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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## POTENTIOMETRIC TITRATION OF ALKALOIDS WITH BIMETALLIC ELECTRODES.

BY M. LESLIE HOLT[1] AND LOUIS KAHLENBERG.[2]

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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[1] Instructor in Chemistry, University of Wisconsin.
[2] Professor of Chemistry, University of Wisconsin.
[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.

A calculated amount of the alkaloid to be titrated (considered as a mono-acid base) was weighed out and dissolved in a known amount of 0.1 *N* HCl, the latter being in excess of that required to form the hydrochloride. Aliquot parts of this solution were taken and the excess of HCl titrated with 0.1 *N* NaOH using the metal couple to indicate the end-point which was also checked with methyl-red indicator. The end-point thus found potentiometrically and colorimetrically was, of course, the point of neutralization of the excess acid before the alkaloid-hydrochloride was decomposed by an excess of NaOH. The remainder of the standard acid was the amount required to neturalize the alkaloid base present in the solution.

The method and apparatus used in the titration was the same as that previously described,[8] and was essentially as follows: The apparatus consisted of a Leeds and Northrup student type potentiometer, a desk galvanometer (sensitivity

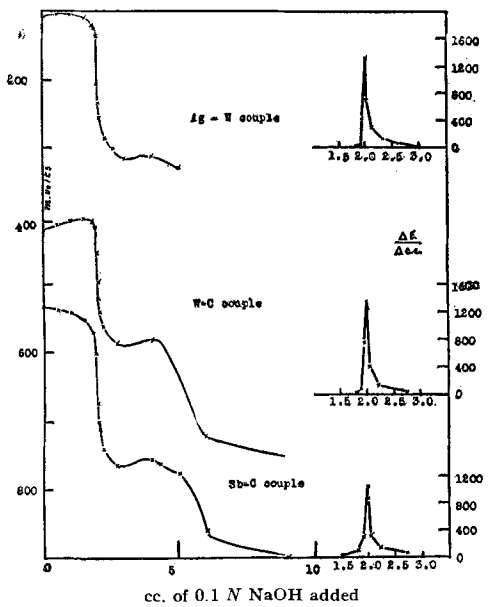


Fig. 1.—Comparing various couples in the potentiometric titration of strychnine (dissolved in excess HCl) with 0.1 *N* NaOH.

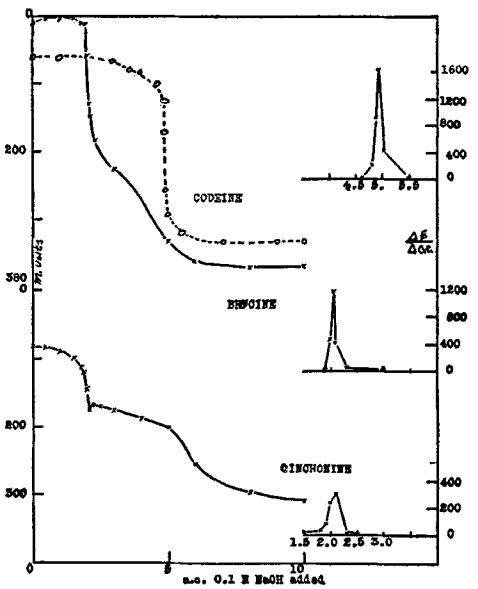


Fig. 2.—Ag-W couple used in the potentiometric titration of various alkaloids (dissolved in excess HCl) with 0.1 *N* NaOH.

2.7 mg.), a motor stirrer, a standard cell, resistance box and tap key. The set-up was the same as that used for the ordinary hydrogen electrode, except that the calomel half cell and platinum black electrode were replaced by the two metal electrodes. The latter were clamped to a bakelite support 1 to 2 cm. apart and connected to the potentiometer through a reversing switch. The electrodes were carefully cleaned, sanded and wiped with clean filter paper each time they were used. The solution to be titrated was introduced into the titration vessel, a 150-cc. beaker, and diluted with water to a volume sufficient to emerse the electrodes 2 to 3 cm. deep. After waiting a few minutes for the couple to attain a reasonably steady difference of potential, the standard solution was introduced from a burette and the change of potential noted on the potentiometer. The solution was stirred continuously with the motor stirrer during the process.

