DETERMINATION OF THE REASONABLE OR PERMISSIBLE MARGIN OF ERROR IN DISPENSING.*

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INTRODUCTION.

The compounding and dispensing of medicines ordered by physicians is the primary function of the pharmacist in his relationship to the public. The education and training which the pharmacist is required to have before he is granted a license to practice and the legal restrictions otherwise thrown about the practice of pharmacy are indicative of the importance which the public attaches to the proper exercise of this function. It is believed that the great majority of pharmacists of this country recognize fully the responsibility which is theirs in this regard and take every precaution that can reasonably be expected of them to compound prescriptions accurately. In spite of the precautions taken, however, errors in compounding and dispensing are made. Occasionally, they are of such magnitude that untoward symptoms of unmistakable origin develop after the medicine is administered, when the error is detected and brought to notice. More frequently, however, the error made is comparatively small or the reaction of the patient is attributed to the malady instead of the remedy and it passes by unnoticed.

To err when reasonable precautions are taken to avoid doing so cannot be attributed to ignorance, carelessness or negligence. It must be attributed to other factors—factors over which even the most careful compounder has little or no control. The personal equation, for instance, enters into every operation involved in the filling of a prescription. In addition, there are the variations in the calibration of measuring utensils and the inaccurate adjustment of scales or balances to be reckoned with. As a matter of fact, it is impossible to fill any prescription without deviating to some extent from the quantities ordered by the prescriber. No measurement or weighing is ever free from error due to one or more of the factors mentioned above; but with the exercise of care, such error can be reduced to a reasonable minimum. To determine the magnitude of this reasonable minimum is the purpose of the studies reported in this series of papers.

Some work has already been done along this line. It is possible that fairly extensive investigations have been made in some of the countries of Continental Europe in which dispensing is carried on under close governmental supervision; but in Great Britain and in this country, where this rigid control is lacking, studies sufficiently extensive and comprehensive to justify the use of the data obtained as a basis for fixing the limit of reasonable or permissible error in the compounding of all but a few of the many types of prescriptions filled in the pharmacies of to-day do not appear to have been made. A résumé of the work of this character done in the two countries last named over the past sixty years follows.

As far back as 1872, C. William Grassley[2] examined 165 samples of Seidlitz powders purchased in this country and in Canada for accuracy with respect to ingredient content.

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[2] PROC. A. PH. A., 20 (1872), 273–300.

Only 2 of the 165 were found to have been accurately prepared. The error in the 163 other samples was attributed largely to the fact that the powders were made by measuring instead of weighing. Depending on the pressure exerted in filling, the capacity of the larger cavity (used for measuring the Seidlitz mixture) of the double-cup measure in general use was found to be 95 to 120 grains and that of the smaller cavity (used for measuring the tartaric acid) 20 to 24 grains.

In an editorial which appeared in the *Pharmaceutical Journal and Pharmacist* for April 12, 1924,[1] mention is made of some dispensing tests carried out in London in 1886. Those who made these tests are reported to have stated that only 6% of the prescriptions compounded by "chemists and druggists" were found to be inaccurate, and to have expressed the view that 10% was an allowable margin of error in individual cases. Unfortunately these are all of the details carried in the editorial and the original report printed in *Chamber's Journal* is not available.

In 1889, E. B. Stuart and E. B. Tainter[2] published a report on the degree of accuracy attained by 37 pharmacists in dispensing the following prescriptions for powders: Prescription No. 1, ferric oxide, 0.1 Gm., sugar 10 Gm., to be divided into 10 powders. Prescription No. 2, Dover's powder, 3.0 Gm., to be divided into 6 powders. Prescription No. 3, powdered rhubarb, magnesia, of each 2.5 Gm., to be divided into 15 powders.

The average error was found to be 4.8% for prescription No. 1, 9.4% for prescription No. 2 and 9.45% for prescription No. 3. For prescription No. 1, the error was less than 5% in 21 instances, between 5% and 10% in 14 instances, between 10% and 15% in one instance and more than 20% in 1 instance. For prescription No. 2, the error was less than 5% in 22 instances, between 5% and 10% in 9 instances, between 10% and 15% in 5 instances and 16.5% in 1 instance. For prescription No. 3, the error was less than 5% in 17 instances, between 5% and 10% in 5 instances, between 10% and 15% in 8 instances and more than 20% in 6 instances.

