CONCLUSIONS.

1. Hydroquinone retards the absorption of oxygen by refined halibut liver oil from air and an atmosphere of pure oxygen.

2. Hydroquinone, as indicated by the Vitamin A color test retards the deterioration of Vitamin A of halibut liver oil upon exposure to air or pure oxygen.

3. Hydroquinone, as shown by the biological test retards the deterioration of Vitamin A of Halibut Liver Oil upon exposure to air.

4. Maleic acid does not act as an antioxidant in halibut liver oil.

Biological assays reported herein were made in the Biological Research Laboratories of E. R. Squibb and Sons and we gratefully acknowledge their assistance; also that of Mr. E. Beaman of Research Laboratories of E. R. Squibb and Sons who assisted in our experimental work.

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ACCURACY AND SPEED FACTORS IN HAND-FILLING CAPSULES.*

BY JOHN W. LEE.[1]

The primary purpose of this paper is to compare two of the usual methods ordinarily employed in hand-filling capsules. One of the first problems that confronts us in either the establishment of a tolerance limit or the comparison of methods in hand-filling capsules, is the method or manner in which the contents of an individual capsule is determined.

Some of the methods that have been used in determining the contents of an empty capsule are:

(1) Dissolving the contents of the capsule in a suitable solvent and subsequent evaporation of the solvent.[2]

(2) Assay of the ingredients by the Official Process.

(3) The emptying of the contents and weighing directly.[3]

(4) Using individual capsules of the same size as a counterpoise.[2]

(5) Weighing a number of filled capsules at the same time using an equal number of empty shells as a counterpoise, changing the empty shells for different ones after one or two operations.[3]

The first method has the disadvantage of requiring too long a time, and it is not always possible to find a suitable solvent, especially, when the capsule contains a mixture of powders.

The second method mentioned also requires too much time and is not practical enough for use by the practicing pharmacist.

The third method, consisting of emptying the contents of the capsule and weighing directly is better suited for general use, but here again too much time is consumed and in the case of adhesive powders it is almost impossible to remove all of the powder from the shell.

The fourth method, using the empty shell as a counterpoise, introduces the error caused by the variance in weight of the individual shells.

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* Section on Practical Pharmacy and Dispensing, A. PH. A., Washington meeting, 1934.

[1] Assistant Professor in Pharmaceutical Chemistry. The George Washington University School of Pharmacy. In collaboration with Prof. W. P. Briggs.

[2] Private communication.

[3] Mathews, Norris W., JOUR. A. PH. A., 22, 321 (1933).

The fifth method eliminates to some degree the variance of the empty shell, but the average weight of the filled capsules must be taken, therefore it is not a true measure of the individual contents.

Experiments were carried out in an effort to eliminate some of the errors as pointed out in the foregoing methods and to find a method accurate enough and practical enough to enable the practising pharmacist to assure himself that, in the great majority of cases, his work is within the reasonable limit of error.

A number of empty shells ranging from twenty to one hundred were taken at random from stock, and each batch was weighed carefully on an analytical balance. The average weight of the individual shells in each batch was determined and then the averages of these averages computed. This figure was used as the tare in all instances where this size of capsule was employed.

In private communications with some of the leading manufacturers of empty capsules the writer was informed that the weight of empty shells of the same lot rarely varied more than three per cent of the average weight of the empty shell. One manufacturer stated that the weight of an individual shell never varied more than seven per cent. This variance was due, it was stated, to the variable viscosity of the gelatin and the moisture content of the air. An additional factor to be taken into consideration is that empty shells made by different manufacturers may show a difference in wall thickness and hence some variation in weight. One manufacturer stated that a 10% error would probably be the maximum. If this be true, then a No. 1 capsule which weighs approximately 80 mg. would show an error of 8 mg. or about $^1/_{10}$ of a grain, which would amount to about a 2% error in a 5-grain capsule.

The following table shows the result obtained by weighing different batches of capsules taken at random from stock.

TABLE I.—WEIGHT EXPRESSED IN GRAMS.

