

This method also has its disadvantages in that care must be taken in tilting the apparatus while running in the urine, or either loss of gas will take place or air will pass into the nitrogen column, thereby spoiling the determination.

Most supply houses are discontinuing to stock the old style apparatus. Our reserve supply of this type having recently become depleted and being obliged to use the newer style apparatus we have employed this in a manner superior to the usual technique advocated for either type.

Instead of pouring the urine to be analysed into the side burette up to the one or to the zero mark and measuring it by aid of the graduations thereon we use the 1-cc. pipette furnished with the old style apparatus and place exactly 1 cc. of urine into the burette arm and then by careful opening and closing the glass stop-cock run the urine into the hypobromite solution. A few drops of distilled water are then run into the burette to wash down residual urine which is also run into the hypobromite column. The apparatus is then ready to receive the next lot to be analysed without the necessity of removing the hypobromite and residual urine to wash out the burette. In this way the same hypobromite reagent can be employed until spent, thereby saving material as well as much time.

Any 1-cc. pipette can be employed for this purpose. Placing an aspirating nipple at the further end makes it unnecessary to resort to mouth aspiration and is much more convenient and rapid. Employing the Doremus Ureameter in this manner will enable the supply houses to furnish the apparatus without the side-arm burette graduation, thereby reducing the production costs for the apparatus.

STUDIES ON THE DETERMINATION OF CAMPHOR IN CAMPHOR LINIMENT.

I. U. S. P. X METHOD.*

BY CHARLES F. POE, GOLDNER LIPSEY AND CLARENCE L. VAUGHN.

INTRODUCTION.

In comparing results obtained from the determination of camphor in camphor liniment by means of the method given in the present Pharmacopœia with the method previously used, it was found that the U. S. P. method gives much lower results. For instance, on samples containing 20.00 per cent camphor the differences were: -0.44% ; -0.26% ; -0.27% ; -0.91% and -1.05% .

In searching the literature very little could be found concerning the evaporation method for the determination of camphor in camphor liniment. Kebler and collaborators,¹ in 1917, reported that the results by the evaporation method may be high, due to the liniment containing volatile materials other than camphor. In eleven out of fourteen analyses reported, the amounts of camphor obtained by this method were higher than the results obtained by using the polariscope. The differences were from $+0.04\%$ to $+0.80\%$.

* Presented before the Scientific Section, A. Ph. A., Philadelphia meeting, 1926. Recently submitted.

¹ Kebler and collaborators, "Camphor Liniment," *Jour. A. Ph. A.*, 6 (1917), 617.

Miller,¹ in 1917, reported that if the heating were conducted at 110° C. instead of 150° C., no decomposition of the oil took place.

Cook,² in 1906, reported that all of the camphor, except one-half per cent, was driven off at 100° C. when heated two and one-half hours.

Cowie and Dickson,³ in 1906, found that when olive oil was heated, there was a change in the weight of the oil averaging 0.162 per cent.

Wallace and Plummer,⁴ in 1921, worked on the changes in oils when heated. They determined the changes in specific gravity, refractive index, weight, iodine number and saponification number. In order to correct for the change in weight, when camphor liniments made from different oils were heated, they recommended that the following percentages should be added: cottonseed oil, 0.35%; peanut oil, 0.26% and olive oil, 0.27%. These authors also found that a sample of camphor liniment, made from cottonseed oil, when heated for five hours showed a loss in weight equivalent to 99.97% camphor. When other oils were used, the loss of camphor was almost quantitative when heated four hours. The results were as follows: peanut oil, 100.33%; olive oil, 99.88%; sesame oil, 100.07%. For camphor liniment, made with cottonseed oil, they recommend heating at 120° C. for five hours.

Since the methods given in the U. S. P. are used by food and drug officials for checking the purity of products sold to the public, it is essential that the methods give accurate results. Any method which will give low results is extremely objectionable, because the manufacturer should always be given the benefit of the doubt. Samples which are really up to standard may be condemned as being low in camphor when the method given in the U. S. P. is used. Since the method given in the U. S. P. X for the determination of camphor in camphor liniments seems to give consistently low results, it was decided to conduct a critical study of the method.

CHEMICALS AND METHODS.

