JOURNAL OF THE

A STUDY OF MANDELIN'S TEST FOR STRYCHNINE.*

BY CHARLES F. POE AND DAVID W. O'DAY.

In general, many tests have been devised for the more common poisons. Strychnine, however, is an exception. There is practically but one class of color tests for strychnine. These tests depend upon the generation of oxygen in a concentrated sulphuric acid solution of the alkaloid. For the generation of oxygen one may use manganese dioxide, cerium oxide, lead peroxide, potassium dichromate, potassium ferrocyanide, ammonium vanadate, etc. When ammonium vanadate is dissolved in sulphuric acid, the test is termed Mandelin's test.

Since the chemical tests for strychnine are rather limited, and also since the test is very important in toxicology, it is extremely important that the limitations and the specificity of the test used for the detection of this alkaloid be well known. For the reasons given, it was decided to make a critical study of the color reactions for strychnine. The investigation to be reported in this paper deals with the detection of strychnine by means of Mandelin's reagent. When strychnine is treated with Mandelin's reagent a violet-blue coloration results, which soon changes to an orange-red, and finally to a yellow.

The experimental work has been carried out with the idea of determining the following points:

(1) Whether or not there are a large number of organic substances, other than strychnine, which will give the same reactions as strychnine with Mandelin's reagent.

(2) Whether the organic substances giving this test can be placed in any special groups, and whether the organic group or groups responsible for this test can be determined.

(3) Whether there are a large number of organic compounds which will interfere with the test and in what amounts they must be present for interference.

In selecting organic compounds for this study, an effort was made to include as many different groups and classes of organic compounds as were available. In the neighborhood of five hundred different organic compounds have been tested.

An ammonium vanadate-sulphuric acid solution, as a test for strychnine, was first proposed by Mandelin (1) in 1883. A few alkaloids besides strychnine will give color reactions with this reagent. According to Witthaus (2) the following alkaloids give strychnine-like reactions with this reagent: 1. Curarin gives about the same play of colors, but the appearance is very much delayed. Curarin, however, is not extracted with organic solvents in alkaline solutions. 2. Gelsemin produces a purple or red-violet color.

Self (3), in 1915, showed that yohimbine, an alkaloid obtained from the bark of *Corynanthe Johimbe*, gives the same purple with Mandelin's reagent as strychnine. However, upon dilution with water the purple color developed by strychnine changes to a beautiful rose-pink coloration, whereas with yohimbine no such color develops upon dilution.

Kundrat (4), in 1889, tested a number of alkaloids with Mandelin's reagent. He obtained distinctive colors with twenty-three of the common alkaloids. Besides with strychnine, he obtained a violet or violet-blue color with apomorphine and papaverin. We were able to confirm only a few of his tests, as will be discussed later on.

^{*} Scientific Section, A. PH. A., Rapid City meeting, 1929.

Efisio Mameli (5, 6), in 1911 and 1914, made a study of the influence of certain compounds employed in therapeutics on the Mandelin color reaction. He found a number of drugs which more or less interfered with the Mandelin color reaction. Mameli does not give the exact amounts of the drugs present as impurities. However, he concluded that, on the whole, the phenols, as well as the aromatic amines with their derivatives, show the greatest tendency to interfere with the characterization of strychnine by means of the Mandelin reaction.

Preparation of Mandelin's Reagent.—One part of finely ground ammonium vanadate was dissolved in 200 parts of cold chemically pure concentrated sulphuric acid.

Preparation of Standard Strychnine Solution.—A solution was prepared in alcohol containing one milligram per cubic centimeter.

Preparation of Solutions to Be Tested.—The compounds to be tested were dissolved in the proper solvent so that one cubic centimeter of the solution was equivalent to one mg. of the compound. Care was taken in selecting a suitable solvent which would both dissolve the compound readily and would volatilize on a water-bath. Substances which were relatively insoluble were finely ground and suspended in water or other solvents. The bottle was shaken before removing a portion of the contents to insure an even suspension of the substance to be tested.

Procedure of Test.—Three tests were made on each compound. For the first test one cubic centimeter of the solution to be tested was evaporated to dryness, and then tested with three or four drops of Mandelin's Reagent. If the color noted was yellow (the same color as Mandelin's Reagent), the test was termed "no reaction." In the second test one cubic centimeter of the solution to be tested and one cubic centimeter of standard strychnine solution were mixed and the test made as described above. If there was no interference, a blue-violet color resulted which soon changed to orange-red. If there was an interference in the color reaction, the colors resulting were recorded. The third test was carried out

 TABLE I.—Color Reactions Obtained When Different Alkaloids Were Tested with Mandelin's Reagent.