Previous work has shown that the Ag-W, Sb-C and W-C (natural graphite carbon) are the most satisfactory pairs for an acid-base titration. These couples were used separately for the potentiometric titration of a solution of strychnine made by dissolving 1.6715 Gm. of the free base (Merck) in 75 cc. of 0.1 *N* HCl and 50 cc. water; 10 cc. parts of this solution were diluted with 25 cc. water and titrated with 0.1 *N* NaOH. When the electrode pair was put into the solution, the stirrer was started and after waiting about 5 minutes for a fair equilibrium, the alkali was added at definite intervals. The total titration time was twenty to twenty-five minutes, depending on the number of readings taken. The three pairs gave very good results (Fig. 1), the potentiometric end-point checking exactly with the methyl red end-point. The results are presented graphically as the ordinary titration curve (e. m. f. as ordinates against cc. standard alkali added as abscissas) and also with the rate of change of potential $\left(\frac{\Delta E}{\Delta cc.}\right)$ plotted against the volume of added alkali. The data are presented in Table I. The Ag-W couple was selected

TABLE I.—DATA FOR FIG. 1, TITRATION OF STRYCHNINE WITH Ag-W, W-C AND Sb-C COUPLES.

| Ag-W Couple. | | | | W-C Couple. | | | | Sb-C Couple. | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 0.1 *N* NaOH cc. | E. m. f. mv. | $\Delta E.$ | $\frac{\Delta E.}{\Delta cc.}$ | 0.1 *N* NaOH cc. | E. m. f. mv. | $\Delta E.$ | $\frac{\Delta E.}{\Delta cc.}$ | 0.1 *N* NaOH cc. | E. m. f. mv. | $\Delta E.$ | $\frac{\Delta E.}{\Delta cc.}$ |
| 0.0 | 108 | | | 0.0 | 420 | | | 0.0 | 534 | | |
| 0.5 | 104 | | | 0.5 | 412 | | | 0.5 | 538 | | |
| 1.0 | 105 | | | 1.0 | 407 | | | 1.0 | 542 | | |
| 1.5 | 108 | | | 1.5 | 402 | | | 1.5 | 552 | 10 | 20 |
| 1.8 | 120 | 12 | 40 | 1.8 | 407 | 5 | 16 | 1.8 | 570 | 28 | 93 |
| 1.9 | 125 | 5 | 50 | 1.9 | 417 | 10 | 100 | 1.9 | 600 | 30 | 300 |
| 1.93 | 138 | 13 | 433 | 1.95 | 455 | 38 | 760 | 1.97 | 672 | 72 | 1029 |
| 1.98 | 205 | 67 | 1340 | 1.98 | 495 | 40 | 1330 | 2.0 | 698 | 26 | 866 |
| 2.02 | 234 | 29 | 725 | 2.0 | 520 | 25 | 1250 | 2.04 | 710 | 12 | 300 |
| 2.08 | 252 | 18 | 300 | 2.05 | 540 | 20 | 400 | 2.2 | 739 | 29 | 170 |
| 2.3 | 284 | 32 | 145 | 2.2 | 560 | 20 | 135 | 2.7 | 764 | 25 | 50 |
| 2.6 | 300 | 16 | 53 | 2.7 | 585 | 25 | 50 | 4.0 | 755 | | |
| 3.0 | 314 | 14 | 35 | 4.0 | 580 | | | 4.3 | 762 | | |
| 4.0 | 310 | | | 6.0 | 720 | | | 5.0 | 775 | | |
| 5.0 | 328 | | | 9.0 | 750 | | | 6.0 | 860 | | |
| | | | | 11.0 | 750 | | | 9.0 | 940 | | |
| | | | | | | | | 11.0 | 950 | | |

