

I. M. Kolthoff, "Die Verwendung der Chimhydronstatt Wasserstoffelektrode bei potentiometrischen Aciditätsbestimmungen," *Rec. Trav. Chim. des Pays-Bas XLII*.

S. P. L. S. Soerensen, Margrethe Soerensen and K. Linderstroen Lang-, "Sur l'erreur de sel inherente a l'electrode de quinhydrone," *Ann. de Chimie*, 16 (1921), 9's, 283.

FOOD AND DRUG DEPARTMENT,
COLLEGE OF PHARMACY,
UNIVERSITY OF MICHIGAN,
ANN ARBOR.

THE USE OF THE POTENTIOMETER IN THE QUANTITATIVE ANALYSIS OF ALKALOIDAL SOLUTIONS.*

BY JOHN C. KRANTZ, JR.

INTRODUCTION.

There is no instrument which, in recent years, has helped the scientist in the study of chemical phenomena more than the potentiometer. The pharmacist has not been slow to recognize the possibilities of the use of this instrument in solving many of the pharmaceutical problems which have confronted the manufacturer, retailer and drug analyst. Thus Masucci and Moffat¹ have very comprehensively shown how easily the actual acidity of medicinal solutions may be determined by this instrument in conjunction with the other apparatus necessary for its proper use. Smith and Giesy² have employed the potentiometer in the determination of the alkalinity of Magma Magnesiae. McGill³ and his associates have begun a pioneer phase of research in employing electrical instruments to evaluate the alkaloidal value of crude drugs.

In this work McGill has determined the voltage end-point for several alkaloidal residues and consequently he has been able to employ the potentiometer as an indicator in the residual titration of the excess of acid. After carefully reviewing this important investigation, it occurred to the writer that, based upon definite physical chemical principles, a method of analysis might be devised, in which the potentiometer would not only replace a chemical indicator but, at the same time, take the place of the alkali solution.

THEORETICAL CONSIDERATIONS.

McGill pointed out, in his experiments with Cinchona residues, that the concentration of the alkaloidal salts has very little effect upon the hydrogen-ion concentration of the solution. This fact was verified by the author as can be observed from the results tabulated in this paper. Based upon this fact—if the molarity of the alkaloidal salt solution does not influence the p_H of the solution, a definite excess of acid added to variable amounts of alkaloidal salts and made up to a definite volume, at which the ionization of the acid is practically complete, will yield solutions with a p_H which is a function of the excess of acid present. The

* Scientific Section A. PH. A., Buffalo meeting, 1924.

¹ JOUR. A. PH. A., 12, 609 (1923).

² *Ibid.*, 12, 955 (1923).

³ *Ibid.*, 11, 1003 (1922).

hydrogen-ion concentration produced by the alkaloidal salt can be subtracted from the hydrogen-ion concentration of the solution, and the difference can then be calculated as excess of tenth normal acid. This would of course involve several calculations and present practical difficulties which are not apparent when considered from the standpoint of theory alone. Thus, in order to obviate lengthy calculations and any difficulties that might arise from the buffer action of the alkaloidal salt, a quantity of alkaloid was dissolved in just enough tenth normal hydrochloric acid to combine with it, and a curve was plotted using various amounts of $N/10$ hydrochloric acid in excess as abscissae and the p_H of the solutions as ordinates. If then in any alkaloidal salt solution in which the quantity of acid is known and a curve has been prepared, the p_H of the solution is estimated as

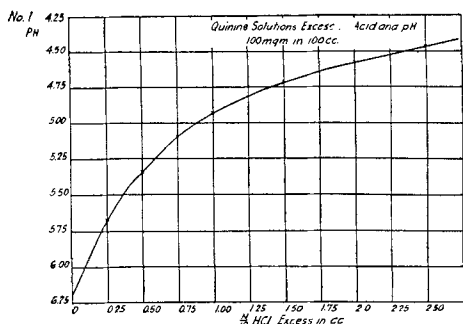


Fig. 1.

