A TOXICOLOGICAL INVESTIGATION OF MORPHINE AND COCAINE.*

BY L. W. RISING AND E. V. LYNN.

Of the common alkaloidal poisons causing death, strychnine is used most frequently. It is, however, an extremely stable substance, easily isolated and identified, hence presenting no particular problem to the analyst. Next in the order of frequency, morphine and cocaine, in the sequence named, are the direct causes of death, either intentional or accidental. Both of these drugs have been the subjects of controversy when their stability in contact with biological material and when other points pertinent to legal medicine were considered.

It was decided to investigate the poisons quantitatively, in order to secure data which would in part settle these questions. It was especially hoped that the study would yield information indicating the probable rate of disappearance of both drugs in a body after death, the analytical significance of preservatives present, and of putrefaction. The general plan of the work was that followed in the initial investigation of this series (1).[1]

Selection of analytical procedures, particularly for morphine, from the maze of published methods was a difficult task. Morphine has long presented a problem to analysts. None of the great number of technics for its determination seem to have attained general favor, probably because it is difficult with any one of them to obtain concordant results. The method finally worked out is a colorimetric one. The material containing the morphine is finely divided, treated with 2% tartaric acid solution, and heated 30 minutes to an hour on a water-bath at a low temperature. On cooling, the substance is filtered, thoroughly washed, evaporated to a thick syrup, and sodium bicarbonate is added until a slight excess is present. The morphine tartrate is thus decomposed and the alkaloid freed. The mass is evaporated to dryness over a water-bath, powdered in a mortar, extracted with a chloroform-acetone mixture, and the morphine determined colorimetrically. This is

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[1] The plan was to subject the poisons as nearly as possible to all of the conditions they might encounter in a body after death. Some of the specimens to be made up for analysis were to be preserved with the common tissue preservative, including embalmer's cavity fluid, and others left unpreserved and allowed to undergo natural putrefaction. Therefore, using stomachs from freshly killed sheep as carriers for the drugs, a series of small, wide-mouthed bottles were set up, each containing a weighed quantity of minced stomach together with a known amount of one poison and one or no preservative.

The preservatives used were alcohol, a 10% solution of formaldehyde, a 1% solution of mercuric chloride, a saturated solution of arsenous acid, and embalmer's cavity fluid. The formula for the cavity fluid is approximately as follows:

Absolute alcohol	(Volume)	35.00 per cent
Methyl alcohol	(Volume)	14.70 per cent
Glycerin	(Volume)	2.00 per cent
Ethereal constituents	(Volume)	4.00 per cent
Water and other constituents	(Volume)	44.30 per cent

All bottles were stoppered and sealed with paraffin except one set of the unpreserved samples which were to be partially exposed to the elements. In all, enough specimens were arranged so that there were three complete sets of bottles containing the poison in contact with one or no preservative. This permitted, during the period of the investigation, three quantitative determinations of the poisons under every condition considered.

carried out by comparing the color from a known sample with the color obtained by treating with Marquis reagent. The principle of the procedure is the same as that practiced by Morgulis and Levine (2).

One of the greatest difficulties in the determination of morphine by this method is its extraction from even simple contaminating agents such as sodium bicarbonate. Cold chloroform-acetone extraction must be repeated 15–20 times before removal is complete. Hot extraction necessitates at least seven attempts.

TABLE I.—RESULTS OF ANALYSES OF MORPHINE-BEARING SPECIMENS.

Set Number.	1.	2.	3.	4.	5.	6.	7.
Preservative % found in.	Alcohol.	HCHO.	$HgCl_2$.	As_2O_3.	Cav. Fld.	Unpreserved. Exposed.	Unexposed.
1.	89	92	94	85	90	91	79
2.	70	82	81	80	63	85	73
3.	58	53	52	55	60	69	62

1. Per cent recovered at the end of one month.
2. Per cent recovered at the end of three months.
3. Per cent recovered at the end of seven months.

