect on the ability of the test to screen out the bad batches. A sample of only 10 tablets seems to provide very meagre protection against inferior products being marketed and it would seem to be desirable to employ sample sizes of 50 or 100 tablets if possible. Whether the increased discriminating ability of the test when the larger sample sizes are used is worth the extra labour in examining the greater number of tablets is, of course, for the controlling authorities to decide. In addition to requiring a greater expenditure of effort in weighing the tablets, there may be difficulties at times in obtaining market samples with the required number of tablets.

Possible Alternative Weight Variation Tests

The weight variation tests defined in the pharmacopœias mentioned in the introductory paragraph have the advantage of being simple to apply. All that is required is to weigh the individual tablet and to count the number which deviate from the mean by more than the specified amount. However, this procedure does not utilise all of the information provided by the knowledge of the individual tablet weights. There is the possibility, then, of improving the OC curve, without changing the sample size, by adopting a procedure which makes more efficient use of the available information.

In statistical populations which are approximately normally distributed, the most efficient measure of variability is the standard deviation. If the weights of the individual tablets in the sample are known, the standard deviation of the weights can be readily calculated. A rejection criterion may be based on the requirement that the standard deviation should not exceed some specified percentage of the mean.

In Figure 2 are shown the OC curves for tests based on 10 and 20 tablets using a criterion based on the standard deviation. In computing

these curves, the upper tolerance on the standard deviation was taken to be 3·5 per cent. of the mean for a sample of 10 and 3·25 per cent. of the mean for a sample of 20. By these choices, the OC curves of the standard deviation tests coincided approximately with the OC curves of the official tests at 8 per cent. defective tablets. It was not necessary to estimate the OC curves of the standard deviation test by the experimental sampling method used in the case of the official tests, since the statistical theory for determining them is given by Johnson and Welch[5].

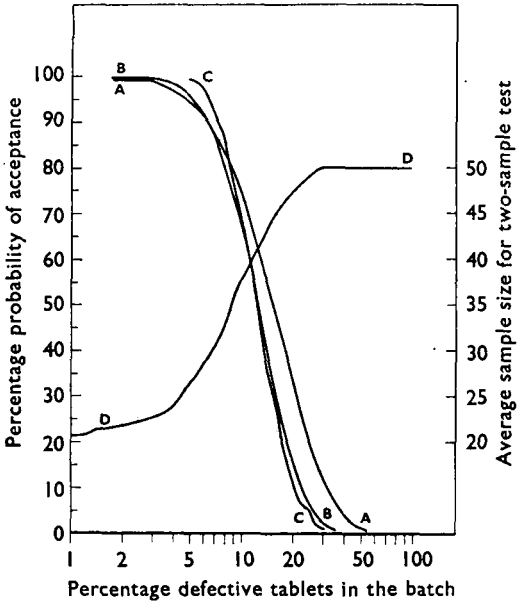

FIG. 2. OC curves for some alternative weight variation tests.

A. Standard deviation test, 10 tablets.
B. Standard deviation test, 20 tablets.
C. Two-sample test.
D. ASN curve for two-sample test.

Hence these OC curves are exact and are not subject to the sampling variations of the curves in Figure 1.

If it is considered essential to retain the form of the present official procedures, then an increase in the sample size is necessary to increase the efficiency of the test. The increase in sample size from 20 to 50 or 100 tablets would entail, of course, considerable extra effort to carry out the test, which is perhaps not justified in the case of most products on the market. It is possible, however, by using a "two-sample" test, to increase the efficiency of the procedure while retaining the advantage of having a small sample size when the batch being examined is a satisfactory one. As its name implies, a two-sample test is based on two samples instead of one. However, since the decision to examine the second sample depends on the results observed in the first, it is possible that the first sample alone may be sufficient for determining whether the batch in question satisfies the requirements. For example, a total sample size of 50 tablets may be specified, and a rule adopted which determines, after the examination of 20 tablets, whether the remaining 30 need be examined. Such a weight variation test might be formulated as follows:

