

The paste remaining in the distillation flask is mixed with starch and aliquot parts of the starch mixture are fed as known doses of the material of the bouillon cube.

It is obvious that this method will be inapplicable for the separation of the vitamin B complex from interfering substances which are soluble in glacial acetic acid.

2. A simple method is described which employs each test animal used in an assay for the vitamin B complex as its own control. Experimental animals, depleted of the vitamin B complex, are fed on given doses of the material to be tested. At the end of the test period a daily dose of a material (dried brewers' yeast) known to contain several times the minimum adequate dose of the vitamin B complex required for normal growth is substituted for the daily dose of the test material under investigation. If the growth curve breaks upward with the feeding of the large dose of brewers' yeast, the given dose of the test material was inadequate for normal growth.

3. Dried brewers' yeast known to be stable for a period of at least three years is suggested as a physical standard of reference of assays for the vitamin B complex.

4. It has been found that 100 mg. of brewers' yeast, 300 mg. of bouillon cube and 1500 mg. of yeast cake are equivalent in vitamin B complex potency.

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THE COLORIMETRIC AND ELECTROMETRIC p_H DETERMINATIONS OF SOLUTIONS OF CERTAIN ALKALOIDAL SALTS.*¹

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A review of the literature reveals several reports of investigations on the determination of the hydrogen-ion concentration of solutions of alkaloidal salts. Evers (1) determined the colorimetric p_H values of solutions of the pure hydrochlorides of morphine, quinine and atropine and suggested the use of certain indicators which would give more accurate results in the titration of the corresponding free alkaloids. McGill (2), and later Wagener and McGill (3), using electrometric methods of measurement, obtained values for pure quinine, morphine, strychnine and atropine salts. Krantz (4), using a hydrogen electrode, determined the p_H values of pure quinine hydrochloride and also obtained data on the p_H values of quinine, strychnine and atropine dissolved in varying quantities of tenth-normal hydrochloric acid in excess.

Masucci and Moffat (5) reported electrometric values for many commercial samples of morphine, codeine, quinine, strychnine, atropine and caffeine salts. Wales (6) determined titration curves for various alkaloids and from these he obtained p_H values for pure salts. Based on the latter, he recommended the use of certain indicators to minimize titration errors. Finding great variations in commercial samples of alkaloidal salts, Eder (7) recommended the adoption of definite p_H limits for alkaloidal salt solutions. More recently, Mellon and Tigelaar (8)

* Abstracted from the thesis of Allen F. Peters, submitted to the Faculty of the Philadelphia College of Pharmacy and Science in partial fulfillment of the requirements for the degree of Master of Science in Chemistry. ¹ Scientific Section, A. P. H. A., Madison meeting, 1933.

compared the results of alkaloidal titrations using various indicators and constructed titration curves for atropine, strychnine and brucine.

As many of the measurements reported in previous investigations were obtained from titration curves the authors of this paper considered it advisable to prepare certain pure salts from the corresponding pure alkaloids and to determine electrometric and colorimetric values of solutions of the salts. The effect of dilution was likewise considered to be worth while investigating. The results obtained in a study of this kind would be of value in setting p_H standards for testing for the presence of excess acidity or alkalinity in alkaloidal salts.

EXPERIMENTAL.

Pure brucine sulphate, strychnine hydrochloride, strychnine sulphate, quinine sulphate and quinine sulphate were prepared by shaking a nearly saturated chloroform solution of the pure alkaloid with a quantity of the proper acid equivalent to approximately 75% of the alkaloid used. The concentration of acid was sufficiently high to produce precipitation of the alkaloidal salt in the aqueous solution. After filtration on a Büchner funnel, the salt was successively washed with chloroform, alcohol and water. The residue was recrystallized from hot water, filtered, washed with water and dried between filter papers.

Quinine bisulphate, quinine hydrochloride, quinine and urea hydrochloride and quinine hydrobromide were purified by repeated crystallization of commercial samples.

The indicators listed in the tables were those which could be most easily matched with the standards. Although slight precipitation was observed with certain solutions in the higher concentration range, the matching of colors was easily made.

