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THE CODETERMINATION OF IODINE-127, IODINE-131,
AND ASTATINE-211 IN TISSUE

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November 1954

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ABSTRACT

Astatine-211 and iodine, both stable and radioactive, in biological material in samples up to 50 grams can be determined by the procedure described. Tissue is digested with chromic acid, the mixture is reduced with oxalic acid, and the iodine and astatine are distilled quantitatively. At^{211} and I^{131} are then determined by radioactive assay, and stable iodine by spectrophotometry.

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The thyroid glands of experimental animals have been shown to accumulate astatine-211, but to a lesser degree than iodine-131. ^(1,2) Investigation of the radiotoxicity of At^{211} in rats and monkeys indicated that it would be safe to attempt tracer studies on the accumulation and retention of At^{211} in the human thyroid gland. ^(2,3) The results of a preliminary study of the uptake in the thyroid glands of 50 μc of At^{211} administered orally to patients who were to undergo thyroid surgery have been reported elsewhere. ⁽⁴⁾

In order to properly evaluate the results of tracer studies with At^{211} in the thyroid gland of man, it was felt that data should be obtained on stable iodine content, and the accumulation of At^{211} and a tracer dose of I^{131} simultaneously in the same individual.

The chemical and physical properties of At^{211} are given in detail by Johnson et al. ⁽⁵⁾ and by Hollander et al. ⁽⁶⁾ Astatine-211 decays both by alpha-particle emission and by K-capture which is associated with 80-kev x-rays. Iodine-131 decays by beta-particle emission associated with a complex cascade of gamma rays. Since the decay of both radioisotopes involves the emission of photons, it is possible to assay wet tissue samples directly with a scintillation counter when only one is present. When both At^{211} and I^{131} are present in the same sample, it is necessary to measure the alpha particles of the At^{211} in an ionization chamber which is insensitive to beta particles. In order to count alpha particles accurately, the samples must be nearly massless. A lead filter, 0.5 g/cm^2 is then placed over the samples to absorb the At^{211} alpha particles and x-rays, and the beta particles from the I^{131} . The gamma activity of the I^{131} can be measured with an NaI-Tl scintillating crystal

* This work was performed under contract of the University of California under the U.S. Atomic Energy Commission.

gamma counter. A detailed discussion of the problems involved in the radioactive assay of At^{211} is given by Hamilton et al. (2)

It was therefore necessary to subject the surgically removed human thyroid specimens to an analytical procedure that would meet the following requirements: The determination should be quantitative for At^{211} and for the total iodine present, both stable and radioactive. The final product should be a neutral or slightly basic aqueous solution which when dried would be nearly free from mass, the procedure should not be too time-consuming because of the short half life of the At^{211} , and the method should be applicable to fairly large samples, since goiterous human thyroids often weigh more than 50 grams.

The procedure to be described is based on earlier work by Hamilton and Soley. (7)

The following reactions are presumed to occur: During the digestion of the tissue with a mixture of chromium trioxide and 18 N sulfuric acid the iodine is oxidized to iodate and the At^{211} to a high positive-valence state; oxalic acid is added, reducing the iodate to volatile I_2 and some of the At^{211} to At^0 , which is also volatile; (5) and ferrous ion is added to complete the reduction of At^{211} to the zero-valence state.

Materials and Methods

The apparatus consisted of a one-liter Claisen flask fitted by a ground-glass joint to a thistle tube with a stopcock and by a second joint to an all-glass water-jacket condenser with a delivery tube bent nearly to a right angle. Erlenmeyer flasks one-third full of CCl_4 and surrounded by an ice bath served as receivers. The receiving flasks were placed so that the delivery tube dipped well below the surface of the CCl_4 .

The At^{211} was prepared by a modification of the method of Garrison et al. (8) The details of the administration of the At^{211} to the patients and the handling of the thyroid glands after their surgical removal are given elsewhere. (4) The thyroid glands were weighed, and no more than 50 grams was employed in a single determination. Thyroid glands weighing more than 50 grams were divided into approximately equal portions which were assayed separately. The tissue sample and some glass beads were placed in the flask with approximately three times the tissue weight of chromium trioxide. The neck of the flask was washed with three times the tissue weight of water. After the initial bubbling had subsided, a volume of 36 N sulfuric acid equal to that of the water was added slowly

through the thistle tube. Since the reducing capacity of biological materials is variable, it was sometimes necessary to use more than the stated amounts of reagents. The color of the reaction mixture usually was indicative of the progress of the oxidation. Persistence of the dark-green chromic ion indicated that the oxidation was not complete and more chromium trioxide, water, and sulfuric acid were added. All the reagents used in these experiments were c.p. grade.