The mean tablet weight is determined by weighing 50 tablets. Provided no more than one of the first 20 tablets examined deviates from the mean by more than 5 per cent. of the mean, the batch is accepted. Otherwise, the entire 50 tablets are to be examined and the batch accepted if no more

TABLE I

RESULTS OF WEIGHT VARIATION STUDIES; SAMPLES FROM THE MANUFACTURER

Tablet	Machine	Sample	No. of tablets	Mean weight, mg.	Standard deviation, per cent. of mean	Skewness	Kurtosis
A (Phenobarbital)	Single-punch	1	250	28·58	2·2	−0·07	0·81
		2	100	28·48			
		3	100	28·16			
		4	250	28·28	2·4	0·08	0·78
		5	100	28·25			
		6	100	28·17			
		7	250	28·16	2·4	0·33*	0·76*
		8	100	28·11			
		9	92	28·30			
		10	239	28·76	2·3	0·18	0·80
B (A.B.S. & C.)	Double-punch	1	100	66·56	5·4	−0·21	0·88*
		2	100	65·56			
		3	100	67·30	4·1	−0·45*	0·86*
		4	100	66·87			
		5	100	68·28	4·8	−0·32	0·83*
		6	100	66·92			
		7	100	66·53	3·9	−0·00	0·82
		8	100	65·63			
		9	100	66·85	4·6	−0·17	0·87*
		10	100	66·91			
C (Chlorcyclizine Hydrochloride)	Single-punch 1	1*a*	250	148·9	0·5	−0·02	0·81
		2*a*	250	148·6	0·5	0·15	0·80
	2	1*b*	248	146·5	1·1	−0·12	0·79
		2*b*	250	146·3	1·0	−0·29*	0·80
	3	1*c*	250	147·0	0·9	0·12	0·81
		2*c*	250	148·0	0·7	−0·04	0·81
D (Butethal)	Rotary	1	250	223·8	2·0	0·08	0·82
		2	100	218·2			
		3	100	216·1			
		4	250	218·4	1·8	−0·01	0·79
	(selected punch)	5*a*	100	216·8			
		6	100	217·1			
	(selected punch)	6*a*	100	217·7	1·0	−0·59*	0·78
		7	100	217·5	1·7	−0·04	0·80
	(selected punch)	7*a*	100	216·7			
		8	100	216·4			
	(selected punch)	8*a*	100	217·0	1·0	0·36	0·76*
		9	100	216·4	1·4	−0·25	0·75*
	(selected punch)	9*a*	100	217·0	1·0	−0·42*	0·81
E (Sodium Salicylate)	Single-punch	1	100	330·2	1·2	−0·02	0·79
		2	100	329·6			
		3	100	328·5			
		4	250	330·7	1·3	0·25	0·78
		5	100	328·4			
		6	100	328·7			
		7	250	330·5	1·6	−0·28*	0·80
		8	100	331·5			
		9	100	328·6			
		10	250	328·4	1·4	0·33*	0·80
F (A.S.A.)	Single-punch	1	50	362·8	1·4	−0·11	0·81
		2	50	362·7	1·3	0·36	0·79
		3	50	362·2	1·4	−0·02	0·81
		4	50	360·7	1·2	0·95*	0·77
		5	50	362·4	1·5	−0·66	0·78
		6	50	361·8	1·6	0·27	0·80
		7	50	360·5	1·0	−0·22	0·81
		8	49	361·4	1·1	0·21	0·80
		9	50	362·8	1·2	0·28	0·79
		10	50	358·5	0·8	0·67*	0·79
G (A.S.A.)	Rotary	1	250	372·2	1·2	−0·25	0·79
		2	100	371·3			
		3	100	370·6			
		4	250	371·8	1·1	0·16	0·80
		5	100	368·3			
		6	100	370·2			
		7	154	370·6	1·0	−0·09	0·79
		8	100	371·4			
		9	100	370·5			
		10	158	373·1	1·1	−0·16	0·82
H (Ferrous Sulphate)	Rotary	1	50	474·2	1·3	−0·18	0·80
		2	50	471·5	1·2	0·22	0·77
		3	50	474·4	1·3	0·29	0·76
		4	50	478·4	1·4	0·03	0·84

