TABLE II.—DETERMINATION OF CAMPHOR BY USE OF ANTIOXIDANTS.

20 Per cent Liniments Used. 110° C.

Antioxidant Parts.	Sample No. 7. 2 Hrs.	4 Hrs.	6 Hrs.	Sample No. 8. 2 Hrs.	4 Hrs.	6 Hrs.	Sample No. 12. 2 Hrs.	4 Hrs.	6 Hrs.	Average. 2 Hrs.	4 Hrs.	6 Hrs.
Pyrogallol.												
1:250	19.12[a]	19.88	19.92	19.50	19.87	19.73	19.42	19.94	19.90	19.35	19.90	19.85
1:500	18.98	19.92	19.94	18.48	19.70	19.60	19.00	19.80	19.56	18.22	19.81	19.70
Alpha Naphthol.												
1:250	18.30	19.88	19.92	18.54	19.84	19.80	18.75	19.86	19.70	18.53	19.86	19.81
1:500	18.82	19.84	19.90	18.44	19.80	19.65	18.80	19.72	19.52	18.69	19.79	19.70
Hydroquinone.												
1:250	19.60	19.90	19.94	19.60	19.96	20.00	19.00	19.94	19.80	19.40	19.93	19.91
1:500	18.10	20.04	19.99	19.40	19.82	19.50	19.08	19.84	19.54	18.86	19.90	19.68
Para-phenylene Diamine.												
1:250	17.94	19.74	19.68	18.34	19.14	19.08	18.60	19.80	19.67	18.29	19.56	19.48
1:500	19.04	19.95	19.70	18.22	19.28	19.26	18.34	19.56	19.53	18.53	19.60	19.50
No antioxidant	19.50	19.40	19.18	18.60	19.26	19.14	19.62	19.36	19.13	19.24	19.34	19.15

[a] All results expressed in per cent.

CONCLUSION.

1. Certain antioxidants have been investigated for use in the determination of camphor in camphor liniment.

2. Several antioxidants seem to show promise as a means of preventing the oxidation of the cottonseed oil used as a base for camphor liniment.

3. The results obtained with the use of the antioxidants seem to be more satisfactory than the results obtained by means of the U. S. P. X method, but less satisfactory than with the vacuum oven method.

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THE ASSAY OF ORGANIC MEDICINAL PREPARATIONS CONTAINING ARSENIC.*

BY EDWARD J. HUGHES.

During the past thirty years no less than a dozen distinctly different methods have been proposed for the estimation of arsenic in organic medicinals. Yet, up to the present time, no general method having the desirable qualities of accuracy, practical simplicity and rapidity has apparently been evolved.

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Splendid work has been done by a number of investigators in developing assay procedures that apply to a given arsenical, or, in some cases, to a group of arsenicals. It is when an attempt is made to apply a given assay method to the ever-increasing list of organic arsenicals that the analytical limitations of the method are discovered. There are also a number of very dependable methods that either require special equipment or are too involved and time-consuming to be acceptable for general use.

It is endeavored, with these thoughts in mind, to draw upon the experiences of other investigators and to develop, if possible, an improved method having the elements of precision and speed, which at the same time might be generally applied by the routine analyst to a relatively large proportion of medicinal arsenicals.

Among the earlier quantitative methods were those in which the arsenic was estimated by difference and others depending upon the increase in weight of a combustion tube after the elementary analysis of the organic arsenical. Later methods involved various types of fusions and distillations which were followed by gravimetric or by volumetric estimation of the arsenic. These earlier methods have been pronounced unreliable, either because of the inexact nature of the procedure, or because of the loss of part of the arsenic through volatilization. Continued investigation has resulted in the development of methods involving the use of the potentiometer and of the Marsh apparatus. One of the more recent methods depends upon the formation of hydrogen arsenide, which is subsequently determined by means of a combination iodometric and acidimetric titration. A very trustworthy although tedious procedure is the one in which the arsenic is oxidized by the Carius method to arsenic acid and subsequently weighed as magnesium pyroarsenate.