for titration of other alkaloids because the potentials are more nearly reproducible and the couple is very convenient to use. The tungsten electrode used was 2 cm. wide, 8 cm. long and 1 mm. thick. The silver electrode was 1 cm. by 5 cm. It was cut from a sheet of pure silver. The size of the electrode apparently has very little effect on the titration, for a small tungsten rod and a silver wire were just as satisfactory as the larger electrodes. The same procedure was followed in all the following titrations using 10-cc. portions of the solutions as made up and diluting with 25 cc. water.

The codeine solution was made by dissolving 0.7982 Gm. of the free base (Mallinckrodt, U. S. P.) in 75 cc. 0.1 *N* HCl and 50 cc. water. As shown in Fig. 2 the results of the titration were very satisfactory. The end-point was easily found. The potentiometric and colorimetric (methyl-red) end-points checked very closely.

The brucine solution was made by dissolving 1.1611 Gm. of the free base

(Merck) in 50 cc. 0.1 *N* HCl and 50 cc. water. The results of the titration of 10 cc. of this solution are shown in Fig. 2. The end-point was entirely satisfactory. There was a secondary potential change on addition of excess of alkali, giving evidence of the decomposition of the brucine hydrochloride.

The titration of cinchonine was not very successful, 1.4713 Gm. of the free base (Lehn and Fink) were dissolved in 75 cc. 0.1 *N* HCl and 50 cc. water. The methyl-red end-point was very vague but the potentiometric end-point was fairly definite as shown in Fig. 2. Here also there was a secondary potential change indicating the breaking down of the hydrochloride.

The morphine solution contained 0.7852 Gm. of the free base (Merck U. S. P.) with 75 cc. of 0.1 *N* HCl and made up to a volume of 125 cc. with water. In this titration the indicated potentiometric end-point was very sharp and definite and the salt decomposition hardly noticeable—Fig. 3.

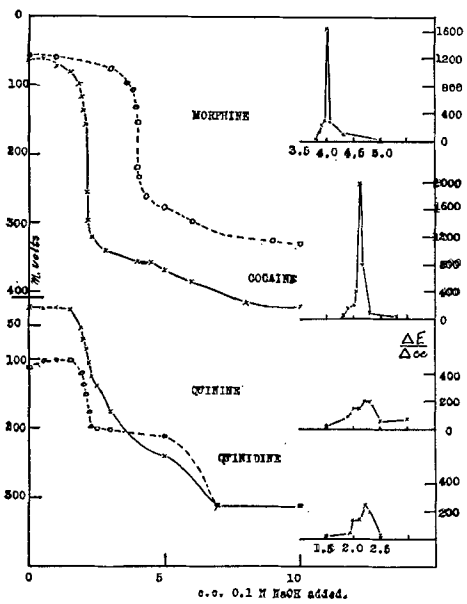


Fig. 3.—Ag-W couple used in the potentiometric titration of various alkaloids (dissolved in excess HCl) with 0.1 *N* NaOH.

The cocaine solution was made by dissolving 1.5163 Gm. of the free base (Mallinckrodt U. S. P.) in 75 cc. 0.1 *N* HCl and 50 cc. water. The potentiometric end-point was very good—Fig. 3. There was a secondary potential change for the decomposition of the hydrochloride.

The titrations of quinine and quinidine were perhaps the least successful of those attempted. The solutions were made by dissolving 1.6216 Gm. of the free base (Quinine, Merck U. S. P.; Quinidine, Merck N. F. V) in 75 cc. 0.1 *N* HCl and diluting each to a volume of 125 cc. Methyl-red gave no indication of the end-point and the potentiometric end-points (Fig. 3) were very poor. The hydrochloride formed is decomposed so easily that the titration of the free base in excess of HCl is hardly feasible.