TABLE I (*contd.*)

Tablet	Machine	Sample	No. of tablets	Mean weight, mg.	Standard deviation, per cent. of mean	Skewness	Kurtosis
		5	50	476·8	1·5	0·25	0·82
		6	50	477·0	1·5	−0·29	0·78
		7	50	475·3	1·9	−0·37	0·78
		8	50	474·5	1·4	−0·20	0·77
		9	50	473·6	1·6	0·32	0·83
		10	50	476·5	1·5	−0·20	0·82
I (A.P.C.)	Rotary	1	50	482·3	1·4	−0·10	0·83
		2	50	486·6	1·6	−0·11	0·79
		3	50	477·1	1·4	−0·89*	0·74*
		4	50	472·0	2·0	−0·58*	0·83
		5	50	476·3	1·6	−0·10	0·73*
		6	50	470·4	1·6	0·46	0·80
		7	50	475·0	1·3	−0·14	0·85
		8	50	481·2	1·6	0·35	0·80
		9	50	478·2	1·6	0·16	0·82
		10	50	483·7	1·6	0·11	0·78
		11	50	473·5	1·8	−0·09	0·78
J (Milk of Magnesia)	Single-punch	1	100	499·1	1·0	−0·19	0·81
		2	100	501·9			
		3	100	501·8	1·1	0·19	0·80
		4	98	501·9			
		5	100	504·7	1·0	−0·20	0·79
		6	99	505·8			
		7	100	503·3	1·2	0·24	0·83
		8	100	498·1			
		9	100	497·1	1·2	−0·79*	0·79
		10	97	496·5			
K (Ammonium Chloride)	Rotary	1	50	517·3	1·4	−0·10	0·75*
		2	50	517·3	1·3	−0·36	0·75
		3	50	518·6	1·7	−2·06*	0·68*
		4	50	521·0	1·4	−0·76*	0·74*
		5	50	516·9	1·6	−0·65*	0·76
		6	50	515·5	2·0	−0·37	0·82
		7	50	518·7	2·1	−0·27	0·85
		8	50	519·9	1·6	−0·13	0·74*
		9	50	523·2	1·6	0·10	0·79
		10	50	523·5	1·7	−0·39	0·84
		11	50	529·9	1·8	−0·25	0·82
		12	50	517·7	1·8	−0·53	0·75
		13	50	524·4	2·2	−0·03	0·80

* Here and Table II denotes values for tablet samples falling beyond the upper or lower 5 per cent. points.

than 5 tablets deviate from the mean by more than 5 per cent. of the mean and none deviate by more than twice this amount.

In Figure 2 the estimated OC curve corresponding to this procedure is shown. In addition to the OC curve, the average number of tablets which will be required by the test is of interest. This is also shown in Figure 2 as a function of the percentage of defective tablets in the batch and is known as the "Average Sample Number" curve (ASN curve). From the ASN curve it may be seen that for a batch of tablets which is 4 per cent. defective, the average sample size is about 26 tablets. This means that, although part of the time 20 tablets will be sufficient while in the remaining instances 50 tablets will be required, on the average, for batches which are 4 per cent. defective, 26 tablets will be examined. The ASN curve in Figure 2 shows that this two-sample procedure has the desirable property of concentrating the efforts of the examiner on the more heterogeneous batches. The satisfactory batches are usually accepted after the examination of only 20 tablets while the more variable batches usually require the examination of all 50 tablets before they are either passed or rejected.

The curves in Figure 2 of the two-sample procedure were obtained by the same experimental sampling procedures used to obtain the curves in Figure 1.

Part II. Weight Variation Studies

The purpose of this phase of the study was to investigate the variation in weight of individual tablets made from the same batch of material. Several samples of various types of tablet were obtained and weighed on a semimicro balance. The data were subjected to a statistical analysis, the main results of which are summarised in Tables I and II.

