

ACKNOWLEDGMENT

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Determination of Iodine in Thyroid

Comparison of a Rapid Method with the U. S. P. XI Method

By Charles E. Nicklaus* and Nelson Tippett*

Previous investigations have emphasized the need of an assay method for Thyroid, that is both quick and accurate. Tippett (1) simplified the U. S. P. XI Method and increased the accuracy by consideration of a titration time factor. The one inherent disadvantage of the alkaline ash method remained however—one assay taking the better part of a working day. Nicklaus has adapted the Matthews, Curtis and Brode modification of the Leipert procedure (2) to Thyroid products and obtained a method having the triple advantage of speed, accuracy and manipulative ease. In substance this method depends upon an initial chromium trioxide oxidation and distillation in a special, but quite simple apparatus, and a subsequent titration with hundredth-normal sodium thiosulfate, the complete procedure requiring a maximum time of one hour. Over a period of six months, numerous assays by each method have shown practically no variation. For the appended table a representative few have been chosen.

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If care is taken to use reagent grade chemicals, no blank is needed.

EXPERIMENTAL

Preparation of Reagents.—30*N* Chromium Trioxide: Dissolve 165.0 Gm. chromium trioxide in 100 cc. water.

N Potassium Carbonate: Dissolve 14.0 Gm. of the salt in 100 cc. water.

0.2*M* Potassium Permanganate: Dissolve 3.16 Gm. in 100 cc. water.

1.5*N* Sodium Nitrite: Dissolve 10.4 Gm. in 100 cc. water.

5*M* Urea Solution: Dissolve 30.0 Gm. in 100 cc. water.

Determination of Iodine.—Weigh accurately about 0.5 Gm. of Thyroid and place it in a 500-cc. Kjeldahl flask (containing an antibump) and wash down the inside of the flask with about 10 cc. of distilled water. If the assay is to be run on a tablet, a representative number are weighed and powdered and an aliquot part of the powder, equivalent to about 0.5 Gm. of Thyroid, is treated in the same manner. No trouble is experienced with tablets of any grainage.

With constant rotation of the flask, slowly add 10 cc. of 30*N* chromium trioxide, and after the reaction has subsided add slowly 50 cc. of sulfuric acid. Place the flask in a ring stand and fit it with a three-hole rubber stopper containing a 0–220°C. thermometer and two tubes for ventilation. Heat the contents at a temperature of 210–220°C. until the liquid acquires a clear bluish green coloration; when the bubbles cease to aggregate on the surface of the liquid, oxidation is complete. Prolonged heating at high temperature results in the formation of an insoluble chromium sulfate precipitate leading to bumping difficulties during distillation. Remove the flask from the ring stand and cool it first under the hot-water tap and then under the cold. Wash the thermometer and remove it. Add 100 cc. of distilled water cautiously while rotating the flask. Connect the flask with the distillation apparatus. To a 250-cc. flask containing an antibump, add 2-cc. of *N* potassium carbonate and place the flask under the condenser stem in such a manner that the tip of the stem dips into the liquid. Place 10 cc. of phosphorous acid 50% in the reservoir on the top of the apparatus and after bringing the liquid to a boil so as to wet the glass joints, allow the acid to run in slowly by turning the stop-cock. Rapidly distil over 75 cc. Lower the flask containing the distillate, open the stop-cock, and wash down the condenser stem permitting the washings to join the distillate. Remove the flask to a burner and boil down to a volume of 4.5 to 5.0 cc. Wash the antibump and remove it. Place the flask on a steam-bath and add from a dropper enough 0.2*M* potassium permanganate to establish a permanent wine-red coloration. Heat five minutes with frequent rotation. Add 10 drops of syrupy phosphoric acid and continue to heat for five minutes. No decoloration of the permanganate

