MOLYBDENUM TRIOXIDE PURIFICATION METHODS

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Abstract

Radiopharmaceutical products based on technetium - 99 metastable (^{99m}Tc) have become very important instruments for the diagnosis of a wide range of diseases. An extremely important aspect in the process of obtaining ^{99m}Tc through Mo activation is the purity of the raw material, specifically molybdenum trioxide (MoO_3). A problematic impurity within MoO_3 is the tungsten which even at trace levels produces through irradiation the radioisotope ^{188}W which further decays into ^{188}Re. The presence of ^{188}Re raises challenges in the separation and purification process of the final solution containing the radionuclide of interest, ^{99m}Tc, due to their similar chemical properties. The objective of this study was to assess two purification methods for molybdenum trioxide to eliminate tungsten intrinsic impurities, aiming to produce a tungsten-free oxide suitable for generating the medical radioisotope ^{99m}Tc through neutron activation. Both methods use a liquid-solid selective separation technique to isolate the tungsten impurities. One approach relies on the preferential adsorption of tungsten by hydrated tin oxide (SnO_2 x nH_2O), while the alternative method utilizes activated charcoal as an adsorbent material. The paper presents comparative results of the MoO_3 obtained after separation using the two methods described above. To evaluate the efficiency of each method of purification, the inductively coupled plasma mass spectrometry technique was used by measuring the W concentration in the purified MoO_3 samples.

Keywords: *Purification, Molybdenum trioxide, Tungsten, Medical radioisotope*

Introduction

The use of radioisotopes with special characteristics is of great importance in modern medical practice. ^{99m}Tc is the most used marker in obtaining physiological information from the main organs of the body: brain, thyroid, lungs, liver, spleen, kidneys (structure and rate of filtration), gall bladder, heart muscle, but also in the imaging of the skeleton and bone marrow [1].

^{99m}Tc obtained from the generator ^{99}Mo/ ^{99m}Tc is one of the most widely used radionuclides in medicine for diagnosis using scintigraphic technique. ^{99}Mo, the parent radionuclide for this generator, is obtained either by neutron irradiation through (n, γ) reaction of the stable isotope ^{98}Mo, or from the fission products of ^{235}U [2].

^{99m}Tc is used in imaging diagnostics due to its advantages:
▪ It can be chemically embedded in various pharmaceutical products used to study organs and identify diseases;
▪ The half-life of 6 hours is considered sufficient to be used in nuclear medicine procedures;
▪ It can be easily transported to hospitals with the help of technetium generators;
▪ The doses received by patients are very small in certain procedures due to the reduced half-life of the isotope and because it does not emit alpha and beta radiation [3].

In order to be used in nuclear medicine, the nuclear characteristics of ^{99m}Tc must be supplemented with the chemical, radiochemical and biological properties of the solution containing it, allowing intravenous injection into the human body.

According to the Romanian Pharmacopoeia [4], the solution containing ^{99m}Tc must meet the following conditions:
- to be salt solution (0.9% NaCl) with a clear appearance;
- to have a pH between 5 - 7;
- to have a radioactive concentration between 10 and 100 mCi ^{99m}Tc/mL;
- to have a concentration of Al^{3+} < 5 ppm;
- to have a radionuclide purity > 99.9%;
- to have a radiochemical purity > 99%;
- do not contain pyrogenic substances, such as peroxides, or organic substances;
- to be sterile.

To produce ^{99}Mo (n,γ), two types of materials are usually used: molybdenum trioxide and metallic molybdenum.

The purity of the raw material used is an extremely important aspect and for this reason it is recommended that, before irradiation, the molybdenum trioxide will be initially purified from rhenium traces because as a result of nuclear reactions these will lead to the formation of ^{186}Re ($t_{1/2}$=90.8 hours) and ^{188}Re ($T_{1/2}$ =16.8 hours) isotopes. These isotopes are usually removed at the first elution of ^{99m}Tc on the generator; therefore the first elution must be discarded. Particular attention is also paid to tungsten impurities because as a result of the irradiation process, ^{188}W is obtained which further disintegrates in ^{188}Re. [5]

Materials and methods

An extremely important aspect is the purity of the raw material used and for this reason it is recommended that the molybdenum trioxide that will be irradiated should be initially purified from tungsten traces because as a result of the irradiation process ^{188}W is produced which disintegrates in ^{188}Re. ^{188}Re is very difficult to separate from ^{99m}Tc due to their similar chemical properties. [5]

This paper deals with the following processes developed on laboratory scales: the first method is based on the preferential adsorption of tungsten by hydrated tin oxides (SnO_2 x nH_2O); the second method uses the activated charcoal as an adsorbent material of tungsten impurities.