TABLE II

Results of weight variation studies; A.S.A. samples from retail outlets

Mfr.	Mean weight, mg.	Standard deviation, per cent. of mean	Skewness	Kurtosis
1	345·1	2·4	−0·14	0·91*
2	347·1	1·8	0·61	0·80
3	349·3	6·7	−2·60*	0·59*
4	352·0	3·3	−0·75	0·79
5	353·4	2·2	0·07	0·74
6	355·7	2·4	−0·18	0·78
7	359·9	2·0	0·10	0·78
8	362·0	0·9	−0·09	0·84
9	364·6	2·3	0·01	0·84
10	364·7	1·6	0·03	0·81
11	365·7	1·2	−0·31	0·80
12	365·8	2·7	−1·02*	0·75
13	365·8	3·2	−0·40	0·89*
14	366·7	2·7	2·27*	0·65*
15	367·3	2·0	−0·62	0·76
16	367·7	2·4	−0·43	0·81
17	368·5	1·6	−0·78	0·72*
18	368·7	1·4	−0·37	0·77
19	369·7	1·8	1·14*	0·75
20	370·0	2·5	−0·24	0·80
21	370·2	2·3	0·89*	0·81
22	370·3	1·3	0·32	0·84
23	375·4	5·0	−0·60	0·74
24	375·7	2·1	1·14*	0·71*
25	378·1	1·8	−0·02	0·76
26	378·1	2·9	0·20	0·81
27	380·0	1·3	0·60	0·82
28	382·9	2·3	−0·17	0·87
29	383·3	3·5	0·06	0·87
30	384·3	1·8	1·13*	0·77
31	385·8	2·5	−0·02	0·89*
32	386·1	1·9	−0·04	0·72*
33	386·9	1·5	0·46	0·82
34	387·6	1·6	−0·41	0·83
35	387·6	2·6	1·86*	0·68*
36	388·4	2·5	−2·50*	0·59*
37	390·6	2·6	0·93*	0·79
38	391·2	2·8	0·34	0·89*
39	401·1	0·8	0·05	0·86
40	409·0	1·7	0·53	0·81

The data in Table I refer to tablets obtained directly from the manufacturers. The plants of five Canadian producers were visited and samples obtained of eleven different types of tablet, denoted in Table I by the code letters A to K. Nearly 12,000 tablets were collected, of which over 8000 were individually weighed. For each type of tablet, the samples collected were from the same batch of material and, except for tablet C, from the same tableting machine. The six samples of tablet C were taken from three different machines. Except for tablets C, F and I, all samples were taken directly from the ejection spout of the machine, so that the

individual tablets in these samples were punched out consecutively, and successive samples were taken at equal time intervals of 10 to 20 minutes. The samples of tablet C were also taken directly from the three machines, the first samples in the morning and the second in the afternoon of the same day. Tablet types F and I were sampled from several large containers serving as receptacles for the tablets after ejection from the machine. One sample was taken from the top of each such container. Machines of the single, double and rotary types of punch were represented as indicated in Table I. For tablet type D, which was punched on a machine with a rotary type of punch, five of the samples were confined to a selected punch.

The data in Table II refer to 5-grain tablets of acetylsalicylic acid obtained from various retail outlets. Samples, each of 20 tablets, were collected of 40 different brands of this type of tablet. The tablets of each sample were taken from the same package or bottle; this is one way that an official sample is usually obtained. Each of the 800 tablets was individually weighed.

In the statistical analysis of the tablet weight data, the mean tablet weight was determined for each sample. For those samples whose tablets were individually weighed, the standard deviation and coefficients of skewness and kurtosis* were also computed. The numerical results obtained are given in Tables I and II.