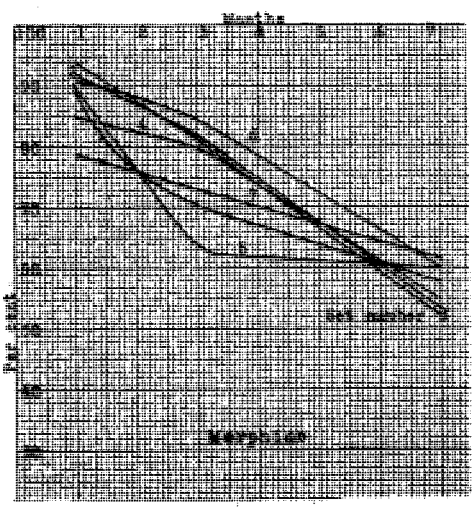

Fig. 1.—Morphine.

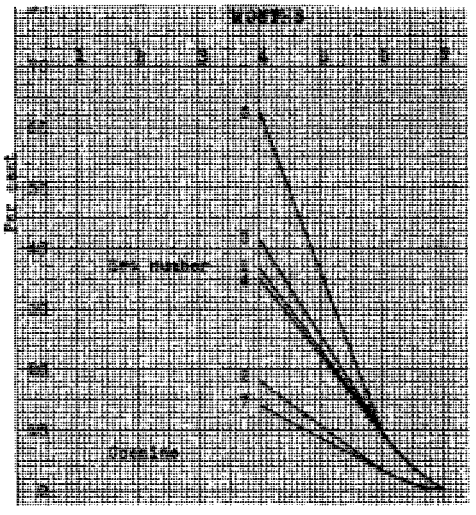

Fig. 2.—Cocaine.

Much has been written about the stability of morphine under various conditions. That opinion is divided is well illustrated by two typically diverse statements: Woodman and Tidy (3) isolated morphine from the stomach of a body after it had been exposed in an unfinished house for four months. Ogier (4), in contrast, states that he has frequently been unable to detect the drug after exposure in viscera putrefied from two to four weeks.

It is certain that morphine can be detected in a body for approximately a year after death, regardless of the condition of the tissue or the presence of the ordinary preservatives. Decomposition sets in immediately and continues more or less gradually until the alkaloid is entirely destroyed. This should require a little more than a year. The rate of decomposition is affected very little by the agents used to prevent putrefaction. If there is any real effect, it is an accelerating, rather than a

depressing one. It is doubtful that an analyst can recover over 50 per cent of the alkaloid from any tissue after the latter has stood longer than 8 months. Within a month after ingestion he should isolate 90 per cent or over and within three months probably between 70 and 80 per cent. Aqueous solutions of morphine contain only 4–5 per cent of the original alkaloid at the end of the year.

In order to isolate the cocaine for analysis, it was separated from the organic carrier by means of an acid-alcohol mixture, from which the alkaloid was then extracted with chloroform. Before making use of the immiscible solvent, all the acid-alcohol solutions of cocaine were concentrated *in vacuo* at temperatures never exceeding 35–40° C. This made the working quantities of liquids much more convenient. Finally the chloroform extract was allowed to evaporate spontaneously, the alkaloid taken up in an excess of dilute acid, and the excess determined by means of a standard alkali.

TABLE II.—RESULTS OF ANALYSES OF COCAINE-BEARING SPECIMENS.

Set number.	1.	2.	3.	4.	5.	6.	7.
						Unpreserved.	
Preservative % found in.	Alcohol.	HCHO.	$HgCl_2$.	As_2O_3.	Cav. Fld.	Exposed.	Unexposed.
1.	37	18	41	35	63	13	14
2.	9	3	9	9	9	..	3
3.	0	0	0	0	0	0	0

1. Per cent recovered at the end of four months.
2. Per cent recovered at the end of six months.
3. Per cent recovered at the end of seven and one-half months.

