Argonne Chemical-Processing Activities in Support of the Development of γ,n Production of Mo-99

D.A. Rotsch, P. Tkac, G.F. Vandegrift

Chemical Science and Engineering
Argonne National Laboratory, 9700 Cass Avenue, Argonne IL. 60439 – USA

and

J.T. Harvey
Northstar, 5249 Femrite Drive, Madison WI. 53718 – USA

ABSTRACT

Technetium-99m, currently provided to consumers from ^{99}Mo/^{99m}Tc generators, is well-known for its uses in radiopharmaceuticals. Argonne National Laboratory is assisting NorthStar Medical Radioisotopes in developing accelerator-based production of ^{99}Mo using photonuclear reaction ^{100}Mo(γ,n)^{99}Mo with enriched ^{100}Mo targets. Enriched-^{100}Mo metallic disks are irradiated, dissolved in H_2O_2, converted to K_2MoO_4 in a KOH solution, and then loaded onto a NorthStar Generator, RadioGenix^{TM}, formally known as TechneGen. The alkaline solution containing ^{99m}Tc and $^{99/100}$Mo is fed to the RadioGenix and the technetium is sorbed by the ABEC column. After a wash step, pure $^{99m/g}$Tc is eluted from the column and ready for chelation. Once the ^{99}Mo in the feed solution has decayed, the solution needs to be treated to recover and recycle the valuable ^{100}Mo. To reuse ^{100}Mo, NorthStar will require that recycled materials meet the purchase specifications of the original material. Experimental data on dissolution of sintered Mo disks, separation of $^{99m/g}$Tc from $^{99/100}$Mo using RadioGenix generator, and recovery of ^{100}Mo will be presented.

1. Introduction

Technetium-99m is a widely used radioisotope for single-photon emission computed tomography (SPECT) imaging because of its ideal characteristics such as a sufficiently short half-life (6 hrs) and single gamma emission (140 keV). SPECT utilizes gamma emissions from select radioisotopes such as ^{99m}Tc (140 keV) to collect multiple 2D images that can later be combined into 3D images that map the interior of a patient. Information such as this provides insight on diseases that will help doctors cure certain ailments.

There is currently no US-domestic supply of ^{99m}Tc which is a decay product of ^{99}Mo. Argonne National Laboratory with the National Nuclear Security Admiration's (NNSA) Global Threat Reduction Initiate (GTRI), in partnership with commercial entities like NorthStar Medical Isotopes are developing technologies for the domestic production of ^{99}Mo for nuclear medicine while minimizing civilian use of highly enriched uranium (HEU). Currently, most of the ^{99}Mo being produced is a fission product isolated from HEU targets irradiated in HEU-fueled reactors. It is because of the GTRI program that other methods for the production of Mo-99 are being targeted. One such method is the photonuclear reaction ^{100}Mo$(\gamma,n)^{99}$Mo. The targets, enriched-^{100}Mo pressed and sintered Mo-powder disks, represent a large investment and the ^{100}Mo must be recycled. Herein we report strides taken towards dissolving irradiated ^{100}Mo disks, separation of ^{99m}Tc from $^{99/100}$Mo product solution, and recycling of ^{100}Mo in waste streams.

2. Experimental

2.1. Dissolution of Mo Disks

After the 1-g enriched-^{100}Mo disks have been irradiated, they are transferred using a shielded cask to a hot cell. The cell is specially designed to allow for samples to be brought in through the floor of the cell with a lift. Once inside the hot cell, the pressed Mo-powder disks are removed from the 25-disk holder using specialized tools. The disks are placed in individual holders in lead pigs, removed from the hot cell, and gamma counted. Six disks having the highest ^{99}Mo content are brought back into the cell and dissolved.

The Mo-metal disks are dissolved using 30% H_2O_2 at 70°C. The amount of H_2O_2 required for the dissolution is dependent on the physical properties of the disks themselves (pressing and sintering conditions, pore size, grain size, density, etc.)[1]. The reaction is exothermic and shown below as Equation 1.

$$2Mo_{(s)} + 10H_2O_{2(aq)} \rightarrow (H_3O)_2[Mo_2O_3(O_2)_4(H_2O)_2]_{(aq)} + 5H_2O_{(l)} \qquad \textbf{(Eq. 1)}$$
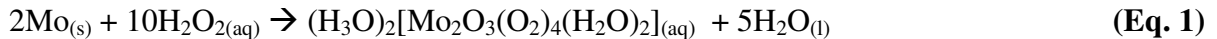
The metallic disks rapidly dissolve and produce a yellow/orange solution. After complete dissolution, the solution is converted to a highly alkaline solution by slow addition of potassium hydroxide. The Mo-peroxo species is converted as shown in Equation 2. Potassium hydroxide is added until the solution is clear and colorless.