The samples of camphor used were lots which had been saved at different intervals during the last twelve years. They apparently represented samples of camphor from widely different sources. The camphor was resublimed at least once, and in some cases twice. Any drops coming over at the beginning of the process, which did not solidify, were discarded. The purity was tested by determining the specific rotation in 95% alcohol. The samples of oil were obtained on the open market. These were tested for the usual oil constants: refractive index, specific gravity, iodine number and saponification number. Any sample which did not meet the U. S. P. standard was rejected. Samples of camphor liniment were made from the above constituents. The camphor was accurately weighed to the fourth decimal place in a tared glass-stoppered flask and the required amount of oil was added. This was weighed to the third decimal place. The camphor was allowed to dissolve either at room temperature or at a slightly higher temperature. Care was taken,

¹ Miller, "Note on Determination of Camphor," *JOUR. A. PH. A.*, 6 (1917), 683.

² Cook, "Camphor Liniment. Assay by Evaporation," *PROC. A. PH. A.*, 54 (1906), 637.

³ Cowie and Dickson, "Linimentum Camphoræ B. P. Method of Assay," *PROC. A. PH. A.*, 54 (1906), 638. *Pharm. J. & Pharm.* (1906), 281.

⁴ Wallace and Plummer, "Determination of Camphor in Camphorated Oils," *A. J. P.*, 93 (1921), 600.

however, that the ground glass stopper was not removed during the time the camphor was going into solution. The accuracy of the preparation of each sample was checked by reading the sample in the polariscope.

The method of analysis was the official method given in the U. S. P. X. The procedure follows:

"Place 5 cc. of camphor liniment in a tared porcelain dish, having a diameter of about 75 mm., weigh accurately, heat at about 110° C. for ninety minutes, or until the odor of camphor is no longer discernible, cool and weigh."

The ovens used for the determinations of the camphor were the Freas and DeKhotinsky constant-temperature ovens. These were set at 110° C. and maintained at this temperature during the heating process. Two other methods of heating were also used: the water-bath and hot-plate. It was thought that the water-bath could be used and the oxidation might be reduced, owing to the lower temperature (94.6° C.). Some slight variations of the above methods were made in certain cases. These will be mentioned at the proper place.

EXPERIMENTAL.

A series of samples was made up with varying amounts of camphor from 2.5% to 25%. Five grams of each of the samples were weighed into flat-bottom milk dishes made of aluminum. These were heated according to the U. S. P. method with results as listed in Table I. The time of heating was three hours.

TABLE I.

Per cent camphor in sample.	Loss in weight in Gm.	Per cent camphor found.	Per cent difference.
2.5	0.0869	1.74	-0.76
5.0	0.2030	4.06	-0.94
7.5	0.3552	7.10	-0.40
10.0	0.4776	9.55	-0.45
12.5	0.5824	11.65	-0.85
15.0	0.6749	13.50	-1.50
17.5	0.8280	16.36	-0.94
20.0	0.9376	18.75	-1.25
22.5	1.0796	21.59	-0.91
25.0	1.1997	23.99	-1.01

As may be seen from the above table, the error was considerable: the greatest, -1.50% and the least, -0.40%. These differences appeared even though the same lots of cottonseed oil and camphor were used in making up the different

TABLE II.

Per cent camphor in sample.	Per cent camphor found.					
	1/2 hour.	1 hour.	1 1/2 hour.	2 hours.	3 hours.	5 hours.
5.0	1.70	3.26	4.25	4.46	4.52	4.38
7.5	2.61	5.70	6.82	7.25	7.00	6.33
10.0	4.54	7.89	9.28	9.63	9.60	9.28
12.5	6.61	10.48	11.45	11.94	11.96	11.76
15.0	7.30	13.22	14.12	14.48	14.31	14.22
17.5	11.47	15.32	16.64	17.38	16.56	16.48
20.0	15.22	17.33	19.05	19.52	19.28	18.61
25.0	15.14	19.42	21.24	22.27	22.03	21.55

members of this series. It would be expected that the error would be about the same in all the percentages, but there seems to be no consistency.

The effect of time of heating was tried on a series of liniments made from the same oil and camphor. These samples were heated in aluminum dishes in the constant temperature-oven for varying lengths of time up to five hours. The results are recorded in Table II.

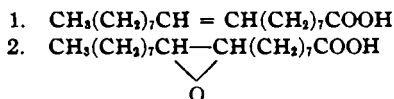
In most cases the maximum amount of camphor was found in two hours. After this time the percentage began to decrease. There is probably a certain time in which the results would be at a maximum, but it would be impossible to find this time for every sample.

It was now decided to heat the sample of oil alone so as to determine the change of weight from this source. Five grams of oil were heated in an oven for the varying lengths of time as indicated in Table III.

TABLE III.

Time in minutes.	Increase in weight (Gm.).	Equivalent to camphor in per cent.
30	0.0060	-0.12
60	0.0172	-0.34
90	0.0385	-0.77
180	0.0419	-0.84
300	0.0464	-0.95

During the heating something happened to the oil which caused an increase in weight. As is well known, cottonseed oil contains an ester of oleic acid called olein. Oleic acid, Formula I, contains a double bond, and this double bond is very susceptible to oxidation, forming a substance having Formula 2.