Method 1

The process presented in the following can reduce the level of tungsten impurities to about 10 ppm. Traces of tungsten can be removed using hydrated tin oxide. This method is based on preferential adsorption of tungsten with hydrated tin oxide (SnO_2 x nH_2O) [6].

SnO_2 x nH_2O can be synthesized by the reaction of $SnCl_4$ 1M solution with NH_4OH 28%, washing the precipitate with water, drying at 70°C, and grinding to obtain particles with a diameter of 0.1-0.3 mm. Once prepared, SnO_2 x $11H_2O$ can be stored for up to 1 year.

Mix 1L of $(NH_4)_2MoO_4$ 0.7M solution, in which $W^{187}O_4^{2-}$ has been added as a W content tracer, with 8g SnO_2 x $11H_2O$, stirring and bringing the solution at a pH of 8-9. Within 2 hours, 20% of W was removed from the solution, followed by ~34% in 4 hours, ~41% in 7 hours and ~ 90-95% in 24 hours. The solution of $(NH_4)_2MoO_4$ was filtered from SnO_2 x nH_2O through the Whatman N1 filter sequence of 0.22µ under suction, followed by MoO_3 precipitation by careful addition of concentrated HNO_3. The precipitate was washed with water, dried at 100°C and then calcined at 400°C for 6 hours [5].

Method 2

The method presented below is based on the preferential adsorption of tungsten on an activated charcoal column, and it includes the following steps [4]:

- Mix 10 kg of molybdenum trioxide with 40 L of water;
- Add about 6 L of concentrated ammonia solution under continuous stirring;
- Filter the resulting solution with a folded paper filter;
- Pass the solution on an activated charcoal column with a diameter of 2 cm and a length of 3 m; the flow rate is approximately 1.2 L/h;
- Slowly add about 2-3 L of HNO_3 for precipitation;
- Filter the hydrated molybdenum trioxide precipitate and then wash with warm distilled water;
- Dry the precipitate at 200°C for 24 hours, and after cooling, crush it until a fine powder is obtained;
- Heat the powder in the oven to 380°C for 24 hours in the current of hot air.
- After cooling, the powder is kept in plastic containers until irradiation;
- A sample of molybdenum trioxide is recommended to be irradiated and checked for impurities.
- Purified molybdenum trioxide has a validity of 5 years.

MoO_3 purification method using SnO_2 x nH_2O

According to the working method for the purification of MoO_3 from rhenium and tungsten impurities described above, as first step, it is necessary to prepare the hydrated tin oxide SnO_2 x nH_2O by the reaction of 11.94 ml of 1M $SnCl_4$ solution with 28% NH_4OH.

Ammonium hydroxide is gradually added until the solution stops precipitating, the precipitate is collected and the volume of used ammonium hydroxide is recorded. For 11.94 ml of $SnCl_4$ solution, 40 ml of NH_4OH were required. The resulting precipitate is washed with demineralized water, dried in the oven at 70°C, and then crushed until particles with a diameter of 0.1÷0.3 mm are obtained. The hydrated tin oxide, SnO_2 x $11H_2O$, obtained can be stored for up to 1 year.

The second stage is represented by the purification process itself. Two samples of 10.08 g MoO_3 each were weighed to perform two tests. The samples were labeled as follows: sample 1 – will be the reference sample with no tracer added, sample 2 – sample in which a solution of 500 µL W of known concentration will be added (tracer). In both samples, 100 mL of distilled water was added, then stirred on the electric stove and heated (at about 65°C) until all the amount of MoO_3 was incorporated into the bulk solution. Subsequently, 5.58 mL of 25% NH_4OH solution was added. The resulting solutions are clear and colorless as can be seen in Figs. 1 and 2.



Fig. 1. Samples 1 and 2 – MoO_3 dissolution



Fig. 2. Samples 1 and 2 – the resulting solutions

After MoO_3 complete dissolution, the ammonium molybdate solution was filtered on a paper filter, the resulting volume of supernatant being of 100.5 mL for test 1 and of 101 mL for test 2, respectively.

