Radiation Chemistry of Simulated ^{99}Mo Product

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Pharmaceutical houses that produce $^{99\text{m}}\text{Tc}/^{99}\text{Tc}$ generators have on occasion received ^{99}Mo that contained a black precipitate. Addition of sodium hypochlorite to product bottles prior to shipment prevents precipitate formation, indicating the precipitate is a reduced form of Mo. The radiation effects of the dose from ^{99}Mo on the product and product bottle have been determined by irradiating simulated ^{99}Mo product solutions with the ^{60}Co source at Sandia National Laboratories' Gamma Irradiation Facility (GIF). The GIF experiment successfully generated a black precipitate in amounts sufficient for isolation and analysis by infrared and Raman spectroscopy. Changes in the pH of the basic ^{99}Mo product solution during irradiation were monitored by titration. Results of these analyses and the nature of the process that generates the precipitate, a mixture of molybdenum oxides that forms in plastic bottles, but not in glass containers, are discussed.

Key Words

Radiation chemistry, ^{99}Mo , self-irradiation.

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Introduction

^{99m}Tc , the decay product of ^{99}Mo , is the most widely used radioactive isotope for diagnostic studies in nuclear medicine. ^{99}Mo is one of the fission products produced by neutron bombardment of a $^{235}\text{UO}_2$ -coated stainless steel target in a reactor. After irradiation, the uranium coating is dissolved in acid and the ^{99}Mo is isolated and purified in a hot cell facility. Because the half-life of ^{99}Mo is only 66 hours, the supply must be continuously produced and shipped to the pharmaceutical houses within 24 hours of production. There is currently only one commercial producer of ^{99}Mo in the western hemisphere, MDS Nordion of Canada.

Concerned that they were limited to a single source for ^{99m}Tc , the U.S. medical community approached Congress to seek support for the development of a domestic production source of ^{99}Mo . Congress tasked the Department of Energy (DOE) with the development of this production capability. In September 1996 the DOE signed a Record of Decision authorizing Sandia National Laboratories in Albuquerque to establish a production capability for ^{99}Mo and related medical isotopes at its reactor and hot cell facilities.¹ Using the existing facilities, pilot batches of ^{99}Mo that passed industry purity specifications were produced in 1996 and shipped to pharmaceutical houses for evaluation of compatibility with their processes. Once this milestone was achieved, facilities modifications and the Food and Drug Administration validation process for full-scale production were begun. As part of process validation, possible negative effects of the high radiation field produced by ^{99}Mo on both processing reagents and fission products were considered. Beta irradiation from ^{99}Mo averages 1.12 Mrad/hr and can degrade both reagents during isotope separation and the product during shipping. In the

past, pharmaceutical houses have reported receiving ^{99}Mo product solutions containing a black precipitate that forms during shipment, presumably as a result of self-irradiation.^{2,3} Addition of sodium hypochlorite to the product solution prior to shipment prevents precipitate formation, indicating the precipitate is a reduced form of ^{99}Mo .

Based on target irradiation time, ^{99}Mo product activity can range from approximately 2.5 Ci/mL to approximately 7.5 Ci/mL. The corresponding total dose is 17 Mrad to 104 Mrad for shipping times of 15 to 30 hours. This study has used the ^{60}Co source at Sandia's Gamma Irradiation Facility (GIF), which produces a field intensity of approximately 1.2 Mrad/hr two inches from the source, to determine the effects of irradiation on a simulated product solution of sodium molybdate under a simulated ^{99}Mo radiation environment.

Experimental Methods

Simulated Product Irradiation. Four high density polyethylene (HDPE) product bottles, each containing 80-mL aliquots (the standard product volume) of a 2% solution of $\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$ in 0.2N NaOH, were irradiated in the GIF. Bottles were removed after 14.4 hours (sample 1-A, corresponding to a product activity of 2.5 Ci/mL and 15 hours' shipping time), 28.8 hours (sample 1-B, same activity, 30 hours' shipping time), 43.2 hours (sample 1-C, product activity of 7.5 Ci/mL, 15 hours' shipping time), and 86.4 hours (sample 1-D, same activity, 30 hours' shipping time). The initial molybdate solution irradiated was approximately 54 times more concentrated than an average product solution to ensure that, if formed, enough precipitate would be available for isolation and identification. However, since black precipitate readily formed in these solutions after 14.4 hours, it was decided to irradiate three additional sets of samples:

