DETERMINATION OF SMALL AMOUNTS OF ETHYL IODIDE

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The use of ethyl iodide in the indirect determination of cardiac output in man gives importance to methods for the determination of low concentrations of its vapor in air. The iodine pentoxide method advocated by Henderson and Haggard (1) was found by Starr and Gamble (2) to give variable results, depending on the sample of iodine pentoxide used and the rate at which the ethyl iodide-air mixture was passed through it. The silver nitrate method developed by Starr and Gamble (2) gave results of a relatively high degree of accuracy; average error, 0.03 mg. of ethyl iodide in a 500 cc. air sample. This probable analytical error, however, introduces an error of 6 to 7 per cent in the calculated cardiac output (3 p. 471). Further efforts in the direction of greater analytical accuracy seemed advisable.

In the method described in this paper the ethyl iodide is treated with chlorine, or bromine, which promptly oxidizes the iodide to iodate (4, 5). The excess halogen is removed with phenol and the iodine, liberated from potassium iodide by the iodate, is determined by titration with thiosulfate. With vaporized samples of the order of 3 mg. the average error was only 0.5 per cent (Table II) in terms of ethyl iodide, equivalent to an error of only 2 to 3 per cent in the value for cardiac output as determined by the method of Starr and Gamble (3). The advantages of the method are the definiteness of the titration end-point, the sixfold increase in amount of iodine titrated, and the elimination of the 16 to 24 hours delay necessary in the Starr and Gamble method (2) for the completion of the ethyl iodide-silver nitrate reaction.
Ethyl Iodide Determination

Procedure

The procedure applicable to air samples containing vaporized ethyl iodide is as follows: The ethyl iodide-air mixtures are collected in 500 cc. gas sampling tubes previously described (1–3). 10 cc. of chlorine water not more than a day old are placed in a reagent tube which is inserted into the end of one of the rubber connections on the sampling tube so that the pinch-clamp can be removed without allowing gas to escape. After removing the pinch-clamp, the mouth of the reagent tube is pushed through the rubber tubing until it is 2 to 3 cm. within the glass neck of the sampling tube. The chlorine water is allowed to run into the main body of the sampling tube, but not into the opposite neck. The tube is leveled and rotated so that the walls are washed with the reagent. The contents of the reagent and sampling tubes are washed into an Erlenmeyer flask with a total of 30 to 35 cc. of distilled water divided into at least three portions. The liquid in the flask is set into rotation and 10 cc. of 10 per cent phenol-water mixture are added rapidly from a graduated cylinder. After standing for at least 20 minutes, 25 cc. of water and 5 cc. of 20 per cent potassium iodide solution, which has been prepared on the day it is to be used, are added, and the iodine liberated is titrated, at once, with 0.005 N sodium thiosulfate. When the

1 The chlorine water used in testing the method contained approximately 0.35 per cent of Cl. Since the concentration need be known only approximately, the strength of the reagent can be judged with sufficient accuracy by its appearance. Cf. The Pharmacopoeia of the United States of America, tenth decennial revision, Philadelphia, 487 (1926).

2 The reagent tubes were made from glass tubing the outside diameter of which was slightly less than the inside diameter of the neck of the sampling tube. At one end a 10 cc. bulb was blown, giving the tube the appearance of a small retort.

3 If the phenol is added slowly it is partially oxidized, producing colored compounds (Kendall ((6) p. 896)). In such cases high values for ethyl iodide were obtained.

4 When the highest analytical accuracy is required, as in the tests which follow, the 0.005 N sodium thiosulfate must be made with recently boiled distilled water, must not be more than 2 weeks old, and must be standardized each day. If proportionate concentrations only are required, as in the application to the cardiac output method, standardization is unnecessary. The stability of 0.1 N thiosulfate solution is much greater than that of the weaker solution and may conveniently be used as a stock solution.
yellow color of the iodine has nearly disappeared, 5 cc. of 0.2 per cent starch solution are added and the titration is continued until the solution is colorless. 1 cc. of 0.005 N sodium thiosulfate is equivalent to 0.130 mg. of ethyl iodide in the original sample. 5 cc. of approximately saturated bromine water may be used, instead of the 10 cc. of chlorine water, in the above procedure and the excess removed with 5 cc. of 10 per cent phenol.