Due to the 99.99% purity of the molybdenum trioxide used, a standard known concentration solution of tungsten, as a tracer, was added to sample 2.

On top of the ammonium molybdate solutions 1 and 2, 0.8 g of hydrated tin oxide was added and continuously stirred until obtain a pH of 8-9. The pH adjustment was performed by adding up to 30 mL of 3M NaOH solution. The hydrated tin oxide was allowed to stand in the ammonium molybdate solution for 20 hours.

The ammonium molybdate solution was filtered (through 0.22µ filter paper) using a filter system equipped with a Millipore vacuum pump (see Fig. 3). The filtering system consists of the Buchner funnel, inside which a filter paper for quantitative analysis and a collector vessel are attached. The resulting filtration solution volume was of 119 mL for test 1 and 120.5 mL for test 2, respectively.



Fig. 3. Filtration and washing of molybdenum

In the next step, the molybdenum resulting from the filter solution was precipitated by gradually adding 14 mL of concentrated HNO_3 under continuous stirring on the electric stove. The MoO_3 precipitate was washed with demineralized water and the supernatant final volume was of 115 mL for test 1 and 118 mL for test 2, respectively.

The gels resulting from the filtration were placed in glass Petri dishes and then dried for 2 hours at 100°C in the laboratory oven type POL-EKO-APARATURA, model SLN 53 STD (see Fig. 4) equipped with a control panel of the working parameters and having the possibility of setting up gradients of time and temperature that can reach the maximum value of 250°C.



Fig. 4. Drying of samples

MoO_3 purification method using activated charcoal (CA)

This method uses activated charcoal (CA) as adsorbent material of W impurities. A quantity of 20 g of activated charcoal (granulation 50÷100 mesh) was washed with demineralized water until the washing water remained clear.

MoO_3 was cleaned from W impurities using a glass column with an outer diameter of 1.8 cm and a height of 13 cm filled with a layer of 5 cm activated charcoal (about 10 g). The conditioning of the column with CA was done using a 0.2 M NaOH solution.

A quantity of 10 g of MoO_3 was dissolved in 40 ml of demineralized water and 27 ml of 25% NH_4OH. The dissolving process was performed on the electric stove at 60°C with a second stage of stirring. The ammonium molybdate solution was filtered through a paper cut filter, yielding an eluate volume of 72 ml.

The resulting solution was passed through an elution column to retain the W impurities. Passing the entire solution through the elution system took 48 hours, and the final eluent volume was 32 ml (Fig. 5).



Fig. 5. Filtering the solution on CA

In the next step, the molybdenum obtained from the filter solution was precipitated by gradually adding 6 ml of concentrated HNO_3 under continuous stirring on the electric stove. The ammonium molybdate solution was filtered (through a 0.22µ filter paper) using a filtering system equipped with the Millipore vacuum pump. Because it has been precipitated into the supernatant solution, another filtration was performed through a cut filter paper. The precipitate was washed using 105 ml of demineralized water, and the final supernatant volume was 105 ml. The MoO_3 gel was transferred into a Petri dish and was dried at 100°C for 3 hours in the laboratory oven.

After drying, the purified MoO_3 samples were grinded with a porcelain jar and weighed.

The final step in achieving purified MoO_3 for both methods consists in the calcination at a temperature of 380°C for 6 hours. The samples were calcined in the NABERTHERM type LT5/13/P330 calcining oven, equipped with a display and programs allowing to set-up the time and temperature gradients that can reach a maximum of 1300°C.

The dried samples of MoO_3 purified by the two methods have a light gray color which is the specific MoO_3-colour (see Fig. 6).

To determine the amount of tungsten resulting from the purification tests, 1 mL sample of solutions resulting from the initial step of molybdenum trioxide dissolving, 1 mL after the purifying step, and 1 mL after the precipitation stage were collected (Table 1). The samples were collected in 50 mL glass balloons.