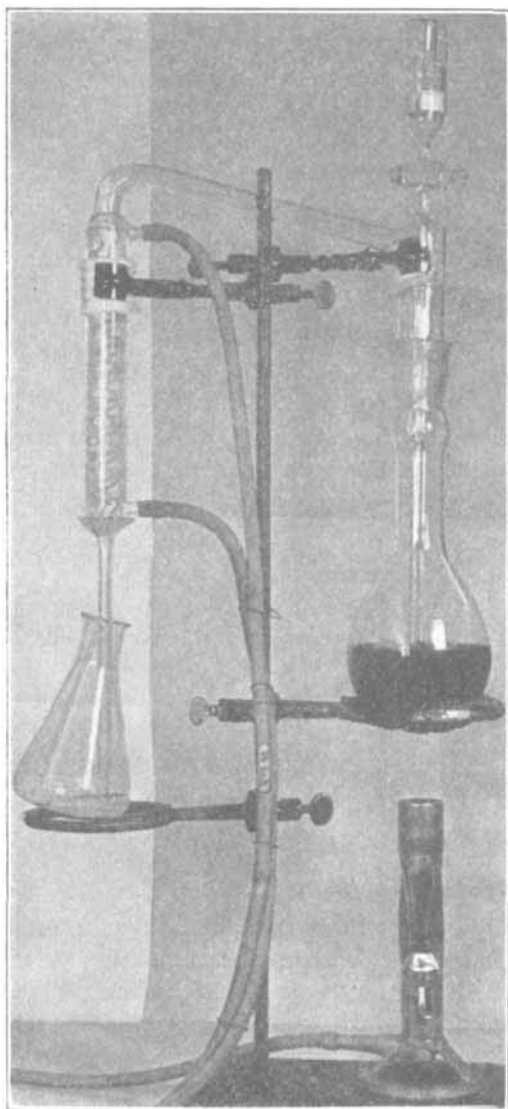


Photo by Walter Hobbs, Jr.

Fig. 1—Photograph of distillation apparatus.

should occur. If decoloration does occur, more permanganate should be immediately added. Then add just enough 1.5*N* sodium nitrite to decolorize it, plus one drop in excess. Heat five minutes. Add eight drops of 5*M* urea solution and after five minutes' heating remove from the steam-bath and cool to room temperature. The flask should be rotated frequently during the five-minute heating intervals, and additions of the permanganate, acid, nitrite and urea solutions should be made dropwise directly into the liquid, care being taken not to get any on the sides of the flask. Add crystalline potassium iodide in slight excess and immediately titrate the liberated iodine with hundredth-normal sodium thiosulfate, using starch T.S. as the indicator. Each cc. of hundredth-normal sodium thiosulfate is equivalent to 0.0002115 Gm. iodine.

Apparatus.—The apparatus designed for the distillation is presented in the accompanying photo-

graph and figure. *A* is the oxidation and distillation flask which has the usual Kjeldahl shape and which may be of any convenient size (500-cc. capacity found to be quite satisfactory). *B* is the entry tube which is 16.5 cm. in length with an inside diameter of 3 mm. and an outside diameter of 9 mm. It should reach to within 5 mm. of the bottom of the flask. *C* is a standard ground glass joint of 25- or 30-mm. size. *D* is a cup into which solutions are measured before they are let through the stop-cock and entry tube into the flask. *G* is a coil condenser which has a dew cup attached. The condenser stem is about 17 cm. long with an inside diameter of 6 mm. and 9 mm. outside diameter. *F* is a connecting tube 1½ cm. in diameter and about 21 cm. long. *H* is the receiving flask of 250-cc. capacity containing an antirump. *K* is an antirump constructed from 3-mm. glass rod on the one end of which is sealed a piece of 3-mm. glass tubing 5 mm. long. Its length should be such that it stands vertically in the flask. The inset shows the detail of the entrainment trap which has been designed for this distillation. On leaving the flask, vapors enter *L* and pass up into the large chamber in which partial condensation occurs. Three small holes (*M*) 0.2 mm. in diameter are located at the top of the lower entry tube, but not in it, in order to permit the condensed liquid to flow back into the flask. Any microburet of at least five-cc. capacity and readable to fiftieths is satisfactory for the titration.