$$(H_3O)_2[Mo_2O_3(O_2)_4(H_2O)_2]_{(aq)} + 4KOH_{(aq)} \rightarrow 2K_2MoO_{4(aq)} + 7H_2O_{(l)} + 2O_{2(g)} \qquad \textbf{(Eq. 2)}$$

The solution is heated to destroy any residual H_2O_2 and then diluted as necessary to render a 0.2 g-Mo/mL K_2MoO_4 solution in 5 M KOH . With no further treatment, the solution is allowed to cool and loaded into a RadioGenix transfer pot, which is later connected to the RadioGenix system.

2.2. RadioGenix

Once the $^{99/100}$Mo disks have been dissolved and loaded into the RadioGenix transfer pot, the pot is brought to the RadioGenix system and connected. The RadioGenix system is shown below (Figure 1). The ^{99m}Tc/$^{99/100}$Mo solution is passed through the system where ^{99m}Tc is

trapped on a column and the remainder of the $^{99/100}$Mo is rinsed from the column into a collection pot. The column is further washed and these washes collected in a waste container. ^{99m}Tc is then eluted from the column in saline ready for use.

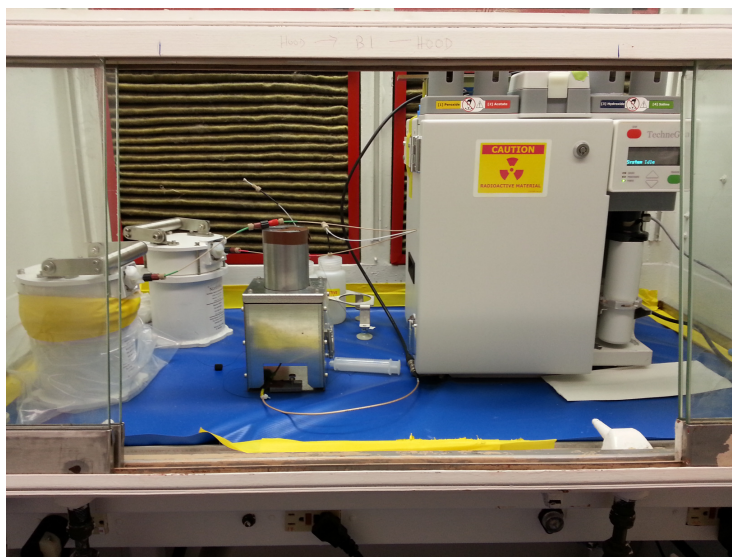**Figure 1.** RadioGenix System: $^{99/100}$Mo Transfer Pot (left front); ^{100}Mo Collection Pot (left rear); waste vessel (middle rear); purification system and final product isolation (right).

2.3. Mo-100 Recycling

Mo-100 is in the range of $750/g and must be recycled for cost efficiency. $^{99/100}$Mo that is rinsed from the RadioGenix column is stored in a lead-lined pot until ^{99}Mo decays. Once ^{99}Mo is decayed, the ~0.2 g-Mo/mL solution (in 5M KOH) is treated to recover and purify the ^{100}Mo. Two methods are currently under investigation. $MoO_{3(s)}$ will precipitate from acidic solutions (Method 1); molybdenum also has rich and well-known chemistry and will readily form water-insoluble polyoxometalates (POMs, Method 2).

2.3.1 Method 1 $MoO_{3(s)}$

Precipitation of Mo was performed by adding glacial acetic acid to a solution of ~0.2 g-Mo/mL in 5M KOH (Equation 3). The Mo-trioxide precipitate was then washed repeatedly with concentrated nitric acid.

$$K_2MoO_{4(aq)} + 2HOOCH_{3(aq)} \rightarrow MoO_{3(s)} + 2KOOCH_{3(aq)} + H_2O_{(l)} \tag{Eq. 3}$$