Table II shows the results of these alkaloid titrations. The point of maximum change of potential per volume of added alkali $\left(\frac{\Delta E}{\Delta \text{cc.}}\right)$ was taken as the end-point. These were sharp and definite except in the cases of quinine and quinidine. The potentials were steady and quick to reach a reasonable equilibrium after each addition of reagent. The change at the end-point was definite and rapid. All results were checked and found entirely reproducible, particularly for the observed end-points. However, the initial and final potentials were not always repeatable because these potentials are affected by the conditions of the titration. This is in general true of all titrations with bi-metallic electrodes.

The effect of quinhydrone on Ag-W and Sb-C couples in the titration of strych-

TABLE II.—RESULTS OF INDIRECT POTENTIOMETRIC TITRATIONS OF VARIOUS ALKALOIDS WITH THE Ag-W COUPLE.

| Alkaloid. | 0.1 *N* NaOH to Neutralize Excess HCl. | | Grams of Alkaloid. | |
|---|---|---|---|---|
| | Calc. NaOH cc. | Required NaOH cc. | Present. | Found. |
| Brucine | 2.05 cc. | 2.06 cc. | 0.1161 Gm. | 0.1157 Gm. |
| Cinchonine | 2.0 cc. | 2.1 cc. | 0.1177 Gm. | 0.1148 Gm. |
| Codeine | 5.0 cc. | 4.91 cc. | 0.0639 Gm. | 0.0696 Gm. |
| Cocaine | 2.0 cc. | 2.1 cc. | 0.1213 Gm. | 0.1183 Gm. |
| Morphine | 4.0 cc. | 4.0 cc. | 0.0628 Gm. | 0.0628 Gm. |
| Quinidine | 2.0 cc. | 2.2 cc. | 0.1297 Gm. | 0.1232 Gm. |
| Quinine | 2.0 cc. | 2.2 cc. | 0.1297 Gm. | 0.1232 Gm. |
| Strychnine | 2.0 cc. | 1.97 cc. | 0.1337 Gm. | 0.1347 Gm. |

nine was studied. A small amount of quinhydrone was added to the solution in the titrating vessel and the titration was carried out in the usual manner. The quinhydrone altered the difference of potential between the electrodes, but did not aid in the determination of the end-point, for it neither increased the magnitude nor the sharpness of the potential change. In fact the indication of the end-point was rather less satisfactory, so this effect was not studied further.

SUMMARY.

1. The bi-metallic electrodes Sb-C, W-C and Ag-W have been used in the indirect electrometric titration of strychnine.

2. The Ag-W pair was used in the titration of brucine, cinchonine, codeine, cocaine and morphine.

3. The titration of quinine and quinidine with the Ag-W couple was not satisfactory.

4. Quinhydrone does not enhance the value of the Ag-W and Sb-C couples in the titration of strychnine.

CHEMICAL LABORATORY,
UNIVERSITY OF WISCONSIN, MADISON,
November 1930.

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# THE SPECIFIC GRAVITY OF MIXTURES OF CHLOROFORM (U. S. P.) AND BENZYL ALCOHOL.*

BY SAMUEL M. GORDON.

An examination of several proprietary remedies, exploited extensively to the dental profession as local anesthetics, revealed that they consisted of mixtures of benzyl alcohol and chloroform.

Benzyl alcohol has found limited use as a local anesthetic by injection or by infiltration in minor surgical operation, including the extraction of teeth. In ordinary doses it is stated to be practically non-irritant and non-toxic. In addition, pure benzyl alcohol is reported to possess antiseptic properties.[1]

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* Contribution from the American Dental Association Bureau of Chemistry and the American Medical Association Chemical Laboratory.

[1] A more complete description of benzyl alcohol may be found in "New and Nonofficial Remedies," 1930, published by the American Medical Association.