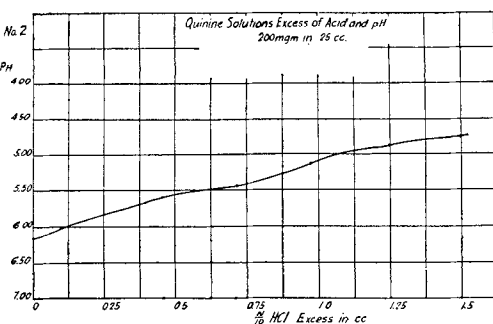


Fig. 2.

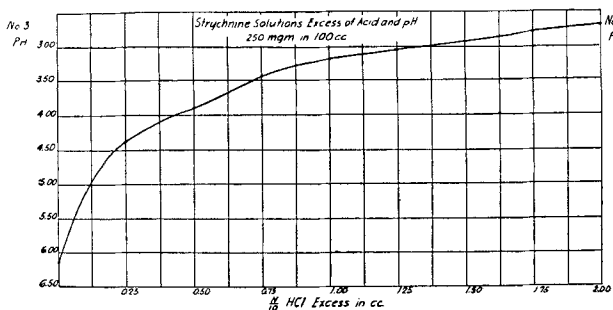


Fig. 3.

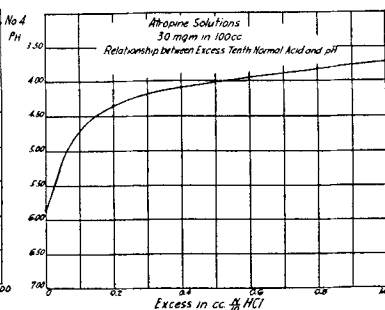


Fig. 4.

excess acid from the curve, and from these data—the variables, *i. e.*, the quantity of alkaloid present may be calculated in the usual manner.

METHODS EMPLOYED AND RESULTS.

Throughout this work a Leeds and Northrup hydrogen-ion outfit was employed with a Bailey electrode and normal calomel electrode.

A. *Quinine*.—Curve number one was prepared by dissolving 0.100 Gm. of quinine (equivalent in quantity to the amount of alkaloids obtained from 2 Gms. of cinchona) in a molecular equivalent quantity of $N/10$ hydrochloric acid and the solution was made up to 100 cc. with boiled distilled water. The p_H was determined immediately. A number of solutions were prepared in a similar manner keeping the amounts of quinine constant, but increasing the quantities of acid

as shown by the curve. After plotting the curve, the amount of quinine was varied and an excess of acid added comparable to that contained in solutions previously studied and the following results were obtained.

0.200 Gm. Quinine, 0.75 cc. <i>N</i> /10 HCl, p_H 5.09
0.100 Gm. Quinine, 0.75 cc. <i>N</i> /10 HCl, p_H 5.10
0.100 Gm. Quinine, 1.5 cc. <i>N</i> /10 HCl, p_H 4.72
0.120 Gm. Quinine, 1.5 cc. <i>N</i> /10 HCl, p_H 4.71
0.100 Gm. Quinine, no excess HCl, p_H 6.19
0.800 Gm. Quinine, no excess HCl, p_H 6.15

These results indicate that the amount of quinine present has little effect upon the p_H of the solution.

Several solutions of quinine alkaloid were prepared using 4.7 cc. *N*/10 hydrochloric acid and made up to 100 cc. with distilled water. After the determination of the p_H the solutions were analyzed by curve No. 1 and the following results were obtained.

	Grams of quinine in 100 cc.	p_H .	Grams found.
No. 1	0.120	4.71	0.1192
No. 2	0.140	5.02	0.1445
No. 3	0.160	5.42	0.1611
No. 4	0.170	5.77	0.1702

Some of the solutions used in the preliminary work with a much higher quinine content containing 9 cc. *N*/10 hydrochloric acid were analyzed by this curve and the following results obtained.

	Grams of quinine in 100 cc.	p_H .	Grams found.
No. 1	0.300	5.16	0.313
No. 2	0.290	4.74	0.286

Naturally the best plan to follow in analysis by this method is to have the curve to be used plotted with solutions containing an amount of the alkaloid that corresponds more or less closely to the amounts present in the solutions to be analyzed.

CURVE NO. 1.

Another curve was prepared using 25 cc. as the total volume and excess of acid up to 1.5 cc. Four quinine solutions were prepared in a similar way containing 7.05 cc. *N*/10 hydrochloric acid and analyzed by this curve, *i. e.*, No. 2. The following results were obtained.