The *Pharmaceutical Journal and Pharmacist* for December 9, 1922[3] calls attention to some of the results of an investigation made by the Public Health Committee of the Middlesex County Council to ascertain the accuracy with which medicinal powders were dispensed. In one case, the 6 powders supplied weighed from $2^3/_4$ to 5 grains each, averaging 4 grains. In two other instances, the 6 powders supplied varied in weight from 5 to 7 grains each. In two cases, no powder weighed more than $5^1/_2$ grains. A subsequent examination of the scales and weights of the pharmacists concerned is reported to have revealed that the inaccuracies were not wholly due to maladjustment of the weighing appliances.

Within the past year and a half, two papers dealing with the subject have appeared in print, one by John Butler[4] reporting the results of an investigation made in England and the other by Dr. John C. Krantz, Jr.,[5] reporting the results of the examination of certain preparations purchased from pharmacists in Baltimore, Maryland.

In the report made by Mr. Butler, data are given to show the error made by 40 "dispensing chemists" in the compounding of certain liquid potassium bromide mixtures. These data show that in 4 of the 40 potassium bromide mixtures examined, the error with respect to potassium bromide content was greater than 10%; in 34, the error was below 5% and in 27 the error was below 3.5%. Mr. Butler states further that most "chemists" are of the opinion that an error of 10% should be allowed, and that this is accepted by most Pharmaceutical Service Sub-Committees as a fair margin in the dispensing of certain types of mixtures.

Dr. Krantz reported the probable error with respect to potassium iodide content to be 9.55% for 10 samples of Saturated Solution of Potassium Iodide, N. F. V, examined.

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[1] *Pharm. J. & Pharm.*, 112 (1924), 397.

[2] PROC. A. PH. A., 37 (1889), 183–188.

[3] *Pharm. J. & Pharm.*, 109 (1922), 545.

[4] *Ibid.*, 128 (1932), 149.

[5] *Maryland Pharmacist*, 7 (1932), 543–545.

For 17 samples of Tincture of Ferric Chloride, U. S. P. X, examined, the probable error with respect to iron content was computed to be 6.45%. In two batches of twelve 5-grain quinine capsules prepared by pharmacists, the probable error with respect to quinine content was computed to be 25.11% and 5.08%, respectively.

The data presented in the foregoing reports, although inadequate and in some instances unsuited for the purposes of this study, are nevertheless of some value. They at least lend weight to the statement already made, that deviation from the quantities ordered is the general rule in dispensing rather than the exception, and show that there is need for further systematic investigation along these lines to enable us to fix the margin of error which may be accepted as reasonable or permissible. The British appear to have accepted 10% as the "allowable" margin of error for certain types of prescriptions, at least. Whether or not this margin is the proper one for all types of prescriptions still remains to be proven.

EXPERIMENTAL PART.

The different types of prescriptions which the pharmacist is ordinarily called upon to fill may be divided, roughly, into two classes, namely, liquids and solids. With respect to the magnitude and frequency of the error to be expected, the latter class seemed to offer the greatest possibilities because of the more complicated nature of the operations involved in filling prescriptions of that type. For these reasons and because powders and capsules are actually prepared by the pharmacist more frequently than any of the other types of this class, they were selected as the types to be used in beginning this study.

POWDERS.

With respect to the preparation of powders, and this applies to the preparation of capsules as well, the division of the bulk powder into individual doses constitutes the greatest source of error. Furthermore, the error from this source is not constant since the magnitude is dependent to a considerable extent upon the *modus operandi* by which the division is made. Of the many methods which have been suggested for effecting this division, the majority have as their chief aim speed in completing the task rather than accuracy. The following are the methods which are in general use. They were, therefore, used in making the studies reported herein.

(1) The guess by eye method in which small portions of the powder are transferred to papers by means of a spatula; and when all has been thus transferred, the quantities on the different papers equalized as nearly as possible by eye.

