

New prototype ^{99m}Tc extraction system

Aleš Fajgelj and Jože Novak

“Jožef Stefan” Institute, Ljubljana, Slovenia

A new semi-automatic extraction system for production of ^{99m}Tc from low specific activity ^{99}Mo , developed in the Department of Nuclear Chemistry of the “J. Stefan” Institute in Ljubljana is described. ^{99m}Tc is separated from reactor irradiated natural molybdenum(VI) oxide by continuous solvent extraction with methyl-ethyl ketone (MEK). The important characteristics and problems related to this new extraction system are discussed.

Key words: technetium-99m, technetium-isolation and purification, isotope production, solvent extraction; molybdenum, molybdenum oxide; nuclear reactors

Introduction

Three decades after the introduction of ^{99m}Tc as an “ideal” radiotracer, it still remains the most widely used isotope for nuclear medicine studies. The pre-eminence of ^{99m}Tc as a medically useful radionuclide is directly attributable to its excellent physical and chemical properties.^{1, 2} Technetium, in the form of ^{99m}Tc , is obtained from ^{99}Mo , which is produced by neutron irradiation of molybdenum (of natural isotopic composition or enriched in ^{98}Mo); alternatively, ^{99}Mo may be obtained as a fission product of uranium. Chromatography, sublimation and solvent extraction are three commonest methods used to separate ^{99m}Tc from ^{99}Mo .^{3,4,5}

In a nuclear reactor with a relatively low neutron flux (below say $5 \times 10^{13} \text{ n.cm}^{-2}\text{s}^{-1}$) the specific activity of ^{99}Mo is such that only the solvent extraction and sublimation methods can be used, as the mass of molybdenum required to be loaded on to a generator column would be too great.

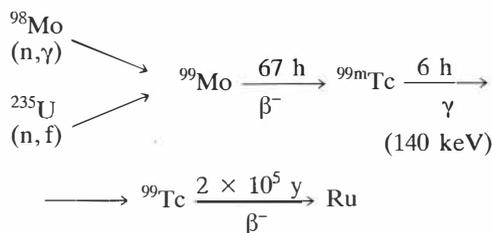


Figure 1. Production of ^{99m}Tc by nuclear reactions.

Correspondence to: Aleš Fajgelj Ph. D., “Jožef Stefan” Institute, Nuclear Chemistry Department, Jamova 39, P.O. Box 100, 61111 Ljubljana, Slovenia.

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^{99m}Tc has been successfully produced at the TRIGA Mark low power research reactor (250 kW) of the “J. Stefan” Institute in Ljubljana for almost ten years. By the use of manually

operated solvent extraction system where separation of ^{99m}Tc from ^{99}Mo was based on bubbler extraction, the needs of the two Slovenian largest nuclear medicine institutions, the University Clinic for Nuclear Medicine and the Institute of Oncology has been covered.⁶ For the same purposes a new semi-automatic, centralized, computer controlled continuous extraction system has been developed and is described in the present work.

Materials and methods

Apparatus

The purpose of the apparatus is to separate ^{99m}Tc from low specific activity ^{99}Mo by solvent extraction, where some steps of the procedure are automated, and finally to obtain a sterile, chemically pure product in a small volume (cca. 10 ml) of physiological solution for direct medical use.⁷ Block and schematic diagrams are shown in Figures 2 and 3. The main parts of the prototype apparatus are as follows:

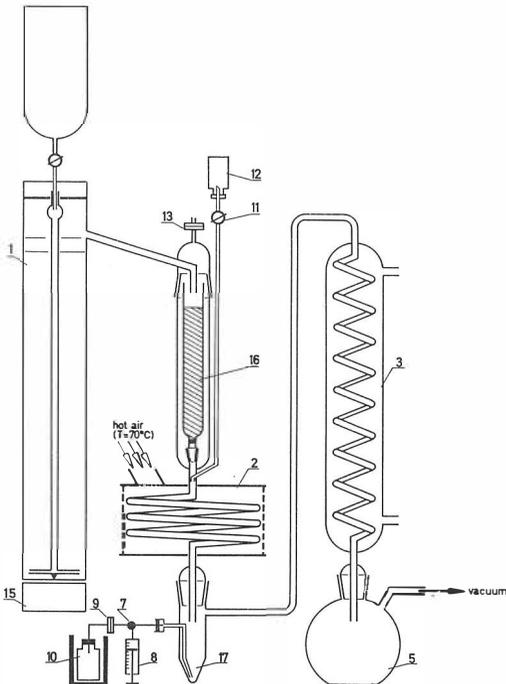
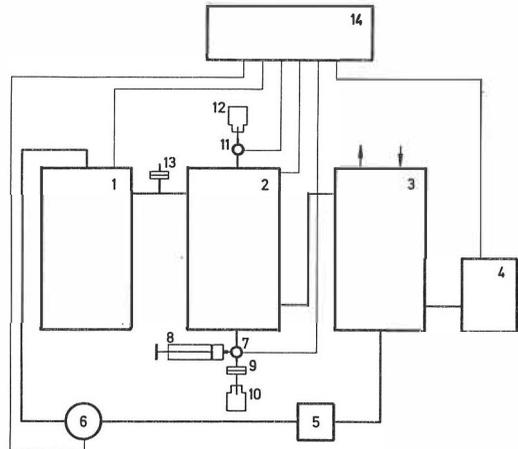