Number in Batch.	No. 0 Capsule. Wt. of Batch.	No. 0 Capsule. Average Wt. per Capsule.	No. 1 Capsule. Wt. of Batch.	No. 1 Capsule. Average Wt. per Capsule.
20	2.1748	0.1087	1.6670	0.0833
20	2.1642	0.1082	1.6540	0.0827
20	2.1780	0.1089	1.6704	0.0835
50	5.3830	0.1076	4.1590	0.0831
50	5.4010	0.1080	4.1165	0.0823
100	10.8230	0.10823	8.1200	0.0812
260—Total				
Average weight per capsule		0.1083		0.0827
Maximum variation per capsule, av. wt.		0.0012		0.0023

	No. 2 Capsule.		No. 3 Capsule.	
20	1.3598	0.0679	1.0566	0.0518
20	1.3610	0.0680	1.0584	0.0524
20	1.3400	0.0670	1.0278	0.0513
50	3.3495	0.0669	2.5770	0.0514
50	3.4000	0.0680	2.4535	0.04907
100	6.7550	0.0675	5.2030	0.0520
260—Total				
Average weight per capsule		0.0675		0.0513
Maximum variation per capsule, av. wt.		0.0010		0.0033

Observing the table it will be noted that the maximum variation in weight per capsule based on the average weight is in the case of the No. 3 capsule. This variation is 3.3 mg. or about five hundredths of a grain. Now by using the average weight 0.0513 this variation is reduced by about one-half, so it could be considered as practically negligible.

Two prescriptions of 12 capsules each were used in Table II. In both cases the theoretical content of the individual capsules was exactly five grains. Two methods were employed in determining the actual contents of each capsule. Method A consisted of weighing the capsule directly on an analytical balance and then subtracting the average weight of the same size empty capsule, as determined in Table I. Method B consisted of emptying the contents of the capsule on to a tared watch glass and then weighing on the analytical balance.

TABLE II.—THE WEIGHTS ARE RECORDED IN GRAMS.

Theoretical weight of 5-grain capsule in Gm. is 0.3240.

	Prescription No. 1.		Prescription No. 2.	
Capsule.	Method A.	Method B.	Method A.	Method B.
1	0.3355	0.3292	0.3013	0.2994
2	0.3303	0.3230	0.3163	0.3100
3	0.3179	0.3036	0.2859	0.2801
4	0.3319	0.3290	0.3243	0.3196
5	0.3067	0.3036	0.3577	0.3480
6	0.2597	0.2532	0.2633	0.2583
7	0.3073	0.2990	0.3163	0.3095
8	0.3443	0.3300	0.3917	0.3900
9	0.3369	0.3368	0.2973	0.2921
10	0.3099	0.3074	0.3133	0.3137
11	0.3189	0.3334	0.3743	0.3682
12	0.3093	0.3094	0.3423	0.3410
Totals	3.8086	3.7576	3.8840	3.8299
	2.83%	3.35%	0.10%	1.52%

Percentage error based on theoretical weight 3.888.

Table II shows that in both instances, using the average weight of the empty shell as a tare, the results were nearer the theoretical. Furthermore, in a comparison of the weight of the contents of individual capsules, the weights obtained by Method A are practically uniform, being slightly higher than the individual weight obtained by Method B.

There are three general methods usually employed in filling capsules by hand. The individual weighing of each capsule is undoubtably the most accurate method, but it is not practical for ordinary dispensing.

The two methods upon which the comparison of accuracy and speed are determined in this paper are:

(1) *The Punching Method*, consisting of filling the capsule directly from the entire quantity of the material either by repeatedly punching the shell in the powder until filled or forcing the powder into the shell by the aid of a spatula.

(2) *The Blocking Method*, in which the material is divided into a uniform square and then into the desired number of divisions, the material in each division being placed in a capsule.

There are several factors to be taken into consideration in the comparison of the accuracy of these two methods. *First*, the comparison must be based upon the quantity of material per capsule, since it is uniform distribution of the material throughout the desired number of capsules that is important. To base it upon the theoretical average weight per capsule determined from the theoretical total weight of the ingredients would not be correct but would merely be a measure of the error

in weighing plus the error in loss of material on the tile, etc. In the case of tolerance establishment this weighing error would be important, but not in a comparison of the accuracy of the two methods of filling. The true index as to the accuracy of filling then must be based upon the distribution of the material contained in the entire lot of capsules, not the amount that should have been placed in them. If, then, the average weight of the contents per capsule is based upon the actual weight of the total contents as determined by weighing on an analytical balance, we have a true estimate as to the quantity each capsule should contain. *Secondly*, the nature of the material would have some effect on the accuracy, so the prescriptions selected, bearing this in mind, consist of: (1) a powder of medium weight and bulk, (2) a bulky powder, (3) a compact powder, (4) a mixture of bulky powders and (5) a mixture of heavy powders. *Third*, the comparison must be based upon the same prescription so every operator filled each prescription twice, once by each method.