Tests of Method

The accuracy of the method has been proved by the following experiments.

Eastman's ethyl iodide was redistilled, first over powdered silver, then over mercury. Samples weighing from 1 to 12 mg. were introduced into weighed capillary tubes or bulbs with capillary stems. These were sealed after waiting until the ethyl iodide at the end of the capillary had evaporated, and weighed again on the following day. The weighings were made on an assay balance with weights calibrated by Richards' method (7); the average change in weight from handling and sealing alone (determined by eight experiments) was ±0.007 mg. The capillary tube, or bulb, was placed in an Erlenmeyer flask containing 25 cc. of water plus 10 cc. of freshly prepared chlorine water and thoroughly crushed with a glass rod. The flask was rotated while 10 cc. of 10 per cent phenol in water were added rapidly. After standing for at least 20 minutes, 25 cc. of water and 5 cc. of freshly prepared 20 per cent potassium iodide solution were added and the liberated iodine was titrated with 0.005 N sodium thiosulfate, 5 cc. of 0.2 per cent starch solution being used as indicator.

The sodium thiosulfate solutions, never more than 2 weeks old, were standardized each day that they were used. Bureau of Standards arsenious oxide was used as the ultimate standard, while standard potassium biiodate, which was compared with the arsenious oxide several times during the investigation, was used for daily standardizations. Blanks were run on all the reagents and the distilled water used. Standardizations, comparisons, and blanks were made under the same conditions as the

6 The bromine water used contained approximately 2.5 per cent of Br (cf. foot-note 1).
determinations. Solution volumes were corrected for temperature.

The results of consecutive determinations, made on 2 different days, are given in Table I. The greatest error in this series is $+1.8$ per cent, the arithmetical mean of the errors is $+0.4$ per cent, and the average deviation from this is $+0.6$ per cent. In other series of analyses of ethyl iodide, in accurately measured volumes of water solutions, evidence was obtained that the errors involved in weighing the ethyl iodide samples were an important factor in the inconsistencies, small as they were, in these results. A solution of ethyl iodide was prepared containing approximately 0.58 mg. in 10 cc. Analyses in triplicate (two with chlorine, one with bromine) were made of 10, 20, 30, 40, and 50 cc. samples, the same 10 cc. pipette being used in each measurement. Each result was compared with the amount of ethyl iodide calculated to be present from the average of all fifteen determinations. The maximum deviation from the arithmetical mean of the series was $+0.004$

### Table I

**Determination of Weighed Samples of Ethyl Iodide Released under Chlorine Water in Erlenmeyer Flask**

Excess chlorine was removed with phenol.

<table>
<thead>
<tr>
<th>Sample taken</th>
<th>Found</th>
<th>Error per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>mg.</td>
<td>mg.</td>
<td></td>
</tr>
<tr>
<td>4.390*</td>
<td>4.380</td>
<td>$-0.2$</td>
</tr>
<tr>
<td>6.048</td>
<td>6.083</td>
<td>$+0.6$</td>
</tr>
<tr>
<td>12.516</td>
<td>12.354</td>
<td>$-1.3$</td>
</tr>
<tr>
<td>3.425</td>
<td>3.414</td>
<td>$-0.3$</td>
</tr>
<tr>
<td>4.370</td>
<td>4.379</td>
<td>$+0.2$</td>
</tr>
<tr>
<td>3.894*</td>
<td>3.930</td>
<td>$+0.9$</td>
</tr>
<tr>
<td>2.245*</td>
<td>2.286</td>
<td>$+1.8$</td>
</tr>
<tr>
<td>1.704</td>
<td>1.721</td>
<td>$+1.0$</td>
</tr>
<tr>
<td>1.744</td>
<td>1.752</td>
<td>$+0.5$</td>
</tr>
<tr>
<td>1.055</td>
<td>1.057</td>
<td>$+0.2$</td>
</tr>
<tr>
<td>2.063</td>
<td>2.080</td>
<td>$+0.8$</td>
</tr>
<tr>
<td>3.456*</td>
<td>3.460</td>
<td>$+0.1$</td>
</tr>
</tbody>
</table>