Figure 2. Schematic presentation of the newly developed extraction system.



1. Extraction vessel (V = 200 ml)
2. Evaporator
3. Condenser
4. Diaphragm pump
5. Reservoir for MEK
6. Peristaltic pump
7. Three-way tap
8. Self-filling syringe
9. Membrane filter (0.22 μm)
10. Sterile vial
11. Valve for 0.9 % NaCl
12. 0.9 % NaCl solution
13. Membrane filter (0.45 μm)
14. Control unit
15. Motor
16. Silica-Gel column
17. Reservoir for TcO_4

Figure 3. Block scheme of the extraction system.

- extraction vessel (see also Figure 4);
- funnel for methyl-ethyl ketone (MEK); the volume of the glass vessel is 50 ml;
- reservoir for NaCl (0.9 % NaCl); physiological solution is kept in commercial sterile flasks;
- evaporator;
- condenser for MEK: a glass apparatus of 400 ml capacity, connected to the reservoir for MEK;
- silica-gel column, maintained in position inside a glass holder;
- automatic self-filling and dispersing syringe;
- 0.22 μm membrane filters (Millipore or Sartorius);
- sterile vials (commercial);
- Masterflex peristaltic pump with flow rates of 1 – 20 ml per minute;

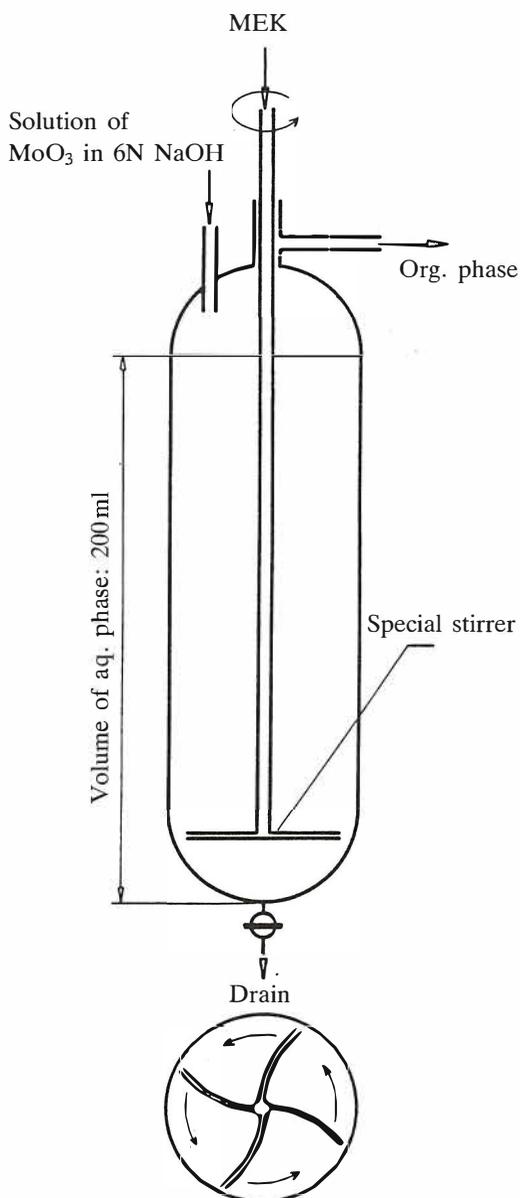


Figure 4. Schematic drawing of new prototype extraction vessel.

