pletely precipitated. Filter through a small Büchner funnel connected as in Fig. 1 and previously prepared by fitting in a filter paper and overlaying with a thin layer of asbestos filter media. Wash the precipitate with three 15-cc portions of H_2O containing 1% NH_4S and 1% NH_4Cl. Disconnect flask, discard filtrate, rinse flask and reconnect to funnel. Pass five 15-cc portions of hot 10% H_2SO_4 through the funnel, disconnect and boil filtrate until free from H_2S (shown by the vapors not darkening a piece of filter paper moistened with lead acetate solution). Cool and titrate with $N/10$ $KMnO_4$.

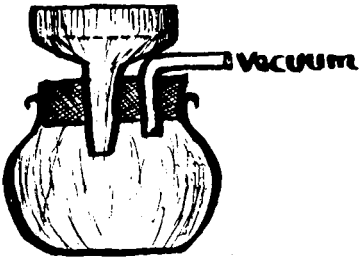

Fig. 1.

A number of preparations were assayed giving results that checked well, but as no other good checking method was available and as the actual iron content was not known, it was thought advisable to repeat the experiments using preparations made by dissolving exact amounts of iron of known purity in the required acids, etc., and then adding the other ingredients.

For the sake of convenience in tabulating and comparing, the iron content in all the liquids was made at one percent instead of the percentage required by formulas.

RESULTS OBTAINED.

	Percent actual.	Percent found.
Solution of Ferric Hypophosphite	1.000	1.005
	1.000	1.005
Elixir Ferric Phosphate	1.000	1.010
	1.000	1.005
Syrup Iron and Manganese Iodide	1.000	1.016
	1.000	1.010
Beef, Iron and Wine	1.000	0.980
	1.000	0.988
Pills of Ferrous Iodide (1 pill)	0.0400 Gm.	0.0405 Gm.
	0.0400 Gm.	0.0410 Gm.

SUMMARY.

An assay has been outlined for the determination of iron in pharmaceutical preparations, which in a number of analyses gave an error not exceeding 0.002 gram.

The time required by the writer, to complete one analysis, was 25 minutes, six analyses having been completed within an hour.

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THE ASSAY OF SALICYLIC ACID AND OFFICIAL SALICYLATES.*

BY ABRAHAM TAUB AND HARRY TAUB.

The present U. S. P. assay of the alkali salts of organic acids having in certain cases proved unsatisfactory, as reported from many authoritative sources, the authors undertook, at the suggestion of Dr. H. V. Arny, Chairman of the Sub-Committee on Inorganic Chemicals, U. S. P. Revision Committee, a study of the

* Read before New York State Pharmaceutical Association meeting, 1922.

relative merits of those methods at present in vogue, with a view of obtaining a method that might be adopted in the next United States Pharmacopoeia. The method, to be suitable for the needs of the U. S. P., should be fairly accurate, rapid and simple. The present investigation was taken up with regard to salicylic acid and salicylates only.

An examination of the bibliography of the subject showed that nearly all of the assay methods fall within the following six groups.

(1) Colorimetric.
(2) Conversion into inorganic sulphates or chlorides by ignition with H_2SO_4 or HCl.
(3) Weighing or titration of liberated organic acid following its extraction with a volatile solvent.
(4) Gravimetric iodine or bromine methods.
(5) Volumetric methods involving iodine.
(6) Volumetric methods involving bromine.

The few miscellaneous assays included one dependent upon the insolubility of crystals of calcium salicylate.[1] However, this does not give strictly quantitative results. Another assay for bismuth salicylate[2] was not investigated, since the present U. S. P. assays this salt for it Bi_2O_3 content.

1. Regarding colorimetric assays[3]—their only value lies in the detection of traces of salicylic acid, as when present as adulterant in foods, aspirin, etc. The presence of free mineral acids, benzoic acid and other substances greatly affects the accuracy of the method.

2. Methods based upon the ignition of salicylate as sulphates or chlorides by treatment with the appropriate acid. Lyons[4] points out that this method is open to the objection that any inorganic impurities present in the original salt will give high results due to their presence in the ash.

3. Assays in which salicylic acid is liberated from its salt, extracted with chloroform and then titrated,[5] although theoretically excellent do not work out satisfactorily when tried out on commercial samples. The presence of benzoic or cinnamic acids or their salts in the original samples is not excluded in this method of assay. Where the liberated salicylic acid is weighed instead of titrated after extraction, the results may be either too high or too low. If a low temperature is used in vaporizing the volatile solvent, some of the latter always remains behind. If too high a temperature is employed a little salicylic acid is lost.

4. Among the gravimetric assays are the following:

The method of W. Autenreith and F. Beuttel[6] depending upon the formation of tribromphenolbromide requires much time. The precipitate of the latter compound is kept on ice for six hours and then dried under reduced pressure before weighing. It does not yield accurate results.

