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PRODUCTION OF HIGH PURITY RADIOACTIVE ISOTOPES

Ephraim Lieberman, Suffern, N.Y., and Wayne J. Gemmill, Milford, Pa., assignors to Union Carbide Corporation, a corporation of New York

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This invention relates to the production of high purity radioactive isotopes, particularly molybdenum-99 and technetium-99m. Technetttium-99m, which has a half-life of six hours, is produced by the spontaneous radioactive beta decay of molybdenum-99. The latter has a half-life of 67 hours.

High purity Tc^{99m} is used primarily as a radioisotope in medical research and diagnosis. It is well suited for liver and brain scanning, and is preferred over other radioactive isotopes because of its short half-life which results in reduced exposure of the organs to radiation.

Since the radioisotope sought to be used has such a short half-life, it is common practice to ship the users of the isotope the parent element; in this case Mo^{99}. The user then extracts the Tc^{99m} from the Mo^{99} as his needs require.

In the past, radioactive molybdenum-99 has been recovered as a fission product formed by the fissioning of uranium-235 in a nuclear reactor. This method of producing Mo^{99} has several important shortcomings. One is that the Mo^{99} has to be separated from the numerous other radioactive fission products of U-235 such as strontium-90, yttrium-91, zirconium-95, niobium-95, ruthenium-103, ruthenium-106, iodine-131, cerium-141, cesium-137, cerium-144, promethium-147 and many others. Some of these fission products are long lived, and due to their radioactivity are difficult to handle without elaborate shielding.

As a result of separation problems, pure molybdenum-99 and consequently pure Tc^{99m} cannot be obtained from U-235 fissioning because traces of fission products such as iodine-131 and ruthenium-103 frequently remain in the separated product. In addition, this technique presents radioactive waste disposal problems.

It is an object of this invention to provide a more efficient method of producing radioactive molybdenum from which radioactive technetium may be extracted. It is another object of this invention to produce radioactive molybdenum by a method which avoids the need for separating radioactive fission products and avoids problems relating to disposing of radioactive waste resulting from the fissioning of U-235. It is another object of this invention to prepare high purity technetium-99 which contains no traces of fission products.

It has now been discovered that the aforementioned objects can be achieved by a process which comprises irradiating a molybdenum containing material in the presence of a neutron flux until the desired amount of Mo^{99} activity is formed, dissolving the irradiated material (containing Mo^{99}) in a base, adjusting the pH of the solution to be acidic and above pH 2.5, contacting an inorganic anion exchange material with the pH adjusted solution (thereby loading the molybdenum on the anion exchange material) and then selectively eluting or extracting technetium-99m, formed by the radioactive decay of molybdenum-99, from the loaded anion exchange material with an acid.

The present method offers several advantages over prior art methods of preparing technetium-99m. One of these is elimination of the need to separate radioactive molybdenum from other radioactive fission products. Another is a considerable reduction in the radioactive waste disposal problem. A still further advantage of this invention is that

a product of high purity is obtained containing no traces of other radioactive fission products. The purity of Tc^{99m} is of considerable importance because of its medicinal use.

In order to more fully understand the invention, the following example, which is the preferred embodiment of the invention, is given by way of illustration only and is not intended to limit the scope of this invention.

EXAMPLE

0.38 gram of MoO_3 were placed in a 3/8 inch aluminum capsule and sealed. The capsule was irradiated for 75 hours in a neutron flux of 5×10^{13} n/cm.^{2}-sec. The resulting material containing radioactive Mo^{99} had an activity of about 135 milicuries. Following irradiation the MoO_3 was dissolved in approximately 10 ml. of 40 percent NH_4OH. The solution of ammonium molybdate

$$(NH_4)_6Mo_7O_{24}\cdot 4H_2O$$

was first neutralized to a pH of 7 with 6 M HNO_3, and then acidified to a pH of 3.0 to 3.5 with 1 M HNO_3.

Prior to loading the above radioactive solution on an alumina anion-exchange column, the column containing 6 grams of 100 to 200 mesh alumina was washed with water and 0.1 M HNO_3. Effluent from the washing step was acidic (pH 2–6) before the column was loaded. The solution of ammonium molybdate after having its pH adjusted to 3.0 to 3.5 (and which contains Mo^{99}) was loaded on the alumina column at a flow rate of about 1–2 ml. per min. After the column was loaded, it was washed with about 150 ml. of 0.1 M HCl in order to remove the small quantities of Mo^{99} that would subsequently wash through during Tc^{99m} elution and contaminate the product solution.

The loaded column which contained about 135 milicuries of activity can subsequently be eluted or milked repeatedly for Tc^{99m} as it is formed with 25 ml. portions of 0.1 M HCl solution. This is done by passing the desired volume of 0.1 M HCl through the column and collecting the effluent.