It was thought that aluminum dishes might act as a catalytic agent and thus increase the rate of oxidation at the double bond. It was, therefore, decided to use porcelain and glass dishes as well as aluminum dishes. The results of these experiments, with the liniment, and oil alone, are recorded in Tables IV and V.

TABLE IV.

Per cent camphor in sample.	Kind of dish used.	Per cent camphor found.	Per cent difference.
20.00	Porcelain 75 mm.	19.28	-0.72
20.00	Porcelain 50 mm.	19.65	-0.35
20.00	Glass	19.53	-0.47
20.00	Aluminum	19.02	-0.98

TABLE V.

Sample oil used in Gm.	Kind of dish used.	Gain in weight in Gm.	Equivalent to camphor in per cent.
5	Porcelain 75 mm.	0.0226	-0.45
5	Porcelain 50 mm.	0.0136	-0.27
5	Glass	0.0358	-0.72
5	Aluminum	0.0475	-0.95

From Tables IV and V it will be seen that the error varied with the different kinds of dishes used. The greatest error was with the aluminum dish and the least with the 50-mm. porcelain dish. There also seemed to be considerable difference in the two porcelain dishes of different sizes. The error was nearly twice as great for the larger dish. This may have been due to the fact that there was a greater surface exposed to oxidation.

A number of examinations were next made using the three methods of heating, *i. e.*, the electric oven, hot-plate and water-bath. Samples were heated for three hours in each method. The results are listed in Table VI.

TABLE VI.

Dish used.	Per cent camphor in sample.	Oven.	Per cent camphor found.	
			Hot plate.	Water-bath.
Aluminum	20.00	19.30	19.54	18.62
Porcelain		19.58	19.76	18.85
Glass		19.48	19.17	18.86
Aluminum	20.00	19.50	19.40	19.73
Porcelain		19.44	19.84	17.58
Glass		19.88	19.57	19.07
Aluminum	20.00	17.73	17.59	18.39
Porcelain		18.84	19.03	18.02
Glass		18.08	18.08	18.16

An examination of the above table plainly shows that none of the methods of heating are entirely satisfactory. The hot-plate method is unsatisfactory because

TABLE VII.

Dish used. ¹	Oil used.	Variation in per cent.		
		2 hours.	3 hours.	5 hours.
Q	2	-0.92	-0.24	-1.51
P		-0.56	-1.03	-1.55
A		-1.00	-1.83	-2.08
Q	3D	-0.44	-0.40	-0.70
P		-0.46	-0.45	-0.67
A		-0.47	-0.63	-1.04
Q	2A	-1.44	-0.73	-1.13
P		-1.09	-0.80	-1.04
A		-2.00	-1.34	-1.96
Q	3B	+0.10	+0.17	+0.03
P		+0.09	+0.18	+0.06
A		-0.23	-0.03	-0.19
Q	3C	-0.54	-0.45	-0.54
P		-0.59	-0.50	-0.48
A		-0.63	-0.53	-0.73
Q	1	-0.47	-0.56	-0.73
P		-0.59	-0.60	-0.74
A		-1.05	-0.85	-0.93
Q	4	-0.80	-0.32	-0.46
P		-0.85	-0.38	-0.47
A		-1.13	-0.48	-0.88
Q	5	-0.55	-0.46	-0.64
P		-0.56	-0.45	-0.84
A		-0.61	-0.41	-1.17

¹Abbreviations: Q—quartz, P—porcelain, A—aluminum.

TABLE VIII.

Dish used. ¹	Oil used.	Per cent gain.		
		2 hours.	3 hours.	5 hours.
Q	2	0.33	0.81	1.04
P		0.25	0.52	0.84
A		0.58	1.06	1.15
Q	3D	0.18	0.33	
P		0.03	0.11	
A		0.69	1.45	
Q	2A	1.34	1.17	
P		1.14	0.95	
A		1.65	1.38	
Q	3C	0.20	0.70	
P		0.33	0.68	
A		0.55	1.09	
Q	1	0.16	0.22	0.55
P		0.12	0.17	0.65
A		0.12	0.24	0.90
Q	4	0.46	0.94	
P		0.28	0.59	
A		0.60	1.05	
Q	5	0.24	0.41	0.42
P		0.43	0.58	0.98
A		0.35	0.62	1.20

¹Abbreviations: Q—quartz, P—porcelain, A—aluminum.

it is nearly impossible to regulate the temperature. Also the oil tended to creep up the sides of the dishes, and in some cases a small amount was lost. The results were in some cases lower than by the other methods, and this may also be due to the fact that there was an ample supply of air and oxidation may have been greater by this method. The water-bath method was unsuitable because the temperature was not high enough to drive off the camphor. In all of the determinations by this method it was necessary to heat the samples at least an additional hour in the electric oven so as to remove all of the camphor.

