

A RAPID ACCURATE METHOD FOR THE DETERMINATION OF ORGANICALLY AND INORGANICALLY COMBINED IODINE.*

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Recently, while investigating the different methods for organically and inorganically combined iodine, it occurred to the writers that the iodine might be liberated by suitable oxidizing agents and advantages taken of its solubility in chloroform. Upon further examination of the subject, we found that other investigators had used several oxidizing agents, *viz.*, potassium permanganate, nitric acid, etc., while several had used sodium nitrite. As far as we were able to ascertain, all reported inaccurate results when assaying products containing iodine, by methods based upon the above reactions. The principal cause of error which they reported was caused by the reagents used to liberate the iodine, being carried mechanically into the chloroform, or being slightly soluble in the latter, thus interfering with the final titration. Nowhere to our knowledge, has anyone used hydrogen peroxide for liberating the iodine. We, therefore, decided to try out this substance, and accordingly we made several determinations upon different compounds containing iodine. The first thing we discovered was the necessity of the presence of a free acid in the solution of sample. We found upon investigation that acetic acid appeared to be the most desirable for this purpose. After several determinations it was evident that the iodine was liberated only slowly by this method, and at times it was difficult to ascertain if the iodine was completely liberated, which led to varying results. It was obvious to us that we must obtain a more rapid and complete oxidation. After experimentation with many different substances, we found that the addition of a small amount of phosphoric acid overcame this difficulty. The following methods have been in use in our laboratories in the past year, and our experience with them has been perfectly satisfactory.

TINCTURE IODINE—U. S. P.

Tincture of iodine, made according to the U. S. P. formula, should contain 70 Gm. of iodine, and 50 Gm. of potassium iodide in each liter. The U. S. P. VIII has appended an assay process for determining the free iodine, but does not include any method for the estimation of the potassium iodide. We have successfully applied the following method for the estimation of both the free iodine and the potassium iodide, using only one sample. Both determinations may be performed in from twenty minutes to one-half hour, according to the speed of the analyst.

METHOD.

Five mls of the tincture are pipetted into an Erlenmeyer flask of a hundred mls capacity and the free iodine estimated by the usual thiosulphate method. The contents of the flask are then transferred to a separatory funnel of 250 mls capacity. Acidify with 10 mls of acetic acid, add 10 mls of hydrogen peroxide

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and 5 mils of phosphoric acid. The whole is carefully mixed by a whirling motion of the funnel and the liberated iodine is shaken out with successive portions of 25 mils each of chloroform. The last portion should not show a pink color indicating that the free iodine has been completely exhausted. The chloroform extractions are collected into a second separatory funnel containing 100 mils of distilled water. In order to free the chloroform from any free acid that may have been dissolved by the chloroform, or carried through mechanically, the contents of the funnel are shaken. After complete separation of the liquids the chloroform solution is drawn off and again washed with 100 mils of distilled water, care being taken that no free iodine is left in the wash water. The chloroform is transferred to a 500-mil flask containing 100 mils of distilled water, the whole thoroughly shaken and if the aqueous layer still shows an acid reaction, a small portion of sodium bicarbonate is added and the flask again shaken. After complete separation, 20 mils of a 10 percent solution of potassium iodide are added. $\frac{N}{10}$ sodium thiosulphate solution is run in from a burette in small portions, and the flask shaken vigorously after each addition. When the chloroform layer shows only a faint pink color a few drops of a starch solution are added and the titration continued, drop by drop, until no blue color persists. From the total number of mils of $\frac{N}{10}$ sodium thiosulphate solution consumed in the latter determination, are subtracted the number of mils consumed in the estimation of the free iodine. The remainder multiplied by 0.0166 and the result by twenty will give the amount of potassium iodide in 100 mils of tincture of iodine.

ESTIMATION OF ORGANICALLY COMBINED IODINE.

TYPE A.—IODOFORM.

Probably the one preparation of iodine in which it has been most difficult to estimate the iodine content is iodoform gauze. Previous to this we have been converting the iodine of the iodoform to potassium iodide with alcoholic potassium hydroxide, evaporating the alcohol, breaking up the resultant iodide with ferric chloride and hydrochloric acid, and distilling the liberated iodine into a solution of potassium iodide and titrating with $\frac{N}{10}$ sodium thiosulphate solution. While this method is theoretically correct, practical demonstration reveals the presence of many possibilities of error which may affect the results. Portions of the ferric chloride and hydrochloric acid may be mechanically carried over into the potassium iodide, thereby liberating free iodine from this solution and causing high results. Another possible source of error is the escape of iodine from the potassium iodide—iodine solution in the receiver. Taken as a whole, we considered the method clumsy and unprofitable for our use, due to the valuable time consumed in setting up the apparatus and evaporation of the alcohol and general manipulation of the process. The following scheme of analysis offers little or no possibilities of error, consumes considerably less time, and is not nearly so complicated as the distillation method. A portion of the moist gauze (about 20 Gm.) is placed into the reservoir of an extraction apparatus, while 50 mils of alcoholic potassium hydroxide are added to the extraction flask. The contents of the flask are boiled, which drives the alcohol up into the condenser; the condensed alcohol falling back on the gauze dissolves the iodoform which is then carried into the flask where it is converted by the potassium hydroxide into potassium iodide by boiling.