The speed factor in hand-filling capsules is important enough in most cases to be considered, but it must not be intimated that accuracy should be sacrificed in order to save time. In determining the time required in the filling operation by the two different methods, it was assumed that since in each method the same weighing and triturations were necessary, the time would be the same. We therefore started measuring time from the point after complete trituration, at which the actual blocking or punching, as the case might be, was started.

The following prescriptions were filled by students of the senior class in Dispensing Pharmacy, at The George Washington University School of Pharmacy. The students were not told that the prescriptions were to be checked for accuracy, but were instructed to fill the first prescription by the blocking method, the second by punching, alternating until all the prescriptions had been filled. At another laboratory period the students were given the same prescriptions and instructed to use the opposite method in filling them than was employed before. In this manner each prescription was filled by each of the two methods and by the same student.

℞ 1	Acidum Acetylsalicylicum	ʒ i	℞ 4	Carbo Ligni		
	m ft. Cap. xii			Phenolphthaleinum	*aa*	gr. ss
℞ 2	Quininæ Sulphas	gr. xxxvi		Acetphenetidinum		
	m ft. Cap. xii			Phenylis Salicylas	*aa*	gr. xx
℞ 3	Bismuthi Subnitras	ʒ i		m ft. Cap. x		
	Ft. Cap. xii		℞ 5	Hydrargyri Chloridum Mite		gr. xii
				Sodii Bicarbonas		gr. xxxvi
				m ft. Cap. xii		

The following tables show the results obtained by each method of filling the prescriptions. In order to have some standard upon which to base the comparison as to the accuracy of the two methods, a ten per cent variance was arbitrarily selected, either plus or minus, from the theoretical average weight of contents per capsule.

TABLE III.—PRESCRIPTION No. 1. Theoretical weight of ingredients in Gm., 3.8880.

Punching Method.

Operator.	Actual Wt. Total Contents of 12 Capsules.	Weighing Error.	Theoret. Wt. per Capsule, Based on Actual Wt. of Total Contents.	No. of Capsules within 10% Error, Plus or Minus.	No. of Capsules Having an Error Greater Than 10%.	Time in Min. to Fill Prescriptions.
1	3.5166	0.3714−	0.2930	7	5	7
2	3.967	0.079+	0.3305	11	1	4
3	3.757	0.131−	0.3130	10	2	9

4	3.9628	0.074+	0.3302	12	0	5
5	3.9242	0.036+	0.3270	9	3	5
6	3.7852	0.1028−	0.3154	8	4	4
7	4.0840	0.196+	0.3605	11	1	6
8	3.9182	0.030+	0.3265	11	1	3
9	3.9956	0.1076+	0.3329	11	1	5
10	4.1756	0.287+	0.3479	10	2	7
Totals				100	20	55
			Blocking Method.			
1	3.823	0.065−	0.3185	8	4	8
2	3.741	0.147−	0.3117	10	2	7
3	3.9946	0.106+	0.3328	6	6	10
4	4.001	0.113+	0.3334	6	6	10
5	3.9672	0.079+	0.3306	8	4	6
6	3.9416	0.0536+	0.3284	10	2	5
7	3.9663	0.078+	0.3305	9	3	9
8	3.8800	0.008−	0.3265	9	3	7
9	3.8100	0.075−	0.3175	10	2	7
10	3.8010	0.087−	0.3167	9	3	8
Totals				85	35	77

TABLE IV.—PRESCRIPTION NO. 2. Theoretical weight of ingredients in Gm., 2.3328.