Arithmetical mean: $+0.4$

Average deviation from arithmetical mean: $+0.6$

* 20 cc. of chlorine water and 20 cc. of 10 per cent phenol were used.
mg., and the average deviation from the arithmetical mean was only ±0.002 mg.

In order to test the method under conditions which more closely resembled those present in measurements of cardiac output, vaporized samples of ethyl iodide were used. Samples weighed in capillary tubes, as described above, were placed in 500 cc. gas sampling tubes, similar to those used by Henderson and Haggard (1) Fig. 6) and Starr and Gamble (2, 3), together with a piece of glass rod. The ends of the tube were closed by rubber tubing and

TABLE II

Determination of Weighed Samples of Ethyl Iodide Vaporized in 500 Cc. Gas Sampling Tubes

The samples were oxidized with chlorine water, and excess chlorine was removed with phenol.

<table>
<thead>
<tr>
<th>Sample taken</th>
<th>Found</th>
<th>Error per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.346</td>
<td>2.375</td>
<td>+1.2</td>
</tr>
<tr>
<td>3.221</td>
<td>3.278</td>
<td>+1.8</td>
</tr>
<tr>
<td>3.590</td>
<td>3.613</td>
<td>+0.6</td>
</tr>
<tr>
<td>4.463</td>
<td>4.496</td>
<td>+0.7</td>
</tr>
<tr>
<td>1.651</td>
<td>1.686</td>
<td>+2.1</td>
</tr>
<tr>
<td>2.168</td>
<td>2.177</td>
<td>+0.4</td>
</tr>
<tr>
<td>2.377</td>
<td>2.398</td>
<td>+0.9</td>
</tr>
<tr>
<td>2.822</td>
<td>2.827</td>
<td>+0.2</td>
</tr>
<tr>
<td>3.731</td>
<td>3.754</td>
<td>+0.6</td>
</tr>
</tbody>
</table>

Arithmetical mean: +0.9
Average deviation from arithmetical mean: ±0.5

Mohr pinch-clamps, and the capillary was thoroughly crushed by whirling the glass rod around inside the sampling tube. When the ethyl iodide had vaporized, the analysis was carried out as described before under "Procedure."

The results of nine consecutive experiments, performed on 2 different days are given in Table II. With seven weighed samples of the same order of magnitude analyzed with bromine water as the oxidizing agent the greatest error was +1.5 per cent; the arithmetical mean of the errors was +0.001 mg. or +0.2 per cent, and the average deviation from the arithmetical mean ±0.011 mg. or 0.5 per cent.
Ethyl Iodide Determination

The method described above is at once directly applicable as an improvement in the analytical technique of the Starr and Gamble cardiac output method. In future developments of the mechanical features of that method it may be found feasible to pass the air to be analyzed directly through chlorine water. Preliminary tests have shown that the absorption of ethyl iodide is rapid and probably adequate to meet the requirements of such a modification of the method.

The author is indebted to Dr. C. J. Gamble for valuable advice throughout the course of this work.

SUMMARY

Low concentrations of ethyl iodide in air and water have been determined by an iodate method in which chlorine or bromine is used as an oxidizing agent, the excess being removed with phenol.

In the range of quantities of ethyl iodide dealt with in an indirect determination of cardiac output the average error was 0.011 mg. This is approximately one-third the error found by Starr and Gamble in their silver nitrate method, and may be held responsible for an error of only 2 to 3 per cent in the value for cardiac output.

BIBLIOGRAPHY