Witthaus (5), in discussing the stability of cocaine after death, states that its decomposition proceeds rapidly. Proelss (6) found that it is not detectable in cadaveric material 14 days after ingestion. The bulk of the literature, in fact, tends to show that cocaine cannot be detected or estimated unless the organs containing it are subjected to almost immediate analysis.

The data obtained in this investigation proves the contrary to be true. Cocaine, when subjected to the action of putrefaction, decomposes rapidly. Complete dissociation, however, is not as immediate as has been generally accepted heretofore. In tissue preserved with a dilute solution of formaldehyde, the disappearance of the alkaloid proceeds at nearly the same rate as it does in the putrefied samples. Arsenous acid, mercuric chloride and alcohol, retard the dissociation considerably. Approximately 40 per cent of the cocaine was recovered in the presence of these preserving agents at the end of four months. Cavity fluid is the best substance with which to treat a body containing cocaine. The first analysis of tissue in this fluid returned 63 per cent of the poison. In the second series of determinations there was recovered less than 10 per cent of the alkaloid. At the end of the seven and a half months, complete dissociation of the cocaine had taken place. It should not be taken for granted that cocaine is equally stable under all conditions. The experiments conducted here are only indicative of a general trend of dissociation, but they show that it will persist in a body longer than toxicologists have been wont to believe when exposed to the ordinary influences encountered in a corpse.

SUMMARY.

1. Morphine and cocaine have been shown to be more stable in the presence of biologic material, preserved or decomposed, than many toxicologists have believed.

2. The presence of the common tissue preservatives does not interfere with the analysis of these alkaloids.

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(4) Ogier, Witthaus, "A Manual of Toxicology," 1911.
(5) Witthaus, "A Manual of Toxicology," 1911.
(6) Proelss, *Chem. Cetr.* II (1901), 1321.

STUDIES ON THE DETERMINATION OF CAMPHOR IN CAMPHOR LINIMENT.

III. VACUUM OVEN METHOD.*

BY CHARLES F. POE.

INTRODUCTION.

In previous communications, the author with others (1, 2) has shown that the method given in the U. S. P. X for the determination of camphor in camphor liniment is not accurate. The results were found to be consistently low owing to the fact that the oil was oxidized during the heating process and consequently gained in weight. The investigation covered by this paper proposes a more accurate method for the determination of camphor in the liniment by means of the vacuum oven.

EXPERIMENTAL.

The materials and methods of preparation of the liniments were similar to those described in the previous papers (1, 2). The vacuum oven used was the latest type of the Freas constant-temperature vacuum oven.

A sample of camphor liniment containing 20 per cent camphor was selected for the first tests. Determinations were made using the vacuum oven and also the ordinary air oven according to the U. S. P. X method. A number of dishes made of different materials were used for the determination of the camphor and for the heating of the cottonseed oil. Table I gives the results of this series of tests.

TABLE I.—COMPARISON OF THE DETERMINATION OF CAMPHOR BY THE U. S. P. X AND VACUUM OVEN METHODS USING VARIOUS DISHES. 20 PER CENT CAMPHORATED OIL USED. 4 HOURS' HEATING.

	Air Oven 110° C. Camphorated Oil.			Vacuum Oven 100° C. Camphorated Oil.		
*	Camphor, per cent found.	Variation.	Oil alone, per cent gain.	Camphor, per cent found.	Variation.	Oil alone, per cent gain.
A	19.38	−0.62	0.95	19.74	−0.26	0.18
G	19.53	−0.47	0.82	19.89	−0.11	0.04
L	19.72	−0.28	0.50	19.92	−0.08	0.08
N	19.66	−0.34	0.56	19.81	−0.19	0.06
Pt	19.62	−0.38	0.54	19.86	−0.14	0.07
P	19.52	−0.48	0.74	19.88	−0.12	0.08

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