Analytical-chemical study of pentamethylenetetrazol
Pharm. Weekbl., 71 (1934), 1170

INORGANIC CHEMICALS.

Dominkiewicz, M.
The commercial synthesis of guaiacol and the possibility of its realization
Arch. Chem. i Farm., Polish, 1 (1934), 1

Dominkiewicz, M.
Studies on the structure of kaolin. II. Stability of the nuclei in kaolin and its derivatives
Arch. Chem. i Farm., Polish, 1 (1934), 115

Dominkiewicz, M.
Studies on the structure of kaolin. III. The Anhydrokaolinates of sodium.
Arch. Chem. i Farm., Polish, 1 (1934), 142

ORGANIC CHEMICALS.

Caldwell, B. P., and Piontkowski, F. A.
The addition of iodine and thiocyanogen to unsaturated compounds
J. Am. Chem. Soc., 56 (1934), 2086

Dominkiewicz, M., and Kijewska, M.
Synthesis of isatin from the economic standpoint
Arch. Chem. i Farm., Polish, 1 (1934), 228

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

BY MARVIN J. ANDREWS.[1]

INTRODUCTION.

This, the fourth paper of this series,[2] deals with pills.

Pills which the pharmacist compounds in the filling of prescriptions are usually made by intimately mixing the ingredients called for in the dry state in a mortar, adding the required amount of liquid excipient and kneading to develope a plastic mass. The mass, when of the proper plasticity, is removed from the mortar and rolled into a pill pipe. The latter is cut into the desired number of parts which are then rolled into pill form by hand. The selection of the excipient and the amount to be used is in most cases left to the judgment of the pharmacist.

The possibilities for error, where operations of the foregoing nature are involved in the filling of prescriptions, are numerous, and to determine to what extent each is a contributing factor would be almost an endless task. Since, however, some investigations to determine the variations in the weight of pills made by pharmacists have been reported, further studies along this line seemed to be warranted, if for no other reason than to demonstrate the difficulties encountered in attempting to determine what constitutes a reasonable margin or error in preparations of this type.

The factors largely responsible for variations in the weight of pills made by the pharmacist are undoubtedly (1) the nature of the excipient used, (2) personal equation and (3) the loss in weight on standing. To determine to what extent each of these factors contribute to the total error, the studies reported in this paper were undertaken.

---

* Joint Session, Scientific Section and Section on Practical Pharmacy and Dispensing, Washington meeting, 1934.

[1] In collaboration with A. G. DuMez, Professor of Pharmacy, School of Pharmacy, University of Maryland.

[2] JOUR. A. PH. A., 22 (1933), 755, 838; 23 (1934), 350, 421.

EXPERIMENTAL PART.

A variety of liquid excipients are used in the compounding of pill masses. Soap and water, honey or glucose are probably as extensively used as any of them. They were, therefore, selected for use in these studies.

Three series of experiments were carried out. In the first series, tests were made to determine the variation in weight of individual pills in the same batch. In the second series, tests were made to determine the effect of the use of different excipients upon weight. The principal objective of the third series of tests was to determine the average loss or gain in weight of the batches of pills prepared in the first series after standing for a period of one and two weeks.

With these objectives in view, the following prescriptions were filled.

No. 1.		No. 2.		No. 3.	
℞		℞		℞	
Aloe	2.600 Gm.	Aloe	3.250 Gm.	Aloe	3.250 Gm.
Soap	0.650 Gm.	Honey, *q. s.*		Glucose, *q. s.*	
Water, *q. s.*		To make 10 pills.		To make 10 pills.	
To make 10 pills.		Sig.:		Sig.:	
Sig.:					

In the actual performance of these tests, the pill prescriptions were filled by 100 members of the senior class in dispensing pharmacy at the School of Pharmacy of the University of Maryland under working conditions described in the first paper. The completed pills were checked for accuracy with respect to weight by using a prescription balance. The standard deviation was computed from the results obtained.

In tests made to determine the variation in weight of pills, the students were instructed to mix the powders intimately, then incorporate sufficient excipient to form a plastic mass and divide it into 10 pills. In some instances the students used a dusting powder such as lycopodium to facilitate rolling and shaping the pills, while in other instances they were prepared without the aid of a dusting powder.

