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PRODUCTION OF HIGH PURITY IODINE-131 RADIOISOTOPE

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ABSTRACT OF THE DISCLOSURE

High purity radioactive iodine-131 is obtained in a stable chemical form by the dry distillation of a neutron-irradiated tellurium containing material, such as tellurium dioxide, onto alumina followed by elution with a base such as a dilute alkaline solution. Radioactive iodine-131 can be prepared by this process with a minimum of radioactive contamination to the immediate environment. The radioactive iodine-131 obtained by this process is a versatile tracer and is useful to determine blood volume, cardiac output and the like.

This invention relates to a novel process for the production of radioactive iodine. In one aspect, this invention relates to a novel process for the production of radioactive iodine-131 in high yields. A further aspect of this invention is directed to a novel process for the production of radioactive iodine-131 which can be obtained in a high degree of purity and in a stable chemical form.

Due to its relative short half-life (8.1 days) and high isotopic abundance, iodine-131 is particularly useful in medical research and diagnosis. It is well suited as a diagnostic tracer both in vivo and in vitro. For instance, it is well known that radioactive iodine isotopes are of great value in tests of thyroid function such as thyroid uptake, urinary iodine excretion, protein bound iodine conversion ratio and scanning of the thyroid or its metastases. In addition to medical uses, radioactive iodine isotopes can also be employed in industrial applications as a point radiation source. For example, they are useful for the determination of structural defects in metals and the like. However, when radioactive iodine isotopes are employed for medical research and diagnosis, the product must of necessity be extremely pure.

In the past, radioactive iodine isotopes have been prepared by a variety of methods. However, the processes employed to prepare isotopes do not always provide a product of the degree of purity necessary for medical applications, or are complex and time consuming. For example, M. Dous et al., U.S. Patent 3,114,608, discloses a process wherein reactor-irradiated TeO_2 target is dissolved into NaOH solution and iodine-131 distilled by adding hydrogen peroxide in the presence of sodium molybdate catalysis. C. R. Evans et al., British Patent 763,865—1956, dry-distilled iodine-131 from TeO_2 target into sodium sulfite solution. F. N. Case et al., U.S. Patent 3,282,655, dissolved the reactor irradiated ^{235}U target into NaOH solution and distilled HI by acidifying the solution with H_2SO_4. The HI that was collected was further purified by Pt adsorption method. K. Taugbol and J. B. Dahl (Jener Report No. 52, Kjeller, Norway, 1957) separated iodine-131 from TeO_2 by one-step dry distillation.

In U.S. Patent 3,226,298 there is disclosed another process for making high purity radioactive iodine-131.

In the referenced process tellurium dioxide is irradiated with thermal neutrons and iodine-131 dry distilled and condensed in a cold trap. However, this method has several disadvantages which do not render it ideally suited for consistently producing a product of a high degree of purity and in a chemically stable form. For example, in order to obtain a highly pure product, free of tellurium dioxide, it is often necessary to redistill the iodine a number of times. This necessarily requires the use of several coldtraps and numerous transfers of the product from one piece of apparatus to another within production facility such as a hot cell. Moreover, the distillation of gaseous iodine-131 can easily contaminate the working areas and, hence, the danger of radio-active contamination is great.

It has also been observed that the chemical form of iodine-131 changes depending on the purity and acidity of the solution. When the dry-distilled iodine is dissolved in an aqueous solution, the iodine is present as iodide (I^-) in an alkaline solution, and as molecular iodine (I_2) or triiodide (I_3^-) in an acidic solution. Molecular iodine is not desirable because it contaminates a laboratory by vaporization. Therefore, the iodide form is safe and more desirable. However, the addition of any reducing chemical reagent is not desirable for many medical uses. Hence, it is desired to control the chemical form of iodine-131 to iodide without adding a reducing agent and by providing a product which has a high degree of purity.