When the iodoform has been exhausted from the gauze, which is recognized by the absence of color in the gauze, the operation is continued for ten minutes, which insures the complete conversion of the iodine in the iodoform into potassium iodide. The contents of the flask are now transferred into a separatory funnel and the method continued as in the determination of potassium iodide in tincture of iodine. One mil of $\frac{N}{10}$ sodium thiosulphate solution is equivalent to 0.0131 Gm. of iodoform. The gauze is removed from the cylinder, dried and accurately weighed, the weight added to the amount of iodoform found, and this total divided into the weight of the iodoform will give the percentage of iodoform in the gauze. The above calculations are based upon the weight of dry gauze which we have found most applicable for the determination of the active constituent of medicated gauze.

ESTIMATION OF ORGANICALLY COMBINED IODINE.

TYPE B.—IODINE ORGANICALLY COMBINED IN OILS.

Recently, there have appeared upon the market several oily preparations containing combined iodine. We were called upon to confirm the statement on the label, which claimed 10 percent iodine, and found that the following method was applicable for the estimation of iodine in this combination.

About 1 Gm. of the preparation is accurately weighed into a tared flask, 30 mls of half-normal alcoholic potassium hydroxide are added and the whole boiled under a reflux condenser until the oil is completely saponified, the contents of the flask transferred to a separatory funnel and about 30 mls of chloroform added and the whole shaken. After separation the chloroform is drawn off and discarded which removes the fats that interfere with the final titration. Should an obstinate emulsion occur here it may be broken up by the addition of acetic acid. Phosphoric acid and hydrogen peroxide are now added and the iodine is shaken out with chloroform as in the preceding methods.

DETERMINATION OF FREE IODINE AND POTASSIUM IODIDE.

IN IODINE OINTMENT.—U. S. P.

The determination of free iodine is essentially the same as that proposed by Mr. Leo S. Fried, *JOURNAL A. PH. A.*, 4, 621. A weighed portion of the sample is dissolved in chloroform, water added and the free iodine titered with $\frac{N}{10}$ sodium thiosulphate solution. To determine the potassium iodide, one gramme of the ointment is accurately weighed into a tared flask and the whole boiled with alcoholic KOH. After removal of the fats with chloroform, the procedure is the same as in the previous methods. From the total iodine subtract the free iodine, and calculate the remainder to potassium iodide.

A sample of iodine ointment was carefully prepared according to the U. S. P. directions. After standing two days it was assayed by the above method and found to contain 3.66 percent free iodine and 4.06 percent of potassium iodide. After standing two weeks the preparation assayed 2.71 percent free iodine, and 4.08 percent potassium iodide.

When we first attempted the assay of this preparation by this method we expected to find about 7.1 percent total iodine, this being the theoretical amount calculated from the potassium iodide plus the free iodine. While we had no

difficulty in obtaining check results, we invariably found that the results were lower than the theoretical amount. This was indeed puzzling to us, but after several determinations we found that the difference between the free iodine and the total iodine was constant, and this difference when calculated to potassium iodide was found to be about 4 percent which is the theoretical amount of potassium iodide incorporated into the preparation. We conclude then that boiling with alcoholic KOH does not free the iodine absorbed by the ointment base. No doubt if a suitable method for converting the absorbed iodine to some iodide which is easily broken down, the entire iodine content of the ointment may be determined by this method. To date, however, we have been unable to accomplish this.

A sample of tincture of iodine was prepared by us according to the U. S. P. formula, the ingredients being accurately weighed upon our analytical balances. When assayed according to the above method the following results were obtained:

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|------------|--------|-------|------------------|-------|
| No. 1..... | Iodine | 6.92% | Potassium Iodide | 4.97% |
| No. 2..... | Iodine | 6.92% | Potassium Iodide | 4.92% |

A sample of potassium iodide, U. S. P., assayed 99.69 percent pure, when broken up and the liberated iodine determined as above and calculated to potassium iodide.

A sample of iodoform, U. S. P., when assayed yielded 100.1 percent pure.

A sample of an oily iodine preparation, labeled 10 percent, assayed 10.23 percent and 10.29 percent iodine.

We have also successfully applied this method for the determination of iodine in the following substances: Ferrous iodide, calcium iodide, and calcium iodized tablets, and conscientiously believe that the method is accurate, rapid and may be applied to practically all combinations of iodine.

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