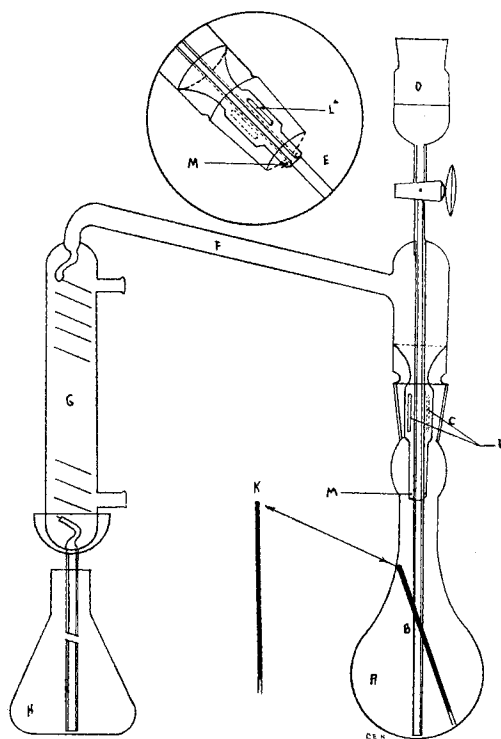


Fig. 2—Drawing showing details of construction of distillation apparatus.

Table I.—Comparative Results of Thyroid Assays

Material	Per Cent Iodine	
	U. S. P. XI Method	Micro-Method
Thyroid Substance	0.2037	0.2090
	0.2040 Av.	0.2024 Av.
C. T. Thyroid 1/2 gr. plain	0.2043	0.1993
	0.0367	0.0366
	0.0365 Av.	0.0365 Av.
C. T. Thyroid 1 gr. S. C. Brown	0.0362	0.0364
	0.0782	0.0785
	0.0786 Av.	0.0786 Av.
C. T. Thyroid 1 gr. Granulation	0.0789	0.0786
	0.0738	0.0739
	0.0738 Av.	0.0752 Av.
C. T. Thyroid 2 grs. Granulation	0.0738	0.0766
	0.0831	0.0836
	0.0834 Av.	0.0837 Av.
	0.0836	0.0838

Since this method has proved itself to be comparatively simple and to take but a fraction of the time spent on other assays, its accuracy remains as the only point to be confirmed. The Research Surgery Department of Ohio State University found the alkaline ash method to yield consistently high results. Tippet's (2) finding that this was due to a personal equation and could be eliminated by equalizing the titration time of the blank with that of the assay proper made nearly perfect iodine recoveries possible. The authors, to prevent any personal favoring of results, enlisted the aid of their laboratory co-worker, Mr. Roger F. Maize, in checking their work. The results of three operators shown in the following table are in remarkably close accord. Although usually a matter of personal preference, the authors suggest that one-hundredth-normal sodium thiosulfate solution be prepared by careful dilution of a tenth-normal solution that has been accurately standardized against pure copper (3).

The single disadvantage of the method lies in the fact that it requires an all-Pyrex glass apparatus of the type shown. This should be easily made by any experienced glass worker or can be ordered from the Leonard Glass Works, 1432 Minnesota Avenue, Columbus, Ohio.

CONCLUSIONS

1. In skilled hands, the U. S. P. XI assay method for Thyroid is accurate, but has the disadvantage of being time-consuming because of the time required to titrate the blank.

2. The method described is fully as accurate and in addition is rapid and easily run.

3. The authors recommend that a study of the method be made with the view of its adoption as a standard Pharmacopoeial procedure.

Credit is due Mr. H. W. Jones, Scientific Director of The Columbus Pharmacal Com-

pany, for his invaluable assistance in many phases of this investigation.

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An Interferometer Method for the Assay of Nitrous Oxide

By Frederick K. Bell and John C. Krantz, Jr.*

For a number of years, the gas interferometer has been used successfully for the analysis of carbon dioxide in air with an accuracy of 0.01 per cent. The fundamental factor which determines the feasibility of the method is the ratio of the indices of refraction of the gases involved and in this case the refractivity¹ of air is 2917×10^{-7} and that of carbon dioxide is 4498×10^{-7} . The value of this ratio also determines the degree of sensitivity that can be expected.

In a survey of the field of possible methods for the assay of nitrous oxide it occurred to the authors that the interferometer method should offer considerable promise. The

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¹ It will be recalled that the refractivity, R , is equal to the index of refraction, n , minus unity, therefore, $R = n - 1$.

The authors are greatly indebted to Carl Zeiss, Inc., of New York, for their generous loan of the interferometer used in these experiments and to the Ohio Chemical and Manufacturing Co. of Cleveland, Ohio, who have supplied us with a considerable number of specially prepared analyzed samples of nitrous oxide.