It is therefore an object of this invention to provide a more efficient method for producing radioactive iodine-131. Another object of this invention is to provide a process for preparing radioactive iodine-131 in a high degree of purity and by an extremely reproducible and simple process. An object of this invention is to produce radioactive iodine-131 by a method wherein the degree of recovery is high. A further object of this invention is to provide a process for preparing radioactive iodine-131 of a high degree of purity and in a chemically stable form which is acceptable for medical research and diagnosis. A still further object of this invention is to provide a method for the preparation of radioactive iodine-131 wherein the danger of radioactive contamination is minimized. These and other objects will readily become apparent to those skilled in the art in the light of the teachings herein set forth.

It has now been discovered that the aforementioned objects can be achieved by a process which comprises the steps of:

(1) Irradiating a tellurium containing material with thermal neutrons;

(2) Dry distilling the radioactive iodine-131 from the said tellurium material onto alumina, and

(3) Selectively extracting the iodine-131 from the alumina with a base.

By the term "tellurium containing material" as employed in the specification and claims, is meant tellurium metal, tellurium oxides, e.g., tellurium monoxide, tellurium dioxide, and tellurium salts, e.g., tellurium nitrate, tellurium sulfide, and the like.

Radioactive iodine-131 prepared by the process of this invention is obtained in a very high degree of purity and in a chemically stable form, i.e., as the iodide, and therefore suitable for use in medical research and diagnosis. In contrast to the known methods referred to above, this process is extremely simple and rapid providing a high recovery of iodine. Moreover, in contrast to the known

methods, the eluted iodine isotope is free of reducing agents. Additionally, the instant process provides a method which minimizes radioactive contamination of the working area.

In the first step of the process of this invention, the tellurium containing material, for example tellurium dioxide, is irradiated with thermal neutrons. If the iodine-131 is to be used for medical diagnostic studies, it is important that the tellurium material be of a high degree of purity, that is, the total of all detectable elements be less than 0.1 weight percent. The selenium content must be less than 0.005 weight percent. If the tellurium material does not meet these limits, then it must be heated to remove the selenium. Heating is effected at temperatures of from about 550° C. to about 700° C. and higher for periods of up to one hour. It has been observed that optimum results are obtained when the tellurium material is heated at 700° C. for 30 minutes, broken up in a ball mill into a powder and refired at 700° C. for 30 minutes. It is broken up again in a ball mill until it has a fine texture.

The tellurium material, for example, tellurium dioxide is then irradiated. After 200 hours of irradiation at a flux of approximately $3\text{–}5\times10^{13}$ n./cm.^{2}/sec., greater than 14 curies of iodine-131 is obtained. A specific activity of greater than 2.5×10^4 Ci/gm. will result one day after processing. Irradiation of the target material to provide the desired isotope is well known and can be effected by placing the tellurium containing material in tht irradiation zone of a nuclear reactor, particle generator or neutron isotopic source. The irradiated tellurium containing material is then transferred to a quartz distillation vessel and mounted in a vacuum system. The vessel is heated to a temperature of from about 450° to about 800° C. and the iodine-131 is distilled, and collected in a removable alumina column. The iodine-131 is removed from the column by dissolution in a base, preferably a dilute alkaline solution.

Although a variety of bases have been found to be suitable for the elution step, sodium hydroxide is preferred. When it is employed, the resulting iodine isotope is obtained in the form of sodium iodide and hence suitable for use in medical diagnosis. However, other bases can also be employed if the radioactive iodine is intended for other than medical uses. Suitable bases include, among others, sodium carbonate, potassium hydroxide, ammonium hydroxide, calcium hydroxide, and the like. The pH of the alkaline eluting solution employed is about 8 or higher, and preferably about 13.

Temperature is not necessarily critical and the elution step can be conducted conveniently at room temperature.

As previously indicated, the present invention provides radioactive iodine-131 which is in a chemically stable form. The oxidation state of iodine-131 to iodide is controlled without the addition of any reagents. The alumina surface shifts the $I_2 \rightleftarrows I^-$ equilibrium to iodide due to surface adsorption. The chemical form of iodine-131 prepared by the process of this invention was investigated by ultraviolet spectroscopy (A. D. Awtrey and R. E. Connick, J.A.C.S. 73, 1842, 1951) and the paper chromatographic method (The United States Pharmacopia (X—VII), pp. 616–617, 1965). The results showed that iodine-131 is present as iodide and does not change to any other forms for three weeks in a significant amount. Tellurium was not detected in the product solution by the cystein hydrochloride color test (the detection limit, $\sim5\times10^{-5}$ M). The radioactive contamination to the environment was essentially eliminated and the operation was simplified.