Alkaloid.	Authors' result.	Kundrat's result.	Alkaloid.	Authors' result.	Kundrat's result.
Aconitine	No	Cof'e-B	Nicotine	No	Darker
Apomorphine	Gr-bk to B-bk	V-bl to l bl	Physostigmine	No	G-Y carmine
Atropine	No	R to Y			to Y-B
Brucine	O-Y	Bl'd R	Pilocarpine	No	10
Caffeine	No	No	Piperidine	No	
Cinchonine	No	O tur'ng gr'nish	Piperine	R-B	R-B to bk-B
Cinchonidine	No		Quinidine	Y to 1 G	bl-G
Cocaine	No	0	Quinine	No	O to bl-G
Codeine	Y to caramel	G to B	Sanguinarine	Gr'nish B to	
Colchicine	G to gr'nish B	G to cof'e-B		dk B	
Emetine	Gr'nish B to B		Scopolamine	No	
Ergotine	No		Spartein	No	
beta-Eucaine	No		Solanine	Gr'nish B	
Homatropine	No		Theobromine	No	
Hydrastine	Red'sh B to B		Veratrine	B to red'sh B	B-R to R-V
Morphine	Gr-bk to B-bk	В			

Abbreviations: No reaction, No; B, brown; bk, black; O, orange; Y, yellow; G, green; Gr, grey; R, red; l, light; V, violet; bl, blue; P, pink; L, lavender.

as above except five cubic centimeters of the solution of the organic compound were used in place of one cubic centimeter.

A number of alkaloids were first tested with the reagent. These were of the highest purity that could be obtained on the market. The results are listed in Table I. There are also recorded the results of the tests as reported by Kundrat (4). It will be noted that in nearly every case this investigator obtained color reactions. A comparison with the results which the authors of this paper obtained show a great difference. The results of Kundrat may be accounted for by the probability of his having impure compounds.

In the pages immediately following, the results of the test with the organic compound alone will be given under the different groups of organic compounds. In order to conserve space the heading will be omitted after the first group. The name of the compound will be given, and immediately opposite will be given the color reactions. In cases where no color reactions were produced, the compounds will be listed with the statement: "No color reaction."

AMINO ACIDS AND DERIVATIVES.

Organic substances.	Color reaction.
Diiodotyrosine	Greyish black
Glycyltryptophane	Traces of purple to yellowish brown
Leucine	Greenish yellow
para-Nitropheny glycine	Dirty lavender to brown
alpha-Phenylalanine	Greenish yellow to blue- green
Phenylglycine	Lavender to brown
Tyrosine	Dirty green to greyish black
Tryptophane	Traces of purple

No Color Reaction.—Acetylphenylglycine, alpha-alanine, para-aminophenylglycine, arginine, asparagine, aspartic acid, *d-l*-benzoylalanine, betaine hydrochloride, creatine, creatinine, edestine, ethylglycollate, glutamic acid, glycine, hippuric acid, iso-leucine, beta-phenylalanine, *d-l*-valine.

ALIPHATIC ACIDS.

No Color Reaction.—Aconitic acid, adipic acid, d-l-alpha-aminoacetylacetic acid, alphabromopropionic acid, beta-bromopropionic acid, formic acid, fumaric acid, lævulinic acid, maleic acid, malic acid—active 1, malonic acid, mesaconic acid, mucic acid, palmitic acid, stearic acid, succinic acid, tartaric acid, tartronic acid, trichloracetic acid.

ALIPHATIC ACID SALTS, ESTERS AND DERIVA-TIVES.

No Color Reaction.—Ethyl oxalate, ethyl succinate, iso-amyl propionate, iso-butyl ace-

tate, iso-butyl iso-thiocyanate, methyl isothiocyanate, sodium formate, sodium oxalate, succinimide, thallous formate, thallous malonate, triacetin, tributryn.

ALIPHATIC ALCOHOLS AND DERIVATIVES.

No Color Reaction.—Cetyl alcohol, dulcitol, erythritol, ethylene glycol, iso-butyl alcohol, iso-propyl alcohol, mannitol, melissyl alcohol, octyl alcohol, trichlorbutyl alcohol.

