SCIENTIFIC SECTION

A TOXICOLOGICAL INVESTIGATION OF CHLORAL HYDRATE.

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One of the most conspicuous deficiencies in the toxicological knowledge regarding chloral hydrate is the lack of information on its stability in the body after death. Analysts have long been in disagreement as to the length of time after death in which the aldehyde could still be isolated from the cadaver and tested for quantitatively, or even qualitatively. There is no experimental data available to indicate the probable curve of disappearance of the drug when in contact with organic tissue.

Knowledge is also lacking about the effect of certain common tissue preservatives or the effect of putrefaction on the stability of chloral hydrate. It is obvious that such information would be of great value in medico-legal cases.

This investigation was initiated in order that such data might be made available. It was decided to make a series of quantitative determinations at intervals of a month or longer on specimens of organic material containing the hypnotic. Some of the specimens were to be preserved with the various preserving agents, and others left unpreserved and allowed to undergo natural putrefactive changes. The general plan was to subject the chloral hydrate as nearly as possible to all of the conditions which it might encounter if the body containing it was embalmed, exposed to the natural action of putrefaction, or the organs removed for analysis and preserved with the usual tissue preservatives. It was hoped that the data obtained from the quantitative analysis of such specimens would furnish certain valuable guides in forensic medicine or court cases wherein the quantitative estimation of the aldehyde was involved.

Stomachs from freshly killed sheep were used as carriers for the poison. These were minced, and weighed portions placed in 4-ounce wide-mouth bottles. Known quantities of the drug in amounts sufficient to have caused death were introduced and thoroughly mixed. A definite amount of the preservative was then added and each bottle stoppered and sealed with paraffin. The preservatives used were alcohol, a one per cent solution of corrosive sublimate, a saturated solution of arsenic trioxide, a ten per cent solution of formaldehyde, and embalmer's cavity fluid.[1] The samples which were to be permitted to decompose were treated in a like manner, except that no preservative was added.

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 determina-

[1] 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

tions of the poison under every condition considered. The analyses were made at approximately the ends of the first, third and seventh months of standing.

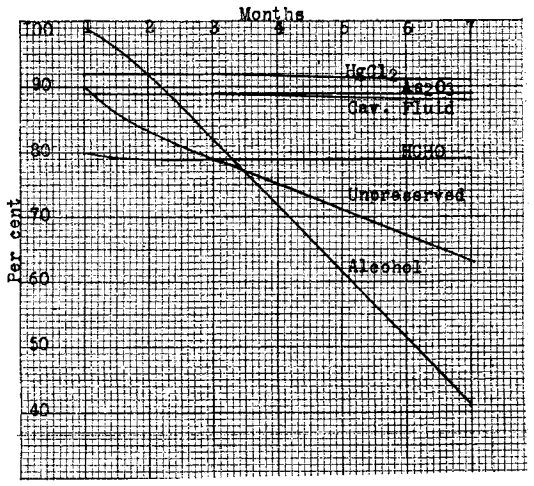

Fig. 1.

Selection of a suitable analytical procedure proved to be a difficult problem. Many of the published technics are subject to the influence of so many variable factors that they are not satisfactory as quantitative methods. On the other hand the isolation of the drug from the tissue offers no particular difficulty. It can best be accomplished by steam distillation. The operation must be continued for several hours but the complete removal of the aldehyde is assured.

The method of estimation (1) finally chosen requires that the chloral hydrate solution from the steam distillation of the organic material be refluxed for one-half hour with zinc dust. The excess zinc is dissolved with acetic acid, the solution filtered and made up to volume. The chloride thus formed is then determined in aliquots by titration with silver nitrate.

RESULTS OF ANALYSES.

Set number		1	2	3	4	5	6
Preserv.		Alcohol	HCHO	$HgCl_2$	As_2O_3	Cav. fld.	Unpreserved
% found in:	I.	99	80	92	89	89	90
	II.	82	79	92	89	89	79
	III.	41	79	91	89	88	63

I. Per cent recovered at the end of one month.
II. Per cent recovered at the end of three months.
III. Per cent recovered at the end of seven months.

CONCLUSIONS.

It will be seen that chloral hydrate is much more stable in putrefied tissue than has been generally accepted. Toxicologists have taken it for granted that the drug would rapidly disappear (2) when subjected to putrefactive action. Such is not the case. It is highly probable that at least a year and a half would elapse before there would be complete dissociation of the aldehyde. The majority of the tissue preservatives exert an unexpected stabilizing influence on it. Bichloride of mercury is the best preserving agent to use in case of chloral poisoning. The maximum loss of the poison in specimens treated with it was less than nine per cent in the seven months.

Arsenous acid and cavity fluid are next most desirable, each yielding approximately 90 per cent of the poison at the end of the seven months. Ten per cent formaldehyde solution permitted an immediate drop of 20 per cent after which no further loss was noted. If there is a likelihood that the viscera will

have to be preserved for a long time, alcohol is a very poor substance to employ. The decline of chloral content in organic material treated with alcohol is quite rapid after the third month. Even putrefaction does not cause such a rapid loss.

The analyst apparently should recover not less than 50 per cent of the poison from tissue, regardless of the preservative used or of putrefaction, if the examination is made within six months after death.

This investigation also showed that there exists a great need for the revision of many of the methods for the quantitative determination of chloral hydrate. The literature contains a number of such methods which cannot be depended upon to give concordant results on aliquots of the same sample.

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(2) W. Autenrieth, "Detection of Poisons" (1928).

POTENTIOMETRIC TITRATION OF ALKALOIDS WITH BIMETALLIC ELECTRODES.

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The alkaloids are such weak bases that their direct titration by means of acids and indicators is unsatisfactory. Usually the alkaloid is dissolved in a definite volume of standard acid representing an excess, and the latter is then titrated with standard alkali in the presence of a suitable indicator. Potentiometric titrations have been fairly satisfactory. McGill and Faulkner[3] used the hydrogen electrode to estimate alkaloids in crude drugs. Krantz[4] employed the hydrogen electrode for the estimation of alkaloids in solutions containing an excess of HCl. His results have been called into question by Kolthoff because of the possibility of the reduction of the alkaloid by hydrogen in presence of platinized platinum. To avoid such possible reduction Wagner and McGill[5] used the quinhydrone electrode for determining alkaloids. They obtained fairly reproducible results with solutions of strychnine, strychnine sulphate, morphine and morphine sulphate. Kolthoff[6] used the antimony electrode for potentiometric titration of some of the alkaloids, but with only fair success. Popoff and McHenry[7] employed a bright platinum wire (against a calomel half cell) for the titration of strychnine, quinine, cinchonidine and cocaine.

In a previous paper[8] it has been shown that certain metallic couples serve very well for the potentiometric titration of various acids and bases. Their application to the titration of amines with HCl led to the present investigation, namely, the use of couples for the titration of alkaloids.

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[3] JOUR. A. PH. A., 11 (1922), 1003.
[4] *Ibid.*, 14 (1925), 294.
[5] *Ibid.*, 14 (1925), 288.
[6] *Rec. trav. chim. Pays-Bas*, 44 (1925), 113.
[7] JOUR. A. PH. A., 14 (1925), 473.
[8] M. Leslie Holt and L. Kahlenberg, *Trans. Am. Electrochem. Soc.*, 57 (1930), 113.