	Grams of quinine in 25 cc.	p_H .	Grams found.
No. 1	0.210	4.74	0.2099
No. 2	0.220	4.94	0.2232
No. 3	0.230	5.20	0.2326
No. 4	0.240	5.46	0.2417

CURVE NO. 2. B. STRYCHNINE.

A third curve was prepared using 0.250 Gm. of strychnine and after the addition of the amounts of acid as indicated by the curve, the solution was made up to 100 cc. and its p_H determined. In a similar manner four solutions were pre-

pared containing different amounts of strychnine and 9.5 cc. of *N*/10 hydrochloric acid. These solutions were analyzed by curve No. 3 and the following results were obtained.

	Grams of strychnine in 100 cc.	p_H .	Grams found.
No. 1	0.305	3.92	0.3015
No. 2	0.290	3.23	0.2857
No. 3	0.275	2.98	0.2701
No. 4	0.260	2.74	0.2583

CURVE NO. 3. C. ATROPINE.

The fourth curve represents the p_H of Atropine solutions with different quantities of *N*/10 hydrochloric acid. Thirty milligrams of atropine was dissolved in a molecular equivalent of *N*/10 hydrochloric acid and the volume was made up to 100 cc. The other solutions containing atropine and hydrochloric acid were prepared in a similar manner and from the hydrogen ion concentrations of these solutions the atropine curve was plotted. Four solutions were prepared containing different amounts of atropine and 2 cc. of *N*/10 hydrochloric acid in 100 cc. These solutions were analyzed by curve No. 4 and the following results obtained.

	Grams of atropine in 100 cc.	p_H .	Grams found.
No. 1	0.035	3.84	0.0359
No. 2	0.040	3.92	0.0393
No. 3	0.045	4.04	0.0445
No. 4	0.050	4.38	0.0507

CURVE NO. 4.

The writer believes that the smoothness of the atropine curve and the more accurate results obtained in the analysis of this compound are due to the fact that the molar concentration of atropine in the solution was exceedingly small compared with that of the hydrochloric acid. Thus there is little possibility of ion repression or buffer action which may be caused by larger quantities of alkaloid.

D. CAFFEINE.

The difficulties presented in the analytical methods used to estimate caffeine volumetrically suggested the application of the potentiometer method to this substance. Accordingly nine solutions of caffeine were prepared containing in 100 cc. 0.100 Gm. of the anhydrous alkaloid. The first solution contained a molecular equivalent of hydrochloric acid or 5.15 cc. of the *N*/10 acid, and the other solutions contained 0.25 cc. *N*/10 hydrochloric acid additional in regular progression until in the ninth solution 2 cc. excess had been added.

The hydrogen ion concentration of the first solution was determined; this showed a p_H of 2.32, far too acidic for the plotting of a caffeine curve. An effort was made to plot milligrams of caffeine directly against p_H in very diluted acid solution; this, however, did not yield satisfactory results. The following data will demonstrate the difficulty involved in this project.

Five and fifteen hundredths cubic centimeters of *N*/10 hydrochloric acid diluted to 100 cc. is equivalent to a normality of 0.0052. At this dilution ionization is practically complete, so that

$$0.0052 \times 1.00 = 5.2 \times 10^{-3} (\text{H}^+)$$

By the potentiometer method this dilution of acid developed a voltage of $0.421 = 2.31 p_{\text{H}}$.

$$\log \frac{1}{(\text{H}^+)} = 2.31$$

$$(\text{H}^+) = 4.9 \times 10^{-3}$$

The voltage developed by the solution containing the same amount of acid and 0.100 Gm. of caffeine was $0.425 = 2.32 p_{\text{H}}$

$$\log \frac{1}{(\text{H}^+)} = 2.32$$

$$(\text{H}^+) = 4.8 \times 10^{-3}$$

This confirms mathematically the statement found frequently in the literature, that the hydrochloride of caffeine is easily decomposed by water. This experiment, although unsuccessful in obtaining a method of estimating caffeine by the potentiometer, shows that at this dilution the hydrolysis of the hydrochloride is practically complete.

CONCLUSIONS.