The results of the first series of tests are presented in Tables I, II and III.

TABLE I.—WEIGHT AND STANDARD DEVIATION IN GRAMS OF BATCHES OF PILLS MADE IN COMPOUNDING PRESCRIPTION NO. 1.

Batch Number.	Weight in Gm.	S. D. in Gm.	Batch Number.	Weight in Gm.	S. D. in Gm.
1	3.969	0.014	51	3.650	0.012
2	3.873	0.009	52	3.500	0.022
3	4.110	0.038	53	3.670	0.028
4	3.532	0.023	54	3.591	0.022
5	4.300	0.038	55	3.585	0.014
6	3.725	0.010	56	3.572	0.034
7	3.870	0.016	57	3.982	0.019
8	3.594	0.026	58	3.575	0.018
9	3.875	0.010	59	3.590	0.022
10	3.650	0.047	60	3.530	0.037
11	3.600	0.011	61	3.575	0.003
12	3.540	0.017	62	3.452	0.003
13	3.475	0.025	63	3.439	0.019
14	3.700	0.026	64	3.390	0.038
15	3.577	0.009	65	3.967	0.033
16	3.685	0.021	66	3.590	0.024
17	3.680	0.032	67	3.480	0.038
18	3.750	0.023	68	3.735	0.018
19	3.770	0.041	69	3.350	0.018
20	3.538	0.032	70	3.652	0.040
21	3.402	0.033	71	3.350	0.033
22	3.620	0.006	72	3.530	0.017

23	4.483	0.041	73	3.395	0.034
24	3.932	0.025	74	3.410	0.046
25	3.573	0.021	75	3.750	0.028
26	3.570	0.037	76	3.900	0.019
27	3.563	0.030	77	3.570	0.019
28	3.740	0.018	78	3.685	0.016
29	3.670	0.018	79	3.592	0.029
30	3.770	0.012	80	3.550	0.009
31	3.820	0.028	81	3.275	0.018
32	3.730	0.031	82	3.970	0.032
33	3.701	0.068	83	3.805	0.017
34	3.280	0.021	84	3.370	0.023
35	4.250	0.004	85	3.575	0.030
36	4.100	0.008	86	3.460	0.028
37	4.170	0.021	87	3.520	0.023
38	3.342	0.003	88	3.750	0.019
39	3.562	0.021	89	3.502	0.022
40	3.492	0.041	90	3.540	0.008
41	3.620	0.038	91	3.650	0.017
42	3.585	0.023	92	3.490	0.029
43	3.677	0.020	93	3.871	0.007
44	3.750	0.021	94	3.565	0.023
45	4.001	0.022	95	3.190	0.010
46	3.765	0.038	96	3.580	0.023
47	3.595	0.034	97	3.655	0.019
48	3.680	0.021	98	3.502	0.042
49	3.735	0.015	99	3.650	0.013
50	3.940	0.030	100	3.530	0.034
	Average weight of batch (10 pills) =			3.659 Gm.	
	Average standard deviation of batches =				0.024 Gm.

TABLE II.—WEIGHT AND STANDARD DEVIATION IN GRAMS OF BATCHES OF PILLS MADE IN COMPOUNDING PRESCRIPTION NO. 2.

Batch Number.	Weight in Gm.	S. D. in Gm.	Batch Number.	Weight in Gm.	S. D. in Gm.
1	4.352	0.019	51	5.120	0.015
2	4.920	0.019	52	4.945	0.042
3	4.675	0.030	53	5.000	0.044
4	5.165	0.035	54	4.810	0.026
5	5.015	0.013	55	5.075	0.022
6	5.425	0.017	56	4.885	0.027
7	4.430	0.042	57	5.100	0.031
8	5.060	0.062	58	4.895	0.019
9	4.820	0.020	59	4.950	0.039
10	4.440	0.021	60	5.165	0.045
11	4.470	0.028	61	4.975	0.008
12	5.037	0.030	62	4.425	0.022
13	4.950	0.007	63	5.090	0.037
14	5.245	0.004	64	4.889	0.020
15	4.992	0.033	65	4.795	0.028
16	4.710	0.035	66	5.277	0.020
17	4.520	0.030	67	4.387	0.017
18	5.535	0.031	68	4.954	0.011
19	5.852	0.026	69	4.647	0.043
20	5.435	0.061	70	4.850	0.041