When the addition of the acid was complete, and the violent reaction had ceased, the flask was heated slowly to a boil, and water was distilled until the amount of water collected in the receiving flask was nearly equal to that originally added, or until excess chromium trioxide precipitated. A small amount of distilled water (10 to 20 ml) was added and the distillation was continued for a few minutes to insure the complete removal of chlorine and to wash out the condenser. Overheating was avoided because of the possibility of carrying spattered dichromate over into the condenser.

The reaction flask was then allowed to cool to about 50°C, and the receiver was replaced by a 500-ml Erlenmeyer flask containing 200 ml of fresh CCl_4 . Neither the At^{211} nor I^{131} was found in measurable quantities in the initial aqueous or organic phases in the first receiving flask.

From 50 to 200 grams of oxalic acid, * depending on the amount of tissue in the sample, was added slowly, a few crystals at a time, until the evolution of CO_2 ceased and the solution was dark green in color. The flask was then heated and water, iodine, and some of the At^{211} were distilled over until the brown iodine color was no longer discernable in the delivery tube. The distillation was continued until another 20 to 30 ml of water had been collected.

After the flask had cooled nearly to room temperature, three times the tissue weight of anhydrous ferrous sulfate was added, and the neck of the flask was washed with 20 ml of water. The distillation was continued, using the same receiving flask, until ferrous sulfate precipitated in the bottom of the flask as a greenish-white solid. The distillate and the CCl_4 were transferred to a large separatory funnel with enough 0.2M Na_2SO_3 to completely reduce the iodine. The layers were separated and the CCl_4 was discarded. The volume of the

*The use of large crystals of oxalic acid is recommended, especially in the early stages of the reaction, which is quite violent.

aqueous layer was recorded, and duplicate aliquots for radioactive assay were pipetted into clean tinned bottle caps.** One ml of 0.2 N KI in 0.1 N NaOH and an excess of 0.1 N AgNO₃ were added. The samples were mixed by carefully rotating the caps and were dried slowly under a heat lamp at 75° C. If a sample of AgI that contains astatine is reduced, all the astatine is found on the precipitated metallic silver. (5) The sampling technique described above is quantitative, presumably as a result of the efficient scavenging of the astatine by the mixed AgI-Ag₂O precipitate, which, on heating in contact with the tinned mount, is reduced to form a thin uniform film of metallic silver completely binding the astatine. The samples were assayed for At²¹¹ alpha activity in an ionization chamber, and for I¹³¹ gamma activity with a scintillation counter as described earlier.

The stable-iodine content of the samples was determined by oxidizing an aliquot of the iodine-containing distillate with dilute HCl and H₂O₂ and re-extracting into a known volume of CCl₄. The concentration of I₂ in the CCl₄ was measured with a previously calibrated Beckman spectrophotometer at a wave length of 570 mμ.

Results

The accuracy of the above method was checked by pilot experiments using samples of rat muscle or beef thyroid to which had been added known amounts of At²¹¹ and I¹³¹. The recovery of the At²¹¹ was 90.2 ± 2.8 % and that of I¹³¹ was 98 ± 1%.

As in the earlier work of Hamilton and Soley⁽⁷⁾, the recovery of iodine, both stable and radioactive, was quantitative after the reduction with oxalic acid and the subsequent distillation as I₂. When the pilot experiments were performed, it was anticipated that At²¹¹ would be recovered quantitatively in the CCl₄ phase following the reduction with oxalic acid, as was iodine. It was found, however, that the recovery of the At²¹¹ was erratic, so that the subsequent reduction with ferrous sulfate was included in the method to insure the accuracy of the determination of At²¹¹.

Summary

A procedure for the determination of At²¹¹ and iodine, both stable and

** When these bottle caps are received from the dealer, they are coated with a thin film of laquer. This is removed by soaking for a few hours in 6 N NaOH warmed on a hot plate.