The work of Norton and Koch (1) in 1905 has resulted in the development of a procedure which is essentially the basis for most of the methods that are now in general use. These investigators found that moist combustion with sulphuric acid can readily be employed to liberate arsenic from organic matter with no loss of arsenic through volatilization and that the resulting acid-digestion mixture may be used for the quantitative estimation of arsenic, either by immediate titration with standard iodine solution after neutralization, or by gravimetric methods. This general idea of moist combustion or digestion has since been utilized by the following investigators, with the modifications that are indicated:

Investigator.	Year.	Digesting Agents.
Lehmann	1912	$H_2SO_4 + KMnO_4$
Ewins	1916	$H_2SO_4 + K_2SO_4$ + Starch
Rogers	1920	$HNO_3 + (NH_4)_2S_2O_8$
Robertson	1921	$H_2SO_4 + HNO_3$ (fuming)
Newbery	1925	$(NH_4)_2S_2O_8$ Solution
Keimatsu and Wada (2)	1931	$H_2SO_4 + K_2SO_4 + KClO_4$
Kahane	1934	$H_2SO_4 + HClO_4 + HNO_3$

It will be noted that among the above examples only in the Ewins (3) method of digestion is the arsenic reduced. In all other cases the arsenic is oxidized to the pentavalent condition. In the Lehmann (4) and the Rogers (5) methods the

oxidized arsenic is caused to liberate iodine from potassium iodide and is ultimately estimated by back titration with standard sodium thiosulphate. In the other digestions the arsenic is reduced to the trivalent form, if not already in that condition, and is finally estimated by direct titration with standard iodine solution or with standard potassium bromate solution as is the case in the recently developed Kahane (10) method.

DuMez and Myers (6) have demonstrated that the Lehmann method, slightly modified, is best adapted for the rapid routine analysis of arsphenamine and of neoarsphenamine. Our investigation has shown that these workers were correct in their contention, although it is our experience that the indefinite nature of the end-point in the final titration is far from being satisfactory. On the other hand, there are certain organic arsenicals for which the Lehmann method of assay is unsuitable. Ewins brought out this point in 1916 and Robertson (7) made the observation in 1921 when he stated that the Lehmann method of oxidation fails with certain of the refractory arsonic acids.

The failure of the Lehmann procedure to yield consistently accurate results in the assay of carbarsone prompted the authors to look elsewhere for a suitable method of assay. The use of ammonium persulphate in the preliminary digestion, as proposed by Newbery (8), proved to be inadequate. The potentiometric method of Cislak and Hamilton (9), which yielded results that checked closely with the calculated amount, was set aside for the reason that the potentiometer is not always readily available in those laboratories that are not accustomed to making a large number of routine arsenic assays.

One of the latest published methods has been proposed by Kahane. This procedure involves digestion and oxidation with a mixture of nitric, perchloric and sulphuric acids, reduction with hydrazine sulphate and direct titration with standard potassium bromate solution in the presence of an excess of sodium bicarbonate. While this method appears to be rapid and relatively simple, the experience so far leads the authors to believe that it is not sufficiently trustworthy for routine application.

Kahane's rapid method of oxidation with perchloric acid mixture has been utilized, however, in formulating a new method having what appeared to be the more desirable elements of the Robertson and the Ewins procedures. The revised perchloric acid method used in this investigation is as follows:

PERCHLORIC ACID METHOD.

To an accurately weighed sample of about 0.25 Gm., in a Kjeldahl flask, add 5 cc. of a mixture containing 7 parts of sulphuric acid (Sp. Gr. 1.82), 2 parts of perchloric acid (Sp. Gr. 1.61) and 1 part of nitric acid (Sp. Gr. 1.39). Apply moderate heat for ten minutes or more after the first appearance of vapors of sulphuric acid. Cool and deliver directly into the liquid 0.25 Gm. of hydrazine sulphate. Keep this mixture at the boiling point for ten minutes. Cool and wash down the inside of the flask with several portions of distilled water, sufficient to make a total volume of about 125 cc. Boil briskly for about one minute, again wash down the neck of the flask with small portions of distilled water, mix thoroughly and allow the mixture to cool. Add 1.0 Gm. of potassium iodide, boil for five minutes, wash down the neck of the flask, mix and allow to cool. Titrate with just sufficient $N/10$ sodium thiosulphate to exactly discharge the color of any liberated iodine. Make alkaline to litmus with 1:1 sodium hydroxide solution, then acidify with sulphuric acid. Dissolve about 5 Gm. of sodium bicarbonate in the solution and titrate with $N/20$ iodine solution.