As previously indicated, the process of the present invention provides a simple method for the preparation of radioactive iodine-131 in a highly pure state and in a chemically stable form. For instance, iodine-131 is obtained by this process having a radionuclide purity of greater than 99.9 percent. When the iodine solution is intended for medical use, the solution can be sterilized according to known techniques without any adverse effect.

The following example is illustrative:

EXAMPLE I

Commercially available tellurium dioxide having a selenium and total heavy metal content of les sthan 0.01 and 0.1 percent by weight respectively was fired in a precalibrated muffle furnace at 700° C., for 30 minutes. It was cooled again and ball milled until it had a fine face-powder texture.

Aluminum tubing, ¾" diameter and 0.035" wall thickness, was cut into 20" lengths. The tube was wire-brushed on the inside and a plug welded in one end. The capsule was washed with trichloroethylene and acetone and dried in an oven. Approximately 300 gms. of TeO_2 was weighed into the capsule. The capsule was held in an aluminum block, a plug inserted and welded to the tubing. The integrity of the weld was determined by subjecting the capsule, immersed in water, to a partial vacuum of at least 27" of Hg.

The tellurium dioxide was then irradiated by reactor neutrons. After 200 hours of irradiation at a flux of approximately $3\text{–}5\times10^{13}$ n./cm.^{2}/sec., greater than 14 curies of iodine-131 were obtained.

After irradiation the aluminum capsule was opened by cutting with a tubing cutter in front of a powder exhaust system to reduce the release of radioactive dust into the hot cell. The tellurium dioxide was transferred to a quartz distillation flask and the empty capsule washed with 1 N NaOH and washings placed in a plastic bottle and capped.

The loaded flask was transferred to the hot cell and total activity checked by use of the in-cell gamma-ray monitor. Thereafter the flask was connected to the system containing a column of Woelm alumina and the system placed under vacuum. When the vacuum gauge indicated 30" of Hg, the furnace was raised up around the flask. Distillation was effected at 650° C. for about one hour. Thereafter, the system was allowed to cool and the column eluted with 5.0 milliliters of 0.1 N NaOH.

The iodine-131 concentration and radionuclidic purity was determined by gamma-ray spectroscopy. The concentration was about 3,000 mCi/ml. and the purity >99.9 percent. The pH of the final solution was 13. The chemical form of iodine-131 was determined by ultra violet spectroscopy and paper chromatography to be iodide. No change was observed in the chemical form of the iodine for a period of three weeks.

Although the invention has been illustrated by the preceding example, it is not to be construed as being limited to the materials employed therein, but rather, the invention encompasses the generic area as hereinbefore disclosed. Various modifications and embodiments of this invention can be made without departing from the spirit and scope thereof.

What is claimed is:

1. A method for producing radioactive iodine-131 which comprises the steps of
   (a) irradiating a tellurium containing material with neutrons,
   (b) dry distilling the radioactive iodine-131 from said tellurium material onto alumina, and
   (c) selectvely eluting the iodine-131 from said alumina with a base.

2. The method of claim 1 wherein said tellurium containing material is tellurium dioxide.

3. The method of claim 1 wherein said tellurium containing material is tellurium metal.

4. The method of claim 1 wherein said dry distilling is effected at a temperature of about 450° to about 800° C.

5. The process of claim 1 wherein said high purity radioactive iodine-131 is removed from said alumina with a dilute alkaline solution.

6. The process of claim 5 wherein said dilute alkaline solution is sodium hydroxide.

7. The method of claim 1 wherein said eluted iodine-131 has a radionuclidic purity of greater than 99.9 percent.

8. The method of claim 5 wherein said dilute alkaline solution containing radioactive iodine-131 is stirilized.

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