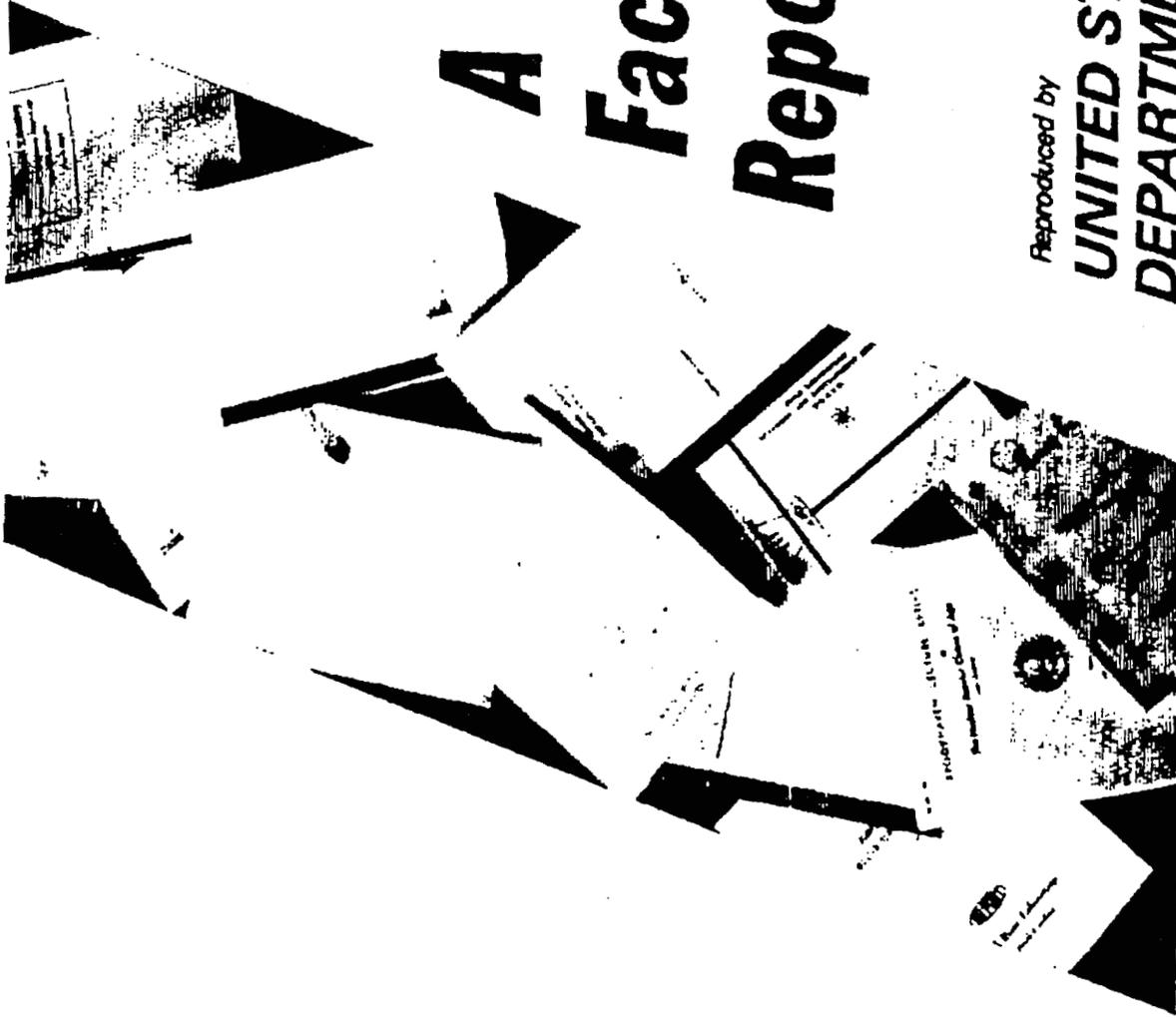
radioactive, in biological material is described. The procedure is applicable to samples weighing up to 50 grams. The tissue is digested with chromic acid and 18 N H_2SO_4 without the loss of either of the radiohalogens by volatilization. Both iodine and At^{211} are distilled quantitatively from the digestion mixture after reduction with oxalic acid and $FeSO_4$. The recovery of the At^{211} is $90 \pm 2.8\%$ and that of I^{131} is $98 \pm 1\%$. The stable iodine is determined spectrophotometrically.

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