Fig. 6. MoO_3 powder

Table 1. Characteristics of the samples taken from the dissolution, purification and precipitation solutions

	Sample code	Collected volume [mL]	Initial volume [mL]	Total volume after the purification step [mL]	Total volume after the precipitation step [mL]
Test 1 Method SnO_2 x $11H_2O$	Sample 1a	1	100.5	-	-
	Sample 1b	1	-	120	-
	Sample 1c	1	-	-	117
Test 2 Method SnO_2 x $11H_2O$ + tracer	Sample 2a	1	101	-	-
	Sample 2b	1	-	121.5	-
	Sample 2c	1	-	-	120
Test 3 Method CA	Sample 3a	1	72		
	Sample 3b	1		32	
	Sample 3c	1			107

Measurement of tungsten content with ICP-MS

To determine the tungsten content needed to calculate the retention and purification percentage, the inductive coupled plasma mass spectrometer PERKIN ELMER ELAN DRC-e was used.

To perform the measurements, several optimization operations of the device are required. Device optimization consists of checking parameters such as: sensitivity, oxides, double loads, background, and accuracy, which are all recorded in a Daily Performance Check report.

To optimize the device, a Smart Tune Solution Standard Elan/ DRC-e solution (10 µg/ L) containing elements Ba, Be, Ce, Co, In, Mg, Pb, Rh, and U in 1% HNO_3 was used.

Preparation of standard solutions

After optimizing the device, the tungsten calibration curve was obtained using a W standard solution of 1000 µg/ mL.

Standard solution A (100 µg/L) contains 1 mL standard solution of tungsten (1000 µg/mL) and 2 mL of 2% HNO_3 diluted in a 100 mL balloon with demineralized water. Several standards were obtained by the appropriate dilution of standard solution A according to Table 2 in four balloons of 50 mL each containing 2% HNO_3 concentrated solution and demineralized water.

To obtain the calibration curve (in the range of 1-1000 µg/L), a blank sample (2% HNO_3) was measured, followed by the standard samples. To clean the route after each measurement, a 2% HNO_3 solution in demineralized water was used.

Table 2. Preparation of standard and blank samples

	Blank	Standard 1 (1 µg/ L) 1 ppb	Standard 2 (20 µg/ L) 20 ppb	Standard 3 (50 µg/ L) 50 ppb	Standard 4 (100 µg/ L) 100 ppb
65% HNO_3 solution	1 mL	1 mL	1 mL	1 mL	1 mL
Standard solution A	-	1 µL	100 µL	500 µL	1000 µL
Demineralized water	49 mL	48.999 mL	48.900 mL	48.500 mL	48 mL

After obtaining the calibration curve (Fig. 7), the samples to be tested were measured. The concentration of tungsten in the samples to be examined should be determined using the intensity indicated on the calibration curve. The report provides the element concentration in µg/L (ppb). The calibration curve is accepted if the correlation coefficient (R) exceeds 0.9965; in our case, R was 0.99997.

Preparation of solutions to be analyzed

After drawing the calibration curve (Fig. 7), the samples measurement was carried out. The samples to be analyzed were diluted in 2% HNO_3 , so that their concentration was within the limits of the calibration curve.

Table 3 shows the measured values, as well as the amount of tungsten in each sample, considering the dilutions performed. According to the data reported in the table, the last samples collected from each test (samples taken from the washing stage of MoO_3 precipitate) had a small amount of tungsten impurities. Therefore, the final amount of W remaining in the MoO_3 sample was calculated as the difference between the amount of W after the purification step and the amount of W after the washing step.

The percentage of W retained after purification of MoO_3 was calculated using the relation:

$$\%\ W\ retained\ after\ purification\ of\ MoO_3 = \frac{initial\ amount\ of\ W\ (mg) - final\ amount\ of\ W\ (mg)}{initial\ amount\ of\ W\ (mg)} \quad (1)$$

Thus, the percentage of W retained as a result of the three tests performed in this study was as follows: 83.57% for Test 1 (hydrated tin oxide method SnO_2 x $11H_2O$), 85.93% for Test 2 (hydrated tin oxide method SnO_2 x $11H_2O$ with tracer) and 43.63% for Test 3 (activated charcoal method, CA).