(2) The method of blocking and dividing, which consists of transferring the bulk powder to a tile or a piece of glazed paper, building it up into a rectangular pile or a parallelogram, by means of two straight-edged spatulas, and dividing the pile thus formed into the desired number of parts by cutting with a spatula.

(3) The method of weighing, in which the amount to be contained in each powder is weighed off separately. When this method is followed, the last powder will be underweight if the scales have been properly adjusted and the weighings accurately made, because some of the material will adhere to the sides of the mortar in which the powder was mixed or be lost in some other way. This expected deficiency is generally avoided by preparing a sufficient amount of the bulk powder to make one or two extra powders.

In addition to the determination of the frequency and magnitude of error traceable to the *modus operandi* of dividing the bulk powder, the effort was also made to determine to what extent, if any, certain other factors influence the final result. It seemed desirable, for instance, to determine the effect of the nature of the ingredients, the number of ingredients, the size of the individual powders and the number of powders prepared. With these objectives in view, the following prescriptions were filled.

No. 1.

Hydrarg. Chlor. Mit.	gr. ii
Lactos.	gr. iii
M. et ft. chart. No. 1	
D. t. d. No. viii	
Sig: One powd. every 15 min.	

No. 2.

Hydrarg. Chlor. Mit.	gr. $^1/_6$
Pulv. Ipecac.	gr. $^1/_{16}$
Lactos.	gr. i
M. et ft. pulv. No. 1	
D. t. d. No. XV	
Sig: One every 2 hrs.	

No. 3.

Sod. Bicarb.	℥i
Mass. Hydrarg.	℈i
M. et ft. chart. No. viii	
Sig: One powd. every 4 hrs. followed by a Seidlitz powder.	

No. 4.

Bism. Subnit.	℥i
Phenyl. Salicyl.	℥ss
Carbo. Lig.	℈ii
M. et div. in chart. No. xii	
Sig: One t. i. d.	

No. 5.

Mag. Oxid.	℥i
Cret. Præp.	℥ii
Pil. Ext. Bellad. Fol.	gr. ii
Ol. Menth. Pip.	gtt. iii
M. et div. in pulv. No. xv	
Sig: One powd. $^1/_2$ hr. p. c.	

No. 6.

Quin. Sulph.	gr. xv
Pulv. Aloe	gr. x
Ext. Ergot.	gr. ii
M. et ft. pulv. No. xii	
Sig: One every 3 hours.	

No. 7.

Ext. Casc. Sagr.	gr. i
Ol. Fœnic.	gtt. i
Lactos. *q. s.*	(gr. iv)
M. et ft. chart. No. xii	
Sig: One powd. every 4 hrs.	

No. 8.

Hydrarg. Chlor. Mit.	gr. ii
Sod. Bicarb.	gr. x
M. et ft. chart. No. vi	
Sig: One powd. every 2 hrs.	

No. 9.

Mag. Oxid. Pond.	gr. lxxx
Ft. pulv. No. viii	
Sig: One powd. in aq. $^1/_2$ hr. p. c.	

No. 10.

Pulv. Ext. Bellad.	gr. i
Acetphen.	gr. lx
M. et ft. pulv. No. xii	
Sig: One powd. every 4 hrs.	

No. 11.

Hydrarg. Chlor. Mit.	gr. i
Bis. Subnit.	gr. xxx
M. et ft. pulv. No. x	
Sig: One every hr.	

In the actual performance of the tests, the foregoing prescriptions were filled by the members of the senior class in dispensing pharmacy at the School of Pharmacy of the University of Maryland under working conditions very similar to those prevailing in the better type of pharmacies. It is true that these students were inexperienced in comparison with the average practitioner; but it is believed that this lack of experience was offset to a large extent, if not completely, by uniformity in measuring and weighing appliances and the close supervision maintained over each operation by the instructors in charge of the work.

For laboratory practice the class in dispensing is divided into sections of approximately 30 students each, and the work of each section is supervised by 4 instructors. Each prescription was filled by the members of at least one section and in some instances by the members of two sections. The completed powders were checked for accuracy with respect to total quantity by weighing on a fairly sensitive balance. No attempt was made in this series of tests to check the amounts of individual ingredients, except in the case of prescription No. 1.