TABLE II.—*Continued.*

Batch Number.	Weight in Gm.	S. D. in Gm.	Batch Number.	Weight in Gm.	S. D. in Gm.
21	4.800	0.026	71	4.845	0.024
22	5.100	0.023	72	5.210	0.058
23	5.115	0.045	73	3.880	0.043
24	5.655	0.060	74	4.420	0.038
25	4.835	0.006	75	4.509	0.032
26	4.300	0.026	76	4.390	0.028
27	4.097	0.035	77	4.340	0.023
28	5.065	0.054	78	4.800	0.032
29	5.560	0.035	79	5.175	0.023
30	5.168	0.034	80	5.020	0.033
31	4.840	0.026	81	4.930	0.023
32	4.725	0.037	82	4.740	0.033
33	4.600	0.030	83	3.700	0.021
34	5.290	0.022	84	5.120	0.034
35	4.757	0.051	85	4.890	0.031
36	4.450	0.008	86	4.000	0.034
37	3.150	0.007	87	5.100	0.045
38	5.300	0.016	88	4.640	0.031
39	5.469	0.021	89	4.889	0.004
40	3.451	0.025	90	4.825	0.023
41	4.652	0.033	91	4.500	0.038
42	4.950	0.019	92	4.840	0.004
43	4.660	0.024	93	5.305	0.013
44	4.520	0.023	94	6.755	0.015
45	5.000	0.033	95	4.920	0.034
46	4.900	0.040	96	4.650	0.062
47	4.895	0.018	97	4.550	0.055
48	4.605	0.043	98	4.700	0.023
49	4.757	0.040	99	4.360	0.031
50	5.180	0.050	100	4.350	0.020

Average weight of batch (10 pills) = 4.795 Gm.

Average standard deviation of batches = 0.029 Gm.

TABLE III.—WEIGHT AND STANDARD DEVIATION IN GRAMS OF BATCHES OF PILLS MADE IN COMPOUNDING PRESCRIPTION NO. 3.

Batch Number.	Weight in Gm.	S. D. in Gm.	Batch Number.	Weight in Gm.	S. D. in Gm.
1	6.075	0.054	51	6.550	0.036
2	3.865	0.002	52	3.300	0.028
3	3.710	0.023	53	5.505	0.055
4	7.010	0.031	54	4.900	0.045
5	7.065	0.035	55	6.102	0.035
6	5.015	0.042	56	5.680	0.027
7	5.775	0.035	57	7.940	0.040
8	5.260	0.027	58	8.870	0.048
9	5.460	0.015	59	5.395	0.041
10	6.370	0.021	60	5.360	0.030
11	5.075	0.011	61	6.330	0.064
12	5.470	0.043	62	5.615	0.007
13	5.097	0.045	63	5.620	0.018
14	5.675	0.039	64	6.000	0.037
15	6.750	0.019	65	5.900	0.032
16	5.808	0.051	66	5.130	0.022

17	5.042	0.021	67	4.350	0.019
18	4.840	0.035	68	4.790	0.012
19	5.300	0.032	69	6.625	0.042
20	5.895	0.028	70	4.620	0.010
21	6.246	0.042	71	5.130	0.036
22	4.878	0.046	72	5.670	0.052
23	5.604	0.040	73	7.870	0.038
24	6.195	0.038	74	6.445	0.075
25	6.552	0.048	75	4.650	0.051
26	7.040	0.007	76	5.500	0.052
27	3.890	0.038	77	5.176	0.030
28	7.360	0.062	78	5.170	0.008
29	5.450	0.055	79	5.670	0.022
30	7.450	0.058	80	5.385	0.041
31	7.380	0.010	81	5.960	0.025
32	6.330	0.048	82	4.485	0.028
33	6.437	0.029	83	5.675	0.022
34	5.755	0.033	84	4.794	0.019
35	6.473	0.055	85	5.330	0.015
36	6.089	0.019	86	5.445	0.021
37	7.120	0.007	87	4.640	0.035
38	5.625	0.019	88	4.312	0.036
39	5.110	0.020	89	4.900	0.039
40	8.155	0.022	90	5.501	0.042
41	5.880	0.021	91	4.834	0.009
42	5.702	0.055	92	5.740	0.025
43	5.230	0.029	93	4.005	0.028
44	7.110	0.035	94	4.770	0.005
45	5.667	0.044	95	7.908	0.015
46	5.385	0.047	96	5.320	0.011
47	5.150	0.037	97	5.960	0.052
48	6.200	0.026	98	4.310	0.027
49	5.210	0.046	99	4.590	0.030
50	6.100	0.028	100	5.910	0.032
				5.689 Gm.	
			Average weight of batch (10 pills) =		
			Average standard deviation of batches =		0.032 Gm.