1. A method of analysis for certain alkaloids by means of the potentiometer has been devised which is rapid and simple in manipulation.
2. Curves which have been prepared for the analysis of alkaloids can be most accurately plotted by employing the minimum amount of alkaloid likely to be found in an unknown specimen and using a total volume of 100 cc.
3. The writer intends to attempt the analysis of colchicine by this method and also apply it to the analysis of crude drugs. The results of these investigations if successful will appear in a subsequent paper.

ABSTRACT OF DISCUSSION.

Chairman J. P. Snyder said that the work presented in this paper showed progress, and hoped that the electrometric method would be satisfactorily employed in alkaloidal determination.

Dr. I. M. Kolthoff did not think it would be possible to have accurate hydrogen electrode measurements of the hydrogen-ion concentration. He had endeavored to apply the method to alkaloidal solutions, but could not obtain very accurate measurements, because of the reduction of the alkaloid by the hydrogen, that is, accelerated by the presence of the platinum. He only succeeded in obtaining good results of the p_{H} of the solution by using the quinhydrone electrode; it is much easier to apply in these determinations.

The author replied to questions propounded that if the concentration of the alkaloid was quite dilute fairly good results were obtained. He did not think the work along the lines of this method had been perfected to the extent that it will be; he was able to get results comparable with the titration method. The touch electrode or drop electrode has been used at the University of Maryland—the electrode comes in contact with the alkaloidal solution only for a moment and the voltage is then read before there is any appreciable amount of reduction.

Dr. Kolthoff said that there can be no equilibrium when there is a reduction.

The author said the Department of Chemistry of the University of Maryland applies the method in the absorption of dyes and their hydrogen-ion concentration difficulties were overcome by using the touch electrode. The method has not been employed in alkaloidal de-

termination, but that would follow an observation as to whether resins and gums would poison the electrode or have any buffer action upon the solutions.

SCHOOL OF PHARMACY,
UNIVERSITY OF MARYLAND.

PLANT COLORING MATTERS.

BY CHARLES E. SANDO.

Recently there appeared in THIS JOURNAL (1) an interesting contribution by Wurdack dealing principally with the distribution, general characteristics, and possible functions in plants of natural coloring matters. While the subject matter of this paper is still fresh in our minds, it seemed desirable to present at this time a number of additional facts of interest which relate to these coloring substances.

It is necessary to mention again only briefly a few salient points concerning the nature of the pigments themselves in view of the well-prepared résumé published. The brief references will be made solely to recall the compounds about which further discussion is to be had.

PLASTID PIGMENTS: CHLOROPHYLLS AND CAROTINOIDS.

That the chlorophyll molecule is exceedingly complex has already been indicated by Wurdack. Endeavors to isolate the pure pigment appeared for many years hopeless because of its instability, its chemical indifference, and on account of the many impurities which accompany it. A knowledge of its structure was finally gained when Willstätter and his collaborators deduced its constitution from a study of the decomposition products formed from it by hydrolysis with acids and alkalis. When the preparation of pure chlorophyll was ultimately accomplished in 1911, the facts learned from its analysis fully corroborated the former deductions as to its chemical makeup. As a result of the work on the decomposition products of chlorophyll, it became possible to compare the green pigment in over two hundred plants from numerous genera of cryptogams and phanerogams. This work demonstrated that leaf-green of all the plants examined consists of two components, chlorophyll *a* ($C_{55}H_{72}O_5N_4Mg$), a blue-black powder, and chlorophyll *b* ($C_{55}H_{70}O_6N_4Mg$), a dark green powder. It was also observed that with the exception of the *Phaeophyceæ*, or brown algæ, all of the plants investigated contained approximately three molecules of chlorophyll *a* to one of chlorophyll *b*. In the case of the brown algæ, the green matter proved to be mostly chlorophyll *a* with but a small percentage of the other component.

It was early recognized that yellow substances accompany the green pigments in the plastid. This mutual occurrence of the coloring matters suggested a significant physiological rôle of the yellow pigments, consequently their separation became an important problem. Ultimately, it was shown that there are present in green leaves two easily crystallizable, nitrogen-free pigments. The members of this group, which are hydrocarbons or their derivatives, are designated carotinoids, but the exact nature of their basic structure or of their function is still unknown. The yellow pigment, carotin, is found not only accompanying chloro-