

more than 26 per cent of ZnO, and not less than 1.8 per cent and not more than 2.2 per cent of $C_7H_6O_3$.

Hard Paste of Zinc Oxide.—Hard Paste of Zinc Oxide contains not less than 23 per cent and not more than 27 per cent of ZnO.

Assays for Iodine and Iodide in Iodine Solutions*

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The iodine solutions considered in this study are the U. S. P. XI preparations: Tinctura Iodi, Tinctura Iodi Mitis and Liquor Iodi Compositus. The proposed assays are applicable also to other iodine-iodide solutions, such as Tinctura Iodi Fortior, N. F. VI.

The United States Pharmacopœia XI directs that the iodine of iodine solutions be determined by titrating a 5-cc. portion with $N/10$ sodium thiosulfate. To determine the iodide, the Pharmacopœia directs that another 5-cc. portion be evaporated on a water-bath to dryness, that it be repeatedly moistened until a white residue remains, which is weighed and calculated as potassium iodide for Tinctura Iodi and Liquor Iodi Compositus, or as sodium iodide for Tinctura Iodi Mitis.

The British Pharmacopœia, 1932, directs that the iodine be determined by titrating a 10-cc. portion of the iodine solution with $N/10$ sodium thiosulfate; and the potassium iodide by treating another 10-cc. portion according to the method of Andrews (1).

The thiosulfate titration for determining iodine is generally regarded as satisfactory and requires no further discussion. The iodide assay according to U. S. P. XI, although simple, is definitely unsatisfactory for several reasons. First, the method does not determine the iodide only, but rather total solids on evaporation. This was pointed out by Schaefer (2). Second, the method is time-consuming, requiring as many as twenty to thirty moistenings, over a period of three to five hours. Schaefer, in his article, states that very often it is

difficult to obtain a white residue, due to impurities present. Third, the method invariably leads to high results. From Table II (see Experimental Part) it can be seen that the potassium iodide by the U. S. P. XI method exceeds the theoretical amount by four to six parts per thousand; and exceeds the iodate method by about four parts per thousand. In the case of sodium iodide, by the U. S. P. method, the theoretical amount is exceeded by about one hundred and thirty parts per thousand; and with the iodate method, it is exceeded by about one hundred and twenty parts per thousand. Fourth, the use of a 5-cc. portion in the assay of Tinctura Iodi Mitis results in decreased accuracy, since only about 7 cc. of the standard solution are used in the titration, and only about 110 mg. of the difficultly weighable sodium iodide are obtained.

The high results in the iodide content when determined by U. S. P. XI method led to the belief that not all of the water which is added in order to volatilize the iodine to obtain a white residue is removed by heating on the water-bath. The white residue obtained by the pharmacopœial method was therefore dried for two hours in an electric oven at $110^\circ C$. Table II (see Experimental Part) shows that the amounts of potassium iodide and sodium iodide were considerably decreased. This, obviously, must be due to water not removed by heating on the water-bath only. The potassium iodide content by the official method is about six parts per thousand higher than the potassium iodide content obtained after drying at $110^\circ C$. for two hours.

As previously indicated, the sodium iodide assay in Tinctura Iodi Mitis is even less satisfactory. The deliquescent nature of sodium iodide renders the attainment of close checks almost impossible. This is indicated by the relative average deviation of fifty-one parts per thousand, for the series of determinations of sodium iodide made by the U. S. P. XI method. Table II (see Experimental Part) shows the diversity of results which may be expected when the sodium iodide is determined by weighing the residue from a 5-cc. sample of the mild tincture.

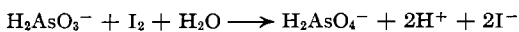
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The British Pharmacopœia, 1932, directs that potassium iodide be determined by titrating with $M/20$ potassium iodate and thus obviates the difficulties encountered with the U. S. P. XI method. However, the B. P. method necessitates the use of separate portions for the iodine and iodide determinations.

A single sample is much to be preferred, as has been shown by Schaefer (2), and by Matthes and Brause (3). In this study a single sample is used for analysis. The iodine is determined by means of $N/10$ sodium arsenite. When the iodine is decolorized, the solution is rendered sufficiently acid, so that it is at least $3N$ at the end of the titration. After being rendered acid, the solution is titrated with $M/20$ potassium iodate until the iodine color is removed from the chloroform, a few cc. of which are added just before the end-point is reached.

In the titration with sodium arsenite no starch test solution is used. The end-point is readily discernible without this indicator. If, however, the starch indicator is preferred to indicate the complete removal of iodine, not more than 1 cc. should be used. It has been found that when too much of the starch indicator is added, it interferes somewhat with detecting the complete removal of the iodine in the chloroform layer. This is due to a turbidity produced in the chloroform. Kolthoff (4) points out that the sensitivity of the detection of free iodine in chloroform exceeds that of the conventional starch indicator and renders a correction factor for the indicator unnecessary.

In the sodium arsenite titration, it is important that enough sodium bicarbonate be added to present the reversibility of the reaction:



The addition of an excessive amount of alkali must be avoided, for too great alkalinity will result in converting some iodine to iodide and hypoiodite or iodate.



Washburn (5) has calculated that optimum results are obtained at a p_{H} range between 4 and 9.

Reinthal (6) and Kolthoff and Sandell

(7) point out that an alkaline solution of arsenous acid will on standing be gradually oxidized by exposure to the atmosphere. According to Reinthal (6), the oxidation is quite rapid at elevated temperatures, but at ordinary temperatures no perceptible change takes place in the titer in a period of four months. The sodium arsenite solution was standardized from time to time during this study over a period of three months and no discernible change in the titer was observed. It is recommended, however, that the sodium arsenite solution be standardized from time to time against a standard solution of potassium iodate, which according to Jamieson (8) will keep its strength indefinitely. Jamieson observed no perceptible change in a solution of potassium iodate, properly kept, in a period of ten years.