Washing steps are repeated until satisfactory purification factors are achieved. Upon completion of wash steps, wet MoO_3 is slowly heated to remove residual HNO_3 and H_2O. Dry MoO_3 is usually yellow but white and blue powders were also isolated (Figure 2).
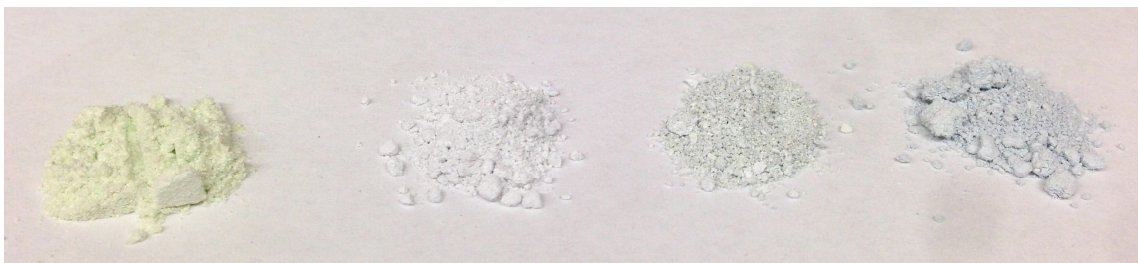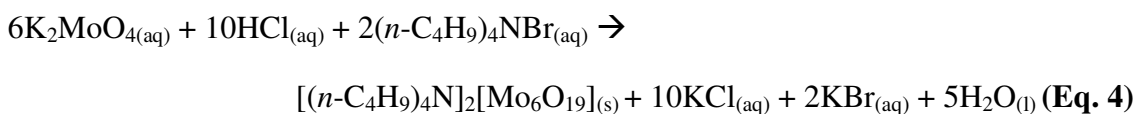
Figure 2. Photographs of Mo oxide powders obtained from Method 1 (3 right piles) from K_2MoO_4 solution in 5 M KOH compared to commercial MoO_3 powder (left)[1].

The recovery of Mo was determined using inductively coupled plasma mass spectrometry (ICP-MS) and verified using [99]Mo spikes. Potassium content was determined using ICP-MS performed on samples that had Mo extracted with tri-*n*-butyl phosphate (TBP).[2] The method is described in detail in recently released reports. [3,4]

2.3.2 Method 2 (Bu$_4$N)$_2$[Mo$_6$O$_{19}$]$_{(s)}$

Molybdenum was precipitated by using a modified procedure from Inorganic Syntheses (Equation 4).[5] A solution of $K_2MoO_{4(aq)}$ (0.2 g-Mo/mL, 1 mL) was neutralized by slow addition of HCl (6M, 1 mL) and further acidified by slow addition of HCl (6M, 1 mL).

$$6K_2MoO_{4(aq)} + 10HCl_{(aq)} + 2(n\text{-}C_4H_9)_4NBr_{(aq)} \rightarrow$$

$$[(n\text{-}C_4H_9)_4N]_2[Mo_6O_{19}]_{(s)} + 10KCl_{(aq)} + 2KBr_{(aq)} + 5H_2O_{(l)} \textbf{ (Eq. 4)}$$

A solid formed upon contact with the second addition of acid and dissolved upon stirring. The solution yellowed upon addition of ~1.5 mL of HCl and precipitated upon complete addition. A solution of tetrabutylammonium bromide ($(n\text{-}C_4H_9)_4$NBr or Bu$_4$NBr; 0.092 g/mL, 1.2 mL) was then added. Precipitation of the solution increased. Stirring became difficult, so the solution was diluted with 10 mL of H_2O. The resultant slurry was heated at 75-80 $^{\circ}$C with stirring for ~45 minutes. During this period, the white solid turned yellow. The suspension was then allowed to cool to room temperature. The slurry was transferred to a centrifuge tube and diluted with water (10 mL).

The sample was centrifuged, and the solution decanted onto a fine porosity glass-fritted funnel. The solution was passed through the funnel; the filtrate was saved for analysis. Water (10 mL) was added to the centrifuge tube and the mixture was mixed by vortex for several minutes and then centrifuged. The solution was again passed through the funnel, and the filtrate collected for analysis. This process was repeated five times. The solid became more and more flocculent with each wash and would not compact with centrifugation. The solids were collected on the fritted funnel. Upon completion of the wash steps, the yellow product was dissolved in warm acetone, passed through the fritted funnel (dissolving the previously collected solid), and collected. A fine white solid was left on the frit. This is presumed to be the hydrolysis product of (Bu$_4$N)$_2$[Mo$_6$O$_{19}$] (this compound will hydrolyze in moist conditions but is indefinitely stable when stored in a desiccator). The white solid was dissolved from the frit with NH_4OH (10 mL) and collected separate from the yellow product. The solvents were evaporated giving

crystalline $(Bu_4N)_2[Mo_6O_{19}]$ and hydrolysis product (Figure 3). Samples were weighed and then prepared for ICP-MS.