Operator.	Actual Wt. Total Contents of 12 Capsules.	Weighing Error.	Theoret. Wt. per Capsule Based on Actual Wt. of Total Contents.	No. of Capsules within 10% Error, Plus or Minus.	No. of Capsules Having an Error Greater Than 10%.	Time in Min. to Fill Prescriptions.
			Punching Method.			
1	2.2932	−0.0396	0.1911	6	6	4
2	2.3768	+0.0440	0.1984	8	4	3
3	2.3708	+0.0380	0.1975	11	1	6
4	2.1396	−0.1932	0.1783	11	1	5
5	2.2656	−0.0672	0.1888	4	8	4
6	2.3036	−0.0292	0.1919	5	7	3
7	2.624	+0.2914	0.2186	10	2	8
8	2.0998	−0.2330	0.1749	10	2	3
9	2.1948	−0.1380	0.1829	10	2	6
10	2.2940	−0.0388	0.1915	12	0	7
Totals				87	33	49
			Blocking Method.			
1	2.3394	+0.0066	0.1949	7	5	9
2	2.2988	−0.0340	0.1916	9	3	9
3	2.5876	+0.2888	0.2156	10	2	6
4	2.3066	−0.0262	0.1922	7	5	11
5	2.3964	+0.0636	0.1977	10	2	8
6	2.3726	+0.0398	0.1969	10	2	6
7	2.3138	−0.0190	0.1928	9	3	10
8	2.7424	+0.4096	0.2287	10	2	8
9	2.2968	−0.0360	0.1914	10	2	8
10	2.4584	+0.1256	0.2048	7	5	6
Totals				89	31	81

TABLE V.—PRESCRIPTION No. 3. Theoretical weight of ingredients in Gm., 3.888.

Punching Method.

Operator.	Actual Wt. Total Contents of 12 Capsules.	Weighing Error.	Theoretical Wt. per Capsule Based on Actual Wt. of Total Contents.	No. of Capsules within 10% Error, Plus or Minus.	No. of Capsules Having an Error Greater Than 10%.	Time in Min. to Fill Prescriptions.
1	3.888	0.000	0.3260	8	4	5
2	3.8688	−0.019	0.3226	5	7	7
3	4.8720	+0.984	0.4060	11	1	3
4	3.9916	+0.103	0.3326	9	3	7
5	4.6544	+0.766	0.3878	8	4	5
6	3.6866	−0.201	0.3072	12	0	5
7	4.0785	+0.1905	0.3398	7	5	7
8	3.7004	−0.187	0.3083	11	1	3
9	4.0240	+0.136	0.3353	5	7	9
10	3.8728	−0.015	0.3227	8	4	5
				—	—	—
Totals				84	36	56

Blocking Method.

1	3.9104	+0.022	0.3258	5	7	8
2	3.9330	+0.045	0.3277	8	4	7
3	3.8792	−0.0088	0.3232	6	6	4
4	3.9527	+0.0647	0.3295	8	4	10
5	4.6544	+0.885	0.3978	7	5	3
6	4.072	+0.184	0.3393	8	4	10
7	4.0224	+0.134	0.3352	6	6	14
8	3.7268	−0.161	0.3105	8	4	5
9	4.1314	+0.243	0.3442	12	0	7
10	3.8738	−0.014	0.3228	7	5	6
				—	—	—
Totals				75	45	74

TABLE VI.—PRESCRIPTION No. 4. Theoretical weight of ingredients in Gm., 2.6556.

Punching Method.

Operator.	Actual Wt. Total Contents of 12 Capsules.	Weighing Error.	Theoretical Wt. Per Capsule Based on Actual Wt. of Total Contents.	No. of Capsules within 10% Error, Plus or Minus.	No. of Capsules Having an Error Greater Than 10%.	Time in Min. to Fill Prescriptions.
1	3.2298	+0.5742	0.3229	10	0	4
2	2.5690	−0.0866	0.2569	9	1	6
3	2.7284	+0.0728	0.2728	10	0	5
4	2.9516	+0.2960	0.2951	7	3	9
5	2.6064	−0.0492	0.2606	6	4	5
6	2.7308	+0.0752	0.2730	8	2	10
7	2.8246	+0.1690	0.2824	10	0	3
8	3.0372	+0.4816	0.3037	9	1	7
9	2.6270	−0.0286	0.2627	10	0	4
10	2.0410	−0.6146	0.2041	2	8	7
				—	—	—
Totals				81	19	60

Blocking Method.

1	2.6382	−0.0174	0.2638	8	2	11
2	2.8260	+0.1704	0.2826	10	0	5
3	2.9838	+0.3282	0.2983	10	0	4
4	2.7166	+0.0610	0.2716	8	2	8
5	2.6072	−0.0484	0.2607	7	3	9
6	2.9600	+0.3046	0.2960	8	2	16
7	2.6722	+0.0166	0.2672	8	2	5
8	2.7014	+0.0458	0.2701	7	3	11
9	2.5394	−0.1162	0.2539	7	3	9
10	2.4910	−0.1646	0.2491	6	4	7
Totals				79	21	85

TABLE VII.—PRESCRIPTION NO. 5. Theoretical weight of ingredients in Gm., 3.1104.