1. Two 80-mL samples, labeled 1-DIL and 2-DIL, each containing 0.145 mmoles of $\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$ in 0.2N NaOH. These samples simulated a typical production scenario and contained the maximum amount of molybdenum (product and carrier) that would be present after a six-hour cooldown from a 20-g target irradiated for seven days at 15kW. It was decided that 1-DIL would be pulled at whatever of the remaining sampling times a precipitate was first detected, and that 2-DIL would be irradiated for the full 72 hours remaining in the test series.
2. Two 25-mL samples, labeled 1-G and 2-G, of the 2% molybdate solution in clear, colorless glass bottles. Due to the pattern of black precipitates seen on the 1-A through 1-D HDPE bottles after 14.4 hours, precipitate appeared to be forming on the bottle surface, building up and then sloughing off to the bottom of the bottle. Bottle surfaces were darkest in the area closest to the ^{60}Co source. Based on these observations, it was decided to determine if the precipitate would form in a glass container. Samples were smaller, due to the size of the glass bottles that were available. These samples were pulled using the same sample protocol as 1-DIL and 2-DIL; i.e., 1-G was removed when precipitate was first observed and 2-G was left in the GIF for 72 hours.
3. Two 50-mL samples, labeled 1-OH and 2-OH, of 0.2N NaOH in the HDPE product bottles. These were run to compare any decrease in base strength that might occur in the molybdate solution with the behavior of a sodium hydroxide blank under the same conditions. Since there was not enough room in the sample container, these two samples were not put in the GIF until the 28.8-hour samples were removed, so they were only irradiated a total of 57.6 hours.

Samples of 2% basic molybdate solution containing NaOCl were also irradiated and removed at the time intervals of 14.4, 28.8, 43.2 and 86.4 hours. Since producers of ^{99}Mo normally add 2 mg hypochlorite/Ci of ^{99}Mo activity, four bottles (samples 2-A through 2-D) contained 3.5 mL of 10-13% aqueous NaOCl (the amount required for 2.5 Ci/mL, 80 mL of product) and four (samples 3-A through 3-D) contained 10.5 mL (the amount required for 7.5 Ci/mL, 80 mL of product).

Titration Data. After removal from the GIF, 20-mL aliquots of samples containing precipitate (1-A through D, 1-DIL, 2-DIL) were set aside and allowed to stand at room temperature. Remaining sample volumes were filtered to remove any precipitate. Duplicate aliquots of the filtered samples were titrated to a phenolphthalein endpoint with standardized 0.1974N HCl that had been standardized with 0.3938N NaOH. The latter was standardized to a phenolphthalein endpoint with potassium hydrogen phthalate. Due to their smaller initial volume, single samples of 1-G, 2-G, 1-OH and 2-OH were titrated. Since each G and OH sample experienced the same total irradiation time, this was equivalent to duplicate samples. Unirradiated samples of the 2% molybdate solution were also titrated prior to irradiation and after standing at room temperature for 86.4 hours.

Infrared and Raman Spectra. Any precipitate that formed was washed to a neutral pH, air dried and analyzed using Fourier transform infrared (FTIR) and Raman spectroscopy. FTIR transmission spectra were obtained using a Nicolet Model 800 SX spectrometer with a SpectraTech microscope attachment (resolution 8 cm^{-1} .) Raman spectra were obtained using 514 nm excitation, a triple spectrograph with a charge-coupled-device (CCD) detector and a microscope accessory ($\sim 1\text{ }\mu\text{m}$ spatial resolution).

Results

Visual Inspection. Samples 1-A through 1-D contained black precipitate after 14.4 hours of irradiation. The amount of precipitate steadily increased with irradiation time. Black precipitate was first noticed in samples 1-DIL and 2-DIL after 28.8 hours of irradiation. No visible changes were observed in sample solutions 2-A through 2-D, 3-A through 3-D, 1-G, 2-G, 1-OH or 2-OH. Gas was released when caps on samples 2-A through 2-D and 3-A through 3-D were loosened. HDPE bottles turned yellow and the glass bottles turned dark brown with increasing irradiation time.

Precipitate in the 20-mL aliquots that were allowed to stand at room temperature slowly returned to solution. Dissolution times ranged from 24 hours (samples 1-A and 1-DIL) to 4 weeks (sample 1-D).

Titration Data. Titration results are summarized in Tables 1 and 2. Data in Table 1 are the average of duplicate aliquots of each sample. Titration of a blank consisting of 2% $\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$ in water required less than 1 drop of HCl. The unirradiated 2% molybdate sample that was titrated at the conclusion of the 86.4 hours of GIF time had a normality of 0.194, in good agreement with initial values.

Table 1. Initial Titration Data

Sample	meq Base/mL Sample*	Δ , meq/mL
Unirrad, t=0	0.198	-
1-A	0.186	-0.012
1-B	0.185	-0.013
1-C	0.193	-0.004
1-D	0.198	-
1-DIL	0.194	-0.004
2-DIL	0.186	-0.012
G	0.185	-0.013
OH	0.186	-0.012
Unirrad, t=86.4	0.194	-0.004

*Avg std dev = ± 0.004 .