The coefficients of skewness and kurtosis are used in standard tests of normality. The coefficient of skewness is a measure of the lack of symmetry with respect to the centre of the distribution. A positive coefficient of skewness indicates an excess of high values over low values in the sample, while a negative skewness coefficient indicates the reverse of this. The coefficient of kurtosis is a measure of the amount of data clustered about the mean relative to the amount remote from the mean. A low value for the coefficient of kurtosis indicates a preponderance of data remote from the mean while a high value indicates that much of the data is close to the mean. For a sample from a population which is exactly normally distributed, the expected value of the coefficient of skewness is 0 and that of the coefficient of kurtosis approximately 0·8. Pearson and Geary (see Table 34 in [6]) have computed the values of these statistics which may be exceeded by chance in certain specified percentages of cases when the population distribution from which the samples are drawn is normal. In Tables I and II, an asterisk has been placed beside

* Denoting the weights of the individual tablets in a sample by $X_1, X_2, ---, Xn$, the coefficient of skewness was computed from the formula

$$\frac{\sqrt{n}\ [(X_1 - \bar{X})^3 + (X_2 - \bar{X})^3 + --- + (Xn - \bar{X})^3]}{[(X_1 - \bar{X})^2 + (X_2 - \bar{X})^2 + --- + (Xn - \bar{X})^2]^{3/2}}$$

and the coefficient of kurtosis from the formula

$$\frac{[X_1 - \bar{X}] + [X_2 - \bar{X}] + -- + [Xn - \bar{X}]}{\sqrt{n}\ [(X_1 - \bar{X})^2 + (X_2 - \bar{X})^2 + --- + (Xn - \bar{X})^2]^{1/2}}$$

where $\bar{X}$ represents the sample mean and $[X - \bar{X}]$ denotes the difference between X and $\bar{X}$ ignoring negative signs.

those values for the tablet samples which fell beyond the upper or lower 5 per cent. points. If all the samples were actually drawn from normally distributed populations, one value in twenty would be expected to exceed the upper 5 per cent. value and one in twenty would be expected to fall short of the lower 5 per cent. value.

Discussion

The first samples obtained and weighed were those denoted by the code letters F and I. These samples were taken from containers and thus the individual tablets in each sample were not necessarily punched out consecutively. Thus the tablets in each sample may have been subject to weight fluctuations caused by adjustments made to the machine by the operator, variations in the tablet material, etc., all of which could

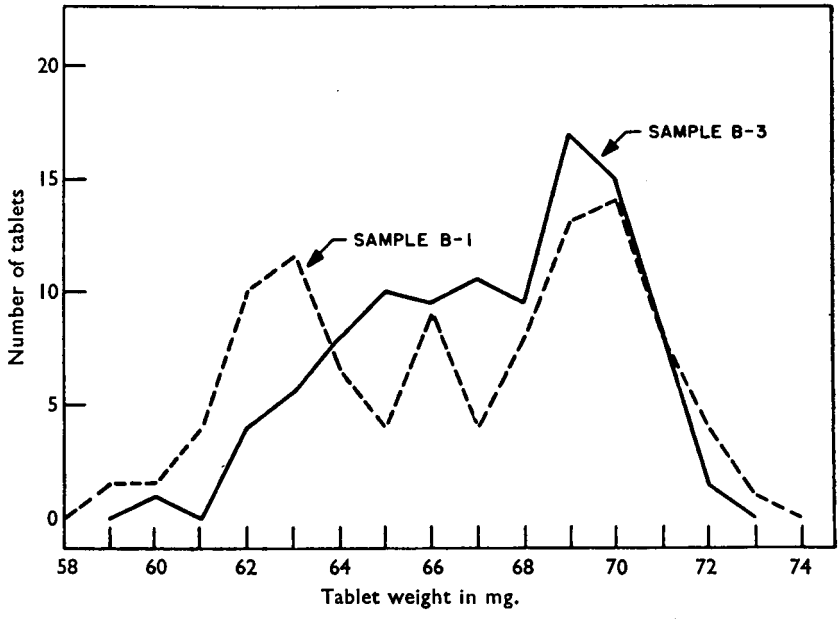

FIG. 3. Weight distributions for two of the double-punch samples.

cause evidence of non-normality to appear in the samples. Of the 21 samples of these two types, 5 showed evidence of skewness (compared with the expectation of 2·1) while only 2 showed kurtosis.