Bougault[7] was the first to utilize iodine in the gravimetric determination of salicylic acid, the resulting product being diiodophenylene oxide, $C_6H_2I_2O$. This

[1] Ewell and Prescott, *Analyst*, 13, 208, 1888.
[2] Kollo, PROC. A. PH. A., 47, 719, 1899.
[3] Muter, *Analyst*, 1, 193, 1877.
[4] JOUR. A. PH. A., 7, 603, 1918.
[5] Ehman, *Ibid.*, 2, 156, 1913.
[6] *Arch. Pharm.*, 248, 112, 1910.
[7] *J. pharm. chim.*, 28, 45, 1908.

method was tried out by the authors and was found to give variable results. However, a recent modification of the above, by W. O. Emery,[1] proved to be satisfactory.

The following 5 assays were carried out by this method:

0.4 Gm. salicylic acid was neutralized with $N/10$ NaOH and made up to 200 cc solution. Weight of precipitate × .4012 = Gm. salicylic acid.

No. of cc of solution.	Gm. salicylic acid.	Weight of precipitate Gm.	Per cent salicylic acid.
25	.05	.1244	99.82
25	.05	.1240	99.50
20	.04	.0993	99.80
20	.04	.0990	99.50
20	.04	.0990	99.50

Since the Emery method is rather lengthy and gives variable results unless strict attention is paid to the many details, as was found out by making slight deviations from the directions, the present authors considered the method unsuitable for the U. S. P., and would fall back upon it only in the event that a simpler method could not be found.

5. Volumetric methods in general are the ideal methods from the standpoint of the Pharmacopoeia and therefore the present authors spent the greater part of their time in investigating these.

Messinger and Vortmann[2] as far as we could find were the first to employ iodine volumetrically in the assay of salicylic acid. This method, with many modifications, was tried out by Seidell[3] and found to give very unsatisfactory results. Experiments conducted by the present authors gave results ranging from 88.5% to 109.2% for a U. S. P. sample of salicylic acid, thereby confirming Seidell's observations. The outstanding flaws of this method are that the amount of NaOH employed can be varied only within narrow limits, which would necessitate having a previous knowledge of the percentage salicylic acid in the sample. Likewise the amount of $N/10$ iodine in excess is an important factor in giving variable results.

Wilkie[4] has submitted a modification of the above iodine method in which he adds the $N/10$ iodine before the NaOH. Seidell, however, finds it unsatisfactory when tried out on thymol.

6. Bromine volumetric methods have their supporters and adversaries. W. Fresenius and L. Grünhut[5] found the original bromate method of Freyer[6] gave fair results. Seidell[7] gets varying results with the same method. Instead he proposes a rather cumbersome method, using bromine vapor and forming dibromosalicylate.

Jones[8] in an article on the assay of sodium salicylate uses Koppeschaar's solution, letting it stand for 15 minutes with the sodium salicylate before titrating.

[1] *J. Ind. Eng. Chem.*, 13, 538, 1921.
[2] *Ber.*, 23, 2753, 1890.
[3] *Jour. Am. Chem. Soc.*, 31, 1168, 1909.
[4] *J. Soc. Chem. Ind.*, 30, 398, 1911.
[5] *Z. anal. Chem.*, 38, 292, 1899.
[6] *Chem.-Ztg.*, 20, 1920, 1896.
[7] *Am. Chem. J.*, 47, 520, 1912.
[8] Jour. A. Ph. A., 9, 878, 1920.

I. M. Kolthoff[1] uses $N/10$ $KBrO_3$ and adds KBr to it before use in determining salicylic acid. He allows the solution to stand 5 to 10 minutes before titrating.

To determine which method gives the best results, the author ran a series of assays based upon the present U. S. P. assay for phenol, varying the amount of sample, excess of bromine, concentration of acid, and length of time of standing before titration.

The following tabulates the results of 16 determinations:

1 Gm. of salicylic acid neutralized with $N/10$ NaOH and made up to 500 cc. (It was found that a slight amount of free NaOH, if present, does not vitiate the results.)

Cc of solution.	Gm. salicylic acid.	Cc $N/10$ Koppeschaar's T.=1000.	Cc $N/10$ $Na_2S_2O_3$ $5H_2O$ T.=0.975.	Cc of conc. HCl.	Time min.	Per cent salicylic acid.
30	.06	30	4.8	5	45	97.1
30	.06	30	4.55	5	45	98.2
30	.06	30	4.3	2	30	99.3
30	.06	30	4.4	5	30	98.9
25	.05	30	8.65	5	40	98.8
25	.05	30	8.6	5	30	99.0
25	.05	30	8.5	2	20	99.4
25	.05	30	8.4	2	20	99.8
25	.05	30	8.5	2	20	99.4
25	.05	30	8.5	2	20	99.4
20	.04	25	9.0	3	5	93.3
20	.04	25	8.7	3	10	95.0
20	.04	25	7.9	3	20	99.5
20	.04	25	7.95	3	25	99.3
20	.04	25	7.85	3	35	99.7
20	.04	25	8.3	3	45	97.2

1 cc $N/10$ Koppeschaar's V. S. = 0.002301 Gm. salicylic acid.