The results given for the electrometric determinations were calculated from electromotive force measurements of quinhydrone and tenth-normal calomel electrode combinations. In the case of the higher concentrations of alkaloidal salt, the electromotive force measurements did not attain equilibrium, hence no p_H values are given in the tables. While the cause of the instability of the potential is not known, it is, perhaps, connected with the precipitation which occurs in all solutions upon the addition of quinhydrone. In the most dilute solutions the precipitation can be seen only with difficulty and the electromotive force remains constant within one or two millivolts, but with increasing salt concentration the precipitation becomes very noticeable and the potential too unsteady to measure. Measurements made with hydrogen electrodes were, in general, also unsatisfactory.

TABLE I.— p_H OF QUINIDINE SULPHATE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red).	Electrometric p_H .	Commercial Sample.
0.25	6.4	6.33	6.2
0.50	6.4	6.35	6.3
1.00	6.5	6.39	6.4

These values for quinidine sulphate are in good agreement with a value of 6.1 obtained by Wales (6) from titration curves for this salt.

In Table I and the following tables are set forth the results of the p_H determinations of pure salts as well as commercial samples. The water used in preparing the solutions was freshly distilled and was found to have a p_H of 6.2 when tested with isohydric chlorphenol red. Solutions made with distilled water of $p_H = 5.7$ as well as solutions through which carbon dioxide-free nitrogen was bubbled rarely differed by as much as 0.1 p_H unit from the values given in the tables.

TABLE II.— p_H OF QUININE SULPHATE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red).	Electrometric p_H .	Commercial Sample.
0.025	6.2	6.26	5.7
0.050	6.2	6.22	5.6
0.100	6.2	6.21	5.6

The values given in Table II are practically identical with the results obtained by Wales for quinine salts of strong acids, namely, 6.12.

TABLE III.— p_H OF QUININE HYDROBROMIDE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red).	Electrometric p_H .	Commercial Sample.
0.10	6.2	6.34	5.8
0.25	6.2	6.29	5.9
0.50	6.2	6.26	6.0
1.00	6.3	6.24	6.2
2.00	6.4	6.21	6.2

Here again the values are comparable with that given by Wales for quinine salts. It should be pointed out that the colorimetric values increase while the electrometric values decrease slightly with increasing salt concentration. The discrepancy, which is rather small, probably originates in the neglect of salt effects in both the electrometric and colorimetric methods, as well as the precipitation which occurs when quinhydrone is used.

TABLE IV.— p_H OF QUININE HYDROCHLORIDE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red).	Electrometric p_H .	Commercial Sample.
0.10	6.1	6.33	6.3
0.25	6.2	6.30	6.3
0.50	6.2	6.21	6.4
1.00	6.2	6.17	6.5
2.00	6.3	6.10	6.5
3.00	6.4	6.5
5.00	6.4	6.5

The corresponding values obtained by Krantz were 6.19 and 6.15 for 0.1% and 0.8% solutions, respectively, while McGill reported values of approximately 6.0.

TABLE V.— p_H OF QUININE BISULPHATE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (LaMotte Yellow).	Electrometric p_H .	Commercial Sample.
0.10	3.6	3.54	3.6
0.25	3.6	3.38	3.6
0.50	3.6	3.30	3.6
1.00	3.6	3.5
2.00	3.5	3.5
5.00	3.5	3.4

No values for quinine bisulphate are available for comparison but Evers reports a value of 3.40 for quinine dihydrochloride.

TABLE VI.— p_H OF QUININE AND UREA HYDROCHLORIDE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (LaMotte Yellow).	Electrometric p_H .	Commercial Sample.
0.10	3.6	3.62	3.6
0.25	3.6	3.51	3.6
0.50	3.5	3.40	3.6
1.00	3.5	3.30	3.6
2.00	3.5	3.6
5.00	3.5	3.6

TABLE VII.— p_H OF BRUCINE SULPHATE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red).	Electrometric p_H .	Commercial Sample.
0.10	5.6	5.74	7.5
0.25	5.5	5.70	7.6
0.50	5.4	5.63	7.7
1.00	5.3	5.52	...

For brucine salts Wales reports a value of 4.85.