The results obtained in these tests are given in the tables which follow. In each case, the standard deviation was computed, and such conclusions as have been drawn are based on the use of this quantity of measurement. Other workers, who have reported tests of this character have stated the results in terms of percentage of deviation from the theoretical amount or from the mean. It seemed, however, more to the point to show the closeness with which the individual results are clustered about the mean; and as the quantity used for this purpose in works on general

statistics is the standard deviation (S. D.), it was used in reporting the results of this study. In the derivation of this quantity, the generally accepted formula, S. D. = $\sqrt{\frac{\Sigma d^2}{n}}$ was used, in which Σd^2 represents the sum of the deviations squared, and n the number of observations made.

PRESCRIPTION NO. 1.

Prescription No. 1 was filled by the "guess by eye method" by one section of the class consisting of 30 students as a part of the regular laboratory work. The fact that the results were to be checked for purposes other than routine grading was not made known. These prescriptions were checked for the weight of individual powders. In addition, 10 batches were selected at random from the 30 batches of 8 powders each, and the calomel content of each powder was determined by the assay method given in the U. S. P. X for calomel. The results obtained are given in the Tables I and II.

TABLE I.—PRESCRIPTION NO. 1 (CORRECT WEIGHT OF EACH POWDER = 5 GRAINS).

Batch No.	Weight of Each Powder in Grains. 1.	2.	3.	4.	5.	6.	7.	8.	Total Wt. in Grains.	Av. Wt. in Grains.	S. D.[1]
1	4.500	5.000	5.000	4.500	5.500	5.250	5.500	4.375	39.625	4.953	0.423
2	5.000	5.125	5.125	5.125	5.125	5.250	5.375	4.875	41.000	5.125	0.139
3	4.750	4.625	5.000	5.250	5.250	4.875	5.375	4.500	39.500	4.937	0.286
4	4.875	5.250	4.625	4.875	5.000	5.125	5.625	4.625	40.000	5.000	0.312
5	4.625	5.875	4.875	5.000	5.125	5.625	6.000	4.375	41.500	5.187	0.552
6	5.500	5.250	5.250	5.125	5.250	5.250	5.750	5.000	42.375	5.296	0.215
7	4.625	5.000	5.000	5.000	5.000	5.000	5.125	4.500	39.250	4.906	0.204
8	4.750	4.625	4.875	5.625	4.625	4.625	5.750	4.500	39.375	4.921	0.454
9	4.875	4.375	5.250	4.875	5.375	4.750	5.625	4.375	39.500	4.937	0.423
10	5.000	4.500	4.750	5.000	5.250	5.500	5.500	4.500	40.000	5.000	0.167
11	5.125	4.750	5.000	5.500	5.250	6.000	5.250	4.750	41.625	5.203	0.313
12	4.500	5.250	4.875	5.000	4.250	5.000	6.000	3.875	38.750	4.843	0.608
13	4.875	5.625	6.375	5.250	4.875	5.125	5.625	4.625	41.375	5.171	0.341
14	4.500	4.875	5.125	4.750	5.000	4.500	5.125	4.500	38.275	4.797	0.256
15	4.750	5.250	4.875	4.625	5.250	5.000	6.000	4.125	39.875	4.984	0.513
16	5.500	5.000	5.500	5.000	5.125	5.000	4.500	4.250	39.875	4.984	0.407
17	5.375	5.750	4.750	4.875	4.875	5.000	4.500	4.625	39.750	4.968	0.384
18	5.625	5.000	4.500	5.125	4.625	4.875	5.250	4.875	39.875	4.984	0.333
19	4.875	5.625	5.250	5.125	4.625	4.625	5.625	5.250	41.000	5.125	0.369
20	5.125	5.000	5.000	4.625	5.250	4.750	5.750	4.125	39.625	4.953	0.446
21	4.875	4.875	4.750	4.875	5.000	5.250	5.375	4.750	39.750	4.968	0.214
22	4.875	4.875	4.500	4.875	5.000	5.125	5.375	4.875	39.500	4.937	0.234
23	5.500	4.250	5.250	5.750	4.875	4.750	5.625	4.875	40.875	5.109	0.477
24	5.750	5.625	5.500	5.125	4.500	5.000	4.750	4.750	41.000	5.125	0.428
25	5.125	5.250	4.500	5.500	5.500	5.000	4.500	4.750	40.125	5.015	0.377
26	4.250	4.375	4.625	5.000	5.250	5.375	4.750	5.125	38.750	4.843	0.384
27	5.000	5.125	4.875	4.500	4.750	4.625	5.250	4.875	39.000	4.875	0.233
28	5.000	5.000	5.125	4.750	5.250	4.875	5.125	4.875	40.000	5.000	0.153
29	5.000	5.125	4.500	4.500	4.625	4.750	5.625	4.875	39.000	4.875	0.353
30	4.875	5.125	4.625	4.875	5.500	4.750	5.125	4.250	39.125	4.890	0.350