All subsequent samples were taken directly from the ejection spout of the machine. Samples taken from machines having more than one punch might show evidence of non-normality if the individual punches were delivering tablets of different average weight. Tablet type B is an interesting example for the machine used had two punches only. All five samples which were individually weighed had negative skewness, although only one fell below the 5 per cent. value, and all five had high coefficients of kurtosis, four of them being above the upper 5 per cent. limit. In Figure 3, the distributions of the individual tablet weights for

samples 1 and 3 are shown. These may be compared with the weight distribution for sample A4, which is more typical, shown in Figure 4. It seems reasonable to assume that the two punches on this machine were delivering tablets which differed in average weight.

Another illustration of the possible effect of differences between the punches in a multiple-punch machine is afforded by tablet type D. These tablets were made by a rotary-punch machine which, however, was not operated with its full complement of punches. One of the punches being used had a blank space on either side of it, making it possible to select tablets from that particular punch. Samples which were confined to that punch (Table I) had smaller standard deviations than the samples from all the punches. This is an indication that the different punches may not have been delivering tablets of the same average weight, or perhaps that some of the punches were more variable than others. However, in this instance there was no marked non-normality in the multiple-punch samples—only one out of four showed evidence of kurtosis and none indicated skewness, while all three samples from the single punch appeared to be non-normal, two of them for negative skewness and one for kurtosis.

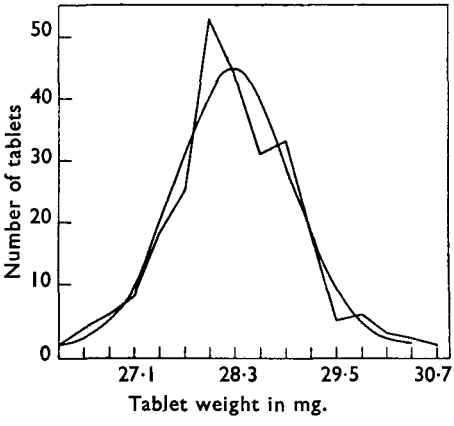

FIG. 4. Weight distribution for a typical sample (A 4) and fitted normal curve.

TABLE III

SAMPLES FROM SINGLE-PUNCH MACHINES SHOWING NON-NORMALITY

Type	Total no. of samples	No. with Skewness		No. with Kurtosis	
		Positive	Negative	Low	High
A	4	1	0	1	0
C	6	0	1	0	0
D (selected punch)	3	0	2	1	0
E	4	1	1	0	0
F	10	2	1	0	0
J	5	0	1	0	0
	32	4	6	2	0

In Table III are shown the numbers of samples from single-punch machines which showed evidence of non-normality by having skewness or kurtosis coefficients outside the 5 per cent. limits. The three samples of tablet D which were obtained from the selected punch are included here. Of the 32 samples, only two had coefficients of kurtosis outside the 5 per cent. limits. This is less than expectation since theoretically about 10 per cent. should have coefficients either below the lower 5 per cent. point

or above the upper 5 per cent. point if the population is normally distributed. However, 10 of the 32 samples showed skewness, 4 in a positive direction and 6 negatively.

In Table IV this information is provided for the rotary-punch machines. Of 42 such samples, only five showed excessive skewness and seven excessive kurtosis, compared with an expectation of 4·2 samples in each category.

TABLE IV

SAMPLES FROM ROTARY-PUNCH MACHINES SHOWING NON-NORMALITY

Type	Total no. of samples	No. with Skewness		No. with Kurtosis	
		Positive	Negative	Low	High
D	4	0	0	1	0
G	4	0	0	0	0
H	10	0	0	0	0
I	11	0	2	2	0
K	13	0	3	4	0
	42	0	5	7	0

Of the three single-punch type machines used on tablet C, the one indicated in Table I by the letter *b* produced tablets which were about twice as variable, in terms of the standard deviation, as those from machine *a*. This is a clear indication that at least part of the short-term variation in tablet weights is due to the machine itself, some machines being more variable than others.