- vacuum line maintained by KOMVAK 1 diaphragm pump;

- control unit: this maintains control over the peristaltic and diaphragm pumps, the mixing of MEK in the generator vessel, the temperature in the evaporator, the dispensing of NaCl (0.9%), and determines the sequence and timing of the operations.

The time sequence of operations is shown in Figure 5. The whole procedure lasts 45 minutes. At the start the mixer and heater of the evaporator spiral are switched on. After 5 minutes the peristaltic pump for MEK and the membrane pump, which carries over the MEK vapour into the condenser, are switched on. After 35 minutes the extraction is complete and the control unit switches off the heater of the evaporator spiral, the mixer for dispersion of MEK in the extraction vessel and the peristaltic pump. The membrane pump continues to operate another 3 minutes in order to remove all the remaining MEK vapour from the system. In the 38th minute the valve opens to allow 6 ml 0.9% NaCl to enter the system, thus washing down sodium pertechnetate from the evaporator spiral to the reservoir. In the 39th minute the membrane pump is switched on for one minute to suck all remaining NaCl solution into the reservoir. In the 40th minute the dispenser is switched on to transfer the sodium pertechnetate solution in physiological saline into a sterile syringe. In the 41st minute the dispenser forces the solution from the syringe via a three-way tap and 0.22 μm membrane filter into a sterile penicillin bottle.

All parts of the generator system are directly connected via glass, teflon or PE tubes. The characteristic of the apparatus developed are as follows:

- dimension of the apparatus: 80 × 80 × 80 cm;
- weight: 35 kg;
- voltage: 220 V;
- cooling system: water cooled;
- preparation time: 45 minutes.

Materials

- MoO₃, p.a., Merck, is used for irradiation;
- NaOH, p.a., Kemika, Zagreb, 6 M solution;

- MEK (methyl-ethyl ketone), p.a., Merck or Kemika, Zagreb, is used for solvent extraction separation of ^{99m}Tc from ⁹⁹Mo in an alkaline solution of Mo(VI) and Tc(VII), distillation before use is required;

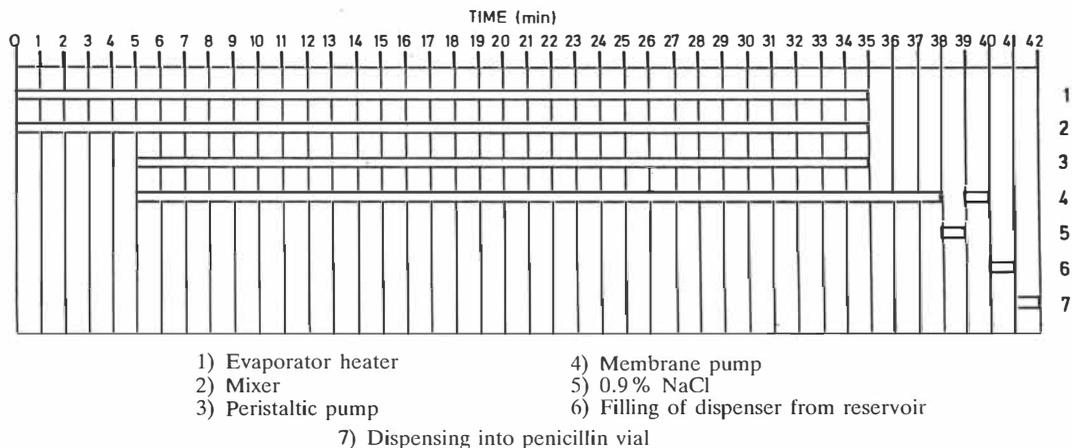


Figure 5. Time sequence of computer controlled operations.

– H_2O_2 , p.a., Belinka, Ljubljana, 3 % solution;

– silica-gel, Kemika, Zagreb, for chromatography, particle size 0.2 – 0.5 mm, washed three times with MEK and then ten times with redistilled water to remove fines, and dried at 105°C , is used for removal of small amounts of water phase which contains dissolved ^{99}Mo ;

– physiological solution (0.9 % NaCl) – sterile.