ALIPHATIC,	AROMATIC	AND	MIXED	KETONES
pa <mark>ra-Am</mark> ido phenone	aceto-	Dark t	orown	
Benzalaceto	phenone	Greeni	sh yello	w
Tetramethy benzophe	ldiamido- none	Caram green	el to 1	yellowish

No Color Reaction.—Acetylacetone, benzalacetone, benzophenone, methylacetophenone, methylheptenone, phorone.

MISCELLANEOUS ALIPHATIC COMPOUNDS.

Chitin	Brown		
Oenanthol	Greenish	yellow	to
	brownis	h green	

No Color Reaction.—Acetal, acetaldoxime, acetamide, acetoxime, aldehydeammonia, aminoguanidine bicarbonate, bromoform, chloral urethane, chloropicrine, dimethylglyoxime, guanidine hydrochloride, hexachloroethane, hexamethylenetetramine, iodoform, iso-butylbromide, iso-euginol, methylglyoxal, sodium bisulphite, monochlorhydrin, nitrosodiethylamine, oxamide, pinakon hydrate, propionamide, sulphonal, tertiary butyl bro-

1295

mide, thialdine, tribromohydrin, trichloroacetyl chloride, trimethylene bromide, trional, veronal.

ANILINE AND ANILINE DERIVATIVES.

Benzanilide	Purple quickly changing to dirty light brown
para-Bromoacetani- lide	Light caramel
para-Bromoaniline	Streaks of lavender to greyish brown
p ara -Nitroaniline	Light brown to red- brown
para-Nitrodimethyl- aniline	Yellowish brown
Nitrosodimethyl- aniline	Dark green

No Color Reaction.—Aniline, ortho-bromoaniline, meta-bromoaniline, ortho-chloroaniline, meta-chloroaniline, para-chloroaniline, 1-2-4dichloroaniline, 2-5-dichloroaniline, 1-2-4dinitroaniline, exalgine, meta-nitroaniline, meta-nitrodimethylaniline, tribromoaniline, trinitroaniline.

AROMATIC ACIDS.

Acetylsalicylic acid	Greenish brown to green
Anisic acid	Greenish brown tinged with purple
Anthranilic acid	Yellowish green to brownish yellow
Arsanilic acid	Yellow to caramel
Benzilic acid	Purple to purplish red
Cinnamic acid	Yellow to brown tinged with lavender
Cumaric acid	Lavender to light brownish green
Diiodosalicylic acid	Yellowish green
Diphenylacetic acid	Blue-green to dark green
Gallic acid	Brown
5-Iodosalicylic acid	Light brown to caramel
Mandelic acid	Dark greenish brown to brown
Naphthionic acid	Greenish yellow to caramel
Phenylcinchoninic acid	Pinkish to brown
Salicylic acid	Light brown to yellow- ish green
Tannic acid	Pinkish brown to light brown

No Color Reaction.—Metanilic acid, terephthalic acid, ortho-toluic acid, para-toluic acid.

AROMATIC ACID DERIVATIVES.

No Color Reaction.—Benzamide, benzoic anhydride, cinchophen, cumarine, neocinchophen (ethyl-6 methyl-2 phenyl quinoline 4 carboxylate), nicotinic acid nitrate, metanitrobenzoyl chloride, paranitrobenzoyl chloride, phthalimide, ortho-tolunitrile, paratolunitrile.

AROMATIC ACID ESTERS.

Benzyl benzoate	Dark brown to brown-
	black
Phenyl salicylate	Yellowish green, blue-
	green to dark green

No Color Reaction.—Butyl benzoate, ethyl benzoate, ethyl salicylate, iso-amyl benzoate, iso-amyl salicylate, iso-butyl benzoate, methyl benzoate, methyl cinnamic ester, methyl salicylate.

AROMATIC ALDEHYDES, AROMATIC ETHERS AND MIXED ALCOHOLS.

Benzhydrol	Orange-red to brownish red
5-Nitrosalicylalde- hyde	Dark green to blue- green
Piperonal	Yellow to greenish yellow
Salicylaldehyde methylether	Reddish purple to brown
Saligenin	Light purplish red to brown
para-Tolylaldehyde	Light purplish red quickly changing to yellow
Vanillin	Green-grey to grey- black

No Color Reaction.—Anisaldehyde, orthobromonitrobenzaldehyde, *1-2-5*-bromosalicylaldehyde, iso-phthalaldehyde, meta-methoxysalicylaldehyde, ortho-nitrobenzaldehyde, salicylaldehyde.

AROMATIC AMINES AND DERIVATIVES.