Numerous variations of the preferred embodiment described above may be practiced, as will be apparent to those skilled in the art, without departing from the basic concepts of the present invention. Thus, while MoO_3 is the preferred target material for the production of Mo^{99}, other molybdenum containing materials may be used. Such materials include, for example, molybdenum sesquioxide, Mo_2O_3; molybdenum dioxide, MoO_2; molybdenum pentoxide, Mo_2O_5; hydrated molybdenum oxide ("moly blue"), $Mo_{2.5-3.0}\cdot xH_2O$; molybdic acid H_2MoO_4, and mixtures thereof.

Separation of Tc^{99m} from Mo^{99} can be effected by contacting the Mo^{99} (in the form of molybdate ions) with alumina, followed by selective removal of Tc^{99m} (in the form of the TcO_4 ion) from the loaded alumina. A column of alumina is preferably used, however, the separation can be made by slurrying the molybdate ion containing solution with finely divided alumina in a container (thereby loading the alumina with molybdate ions), separating the solids from the liquid, for example, by filtration and then removing the Tc^{99} from the alumina particles by reslurrying the alumina in an acid and then separating the dissolved Tc^{99} from the unloaded alumina solids. Use of a column is, of course, far simpler and more efficient.

The exact nature of the "exchange" mechanism by which the molybdenum is loaded on alumina and by which the Tc^{99} is eluted is not entirely certain. While not wishing to be limited to any theory, it is believed to be an ion exchange mechanism whereby molybdate ions are loaded on the acidified alumina column in exchange for OH^- ions. Upon elution, the Tc^{99m} is removed from

the column as pertechnate, TcO_4^- ions in exchange for Cl^- ions. However, the ion exchange reaction appears to be limited to a surface phenomena, and it is therefore possible that the mechanism is actually a surface adsorption phenomena. It is most likely a combination of both ion exchange and adsorption. Thus, while the material is referred to in this disclosure as an inorganic "anion exchange material," it is to be understood that the materials rather than the mechanism whether ion exchange or adsorption are intended thereby. Alumina is the preferred "exchange" material. Other materials, however, which are chemically stable in the system, stable to the radiation emitted in the system, and which are able to "exchange" the molybendum and technetium ions can be used in place of alumina. Such materials include the inorganic refractory oxides of zirconium, thorium, tungsten and silicon. Suitable illustrative materials include zirconia (ZrO_2), thoria (ThO_2), tungsten trioxide (WO_3) and silica (SiO_2). These materials have an affinity for anions when their surfaces have been rendered acidic.

Bases other than NH_4OH may be used to dissolve the irradiated molybdenum containing material, provided they will not interfere with subsequent loading and elution of the inorganic "anion-exchange material." Suitable bases include, for example, NaOH and KOH. Ammonium hydroxide is preferred.

Following dissolution of the irradiated molybdenum containing material it is essential that the solution be acidified and be above pH 2.5. At a pH below 2.5 precipitation results, while at an alkaline pH the molybdate ion will not load properly on the "exchange" material. The preferred range is pH 3.0 to 3.5. Adjustment of the pH and washing of the "exchange" material is preferably done with HNO_3. HCl is the preferred acid used for the preferential elution of Tc^{99m} from the "exchange" material. Other mineral acids, however, such as HNO_3 may also be used.

The amount of radiation to which the molybdenum containing target material is subjected is not critical and both the time and intensity of the neutron flux may be varied considerably from that shown in the preferred embodiment. It is merely necessary that the target material be irradiated until the desired amount of Mo^{99} activity is formed. A convenient amount is about 100–300 millicuries of Mo^{99} per loaded column, or about 200–1000 millicuries per gram of irradiated MoO_3.

What is claimed is:

1. A process for producing radioactive technetium-99m which comprises the steps of:
   (1) irradiating a base-soluble molybdenum containing material in a neutron flux until the desired amount of Mo^{99} activity is formed,
   (2) dissolving the irradiated molybdenum containing material, containing the radioactive Mo^{99}, in a base,
   (3) adjusting the pH of the solution prepared in step (2) to be acidic and above pH 2.5,
   (4) contacting an inorganic anion exchange material with the pH adjusted solution of step (3) thereby loading the molybdenum on the exchange material, and
   (5) extracting technetium-99m, formed by the radioactive decay of Mo^{99}, from the loaded anion exchange material with an acid.

2. The process of claim 1 wherein the inorganic anion exchange material is alumina.

3. The process of claim 2 wherein the base used to dissolve the irradiated material is ammonium hydroxide.

4. The process of claim 2 wherein the pH of the solution prepared in step (2) is adjusted to be within the range of 3.0 to 3.5.