In titrating with potassium iodate, the standard solution should be added with vigorous shaking until the last drop decolorizes the chloroform layer that collects in the neck of the inverted flask. Near the end of the titration, the flask must be closed and thoroughly shaken after the addition of each drop of the standard solution (9). This may appear rather tedious. However, with experience it is quite easy to determine from the color of the solution and from the intensity of the iodine color in the chloroform how much of the standard solution is necessary.

Tables I and II (see Experimental Part) indicate that the suggested procedure is sufficiently accurate and precise for pharmacopœial assays. The precision and accuracy of the suggested procedure in each instance equal or surpass the precision and accuracy of the U. S. P. XI.

EXPERIMENTAL

Iodine Solutions.—A liter of each of Tinctura Iodi, Tinctura Iodi Mitis and Liquor Iodi Compositus was prepared using reagent quality iodine, reagent quality potassium iodide and U. S. P. sodium iodide. The reagents were weighed to the nearest 0.1 mg. and the total volume was exactly 1 liter. In each instance, the chemicals used were assayed according to the U. S. P. XI and the following values were obtained:

Iodine.	99.87 ± 0.09 per cent.
Potassium iodide.	99.93 ± 0.04 per cent.
Sodium iodide.	97.74 ± 0.04 per cent.

Table I.—Results of Assays for Iodine

	Iodine Content in Gm. per 100 Cc.		
	Tr. Iodi	Tr. Iodi Mitis	Liq. Iodi Compositus
Theoretical	6.991 ± 0.006	1.997 ± 0.002	4.994 ± 0.005
U. S. P. XI Method	6.967 ± 0.007	1.983 ± 0.005	4.989 ± 0.005
Arsenite method	6.974 ± 0.007	1.993 ± 0.004	5.001 ± 0.003

Table II.—Results of Assays for Iodide

	Iodide ^a Content in Gm. per 100 Cc.		
	Tr. Iodi	Tr. Iodi Mitis	Liq. Iodi Compositus
Theoretical	4.997 ± 0.002	2.248 ± 0.001	9.993 ± 0.004
U. S. P. XI method	5.019 ± 0.015	2.539 ± 0.130	10.05 ± 0.01
U. S. P. XI method ^b	4.990 ± 0.007	2.299 ± 0.009	9.994 ± 0.017
Iodate method	4.999 ± 0.007	2.269 ± 0.005	10.01 ± 0.01

^a Potassium Iodide in Tr. Iodi and Liq. Iodi Comp.; Sodium Iodide in Tr. Iodi Mitis.

^b U. S. P. XI method modified by drying for two hours at 110° C.

M/20 Potassium Iodate.—This solution was prepared according to U. S. P. XI.

N/10 Sodium Arsenite.—Reagent quality arsenous oxide was dried for one hour at 110° C. and assayed. The assay value was 99.98 per cent. 5.0000 Gm. of the dried arsenous oxide were dissolved in 40 cc. of 5*N* sodium hydroxide. The solution was diluted to 400 cc., rendered neutral with 1*M* hydrochloric acid and then made just slightly acid. To the solution were added 2 Gm. of sodium bicarbonate and when this was dissolved the solution was made up to 1 liter. The theoretical titer of this solution was 0.10108*N*. The *N/10* sodium arsenite was then standardized against *M/20* potassium iodate and was found to be 0.10115*N*. Since an accuracy of one per thousand was regarded as sufficient and since the sodium arsenite solution was to be subsequently used against potassium iodate, the titer used was 0.1012*N*.

PROCEDURE

Tinctura Iodi and Liquor Iodi Compositus.—Transfer 5 cc. of the solution accurately measured with a pipette to a 250-cc. conical flask provided with a ground-glass stopper (iodine flask). Add 20 cc. of distilled water and 0.5 Gm. of sodium bicarbonate. Titrate at once with vigorous shaking with the standard solution of sodium arsenite added dropwise, until the solution turns colorless. One cc. of *N/10* sodium arsenite is the equivalent of 0.01269 Gm. of iodine.

Cool the colorless solution under running water, add 50 cc. of 12*M* hydrochloric acid, and again cool the solution. Titrate with *M/20* potassium iodate, shaking vigorously until the solution becomes light brown in color. Add 5 cc. of chloroform and continue titration by dropwise addition and vigorous shaking until the last drop decolorizes the chloroform layer. Toward the end of the titration, the flask must be closed and thoroughly agitated after the addition of each drop of the standard solution.

From the cc. of *M/20* potassium iodate subtract the cc. of *N/10* sodium arsenite previously required; multiply by 1.660 and divide by the volume of solution taken for analysis.

Tinctura Iodi Mitis.—Proceed as directed above, using a 10-cc. portion of the sample for analysis. Since mild Tincture of Iodine contains sodium iodide and not potassium iodide, subtract from the cc. of *M/20* potassium iodate the cc. of *N/10* sodium arsenite, used in the iodine determination, multiply by 1.499 and divide by the volume of the mild tincture used in the analysis.

SUMMARY

1. The U. S. P. method for the determination of the iodide in the official iodine solutions is not satisfactory and especially is this so for *Tinctura Iodi Mitis*.
2. The white residue of potassium iodide or sodium iodide obtained by the U. S. P. method should be subsequently dried for two hours at 110° C.
3. The suggested procedure for the determination of iodine and iodide requires only a single portion; it is more rapid and more accurate than the U. S. P. XI method.

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