Acetyl-para-anisidine	Dirty greenish grey
Acetylphenetidin	Greenish brown
meta-Acetxylidine	Pinkish brown to grey
meta-Anisidine	Greenish brown to cara- mel
ortho-Anisidine	Greenish yellow with tinge of purple
ortho-Benztoluid	Reddish purple to dirty grey

para-Benztoluid	Old rose to pinkish brown
ortho-Phenetidine	Dirty bluish purple
para-Phenetidine	Brown with streaks of purplish blue
Phenyl-beta-di- phenylamine	Brownish yellow to caramel

No Color Reaction.—Para-anisidine, 1-2-4-xylidine, 1-3-4-xylidine.

BENZENE AND TOLUENE DERIVATIVES.

Azoxybenzene	Greenish brown to red-
	dish brown
Styrole	Greyish green

No Color Reaction.—Para-bromochlorobenzene, ortho-bromonitrobenzene, chloramine, metachloronitrobenzene, ortho-chloronitrobenzene, para-chloronitrobenzene, para-chlorotoluene, orthodichlorobenzene, 2-5-dichloronitrobenzene, iodosobenzene, iso-propylbenzene, ortho-nitroacet-meta-xylidide, metanitrotoluene, ortho-nitrotoluene, para-nitrotoluene, mesitylene.

BENZOIC ACID DERIVATIVES.

No Color Reaction.—Meta-aminobenzoic acid, para-aminobenzoic acid, meta-bromobenzoic acid, ortho-bromobenzoic acid, parabromobenzoic acid, meta-chlorobenzoic acid, ortho-chlorobenzoic acid, para-chlorobenzoic acid, para-mercurichlorobenzoic acid, orthonitrobenzoic acid, meta-nitrobenzoic acid, para-nitrobenzoic acid.

CRESOL AND CRESOL DERIVATIVES.

5-Benzalamino-2cresol Greenish black to greyish black

No Color Reaction.—Meta-cresol, orthocresol, para-cresol, *3-5*-dibromo-ortho-cresol, tetrabromo-*o*-cresol.

GLUCOSIDES.

Aesculin	Purple to dirty brown
Amygdalin	Yellowish green
Arbutin	Brown with tinge of
	purple to brown-black
Salicin	Reddish violet to purple

HETEROCYCLIC COMPOUNDS.

Antipyrine	Dark blue-green to light
	green
Isatin	Brown

No Color Reaction.—Acridine, dimethylpyrone, furoic acid, 6-nitroquinoline, oxyquinoline, quinaldine, skatole.

HYDROAROMATIC COMPOUNDS.

d-l-Camphor (natu-	Dark brown	
ral)		
Carvene	Light brownish	yellow
	to brown	

No Color Reaction.---d-Borneol, d-l-camphor (synthetic), camphoric acid, camphorsulphonic acid, carvenone, limonene, menthol, quercite, terpinol, terpinyl acetate.

NAPHTHALENE AND ANTHRACENE DERIVATIVES.

Acet-alpha-naph- thalide	Grey-black
Acet-beta-naph- thalide	Dirty green to greenish brown
Alizarin	Reddish purple to blood-red green
alpha-Naphthylamine	Dark green to bluish black
beta-Naphthylamine	Greenish brown to brown
alpha-Naphthylamine azobenzene	Purple and greenish black
beta-Naphthalene- sulphonic acid sodium salt	Grey-green to grey-black
beta-Naphthalene- sulphonic acid	Dark grey to grey-black
beta-Naphthol	Dark brownish green to brownish black
beta-Naphthylamine	Dark grey to brownish black
alpha-Naphthyl iso-cyanate	Green to dark green
Nitroso-beta-naphtho	Green to brownish

No Color Reaction.—Alpha-bromonaphthalene, 1-5-dinitronaphthalene, naphthalic anhydride, naphtholmethyl-alpha-ether.

PHENOLS AND PHENOL DERIVATIVES.

Acetyl-meta-amino-	Greenish brown to olive
phenol	green
Acetyl-para-amino- phenol	Dirty green to greenish brown
para-Aminophenol	Greenish blue to dark blue
para-Benzalamino- phenol	Dirty grey-black

ortho-Chloromer-	Green to dark green
curiphenol	
2-4-Dinitrophenol	Green to greenish yellow
meta-Nitrophenol	Dark blue-green to tan
para-Nitrophenol	Dark bluish green

No Color Reaction.—Anisol, ortho-bromanisol, para-bromanisol, para-bromophenol, ortho-chlorophenol, para-chlorophenol, 2-4dichlorophenol, 2-3-dinitrophenol, 2-6-dinitrophenol, para-nitroanisole, ortho-nitrophenol, phenetole, tribromophenol, trichlorophenol.