5. The process of claim 2 wherein the particle size of the alumina is 100 to 200 mesh.

6. The process of claim 2 wherein the acid used for extracting the technetium-99m from the loaded alumina is hydrochloric acid.

7. A process for producing radioactive technetium-99m which comprises the steps of:
   (1) irradiating MoO_3 in a neutron flux until the desired amount of Mo^{99} activity is formed,
   (2) dissolving the irradiated MoO_3, containing radioactive Mo^{99}, in ammonium hydroxide,
   (3) adjusting the pH of the solution formed in step (2) to be acidic and above pH 2.5,
   (4) contacting a column of alumina with the pH adjusted solution of step (3) thereby loading the alumina with molybdate ions, and
   (5) eluting technetium-99m, formed by the radioactive decay of Mo^{99}, from the loaded alumina column with hydrochloric acid.

8. The process of claim 7 wherein the pH of the solution formed in step (2) is adjusted to be within the range of 3.0 to 3.5.

9. A process for producing radioactive technetium-99m which comprises the steps of:
   (1) providing a solution of ammonium molybdate in which at least some of the molybdenum is radioactive Mo^{99},
   (2) adjusting the pH of the solution to be acidic and above pH 2.5,
   (3) contacting a column of alumina with the pH adjusted solution of step (2), thereby loading the column with molybdate ions, and
   (4) eluting technetium-99m, formed by the radioactive decay of Mo^{99}, from the loaded alumina column with an acid.

10. The process of claim 9 wherein the pH of the solution is adjusted to be within the range of 3.0 to 3.5.

11. The process of claim 9 wherein the acid used for eluting the loaded alumina column is hydrochloric acid.

12. A process for producing radioactive technetium-99m which comprises the steps of:
   (1) providing a solution containing molybdate ions, which is acidic, has a pH above 2.5, and in which at least some of the molybdenum is radioactive Mo^{99},
   (2) loading a column of alumina with the solution of step (1) and
   (3) eluting technetium-99m, formed by the radioactive decay of Mo^{99}, from the loaded alumina column with an acid.

13. The process of claim 12 wherein the pH of the solution is adjusted to be within the range of 3.0 to 3.5.

14. The process of claim 12 wherein the acid used for eluting the loaded alumina column is hydrochloric acid.

15. A process for producing a solution containing radioactive molybdenum-99, from which solution radioactive molybdenum-99 can be loaded onto an inorganic anion exchange material, which process comprises the steps of:
   (1) irradiating MoO_3 in a neutron flux until the desired amount of Mo^{99} activity is formed,
   (2) dissolving the irradiated MoO_3, containing radioactive Mo^{99}, in a base, and
   (3) adjusting the pH of the solution formed in step (2) to be acidic and above pH 2.5.

16. A process for producing a solution containing radioactive molybdenum-99, from which solution radioactive molybdenum-99 can be loaded onto alumina, which process comprises the steps of:
   (1) irradiating MoO_3 in a neutron flux until the desired amount of Mo^{99} activity is formed,
   (2) dissolving the irradiated MoO_3, containing radioactive Mo^{99}, in ammonium hydroxide and,
   (3) adjusting the pH of the solution prepared in step (2) to be within the range of 3.0 to 3.5.

17. A process for producing the combination comprising alumina having loaded thereon radioactive molybdenum-99 which process comprises the steps of:
   (1) irradiating MoO_3, in a neutron flux until the desired amount of Mo^{99} activity is formed,
   (2) dissolving the irradiated MoO_3, containing radioactive Mo^{99}, in a base,

(3) adjusting the pH of the solution formed in step (2) to be acidic and above pH 2.5, and

(4) loading the pH adjusted solution of step (3) on a column of alumina.

18. A process for producing the combination comprising alumina having loaded thereon radioactive molybdenum-99 which process comprises the steps of:

(1) irradiating MoO_3 in a neutron flux until the desired amount of Mo^{99} activity is formed,

(2) dissolving the irradiated MoO_3 containing radioactive Mo^{99} in ammonium hydroxide,

(3) adjusting the pH of the solution prepared in step (2) to be within the range of 3.0 to 3.5, and

(4) loading the pH adjusted solution of step (3) on a column of alumina.

References Cited

Atompraxis, vol. 10, Heft 6, June 1964, pp. 263–264.

AEC Document, BNL–595, 1959, page 29.

AEC Document, BNL–864, August 1964, pp. 1, 40–43 and 53–54.

AEC Document, ORNL–3802, May 1965, pp. 8–11.

Handbook of Chemistry and Physics, 40th edition, 1958–1959, pp. 519, 610, 611.

CARL D. QUARFORTH, *Primary Examiner.*

L. DEWAYNE RUTLEDGE, *Examiner.*

H. E. BEHREND, *Assistant Examiner.*