A considerable amount of work has been done with the Ewins method in our laboratories with most encouraging results, particularly as it is applied to the assay of sodium cacodylate, arsanilic acid and carbarsone. This method has been criticized because of the prolonged digestion period which is involved and because of the possible loss of arsenic through volatilization. We have obtained scores of results by this method that agree very closely with the calculated amount of arsenic. Although relatively long in total lapsed time, Ewins method appears to have the advantages of simplicity in technique and to yield a relatively sharp end-point in the final titration with standard iodine solution. Following a suggestion made by Dr. Melvin R. Stevinson (11), the authors have undertaken to modify the Ewins method with the idea of hastening the time of digestion and thereby reducing the possibility of losing arsenic through volatilization to a minimum. The details of this modified method are given as follows:

MODIFIED EWINS METHOD.

Accurately weigh about 0.25 Gm. of sample on a tared, arsenic-free cigarette paper. Fold and deliver the paper and contents into a Kjeldahl flask containing 6 Gm. of reagent potassium sulphate and 20 cc. of concentrated sulphuric acid. Carefully digest the mixture until colorless over a free flame. Cool and dilute with 150 cc. of distilled water. Cautiously make alkaline to litmus with 1:1 sodium hydroxide solution, then make slightly acid with sulphuric acid and allow to cool. Add 2 Gm., in excess, of sodium bicarbonate, mix thoroughly and titrate with *N*/20 iodine solution.

In order to determine the relative values of (1) the Lehmann method, as it is now modified in the U. S. P. XI, (2) the original Ewins method, (3) the perchloric acid method and (4) our modification of Ewins method as general assay procedures, each of the methods has been separately applied to a series of representative arsenicals. The results obtained are tabulated as follows:

	Percentage of Arsenic Found.				
Name of Arsenical.	Lehmann Method.	Ewins Method.	Perchloric Acid Method.	Modified Ewins Method.	Percentage of Arsenic Calculated.
Arsphenamine	32.51	30.29	31.01	31.02	31.55
	32.81	30.29	31.91	30.82	
Neoarsphenamine	19.61	18.01	16.93	18.40	Not less
	19.99	18.01	17.23	18.57	than 19
Acetarsone	28.39	27.14	23.10	26.95	27.24
	28.16	27.14	25.81	27.05	
Tryparsamide	25.34	24.01	24.08	24.40	24.57
	25.49	24.16	24.16	24.30	
Carbarsone	28.08	27.74	27.88	27.86	28.82
	27.85	27.74	27.96	28.01	
Sodium cacodylate	1.52	34.59	34.77	34.93	35.01
	1.83	34.74	26.87	34.83	
Arsanilic acid	41.05	34.28	32.06	33.93	34.53
	41.05	34.20	28.45	34.13	
Approximate amount of time for assay	1 1/2 hrs.	3 hrs.	1 1/4 hrs.	2/3 to 1 1/4 hrs.	..

All of the above results have been obtained from the undried samples. The end-points were relatively sharp in the final titrations in all except Lehmann's method,

in which case considerable difficulty was encountered in making correct interpretations. It will be noted that Lehmann's method yields results that are uniformly higher than those obtained by the other methods, except for sodium cacodylate, and that this method appears to be best adapted for the assay of arsphenamine and neoarsphenamine. On the other hand, the Ewins method, the perchloric acid method and the modified Ewins method all appear to give results that agree more closely with the theoretical amounts which would indicate that the higher figures obtained by Lehmann's method may be due to the nature of the method itself rather than to any loss of arsenic through volatilization in the three other methods.

In conclusion, our experience would indicate that the Ewins method is definitely superior for the assay of arsanilic acid, sodium cacodylate and carbarsone. The substitution of an arsenic-free cigarette paper in place of starch in the digestion mixture makes the Ewins method considerably more rapid, without apparently affecting its accuracy.

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DIALKYLAMINO ACETYL UREAS.*

BY T. C. DANIELS.[1]

There are two general types of ureas that have found relatively wide application as hypnotics, the brominated acyl ureas (Bromural, Adalin) and the cyclic ureids of the barbital type.

An examination of the literature revealed that the dialkylamino acetyl ureids have not been examined and it was decided to prepare the following substances for study: Diethyl, di-*n*-propyl, di-*n*-butyl, di-iso-butyl, di-*n*-amyl, and di-iso-amyl-amino acetyl ureas.

EXPERIMENTAL.

Bromacetyl urea was prepared by reacting 75 Gm. of urea (xs) with 224 Gm. of bromacetyl bromide. The acyl halide was added slowly with stirring to the urea. The reaction product first melts, then solidifies, and the reaction mass after heating on a water-bath for forty-five minutes

* Scientific Section, A. PH. A., Portland meeting, 1936.

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