Figure 3. Photographs of solids isolated from Method 2. Hydrolysis product (left), $(Bu_4N)_2[Mo_6O_{19}]$ (middle), $(Bu_4N)_2[Mo_6O_{19}]$ and hydrolysis product combined (right)

ICP-MS was performed under acidic aqueous conditions. Water-insoluble $(Bu_4N)_2[Mo_6O_{19}]$ was decomposed with NH_4OH. These samples were then diluted with water and two aliquots from each sample ($(Bu_4N)_2[Mo_6O_{19}]$ and hydrolysis product) were taken. The first aliquots were acidified and then submitted for analysis. Molybdenum was extracted from the second aliquots with TBP. The aqueous layer was collected and submitted for analysis. This experiment was repeated (no extraction was performed) using ^{99}Mo spiked solutions to verify Mo recovery.

3. Results and Discussion

3.1. Dissolution of Mo Disks

Processing of irradiated Mo-target disks must be rapid as ^{99}Mo has a relatively short half-life ($t_{1/2} = 66$ hr). Approximately 1% of ^{99}Mo is lost every hour from decay. This means that the dissolution of the disks must be completed quickly. Preparation of Mo disks will greatly affect dissolution rates. Pre-sintering, pressing, and sintering conditions were previously tested.[1,2] In order to achieve high ^{99}Mo and thus ^{99m}Tc yields from irradiated ^{100}Mo disks, high densities (>92%) disks are desired. Disks with high densities are generally formed with high pressing factors and high sintering factors. However, it was determined that high sintering factors greatly reduce dissolution rates. This is most likely a result of grain growth and a decrease in pore sizes. Pre-sintering and sintering are the two conditions that greatly influence dissolution while pressing does not seem to have an effect. The best conditions for quick dissolutions include high pre-sintering and low sintering temperatures. A compromise between high density targets and quick dissolution times needs to be made. Desirable densities and dissolution rates are >92% and 0.6-0.8 g/min (respectively).

3.2. RadioGenix

The RadioGenix System, shown in Figure 1, will be used to test the reproducibility of recovering ^{99m}Tc from dissolved irradiated ^{100}Mo disks. Physical characteristics of the isolated ^{99m}Tc solutions will be examined, from pH to Mo and Al impurities. Each component of the system will be monitored by gamma analysis for ^{99}Mo and ^{99m}Tc. Aluminum content will be monitored by ICP-MS. In previous models, >95% of ^{99m}Tc was recovered in the product vial. Protocols will be modified to adjust parameters to meet United States Pharmacopeia (USP) specifications.

3.3. Mo Recycling

Several MoO_3 precipitation methods were previously tested. The primary method was acidification of the basic starting solution. Precipitation with H_2SO_4 gave a suspension that was difficult to separate. The use of HNO_3 lead to significant losses due to delayed precipitation. Acetic acid was able to precipitate Mo most efficiently and was therefore used. These results are presented in Method 1.

Despite the excellent results of MoO_3 precipitation with acid, the wash steps require abundant amounts of acid, recycling of HNO_3 washes is currently being investigated. Another method that would remove the need to wash the precipitated Mo with acid was attempted. The Mo-POM, $(BuN_4)_2[Mo_6O_{19}]$, is insoluble in water and can be washed repeatedly in water. These results are presented in Method 2.

3.3.1. Method 1 MoO$_{3(s)}$

MoO_3 was precipitated with acetic acid and then allowed to rest at room temperature for 24 hours. The 24-hour wait step was crucial as MoO_3 does not instantaneously and completely precipitate from solution upon acid addition. Over time, a white precipitate formed and clouded the solution. This solid was compacted with the bulk by centrifugation. The solution was then decanted from the solid and the solid washed with HNO_3 by vortex mixing. This solution was centrifuged and again allowed to rest for 24 hours. During this wait step, another slow-forming precipitate formed. The suspension was again decanted and the solid washed. The procedure was repeated until acceptable potassium levels were reached (Table 1). The removal of potassium was dependent on both the mixing/washing time and the number of washes.

Table 1. Mo recovery results using acetic acid precipitation followed by HNO_3 washes. DF: decontamination factor

Mix time	HNO$_3$ wash	Mo recovery (%)	K removed (%)	K (ppm)	DF
4 min	8x	99.51	99.985	261.2	6.6E+03
4 min	10x	99.37	99.992	142.7	1.2E+04
10 min	10x	99.00	99.997	60.7	2.9E+04
4 min	12x	96.74	99.996	71.6	2.5E+04
10 min	12x	~100	99.999	14.7	1.1E+05
10 min	14x	~100	99.999	10.8	1.6E+05
10 min	16x	95.10	99.998	40.5	4.5E+04

Precipitation of MoO_3 with acetic acid has achieved excellent Mo recoveries and K removal when the 24 hour wait steps were performed. Large-scale experiments are currently underway. Full scale experiments will be conducted on two liters of 0.2 g-Mo/mL (400 g of Mo).