**Table 2. Titration of 20-mL Aliquots
with Dissolved Precipitate**

Sample	meq Base/mL Sample*	Δ , meq/mL
1-B	0.183	-0.015
1-C	0.181	-0.017
1-D	0.187	-0.011
1-DIL	0.188	-0.010
2-DIL	0.181	-0.017
OH	0.192	-0.006

*Avg std dev = ± 0.004 .

Once the black precipitate had dissolved, the 20-mL aliquots were titrated, as were samples of residual 1-OH and 2-OH, which were used as controls (Table 2). No data are shown for the 20-mL aliquot of 1-A because it was inadvertently discarded.

Data in Table 1 show a pattern of an initial decrease in sample basicity, followed by an increase at longer irradiation times in samples 1-C and 1-D. A comparable decrease is also seen in 1-OH and 2-OH after 72 hours of irradiation. Once the precipitate dissolves, sample basicity in Table 2 again decreases relative to the residual 1-OH and 2-OH samples, whose basicity appears to have increased slightly with standing.

Infrared Data. $\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$ Mo-O stretching frequencies were observed at 907, 874 and 838 cm^{-1} in samples of pure neat compound. These bands were identical with the $\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$ spectrum in the spectrometer's computer library, and agreed well with literature values (903, 898, 855, 820 and 805 cm^{-1})⁴. As irradiation time increased, the bands narrowed into a single band whose peak tended to shift to lower frequency. Sample 1-D contained a single sharp Mo-O band at 833 cm^{-1} .

Raman Data. A Raman spectrum of unirradiated $\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$ had a strong, sharp Mo-O stretching frequency at 894 cm^{-1} and a medium intensity band at 842 cm^{-1} with an unresolved low-frequency shoulder, in excellent agreement with literature values of 897,

843, 836 and 805 cm^{-1} .⁵ Raman spectra for the black precipitate from samples 1-C, 1-D, 1-DIL and 2-DIL are shown in Figure 1. At low laser excitation power (0.5 mW at the

Figure 1. Raman spectra of the black precipitate formed in ^{99}Mo product solutions after 28.8, 43.2, 72 and 86.4 hours of ^{60}Co irradiation in Sandia's Gamma Irradiation Facility.

microscope entrance and about 10 times lower at the sample) the filtered residues are stable and yield broad Raman bands characteristic of amorphous (glassy) materials. Similar spectra (but with the bands near 870 and 950 cm^{-1} more clearly separated) were obtained by Haro-Poniatowski et al. for amorphous hydrated MoO_3 .⁶

When their samples were exposed to higher laser power, Haro-Poniatowski et al. observed the formation of the α and β crystalline forms of MoO_3 . In an analogous experiment, two areas of sample 1-D and one area of sample 1-C were exposed to 10 mW of laser power in order to crystallize the amorphous material by laser annealing. Results are shown in Figure 2. The narrow Raman bands resulting from laser annealing fall

Figure 2. Raman spectra of laser-annealed precipitate from samples 1-C and 1-D.

within the envelope of bands defined by MoO_3 (Mo-O stretching frequencies at 997 and 820 cm^{-1} for $\alpha\text{-MoO}_3$; 904, 849 and 773 cm^{-1} for $\beta\text{-MoO}_3$)⁷ and $\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$. The differences in the Raman spectra of annealed 1-C and 1-D are most likely due to varying composition in the areas irradiated and localized annealing conditions.

Since the black precipitate is a reduced form of Mo, it is most likely composed of a complex mixture of reduced molybdenum oxides, MoO_x , $2 < x < 3$, and/or the so-called "blue oxides" that contain both oxide and hydroxide, such as $\text{MoO}_{2.0}(\text{OH})$ and $\text{MoO}_{2.5}(\text{OH})_{0.5}$.⁸ All compounds of these types that have been isolated and identified are either brown, black or blue-black and most are air-sensitive. Both $\text{MoO}(\text{OH})_3$ and $\text{Mo}(\text{OH})_3$, two other oxide/hydroxides that may be present, are insoluble in NaOH .⁹

Discussion

HDPE Radiolysis. The fact that precipitate only forms in HDPE bottles and not in glass containers indicates that HDPE radiolysis plays a key role in precipitate formation. The two most common reactions during polymer degradation due to irradiation are crosslinking and increases in chain unsaturation.¹⁰ Crosslinking occurs when free radicals from two separate polymer chains combine; unsaturation increases in a single chain when adjacent hydrogen atoms are removed. In both cases, carbon-carbon double bonds are formed and, in HDPE, hydrogen gas is produced by combination of the hydrogen atoms that are released. The yellow color observed during the irradiation of product bottles is produced by increasing chain unsaturation.¹¹

Molybdate Reduction. Hydrogen gas that diffuses to the surface of the bottle will oxidize in basic solution,

providing electrons that can reduce the Mo from its +6 oxidation state in the molybdate anion,

Reactions (1) and (2) account for the observed initial decrease in solution basicity and subsequent increase (see data, Table 1) in solutions where significant quantities of precipitate formed (1-C and 1-D). The molybdate reaction shown is used as an example of the numerous reactions of ions and radicals that are thermodynamically possible in this solution. MoO_2 will be used as the example of reduced Mo oxide throughout this discussion.

