definite endothermal reaction. Apparently the caramelization of any quantity of sugar can be readily controlled by temperature readings in the mass.

The senior author is continuing the investigation of this point, as well as the standardization of caramel preparations.

URBANA, ILLINOIS,
JULY 1923.

ELECTROMETRIC ASSAY METHODS FOR CRUDE DRUGS. II.*

BY WILLIAM JAMES MCGILL AND LEONARD RANSOM WAGENER.

It has already been pointed out by one of the authors[1] as well as by others,[2] that the indicators at present recommended by the U. S. P. for alkaloidal titrations have been chosen with little regard for the conditions involved in such titrations. The inaccuracies resulting from their use are of relatively small magnitude, and yet if the Pharmacopœia is to be accepted as a compilation of scientific standards, the requirements contained therein should be as rational as is consistent with practicality. Adoption of the proper indicator for official acidimetric titrations can work hardship on no one; the replacement of the litmus paper test for the alkaloidal salts would give more uniform products than are now on the market. In some of our preliminary work on the p_H values of various alkaloidal salts, samples from different lots were found to vary greatly in this respect, although all of them conformed with the U. S. P. litmus paper test. More accurate determinations made possible by the substitution of a Leeds and Northrup type K potentiometer for our earlier portable set-up, have given practically the same results.

We have also previously emphasized the advantages to be gained by the substitution of electrometric methods in the assay of crude drugs, replacing the tedious percolation or shaking-out methods. Admittedly, electrometric crude drug assays give only "proximate" results, which is true of any method we may employ. Actually, the electrometric method of titration gives results closer to the truth than the indicator method.

Much of the literature found in the journals on the determination of hydrogen-ion concentration we believe to be of little value, because the work so reported seems to have been done without any very clear conception of the theoretical considerations underlying the behavior of aqueous solutions of electrolytes or of the apparent anomalies in the behavior of such solutions. For example, the "neutral salt" effect on the end-point of an electro-titration has not been precisely determined, and it is conceivable that there are factors which influence the true end-point in titrating an alkaloidal residue and whose influence cannot be easily formulated so that our results can be accordingly corrected. The very short method of preparation and purification which we employ admittedly retains some of the inert extractive of the crude drug in the residue to be dissolved and titrated. The only criteria

---

* Scientific Section, A. Ph. A., Asheville meeting, 1923.

[1] McGill and Faulkner, JOUR. A. PH. A., 11, 1003, 1922; McGill, *J. A. C. S.*, 44, 2156, 1922.

[2] Evers, *Pharm. J.*, 470, 1921; Masucci and Moffet, JOUR. A. PH. A., 12, 609, 1923.

by which the results obtained by our method can be judged are the exactitude with which they agree among themselves, and their relation to results obtained with other methods. We have already shown in the case of cinchona that, judged from both of these viewpoints, the verdict must be in favor of the electrometric assay, with the further advantage of the shortness of time which the latter method requires.

We have now applied the electrometric method to the assay of three other drugs, namely: nux vomica, belladonna, and opium. In the case of the latter, the electrometric assay involves an application of shaking-out methods to this drug which in turn required considerable study of the various immiscible solvents for morphine. The assay of opium will consequently be discussed in a later paper as will also the determination of the alkaloids of red cinchona.

ELECTROMETRIC ASSAY OF NUX VOMICA.

Method.—15 Gm. of the powdered drug are macerated with immiscible solvent and ammonia water, as in the U. S. P. IX method, except that chloroform may be advantageously substituted for the usual mixture of chloroform and ether. At the end of the prescribed maceration period, an aliquot portion is decanted into a 125-cc Soxhlet flask and the solvent evaporated to almost complete removal. From 15 to 25 cc of neutral alcohol are added to soften the fatty residue. The whole is well mixed with a glass rod, and 1 cc of $N/10$ acid added for every gram of drug represented in the aliquot portion taken. The whole is then rinsed into a 400 cc beaker, or a three-necked titration flask with distilled water, the total final volume amounting to 150 to 200 cc preferably. $N/50$ alkali is used in the titration, the end-point coming at p_H 5.44.