POLYHYDRIC PHENOLS AND OTHER PHENOL DERIVATIVES.

Benzoylthymol	Pinkish brown to dark brown
Carvacrol	Light brownish yellow to brown
Catechol	Green to dark green
Orcinol	Light caramel to brown
Phloroglucinol	Green to blue-green
Pyrogallic acid	Brownish black

No Color Reaction.—Dimethylhydroresorcinol, picric acid, thymol, xylenol.

SUGARS.

Rhamnose	Yellow	to	light	blue-
	green			

No Color Reaction.—Arabinose, galactose, glucose, lactose, levulose, d-mannose, melizitose, raffinose, sucrose, xylose.

THIOURBA AND THIOUREA DERIVATIVES.

Allyl thiourea	Greenish yellow	
d-l-n-Butyl thiourea	Yellow to orange-pink	
Diphenyl thiourea	Dark green to dirt	у
	grey-brown	

No Color Reaction .--- Thiourea.

TOLUIDINE AND TOLUIDINE DERIVATIVES.

Acetyl-ortho-toluidine	Light	lavende	r-pi	nk	to
	dirt	y green			
Acetyl-para-toluidine	Pink-l pink	avender c	to	dir	ty
Toluidine	Yellow	vish brov	vn		

No Color Reaction.—Acetyl-ortho-methyltoluidine, acetyl-para-methyltoluidine, 1-2-3nitrotoluidine, 1-2-4-nitrotoluidine, 1-3-4-nitrotoluidine, ortho-toluidine.

UREA	DERIVATIVES,	URIC	ACID	AND	URIC	ACID
DERIVATIVES.						

Ipral (calcium ethyl- Yellow to yellow-green isopropyl barbiturate)

- Peralga (amidopyrine Brown to green diethyl barbiturate) Phenylethylbarbituric Yellow to light green
- acid Thiobarbituric acid Light blue-green
- Uric acid Greenish yellow

No Color Reaction.—Amytal (iso-amylethylbarbituric acid), acetylmethylurea, allantoin, alloxantin, barbital, barbituric acid, biuret, dibromobarbituric acid, guanine hydrochloride, urethane.

MISCELLANEOUS AROMATIC COMPOUNDS.

Allylphenylthiocar- bamide	Light purple quickly changing to light grey
para-Amidazobenzene	Green to brown
Benzil	Green
Benzoin	Brown to dark green
Benzylphenylhydra-	Streaks of pinkish
zine hydrochloride	lavender to yellow
2-4-Dinitrophenyl-	Greenish yellow
hydrazine	
Fluorene	Blue-green to dark green
Isoamylphenyl-	Dirty purple quickly
hydrazine	changing to brown
meta-Nitrobenz-	Yellow to yellowish
hydrazide	green
para-Nitrophenyl-	Light greenish brown
nydrazine	
Phenanthrene	green to dark
Phenanthrenequin-	Dirty violet-blue to
one dioxide	reddish brown
Phenolphthalein	Orange outlined with purple-red
meta-Phenylenedi- amine hydrochlo- rate	Yellowish brown
Phenylhydrazine hy- drochloride	Blue-green
Tetrabromophenol- phthalein	Purple to brown
Thymolphthalein	Purplish red to brown
Triphenylguanidine	Purplish blue streaks with green to brown
Triphenylmethane	Brown with traces of purple

No Color Reaction.-Diphenyl, nitrobenzyl Rheumatine Brownish green to green chloride, para-toluquinoline sulphate, para-Salvarsan Purplish black toluthioquinanthrene. Saponine Caramel to dark brown Thiosemicarbazide Light blue-green Turmeric Yellow and pink-purple MISCELLANEOUS COMPOUNDS----NOT GROUPED to brown Abietic acid Brown No Color Reaction -Allyl thiocarbamide, Amarine Greenish blue to greyish black santonin.

The color reactions for the tests, where an equal amount of impurity and also those where five times the amount were added to the strychnine, were recorded, but the listing of these would require too much space. Therefore, only those where the violet-blue was completely masked will be given. Reference can be made to the list of substances previously given to obtain the names of the compounds which did not completely cover up the strychnine test. Many of these gave no interference, while others gave more or less interference.

Organic compounds which completely covered up the strychnine test when present in equal amounts:

Acetylsalicylic acid, 5-iodosalicylic acid, salicylic acid, beta naphthol, pyrogallic acid, diphenyl thiourea, and amarine.