Mo oxides with a valence state less than +6 are unstable in air and slowly oxidize to stable MoO_3 , which is soluble in base, e.g.:

The observed disappearance of the black precipitate over time accompanied by a decrease in solution base strength (see data, Table 2) is consistent with these reactions.

The precipitate does not form in solutions in the HDPE bottles containing sodium hypochlorite because the latter is a strong oxidizing agent that reacts to keep the Mo in its +6 oxidation state, e.g.:

Pharmaceutical houses normally add 2mg hypochlorite/Ci Mo-99 to keep the product in solution. Since the stoichiometry of the reaction between the Mo^{+4} and OCl^- ions is 1:1, this is a huge molar excess. In this experiment, the 80-mL aliquots of 2% molybdate solution each contained approximately 7 mmoles of sodium molybdate, or about 48 times more Mo than is present in a product solution with an activity of 7.5 Ci/mL. The 3.5 mL of 10-13% hypochlorite that were added to simulate the amount that would be added if product activity were 2.5 Ci/mL provided approximately 5 mmoles of hypochlorite, almost enough to completely re-oxidize all the Mo in the 2% solution. Solutions containing 10.5 mL of hypochlorite contained an excess. Based on the amount of hydroxide consumed during re-oxidation of the precipitate (Table 2), a maximum of about 10% of the Mo was reduced during irradiation. Therefore, it is not surprising that no precipitate was observed in "2" and "3" samples.

Water Radiolysis. In addition to HDPE bottle degradation, another potential source of hydrogen is water radiolysis. The primary products of the interaction between water and ionizing radiation are H atoms and OH free radicals:¹⁴

The H and OH radicals can combine in any combination:

The above are the primary reactions when aqueous solutions contain solute at concentrations $\leq 0.1 \text{ M}$.¹⁴ Since the molar concentration of the 2% sodium molybdate dihydrate solution is $\sim 0.08 \text{ M}$, direct interaction between the radiation and the molybdate is not likely.

No Precipitate in Glass Bottles. There are two parts to the explanation for the observation that no precipitate is formed when the molybdate solution is irradiated in a glass container:

1. The rate constant for hydrogen production in irradiated water is $1.5 \times 10^8 \text{ M}^{-1}\text{sec}^{-1}$; for peroxide production it is $2 \times 10^8 \text{ M}^{-1}\text{sec}^{-1}$.¹⁴ Approximately equivalent rates of formation and the stoichiometry of the synthesis reactions argue that the steady-state concentrations of hydrogen and peroxide in solution will be roughly equal. While the hydrogen can reduce the molybdate, hydrogen peroxide is an effective oxidizing agent:

If the rate of molybdate reduction by hydrogen is approximately equal to the rate of Mo^{+6} oxidation by peroxide, no precipitate would be observed in the absence of any source of hydrogen other than water radiolysis. The fact that no precipitate is observed when the molybdate solution is in a glass container is an indication that the rates of Mo oxidation and reduction are comparable.

2. Chemical yields of radiolysis products are often expressed in terms of "G" values, the number of molecules of product produced or reactant decomposed per 100 ev of energy absorbed. G values for hydrogen formation from ^{60}Co gamma irradiation of polyethylene range from 3.75 to 4.0¹¹; G_{H_2} from water radiolysis using the same source is on the order of 0.42 - 0.45¹⁴ and $G_{\text{H}_2\text{O}_2} = 0.72 - 0.9$ ¹⁴. Since the amount of hydrogen produced from polymer degradation is approximately ten times the amount produced from water radiolysis, precipitate only forms when an additional source of hydrogen, the HDPE, is present to thermodynamically drive the reaction.

Summary

Hydrogen gas produced from radiolysis of the HDPE product bottle is oxidized at the bottle's surface by the hydroxide present in the product solution. This provides a source of electrons for reduction of molybdenum from the +6 oxidation state of the molybdate anion that is normally present in basic solution. The reduced molybdenum forms a black amorphous precipitate of mixed oxides/hydroxides, MoO_x , $2 < x < 3$. Since the oxides are unstable in air, they slowly re-oxidize to molybdenum trioxide, which dissolves in the sodium hydroxide to regenerate the molybdate anion. The addition of sodium hypochlorite, a strong oxidizing agent, effectively prevents precipitate formation.

The kinetics and thermodynamics of the basic molybdate solution radiation chemistry are such that precipitate does not form when the solution is in a glass bottle. A hydrogen source other than water, in this case HDPE, is necessary for precipitate formation.

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