In Table I, which gives the average weight and the standard deviation of each of the individual batches of pills called for in prescription No. 1, it will be observed that in this series of tests the average weight of a total of the 100 batches is 3.659 Gm. or an increase of 0.409 Gm. over the theoretical weight before adding the excipient. On further examination it will be observed that the average standard deviation is 0.024 Gm. Sixty of the batches of pills filled fall within the average standard deviation, or 0.024 Gm.; thirty-nine batches fall within twice the average standard deviation, or 0.048 Gm.; while one batch (No. 33) falls within three times the average standard deviation, or 0.072 Gm.

In Table II, the results show that the average weight has increased 1.545 Gm. over the theoretical weight of 3.250 Gm. on adding honey as the excipient. The average standard deviation for this series is 0.029 Gm. Fifty of the batches of pills filled fall within the average standard deviation of 0.029 Gm.; forty-six fall within twice the average standard deviation, or 0.058 Gm.; while the remaining four batches fall within three times the average standard deviation, or 0.087 Gm.

In Table III, it will be observed there is an average increase of 2.439 Gm. over the theoretical weight of 3.250 Gm. when glucose is added as the excipient. The average standard deviation for this series of tests is 0.032 Gm. Fifty-one of the batches of pills filled fall within the average standard deviation of 0.032 Gm.; forty-eight batches fall within twice the average standard deviation, or 0.064 Gm.; while the one remaining batch falls within three times the average standard deviation, or 0.096 Gm.

The data obtained in this series of tests show that the use of different excipients in massing the same ingredients has a marked effect upon the weight of the completed pills. The increase in the average weight and in the average standard deviation on adding different excipients is in the following order: (1) soap and water, (2) honey and (3) glucose.

(To be continued.)

NOTES ON EARLY DRUG LEGISLATION.*

BY F. W. NITARDY.

Recent discussions of drug control by the Federal Government have been chiefly restricted to the problems of the present century. Readers might conclude from these discussions that the passage of the present federal law in 1906 was the first considerable achievement in favor of the consumer, and that in the absence of public interest this was instigated and largely supported by a Government bureau, the Department of Chemistry. Even a casual investigation of the periodical literature of the past century will change such view. The Food and Drugs Act of 1906 was not the first legislation of its kind nor was its passage accomplished by an individual or a group of individuals as a result of a few years of agitation. This legislation was the outgrowth of over half a century of effort in which laymen, physicians, pharmacists and drug manufacturers alike participated. The following isolated instances, while not in any sense representing a complete résumé of the subject, illustrate the extent and ramifications of the campaign to obtain pure drugs for the consumer and professions of medicine and pharmacy.

As early as 1848 Congress passed an "Act to prevent the importation of adulterated and spurious drugs and medicines." In its original form it had been introduced into Congress early in the year and was supported by memorials from various organizations including the American Medical Association, Surgeons in the Army and Navy, the physicians and apothecaries of the District of Columbia and by circulars published by the College of Pharmacy of New York in which attention had been publicly drawn to the large quantities of sophisticated chemical and pharmaceutical preparations imported. The gross adulteration of drugs such as opium, blue pill mass and quinine sulphate had been described by Dr. M. J. Baily, examiner of drugs at the New York Customhouse, who further reported in hearing before the House Committee that more than one-half of many of the most important chemical and medical preparations together with large quantities of crude drugs, arrived in this country so much adulterated or otherwise deteriorated as to

* Section on Historical Pharmacy, A. PH. A., Washington meeting, 1934.