[1] Av. S. D. = 0.345, which is equivalent to an average deviation from the theoretical of 6.90%.

It will be observed that in the case of the weight of individual powders, the average standard deviation is 0.345 gr., or 6.91% of the prescribed amount. Fourteen of the 30 batches filled fall within the average S. D. of 0.345 gr., while the remaining 16 fall within twice the average S. D., or 0.691 gr.

TABLE II.—PRESCRIPTION NO. 1 (CORRECT PERCENTAGE OF CALOMEL = 40).

Batch No.	Per Cent of Calomel in Each Powder. 1.	2.	3.	4.	5.	6.	7.	8.	Average Per Cent.	S. D.[1]
1	40.96	35.14	36.36	41.99	41.64	38.05	40.87	39.29	39.29	2.37
2	40.55	46.89	37.06	37.28	39.89	41.56	41.09	40.45	40.59	2.84
3	40.25	40.15	40.05	39.75	39.50	40.30	39.82	40.25	40.01	0.27
4	39.85	39.90	40.12	39.89	40.27	40.15	40.27	39.80	40.03	0.19
5	37.46	37.38	39.60	39.05	37.60	37.83	34.80	40.66	38.05	1.65
6	37.66	42.04	41.32	41.59	39.42	39.67	40.27	39.99	40.24	1.32
7	42.09	40.34	39.79	41.66	40.16	40.16	41.18	41.39	40.85	0.78
8	36.93	36.27	36.24	37.90	36.73	35.67	35.60	34.21	36.19	1.02
9	40.20	40.50	39.32	38.83	39.34	38.43	41.64	32.74	38.87	2.50
10	33.91	39.53	43.07	40.82	39.07	40.15	38.53	38.13	39.15	2.45

[1] Av. S. D. = 1.54, which is equivalent to an average deviation from the theoretical of 3.84%.

In the case of the calomel content, the average standard deviation amounts to 1.54, or 3.84%, based on a calculated content of 40 per cent. Five of the batches assayed for calomel content fall within the average S. D., while the remaining 5 fall within twice the average S. D., or within 7.68% of the correct amount.

On further examination of Table II, it will be observed that the standard deviation for the calomel content in the individual batches of powders is as low as 0.19 and as high as 2.84.

The error in the case of calomel content was probably due in greater part to insufficient trituration in the mixing of the ingredients, or failure to scrape all of the material from the pestle and sides of the mortar. Factors, other than these, affecting the results are errors in weighing, loss during transfer and triturating the calomel in a porous mortar before adding the lactose.

PRESCRIPTIONS NOS. 2–11.

Prescriptions Nos. 2 to 11 were studied with a view to determining to what extent all of the factors heretofore mentioned contribute to the total error. The prescriptions filled in this series of tests were selected with the primary objective in view of determining to what extent, if any, the following contribute to the total error: number of ingredients, nature of the ingredients, number of powders to be made and the amount of material in each powder. To secure data to show to what extent the method used in dividing the bulk powder is responsible for the total error; in some of these prescriptions the bulk powder was divided by the "guess by eye method," in others by the blocking and dividing method and in still others by weighing off quantity for each powder.

The finished prescriptions were checked for accuracy of weight of the individual powders only, and the standard deviation was computed from the results obtained. Before these prescriptions were given out for filling, the students were instructed with respect to the method to be used in dividing the powders, and they were told that their work would be checked for accuracy.

TABLE III.—STANDARD DEVIATION OF PRESCRIPTIONS NOS. 2–7.