Irradiation

120 g of MoO_3 are irradiated in an aluminium container in our TRIGA Mark II research reactor. The optimal irradiation time of MoO_3 for continuous production on a three day cycle with our previous generator system,⁶ determined by experiment, is three weeks in the F-ring, at a neutron flux of $4 \times 10^{12} \text{ n.cm}^{-2}\text{s}^{-1}$, and finally 48 hours in the central channel at a neutron flux of $1.1 \times 10^{13} \text{ n.cm}^{-2}\text{s}^{-1}$. This activity is equivalent to the activity of five 800mCi commercial generators. By (n, γ) reactions, ^{99}Mo ($t_{1/2} = 66 \text{ h}$) and ^{101}Mo ($t_{1/2} = 14.6 \text{ min}$) are formed. Beta decay of these two isotopes gives ^{99m}Tc ($t_{1/2} = 6.02 \text{ h}$) and ^{101}Tc ($t_{1/2} = 14.2 \text{ min}$). ^{101}Tc in the final product could interfere with radiological investigations, so the irradiated MoO_3 is cooled for some hours to allow it to decay away.

Extraction

In the hot cell, 25 g of irradiated MoO_3 are dissolved in 200 ml of 6 M NaOH, and 1 ml of 3 % H_2O_2 is added to oxidize Mo reduced during irradiation. The solution is transferred to the extraction vessel after 10 min vigorous stirring. The new smaller scale prototype extraction vessel allows 200 ml of MEK as organic phase to disperse through the alkaline solution in a single continuous pass. The MEK is dispersed by means of a special stirrer and is siphoned off above the level of the aqueous phase. For the experiments an extraction vessel made of pyrex glass was used.

With this new system the yield of the extraction is around 85 % (see Table 1), which is very close to the yield of the previous, twice repeated bubbler extraction. Extraction without dispersal, or by bubbling as in the previous system did not give good results.

Table 1. Yield of extraction.

Extraction with dispersal, single pass	Without dispersal	Twice repeated bubbler extraction, previous system ⁶
86.2 %	5.4 %	87.1 %
85.1 %	7.1 %	82.8 %
83.7 %	8.3 %	86.3 %

The extraction yield is very dependent on the chemical form of technetium, which has to be

in the pertechnetate form. We compared two methods of oxidation, the first being addition of 3% H_2O_2 , and the second addition of a small amount of $\text{K}_2\text{Cr}_2\text{O}_7$. The oxidation efficiency was the same in both cases. For our new generator system oxidation with 3% H_2O_2 was chosen, as the possibility of contamination of the final product with chromium was eliminated.

Since in the new extraction system continuous extraction is used, we constructed a new continuous evaporator, which is made from a pyrex glass spiral and heated with an electrical heating tape or hot air to 80°C . The bottom part of this evaporator is directly connected with the reservoir for TcO_4^- and the condenser for MEK, where the vacuum is maintained by a KOM-VAK 1 diaphragm pump.

Results and discussion

The final product, solvent extraction produced $^{99\text{m}}\text{TcO}_4^-$ has the following chemical characteristics:

- pH = 6 - 7;
- $^{99\text{m}}\text{Tc}$: 99% as pertechnetate;
- ^{99}Mo content: $< 1 \times 10^{-5}\%$;
- specific activity: $4810 \text{ MBq}\cdot\text{ml}^{-1}$ (130 mCi. ml^{-1});
- volume: 5 - 10 ml;
- trace impurities: ^{95}Nb , ^{188}Re , ^{198}Au .

In quality tests of the final technetium solution we found a measurable activity of ^{186}Re when MoO_3 from Kemika Zagreb was used for preparation of technetium. At the same time, we also found that the chemical purity of MoO_3 produced by Merck is much better, and normally this oxide is used for irradiation. However, if for technical reasons we are obliged to use MoO_3 from Kemika Zagreb, there is possibility to avoid ^{186}Re and ^{188}Re activities by precrystallization of MoO_3 .

Tests carried out at the Microbiological Institute of the Medical Faculty in Ljubljana and LEK - Ljubljana showed the product to be sterile and apyrogenic, and non-toxic, respectively.

The apparatus described is for objective rea-

sons not yet used for daily routine production of technetium, but all the tests performed showed that the final product has the same characteristics as TcO_4^- produced by our previously developed system.⁸ The main part of the new semi-automatic extraction system - the extraction vessel - will in future be changed from glass to a stainless steel extractor to avoid the problems which can arise from leaching of silica from the walls under the combined influence of intense gamma radiation and strong alkali, leading blockage of the membrane filters. The incorporation of additional electronic controls and connection to the micro-computer should make this system more suitable for simple daily routine work.

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