The only method of heating which was used in the additional experiments was the constant temperature-oven method. A large number of samples, made from different camphors and cottonseed oils, were used. Quartz dishes were used in place of glass dishes. The results are recorded in Table VII. The variations from the actual per cent of camphor in the sample are given in lieu of the percentages found. Results are given for 2, 3 and 5 hours' heating. Table VIII shows the results when the oils are heated without the camphor.

The results in Table VII indicate that the method is unsuitable for the determination of camphor in camphor liniment. In all of the samples, except 3B, there was a deficiency of camphor regardless of the time of heating. Sample 3B gave more camphor than was in the original sample. The oil used in this sample was very old and may have contained a little water. Probably considerable oxidation had also taken place in the oil before the sample was made. All of this oil was used in making the sample; so no further examination could be made. In general there was a gradual loss in weight at first owing to the evaporation of the camphor. A maximum was reached in from two to three hours and then there was a gradual gain in weight owing to the oxidation of the oil. At first it was thought that part of the camphor remained in the oil and could not be driven off, but a polariscope examination did not reveal any rotation beyond that of the original oil.

From Table VIII it may be seen that the oxidation is not constant with different samples of oil. This makes this method of analysis extremely objectionable because no correction factor can be applied. The oxidation seemed to be greater in the aluminum dishes and less in the glass dishes.

It was decided to use a number of different kinds of dishes in order to try to reduce the amount of oxidation. In addition to the dishes already used, tin, lead, nickel, silver and platinum dishes were used. The results with these dishes are recorded in Table IX.

TABLE IX.

Dish used.	17.5% camphor.		Oil alone. Per cent gain.
	Per cent found.	Per cent difference.	
Platinum	17.14	-0.36	0.44
Tin	16.96	-0.54	0.84
Aluminum	16.48	-1.02	1.01
Quartz	17.20	-0.30	0.65
Glass	17.11	-0.39	0.78
Lead	17.34	-0.16	0.52
Nickel	16.76	-0.74	0.46
Porcelain	17.14	-0.36	0.61
Silver	17.12	-0.38	0.50

The results in the above table indicate that considerable oxidation took place in every kind of dish. The aluminum dish seemed to give the greatest oxidation and

the lead dish the least. Determinations were repeated in the lead dish and results varying from -0.16 per cent to -0.33 per cent were obtained. None of the dishes gave results sufficiently accurate so as to justify their use in the method.

DISCUSSION.

From the experimental work reported in this paper it may be plainly seen that the official method for the determination of camphor in camphor liniment is far from accurate. The method as described in the U. S. P. X is a method which will give results sometimes more than one per cent low. Any such method is objectionable in enforcement of the Pure Food and Drugs Act. The amount of this oxidation depends upon a number of factors, such as time of heating, kind and size of dish, temperature of heating and amount of air present during heating.

CONCLUSIONS.

1. A critical study of the U. S. P. method for determination of camphor has been made.
2. The method has been found to give consistently low results.
3. The error in this method is due to the oxidation of the olein in the cotton-seed oil.
4. Various kinds of dishes and various methods of heating have been used, but none of these have proved satisfactory.

A more satisfactory method has been developed for this determination by the use of the vacuum oven and will be reported in a later communication.

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THE PREPARATION, ANALYSIS AND LEAD-ION CONCENTRATION OF SOLUTIONS OF COLLOIDAL LEAD.*

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During the course of some work on the preparation of colloidal lead for cancer therapy some observations have been made which are of interest in connection with this problem.

When it was found that colloidal lead solutions which had been prepared without the use of anaerobic technique throughout turned white upon boiling for sterilization, the procedure to be described was developed and found to be entirely satisfactory. The water used for all purposes during the preparation of the colloidal solution was boiled for half an hour, covered with an inch layer of liquid petrolatum and cooled. Where any water was needed, it was siphoned from beneath the oily layer. The granulated lead to be used was exhausted of air by putting it into a vacuum desiccator, evacuating the latter and breaking the vacuum with nitrogen; the process was repeated three times.

One hundred and sixty cc. of a 1% gelatin solution, 148 cc. of a solution containing 1 mg. of potassium chloride per cc. and 92 cc. of water were put into

* Scientific Section, A. Ph. A., Portland meeting, 1928.