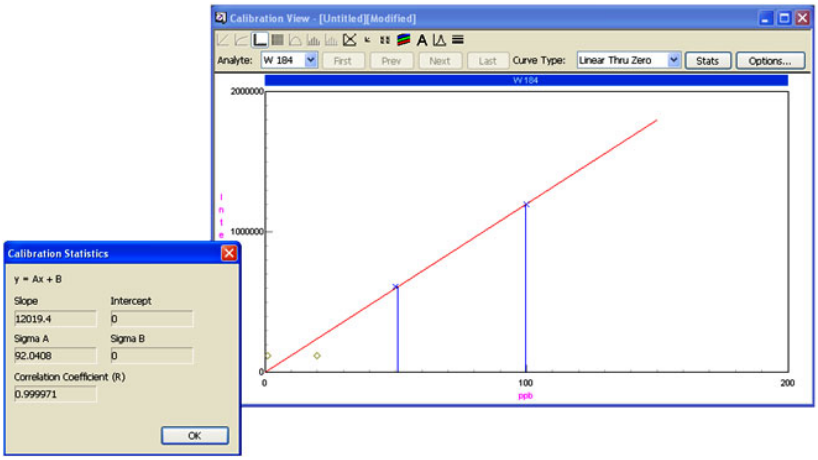


Fig. 7. Tungsten calibration curve

Table 3. Tungsten concentration measurements

	Sample 1a	Sample 1b	Sample 1c	Sample 2a	Sample 2b	Sample 2c	Sample 3a	Sample 3b	Sample 3c
Volume from which sampling was done [mL]	100.5	120	117	101	121.5	120	72	33	107
Collected volume [mL]	1	1	1	1	1	1	1	1	1
Tungsten concentration (µg/ L)	10.72	1.66	0.19	9.81	1.72	0.58	28.05	34.5	0
Total amount of W in the sample [mg]	0.05387	0.00996	0.00115	0.04954	0.01045	0.00348	0.10098	0.057	0

Conclusions

For the chemical characterization of the obtained samples and the efficiency of the purification steps during the process, the method of mass spectrometry with inductively coupled plasma was used to determine the concentrations of the elements.

Based on the tungsten concentration values resulting from the purification process and using the proposed relation, the retention percentages are as follows: 83.57% for test 1, 85.93% for test 2 and 43.63% for test 3, respectively.

A parameter that influences the retention percentage of tungsten is the time; the longer the time in which the ammonium molybdate solution interacts with the hydrated tin oxide, the better the retention percentage.

The experiments demonstrated that the retention of tungsten impurities in the molybdenum solution using the hydrated tin oxide method was significant, leading to the conclusion that the method can be applied to purify the molybdenum trioxide.

References

[1] OECD/NEA (2019) *"The Supply of Medical Isotopes: An Economic Diagnosis and Possible Solutions"*, OECD Publishing, Paris, https://doi.org/10.1787/9b326195-en.

[2] National Research Council (US) Committee on Medical Isotope Production Without Highly Enriched Uranium (2009) *"*Medical Isotope Production Without Highly Enriched Uranium*"*, PMID 25009932, https://doi.org/10.17226/12569, National Academy Press, ISBN 978-0-309-13039-4, USA.

[3] Cimpeanu, C., Barna, C., Neacșu, B., Mihalcea, I., Busuioc, P. (2007) *"Obtaining a new type of $^{99}Mo/^{99m}Tc$ generator based on ^{99}Mo-Zr gel technology using ^{99}Mo obtained by irradiation"*, Sci. and techn. report, Research of Excellence Nat. Programme, Contract No. 71-124, IFIN HH Bucharest, Romania (available in Romanian).

[4] *** (1993) *"Farmacopeea Română"*, Ediția X, Editura Medicală, Bucureşti, Romania (available in Romanian).

[5] Hetherington, E.L.R., Boyd, R.E. (1999) *"*Targets for the production of neutron activated Molybdenum-99*"*, incl. in *"Production technologies for molybdenum-99 and technetium-99m"*, IAEA TECDOC-1065, pp. 19-23, IAEA, Vienna, Austria.

[6] Semenov, M.I., Blokhin, A.A., Taushkanov, V.P. (1984) *"*Use of hydrated oxides of multivalent metals for effective removal of tungsten from molybdenum compounds*", Zh. Prikl. Khimii*, Vol. 57(7), pp. 1501-1506.

[7] Dadachova, K., La Riviere, K., Anderson, P. (1997) *"*Improved Production of Mo-99 at ANSTO*", Proc. of 2nd Int. Conf. on Isotopes*, Sydney, Australia.