Organic compounds which completely covered up the strychnine test when present in amounts five times that of the strychnine:

Apomorphine, colchicine, tryptophane, benzalacetophenone, acetylsalicylic acid, diiodosalicylic acid, diphenylacetic acid, gallic acid, 5-iodosalicylic, salicylic acid, tannic acid, 5-benzalamino-2-cresol, acet-beta-naphthalide, acet-alphanaphthalide, alpha-naphthylamine, betanaphthalenesulphonic acid, beta-naphthol, beta-naphthylamine, acetyl-meta-aminophenol, acetyl-para-aminophenol, para-aminophenol, para-benzalaminophenol, ortho-chloromercuricphenol, catechol, orcinol, phloroglucinol, pyrogallic acid, allyl thiourea, diphenyl thiourea, tolidine, thiobarbituric acid, amidazobenzene, phenylhydrazine hydrochloride, triphenylguanidine, abietic acid, amarine, rheumatine, and thiosemicarbazide.

From a study of the preceding data, we find that there are a number of organic compounds which give various shades of violet, lavender or purple, which might be mistaken for the strychnine test.

In general, the compounds giving a similar strychnine test do not belong to any definite group of organic compounds, nor does any special group seem to be responsible for the characteristic test. However, the characteristic test was not given by any of the aliphatic compounds tested.

There were very few organic compounds which completely covered up the strychnine test when present in small amounts, but when present in amounts five times greater than the strychnine, we find many interferences. Of course, in a carefully conducted examination for strychnine most of the foreign organic substances will be removed by means of different organic solvents.

CONCLUSIONS.

1. A large number of organic compounds have been tested with Mandelin's Reagent. A number have been found to give color reactions similar to strychnine.

2. The interference of organic compounds with Mandelin's test for strychnine have been determined when present in small and large amounts.

3. In toxicological work too much dependence should not be placed in the color reactions for strychnine. The test should be checked by the crystalline form, taste and physiological action.

REFERENCES.

(1) Mandelin, Phar. Zeit. für Russland, 22 (1883), 345; Jahr. der Pharm., Pharmacog. und Toxicologie (1884), 766.

(2) Witthaus, "Manual of Toxicology," 2nd Edition (1911), 1056-1067.

(3) P. A. W. Self, Pharm. J., 94 (1915), 384, 419.

(4) Kundrat, Z. anal. Chem., 28 (1889), 709; Chem.-Zig., 13, 265.

(5) Efisio Mameli, Gazz. chim. ital., 41 (1911), 329.

(6) Efisio Mameli, Boll. chim. farm., 53 (1914), 366.

DEPARTMENT OF CHEMISTRY AND COLLEGE OF PHARMACY, UNIVERSITY OF COLORADO, BOULDER.

A POTENTIOMETRIC ASSAY OF CINCHONA.

BY JOHN C. KRANTZ, JR.*

INTRODUCTION.

The assays of cinchona bark and its preparations have been studied comprehensively by various investigators. A very complete survey of the various methods of evaluating this drug is given by Dubreuil (1). This investigator favors the iodometric method of estimating the alkaloidal residue, as he claims it gives the most satisfactory results. McGill (2) applied electrical titration methods to the assay of this drug and obtained concordant results. The same method was applied to nux vomica and belladonna by McGill and Wagener (3) with an equal degree of success. In this work McGill and his associates (4) were able to eliminate the shaking out process. Very recently Maricq (5) applied the potentiometric titration to the estimation of alkaloidal residues. An excess of a solution of mercuric hydrogen iodide is added and the alkaloid is precipitated with the liberation of an equivalent quantity of hydrogen iodide. In a portion of the filtrate the hydrogen iodide is estimated potentiometrically using a mercuric chloride solution.

In a previous communication to THIS JOURNAL, the author (6) showed that it was possible to determine the quantity of alkaloid present in a solution, the hydrogen-ion concentration of the solution having been determined. From this datum the amount of alkaloid present was calculated.

It is the purpose of this present investigation to apply this method to the evaluation of cinchona alkaloid residues.

EXPERIMENTAL.

Method of Preparing Graph.—In the Pharmacopœial assay of cinchona bark the final extraction of alkaloids represents 4 Gm. of drug. A drug containing 7 per cent of alkaloids would yield 280 mg. of alkaloids. Using 0.0309 as the volumetric equivalent of these alkaloids in terms of 0.1N acid, 9.06 cc. of acid would

^{*} Scientific Section, A. PH. A., Baltimore meeting, 1930.