Batch No.	Prescriptions. No. 2.	No. 3.	No. 4.	No. 5.	No. 6.	No. 7.
1	0.172	0.797	0.305	1.336	0.172	0.371
2	0.241	1.115	0.903	1.425	0.518	0.056
3	0.237	0.605	0.111	0.584	0.260	0.261
4	0.177	0.533	0.226	0.648	0.442	0.310
5	0.158	1.048	0.673	1.342	0.503	0.138
6	0.119	0.162	0.740	0.284	0.500	0.046
7	0.290	0.292	0.711	0.223	0.310	0.116
8	0.219	0.152	0.951	0.218	0.601	0.086
9	0.154	0.140	0.121	0.287	0.228	0.069
10	0.228	0.846	0.579	1.251	0.189	0.063
11	0.128	0.270	0.985	0.861	0.241	0.072
12	0.360	0.697	0.508	1.113	0.165	0.048

13	0.205	0.729	0.217	0.945	0.692	0.067
14	0.169	0.336	0.473	0.351	0.300	0.132
15	0.114	0.863	0.818	1.007	0.241	0.241
16	0.233	0.211	0.072	0.911	0.697	0.180
17	0.140	0.135	0.069	0.226	0.052	0.310
18	0.268	0.460	0.436	0.585	0.036	0.179
19	0.222	0.582	1.180	0.548	0.136	0.275
20	0.115	0.345	1.131	0.530	0.580	0.103
21	0.169	1.025	0.521	0.118	0.276	0.279
22	0.191	0.162	1.043	1.138	0.104	0.276
23	0.069	0.200	0.551	1.190	0.026	0.081
24	0.133	0.787	0.450	0.187	0.513	0.241
25	0.238	0.653	0.830	1.120	0.117	0.210
26	0.128	0.496	0.147	1.027	0.071	0.181
27	0.121	0.330	0.895	0.234	0.117	0.184
28	0.113	1.096	0.582	0.154	0.083	0.352
29	0.191	0.515	0.531	0.374	0.345	0.363
30	0.248	0.168	0.464	0.652	0.314	0.276
Av. S. D. =	0.185	0.525	0.574	0.696	0.294	0.186
Av. % =	18.10	5.25	5.30	5.72	13.06	3.72

TABLE IV.—STANDARD DEVIATION OF PRESCRIPTIONS NOS. 8–11.

Batch No.	Prescriptions. No. 8.	No. 9.	No. 10.	No. 11.	Batch No.	Prescriptions. No. 8.	No. 9.	No. 10.	No. 11.
1	0.246	0.041	0.571	0.267	31	0.392	0.391	0.448	0.120
2	0.473	0.454	0.258	0.224	32	0.213	0.496	0.902	0.365
3	0.261	0.165	0.560	0.229	33	0.212	0.206	0.965	0.107
4	0.238	0.066	0.295	0.256	34	0.116	0.458	0.985	0.150
5	0.239	0.082	0.949	0.327	35	0.257	0.019	0.253	0.373
6	0.327	1.200	0.643	0.097	36	0.062	1.035	0.072	0.129
7	0.294	0.647	0.772	0.335	37	0.171	0.108	0.177	0.150
8	0.471	0.630	0.672	0.074	38	0.133	0.454	0.660	0.075
9	0.042	1.074	0.604	0.245	39	0.232	0.366	0.219	0.150
10	0.363	0.901	0.815	0.333	40	0.276	0.302	0.794	0.075
11	0.132	0.049	0.362	0.322	41	0.089	0.605	0.100	0.150
12	0.432	0.763	0.240	0.069	42	0.387	1.058	0.578	0.172
13	0.221	1.158	0.421	0.377	43	0.314	0.286	0.502	0.064
14	0.133	0.037	0.111	0.365	44	0.205	0.940	0.657	0.150
15	0.208	1.172	0.645	0.225	45	0.198	0.898	0.412	0.149
16	0.232	0.520	0.332	0.154	46	0.057	0.557	0.252	0.074
17	0.152	0.209	0.941	0.150	47	0.243	0.319	0.389	0.075
18	0.392	0.176	0.797	0.261	48	0.199	0.608	0.903	0.110
19	0.162	0.435	0.587	0.160	49	0.365	0.735	0.860	0.112
20	0.151	0.206	0.061	0.075	50	0.267	0.829	0.931	0.078
21	0.450	0.521	0.885	0.098	51	0.085	0.658	0.371	0.168
22	0.335	0.529	0.821	0.075	52	0.126	0.744	0.689	0.098
23	0.306	0.056	0.454	0.152	53	0.191	1.081	0.911	0.178
24	0.352	0.309	0.485	0.100	54	0.086	0.504	0.166	0.331
25	0.204	0.829	0.356	0.182	55	0.156	0.528	0.326	0.180
26	0.161	0.250	0.829	0.077	56	0.046	0.629	0.430	0.337
27	0.186	0.829	0.560	0.331	57	0.112	0.187	0.560	0.224
28	0.221	1.175	0.036	0.140	58	0.046	0.155	0.615	0.375
29	0.227	1.178	0.281	0.093	59	0.260	0.082	0.212	0.267
30	0.450	0.156	0.243	0.044	60	0.151	0.330	0.644	0.367
					Av. S. D. =	0.228	0.523	0.526	0.185
					Av. % =	11.40	5.23	5.26	5.97