3.3.2. Method 2 $(Bu_4N)_2[Mo_6O_{19}]_{(s)}$

As in Method 1, this synthesis has nuances that must be taken into consideration. Acidification of the starting solution must be slow to avoid formation of solid and avoid significant heating of the solution. The end point was just after the solution becomes yellow. If more acid was added, the solution precipitated and the yield of $(Bu_4N)_2[Mo_6O_{19}]$ decreased but this did not affect the Mo recovery yields. The precipitated Mo was still recovered; it simply made the final recovery more intensive. During final recovery, $(Bu_4N)_2[Mo_6O_{19}]$ was dissolved from the fritted funnel in acetone. The other material (presumably a hydrolysis product or MoO_3) was insoluble in acetone and was dissolved in base (NH_4OH).

Initial attempts included isolation of cold Mo as $(Bu_4N)_2[Mo_6O_{19}]$ on a glass fritted-funnel, followed by washing the solid on the funnel. Recoveries by mass were very good (>90%), therefore [99]Mo-spiked trials were conducted while awaiting ICP-MS data. Mo-99 spiked trials were conducting prior to the centrifugation/filtration method (described in the experimental). Washes for these samples were conducted on fritted funnels. These trials determined that 99-100% of the Mo was recovered overall. An average of 55% was collected in the $(Bu_4N)_2[Mo_6O_{19}]$ acetone fraction and 45% was isolated in the NH_4OH fraction. The discrepancy observed between mass yields and gamma counting yields is from loss of material on the frit (powder) and the chemical form of the material complicating yield calculations. This method only used 5 wash steps and will need to be repeated using the newly modified procedure.

ICP-MS data from the filter wash method demonstrated that insufficient washing was occurring. Mo recoveries were >90%; however, the K content (800- 20000 mg-K/kg-Mo) was far above the desired levels (25 mg-K/kg-Mo). The wash method was insufficient because of the inherent nature of the material. $(Bu_4N)_2[Mo_6O_{19}]$ caked on the frit and efficient washing was nearly impossible. A more efficient method was employed in later trials. The solid was centrifuged, solution filtered, solid washed with water, mixed by vortex, and the process repeated. This allowed for adequate washing and little to no loss of material. Initial results are promising, but the data are still pending.

4. Conclusion

Strides have been made for the production of [99]Mo at Argonne National Laboratory with the support of NNSA and NorthStar. Dissolution of irradiated [100]Mo disks depends greatly on the pre-conditioning of [100]Mo powders and the post conditioning of the pressed disks. The formation of the disk (pressing) does not seem to play a major role in dissolution. It was determined that high pre-sintering and low sintering conditions produced disks that were both easily dissolved and had acceptable densities. The RadioGenix system will be used in future studies to determine if samples will meet USP specifications. Two precipitation methods for the recycling of [100]Mo from the RadioGenix system are under investigation. Precipitation of

MoO_3 with acetic acid has achieved excellent Mo recoveries and K removal. However, this method requires various washes with HNO_3 which produces a great deal of acidic waste. This method also requires two 24 hour wait periods. The second method was the precipitation of Mo as $(Bu_4N)_2[Mo_6O_{19}]$. The ability of this material to be washed with water makes this method more desirable. However, it requires more testing.

Future works will focus on the dissolution of irradiated disks and testing the resultant solution in the RadioGenix system. Large scale experiments for the precipitation of MoO_3 by acetic acid are currently underway and testing of the $(BuN_4)_2[Mo_6O_{19}]$ method will continue.

5. Acknowledgments

6. References

[1] P. Tkac, G. Vandegrift, S.D. Nunn, J. Harvey, "Processing of Sintered Mo Disks Using Hydrogen Peroxide," Argonne National Laboratory, ANL/CSE-13/44, September, **2013**.

[2] P. Tkac, A. Paulenova, Speciation of Molybdenum (VI) in Aqueous and Organic Phases of Selected Extraction Systems," Separation Science and Technology, **2008**, *43*, 2641

[3] P. Tkac, G. Vandegrift, S.D. Nunn, J. Harvey, "Recovery of Mo for Accelerator Production of Mo-99 Using (γ,n) Reaction on Mo-100," Argonne National Laboratory, ANL/CSE-13/45, September, **2013**.

[4] P.Tkac, G.F. Vandegrift, "Method for increased accuracy of ICP-MS detection of potassium in sample with high Mo content" Argonne National Laboratory, ANL/CSE-14/16, **2014**.

[5] N.H. Hur, W.G. Klemperer, R.C. Wang, Inorganic Syntheses, **1990**, *27*, 77