From the foregoing the following conclusions can be drawn: The amount of excess of $N/10$ bromine V. S. does not affect the results; 2 to 3 cc of HCl is the best concentration of acid; 5 to 10 minutes' standing is not sufficient, 20 to 30 minutes gives the best results. Longer standing gives poor results. It will be noticed in the above assays, that a difference of 0.1 cc $N/10$ $Na_2S_2O_2$ V. S. gives a variation of about 0.4% of salicylic acid.

In the following determination of salicylic acid and sodium and strontium salicylates, $N/50$ thiosulphate V. S. was employed.

In all the analyses 0.4 Gm. of each chemical was dissolved in 200 cc H_2O. Time of standing—20 minutes; used 3 cc of HCl.

SALICYLIC ACID.

Brand.	Cc of sample.	Gm. sample.	Cc $N/10$ Br. V. S. T. = 1000.	Cc $N/50$ $Na_2S_2O_3$ $5H_2O$ T. = 0.975.	Per cent salicylic acid.
L	25	.05	25	17.7	99.4
L	25	.05	25	17.8	99.3

[1] *Pharm. Weekbl.*, 57, 699, 1921.

Sodium Salicylate.

Brand.	Cc of sample.	Gm. sample.	Cc $N/10$ Br. V. S. T. = 1000.	Cc $N/50$ $Na_2S_2O_3$ $5H_2O$ T. = 0.975.	Per cent sodium salicylate.
L	25	.05	25	32.8	99.2
L	25	.05	25	32.8	99.2
B	25	.05	25	32.6	99.4
B	25	.05	25	32.3	99.7
M	25	.05	25	32.7	99.3
M	25	.05	25	32.6	99.4

Strontium Salicylate.

					Per cent strontium salicylate
L	30	.06	25	36.0	99.3
L	30	.06	25	36.4	99.0
S	30	.06	25	35.8	99.44
S	30	.06	25	35.9	99.36
M	30	.06	25	36.4	99.0
M	30	.06	25	36.2	99.12

1 cc $N/10$ Koppeschaar's Solution V. S. = .002301 Gm. salicylic acid.
1 cc $N/10$ Koppeschaar's Solution V. S. = .003311 Gm. strontium salicylate.
1 cc $N/10$ Koppeschaar's Solution V. S. = .002666 Gm. sodium salicylate.

SUMMARY.

Of all the methods tried, the one we find satisfactory is the following "Bromate" volumetric assay:

About 0.4 Gm. of substance, accurately weighed, is dissolved in H_2O to make 200 cc. Of this solution 25 cc, representing 0.05 Gm. sample, are placed in a 250-cc glass-stoppered flask, preferably one with a long narrow neck. Tenth-normal Br V. S. (25 cc) is added, followed by 3 cc of concentrated hydrochloric acid. Insert the stopper and let stand 20 to 30 minutes with occasional shaking. Remove the stopper, add 5 cc of potassium iodide solution (1.5) and 1 cc chloroform and insert stopper again. Shake until the precipitate is dissolved in the chloroform, remove stopper and rinse it and the neck of the flask with distilled water. Titrate with $N/10$ thiosulphate, V. S., using starch T. S. as indicator.

With strontium salicylate it is preferable to use 30 cc of the solution of the sample, equivalent to 0.06 Gm. of the salt.

COLUMBIA UNIVERSITY COLLEGE OF PHARMACY, JUNE 1922.

CRUDE DRUGS—THEIR SELECTION AND MILLING.*

BY J. L. HOPKINS.

Mankind, from the dawn of his intelligence to the present day, has turned to nature for the means of obtaining relief from his ills. There is hardly a plant that grows that has not somewhere, or somehow, or at sometime, been tried out and sometimes the endeavor to establish its therapeutic worth has resulted in fatalities. To-day botanicals are examined microscopically and by chemical analysis, and human lives are no longer sacrificed in an effort to determine drug values. Some observations along these lines are in keeping at this time.

Every pharmaceutical chemist is aware that the percentage of "active principles" found in botanical drugs varies to such an extent as to render the preparations from many of them of most uncertain value unless the definite amount of active principle is determined by assay. This element of uncertainty attending

* Parts of an address delivered at the annual meeting of the American Pharmaceutical Manufacturers' Association, Bedford Springs, Pa., June 1922.