It may be of some interest to note how the variation between samples in mean weight compares with the within sample variation. In Table V,

TABLE V

WITHIN AND BETWEEN SAMPLES MEAN SQUARES

Tablet	Within sample		Between sample		F
	Mean square	d.f.	Mean square	d.f.	
A	0·440	985	8·72	9	19·8
B	9·36	495	58·60	9	6·3
C	1·40	1492	304·3	5	218
D	12·72	993	819·2	12	64·4
E	21·42	846	196·6	9	9·2
F	21·00	489	94·77	9	4·5
G	17·71	808	221·8	9	12·5
H	47·50	490	200·6	9	4·2
I	59·94	539	1305·0	10	21·8
J	31·10	495	1009·5	9	32·5
K	80·95	637	804·5	12	9·9

NOTE:—
d.f. = degrees of freedom.
F = ratio of between sample mean square to within sample mean square. All F ratios in this table are statistically significant.

the "within sample" and "between sample" mean squares, or variances, are listed for each of the eleven types of tablet. In each case, the between sample mean square exceeds the within sample mean square significantly, indicating that the sample mean weights fluctuate more than can be accounted for by the within sample variations. It was observed that all the tablet manufacturers visited in the course of this study were aware

that the mean tablet weight varied during the course of the manufacturing process and, in fact, the machine operators were instructed to check the tablet weight periodically and to adjust the machine when there were signs of a change from the theoretical value. The results shown in Table V indicate that such periodic adjustments do not entirely eliminate the long-term variation in mean tablet weight.

The data in Table II may perhaps be more nearly representative of the type of variation which would be encountered in the examination of official samples, since these samples were obtained in their final packaged form. Of the 40 samples, 9 showed excessive skewness and 11 showed excessive kurtosis (compared with an expectation of 4 samples in each category). Of the 9 samples which showed skewness, 3 were in a negative direction and the remaining 6 positive. Of the 11 samples which showed abnormal kurtosis, 7 had coefficients below the normal value and the remaining 4 were high. Thus, although the numbers of samples having significant skewness and kurtosis were greater than expected on the assumption that they were drawn from normal populations, there did not appear to be a tendency for either coefficient to depart from its expected value in only one direction.

Conclusions

It is apparent from the results of the weight variation studies reported in Part II of this paper that a higher proportion of the samples deviated from normality than can be accounted for by chance alone. While it was not the purpose of this study to investigate the causes of the variations in individual tablet weights and the lack of normality in the samples, a few obvious conclusions may be drawn from an examination of the data. The results on tablet C indicate that some machines are capable of turning out more uniform tablets than others even when the same material is fed to each one. It was evident also from the data on tablets B and D, machines with more than one punch may have tablets of different average weight coming from the various punches. Finally, as was brought out in Table V, samples taken at different times from the same machine will vary in mean weight more than can be accounted for by the amount of variation within each sample.

Although the majority of the samples showed no evidence of non-normality, it was found that a higher proportion did deviate significantly from normality than could be expected on the basis of chance. However, there was no tendency for the departures from normality to be consistently in one direction rather than in the other since there were, among the non-normal samples, examples of both positive and negative skewness as well as of both high and low kurtosis. Hence there does not appear to be any reason for substituting another distribution in the place of the normal distribution for the purpose of comparing the efficiencies of the various weight variation tests studied in Part I of the paper.

In Part I of the paper, the operating characteristics of four official weight variation tests based on 10, 20, 50 and 100 tablets respectively were obtained. It was shown that increasing the size of the sample had the

effect of considerably decreasing the probability of a non-uniform batch of tablets passing the test and slightly increasing the probability of a highly uniform batch passing. Thus greater protection is afforded to both the consumer and the manufacturer by the examination of the larger numbers of tablets. Two unofficial weight variation tests were also studied, one based on the standard deviation of the observed tablet weights and the other a two-sample criterion. It was shown that the standard deviation test attained a greater efficiency without increasing the sample size and that the two-sample test gained efficiency by concentrating the efforts of the examiner on the less uniform batches.

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