TABLE VIII.— p_H OF STRYCHNINE HYDROCHLORIDE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red) (Methyl Red).	Electrometric p_H .	Commercial Sample.
0.50	5.6	5.62	6.1
1.00	5.5	5.42	6.2
1.50	5.4	5.35	6.2
2.00	5.3	5.16	6.3
2.50	5.3	5.12	6.3

Again Wales' value for strychnine, 4.81, is lower than the values given in this table. However, McGill (2) reports values of 5.45 and 5.42 for 0.002 and 0.02 normal strychnine solutions, respectively.

TABLE IX.— p_H OF STRYCHNINE SULPHATE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red).	Electrometric p_H .	Commercial Sample.
0.50	5.8	5.83	5.2
1.00	5.8	5.74	5.1
1.50	5.7	5.68	5.0
2.00	5.6	5.61	5.0

From an inspection of Table IX it is evident that a slight difference exists between the values for strychnine hydrochloride and strychnine sulphate. Whether or not the difference is real cannot be answered definitely.

CONCLUSIONS.

We have determined the electrometric and colorimetric p_H values of several pure alkaloidal salts. Because of the precipitation which occurs when quinhydrone is added to the solutions, it is recommended that the colorimetric method should be used for routine work in testing for acidity or alkalinity of the salts reported in this paper.

It has been found that, in general, the p_H values for a given salt solution are practically constant over a wide range of concentration.

For a given alkaloidal base, it has been found that variation of the anion produces little if any change in the p_H values of solutions of the salt, provided the anion is of the strong acid type.

It has been shown that the p_H values obtained from measurements of pure salt solutions are, in general, in good agreement with values obtained from titration curves.

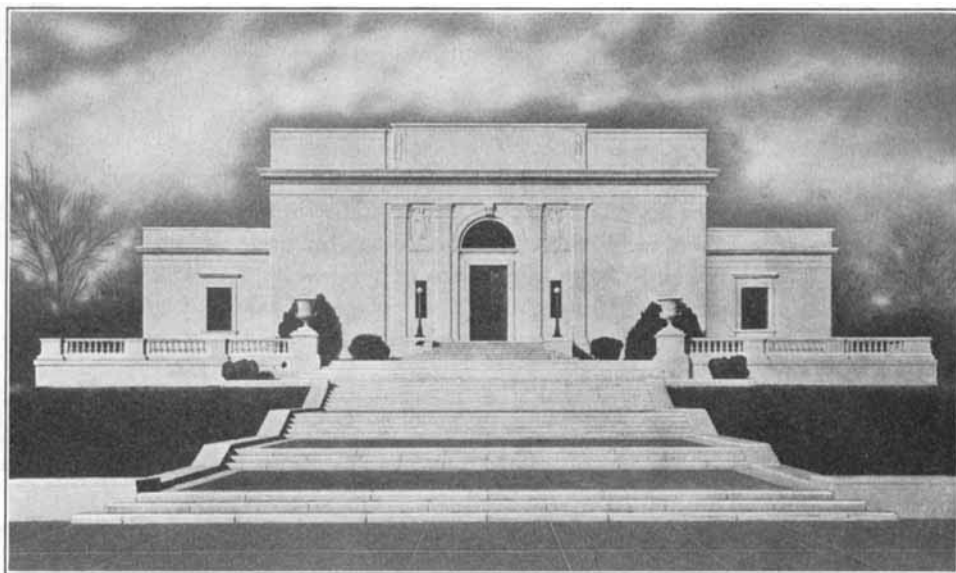
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NOTICE: RESEARCH WORKERS IN PHARMACY.

The returns for the 1934 census of Research in Pharmacy intended for publication are now being taken. If any research worker has not received a blank, or if returns have not been made by workers to whom blanks have been sent, it is requested that they immediately write to JAMES C. MUNCH, 40 North Maple Avenue, Lansdowne, Pa., sending their name, business address and the names of the specific problems, with their nature, which are being studied. In order to facilitate completion of this report it is urged that this information be sent at once.



The American Institute of Pharmacy.

To be dedicated during the week of May 7th. The landscaping has not been completed, but is well under way. The lighting fixtures outside are of bronze as are the main doors, each weighing 1000 pounds. Carved urns, exquisitely done out of a block of solid white marble, flank the main entrance. The panels on either side of the main entrance are indicative of pharmacy and its service.