As already stated, the greatest source of error is the division of the bulk powder into individual doses. It may be said further with respect to the methods of filling that the error will be least in those cases in which the powders are divided by weighing. This is shown to be true by the results obtained for prescription No. 7, in which the average standard deviation is only 0.186, 17 of a total of 30 batches falling within the average S. D., while the remaining 13 fall within twice the average S. D.; and in prescription No. 11, in which the average standard deviation is 0.185, 38 of the total of 60 batches falling within the average S. D., 20 within twice the average S. D. and the remaining 2 within three times the average S. D.

When the blocking and dividing method is used, a slight increase in the average standard deviation results. This is revealed by the results obtained for prescription No. 8, in which the average standard deviation is 0.228, 35 of a total of 60 batches falling within the average S. D., 23 within twice the average S. D., and the remaining 2 within three times the average S. D.; and in prescription No. 6, the average standard deviation of which is 0.294, 17 of a total of 30 batches falling within the average S. D., 10 within twice the average S. D. and 3 within three times the average S. D.

The "guess by eye method" is the least accurate of the methods studied. The results obtained by this method of division are shown in the case of prescription No. 1, in which the average S. D. is 0.345, only 14 of a total of 30 batches falling within the average S. D., and the remaining 16 falling within twice the average S. D.; or in prescription No. 9, in which the average S. D. is 0.523, 33 of a total of 60 batches falling within the average S. D., 19 within twice the average S. D. and 8 within three times the average S. D.

On examination of the results given for prescriptions Nos. 9, 3, 4 and 5, it will be observed that the number of ingredients contained in the powder mixture has a slight effect upon the standard deviation. By increasing the number of ingredients, the number of operations of weighing and transferring are increased, which in turn results in an increase in the standard deviation. When there is only one ingredient, as in prescription No. 9 the average S. D. is 0.523; with two ingredients, as in prescription No. 3 the average S. D. is 0.525; with three ingredients, as in prescription No. 4, the average S. D. is 0.574, and with four ingredients, as in prescription No. 5, the average S. D. is 0.696.

The nature of the ingredients also plays a part in increasing or decreasing the standard deviation in divided powder prescriptions as shown in prescriptions Nos. 1, 5, 10, 6 and 7. The standard deviation for the simple admixture of powders is lower than when the prescription contains a pillular extract or volatile oil in addition to the dry powder. This is to be expected as it is more difficult to weigh a sticky mass, such as a pillular extract, and completely transfer and incorporate it with other material than if it were a dry powder.

The number of powders dispensed also influences the final result. This is shown in the case of prescriptions Nos. 8, 1, 10 and 5, which call for 6, 8, 12 and 15 powders, respectively. The average standard deviation in these instances is 0.228, 0.345, 0.526 and 0.696, which shows that the magnitude of the error increases directly with the number of powders made.

The amount contained in each powder has a decided effect on the standard deviation, as well as on the percentage deviation from the theoretical amount, which is shown in the following table.