Punching Method.

Operator.	Actual Wt. Total Contents of 12 Capsules.	Weighing Error.	Theoretical Wt. per Capsule Based on Actual Wt. of Total Contents.	No. of Capsules within 10% Error, Plus or Minus.	No. of Capsules Having an Error Greater Than 10%.	Time in Min. to Fill Prescriptions.
1	2.9460	−0.1644	0.2455	6	6	4
2	3.5660	+0.4556	0.2972	9	3	5
3	3.2402	+0.1298	0.2700	5	7	6
4	3.2018	+0.0914	0.2668	9	3	6
5	3.2333	+0.1229	0.2693	10	2	5
6	2.7505	−0.3599	0.2292	8	4	7
7	3.0317	−0.0787	0.2526	11	1	4
8	3.0382	−0.0722	0.2531	4	8	3
9	2.9799	−0.1305	0.2483	6	6	4
10	2.8483	−0.2621	0.2373	7	5	6
Totals				75	45	50

Blocking Method.

1	2.9414	−0.1690	0.2452	6	6	6
2	3.1952	+0.0848	0.2663	12	0	7
3	3.7322	+0.6218	0.3110	10	2	5
4	3.2088	+0.0984	0.2674	9	3	8
5	2.9063	−0.2041	0.2422	7	5	8
6	3.0942	−0.0162	0.2578	5	7	11
7	3.0422	−0.0682	0.2535	11	1	5
8	3.0448	−0.0656	0.2537	4	8	4
9	3.0056	−0.1048	0.2508	6	6	7
10	3.0714	−0.0390	0.2559	8	4	7
Totals				78	42	68

SUMMARY OF TABLES III, IV, V, VI AND VII.

Punching Method.

Prescription Number.	Number of Capsules within 10% Error, Plus or Minus.	Number of Capsules Having an Error Greater Than 10%.	Time in Minutes.
1	100	20	55
2	87	33	49

3	84	36	55
4	81	19	60
5	75	45	50
Totals	427	153	269
Percentage of total capsules filled	73.6%	26.4%	
Average time required to fill one capsule			27.6 seconds

Blocking Method.

1	85	35	77
2	89	31	81
3	75	45	74
4	79	21	85
5	78	42	68
Totals	406	174	385
Percentage of total capsules filled	70%	30%	
Average time required to fill one capsule			37.2 seconds

The foregoing tables show a striking uniformity in the degree of accuracy, obtained by average operators, working under ordinary conditions, and filling capsules by punching or blocking methods.

As was expected, the punching method required about $^1/_3$ less time for filling than the blocking method.

Another significant point is that out of the one hundred prescriptions filled only nine came within the arbitrary 10% limit of variance. Of these nine, five were filled by the punching method and four by the blocking method.

CONCLUSIONS.

(1) The comparative accuracy between blocking and punching of capsules is in direct ratio to the skill of the operator.

(2) Considerably less time is required in punching than in blocking and with a comparable degree of accuracy.

(3) The results obtained in this study, which do not contain the weighing error, clearly indicate that a tolerance of more than 10% should be established.

(4) The average weight of an empty gelatin capsule obtained by the method herein described may be used as a tare in determining the weight of filled capsules.

Major General Charles R. Reynolds, the new Surgeon General of the Army, received the degree of M.D. from the University of Pennsylvania in 1899. He entered the service of Medical Corps of the army in 1900 and served through the various grades to Colonel and entered upon his duties as Surgeon General June 2, 1935. He served in the Philippines and had a brilliant record during the World War; was awarded the Distinguished Service Medal and the Silver Star and is an officer of the French Legion of Honor. He has written many professional papers having a bearing on military medical matters.

Dr. James F. Couch, chemist of the Bureau of Animal Industry of the Department of Agriculture and professor of historical science at the National University, has been elected president of the Chemical Society of Washington, D. C.

The New York Pharmacist, with the April issue, became the property of the New York State Pharmaceutical Association and is now known as the *New York State Pharmacist.*