The results obtained by the method follow:

	Electrolytic method. Per cent.	U. S. P. method Per cent.		Electrolytic method Per cent.	U. S. P. method, Per cent.		Electrolytic method. Per cent.	U. S. P. method. Per cent.
Sample 1	2.31	2.21	Sample 2	1.94	1.90	Sample 3	2.09	2.08
	2.39	2.26		1.92	1.88		2.12	2.04
	2.32	2.20		1.95	1.92		2.12	2.09
	2.27	..		..	..		..	..

Nux vomica was selected because of the large amount of fatty matter which it contains, and which conceivably might exert an effect on the electro-titration. It is apparent from the results that this is not the case to any measurable extent. The slightly larger percentage of alkaloids found by the electrometric method was to be expected since the use of methyl red or cochineal as an indicator in titrating nux vomica alkaloids, introduces a small negative error. The avoidance of mechanical loss which is an inevitable concomitant of the shaking-out method also would lead to higher and consequently more accurate results.

ELECTROMETRIC ASSAY OF BELLADONNA.

Method.—Exactly the same procedure was utilized for the preparation of the sample of crude drug as in the case of nux vomica, except that 0.5 cc of $N/10$ acid per gram of drug represented in the aliquot portion decanted, is used. The end-point is reached at p_H 3.84.

Results:

	Electrometric method. Per cent.	U. S. P. method. Per cent.		Electrometric method. Per cent.	U. S. P. method. Per cent.		Electrometric method. Per cent.	U. S. P. method. Percent.
Sample 1	0.29	0.26	Sample 2	0.14	0.12	Sample 3	0.21	0.17
	0.26	0.20		0.18	0.13		0.24	0.20
	0.30	0.24		0.15	0.14		0.18	0.20
	..	..		..	0.10		..	..

Again the electrometric method gives on the average higher results, which theoretically should be more accurate since the use of methyl red or cochineal as an indicator in titrating the mydriatic alkaloids introduces a considerable negative error, while the mechanical losses of the shaking-out process are also avoided.

SUMMARY.

1. Evidence adduced by other workers is cited to emphasize the contention previously made by the authors for a more rational selection of indicators in alkaloidal titrations.

2. Electrometric assay processes are given for nux vomica and belladonna and the advantages of these in time and accuracy reiterated.

FOOD AND DRUG LABORATORY,
UNIVERSITY OF MICHIGAN,
ANN ARBOR, MICHIGAN.

THE TITRATION OF FERRIC CHLORIDE WITH SODIUM HYDROXIDE, USING THE OXYGEN ELECTRODE: A PROOF OF THE NON-EXISTENCE OF IRON OXYCHLORIDE.*

BY R. B. SMITH AND P. M. GIESY.

The National Formulary refers to iron oxychloride, but chemical literature indicates that this is not a definite chemical compound. Solutions have been prepared containing as low as 1 atom of chlorine to 22[1] or 31[2] atoms of iron.

It appeared to be of interest to investigate the curve of the precipitation of ferric hydroxide with sodium hydroxide to determine if there was any indication of the existence of a basic salt.

The hydrogen electrode was first tried but, as had been foreseen, the electrode was poisoned by the ferric chloride and gave only the oxidation-reduction potential of the solution. The oxygen electrode is not objectionable in this respect and while it was realized that it would not measure true hydroxyl ion concentrations, yet the results obtained are so internally consistent that they have justified the use of this method.

A ferric chloride solution was made up from the C. P. salt and standardized by adding nitric acid to a measured volume, evaporating and igniting. The amount of this solution, 84.75 cc, which would be exactly equivalent to 50 cc of $M/3$ solution, was placed in a 250-cc beaker, which was connected by a saturated KCl bridge to a calomel half cell. Normal sodium hydroxide was added in small

* Scientific Section, A. Ph. A., Asheville meeting, 1923.

[1] Malfitano, *Zeitschrift für Physikalische Chemie*, 68, 232, 1909.

[2] Browne, *J. A. C. S.*, 45, 298, 1923.