TABLE V.—EFFECT OF SIZE OF INDIVIDUAL POWDER ON STANDARD DEVIATION.

Prescription Number.	Theoretical Weight of Each Powder in Grains.	Average Standard Deviation.	Percentage Deviation from the Theoretical.
2	1	0.185	18.10
8	2	0.228	11.40
1	5	0.345	6.90
3	10	0.525	5.25
5	12	0.696	5.72

The foregoing data show that the standard deviation increases directly with the weight of the individual powders whereas the percentage deviation from the theoretical amount shows a corresponding decrease. This is to be expected, as a deviation of $^1/_4$ grain in a powder weighing 1 grain results in a 25 per cent error, while a deviation of a $^1/_4$ grain in a powder weighing 10 grains

results in an error of only $2^1/_2$ per cent. The results show further that there is a marked decrease in the error with an increase in weight up to 5 grains, where it remains fairly constant. Incidentally, the practical significance of this is that powders divided by the methods other than weighing should be made to weigh a minimum of 5 grains.

The results of the foregoing tests are summarized in Table VI, which follows. This table shows, in addition to the actual number of batches of powders falling within the standard deviation and multiples thereof, the percentage of the totals which these constitute. It also shows the grand totals falling within these limits.

(*To be continued*)

ASH LIMIT OF DRUGS.

L. W. Winkler (*Pharm. Zentralh.*, 73 (1932), 593, 612, 705). The drug was first freed from adhering earthy matter, then powdered and passed through a sieve of 5-mm. mesh. It was then transferred to a large mortar and stirred for some minutes without pressure from the pestle, in order to assist in removal of impurities. This was continued until no foreign particles were distinguishable under a lens. The powder was then dried for one or two days over quicklime.

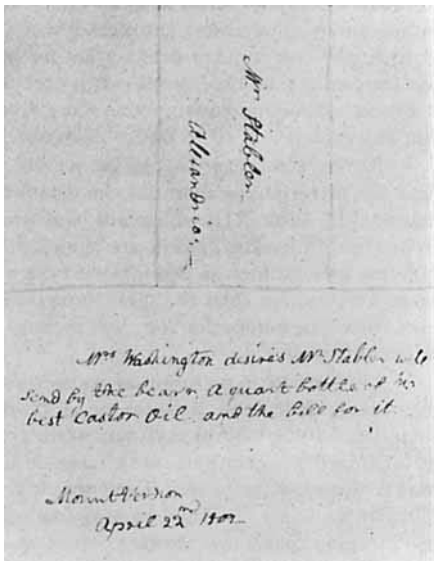
About 1 Gm. of pure sand was placed in a quartz crucible of 5 cc. capacity and 10 drops of fuming nitric acid were added. After evaporation of the acid, the crucible was heated for five minutes, then cooled on a thick metal plate and weighed when cold. About 0.5 Gm. of the powdered prepared drug was added and the drug and sand thoroughly mixed by means of an iron nail. The crucible and contents were weighed, gently heated until the drug was carbonized, and then heated more strongly for five minutes. After cooling, the contents were again carefully mixed with the iron nail in order to break up any large particles of carbonaceous matter, and the crucible again strongly heated. After cooling, the contents were again mixed and then 10 drops of fuming nitric acid were added. The acid was evaporated and the crucible heated to redness, cooled and weighed.

In order to ensure complete decomposition of organic matter a further treatment with nitric acid is advocated. The use of powdered oxalic acid as described in the German Pharmacopœia is not recommended since oxalic acid on combustion always gives rise to some carbon.

Figures for about 100 drugs are given, in most cases for both the whole and the powdered drug, obtained from two or three different sources.

The ash limits of the German Pharmacopœia seem to be too high, it is suggested that both an upper and a lower limit should be set in future editions, and a table of proposed limits is given. In order to evaluate an unground drug, the ash of both the crude drug and the sieved powder should be determined, the difference indicating the amount of earthy matter. The ash of powdered drugs of good quality is not in general greater than that of the cleaned whole drug.

The author suggests that drug houses should always insert the ash limit after the name of the drug, in order to distinguish their goods from inferior grades.—Through *Quarterly Journal of Pharmacy.*



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