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A simple and rapid technique for recovery of ^{99m}Tc from low specific activity (n,γ)^{99}Mo based on solid–liquid extraction and column chromatography methodologies☆

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Abstract

A simple and inexpensive method has been developed for the separation of ^{99m}Tc from ^{99}Mo produced from the neutron activation of ^{98}Mo by ^{98}Mo(n,γ)^{99}Mo nuclear reaction. The recovery of ^{99m}Tc was performed by solid–liquid extraction based on alumina column chromatography. The overall radiochemical yield for the complete separation of ^{99m}Tc was 85–97% (n=5). The separated Na[^{99m}Tc]TcO_4 was of high radionuclidic, radiochemical and chemical purities. The method can be adopted for routine processing and use of ^{99m}Tc in radiopharmacy operations.

Keywords: (n,γ)^{99}Mo; ^{99m}Tc/^{99}Mo solid–liquid extraction generator; Methyl ethyl ketone; Purification; Alumina column chromatography; Na[^{99m}Tc]TcO_4

1. Introduction

Technetium-99m ($t_{1/2}$=6 h; 140 keV), the most widely used radioisotope in diagnostic radiopharmaceuticals, is obtained from the ^{99}Mo-^{99m}Tc generator. Molybdenum-99 is produced either from the thermal fission of ^{235}U(n,f)^{99}Mo reaction [1–3] or from the neutron activation of ^{98}Mo by ^{98}Mo(n,γ)^{99}Mo nuclear reaction. The most widely used method of purifying ^{99m}Tc is through an alumina column (2–5 g) chromatographic generator holding fission-produced ^{99}Mo of high specific activity. ^{99}Mo of low to medium specific activity, 7.4–14.8 GBq/g (200–400 mCi/g), obtained by ^{98}Mo(n,γ)^{99}Mo reaction cannot be used for this purpose since it requires a much larger alumina column to adsorb about 2 g of Mo (capacity up to 20 mg Mo/g of alumina) needed to prepare generators containing ~18.5 GBq (~500 mCi) ^{99}Mo at the reference time. The larger size of the alumina column, in turn, requires larger eluate volumes to recover ^{99m}Tc, and the radioactive concentration of the pertechnetate becomes unacceptably low for radiopharmaceutical use and therefore requires postelution concentration [4,5].

Technetium-99m is obtained in many radiopharmacies in India using the BARC/BRIT methyl ethyl ketone (MEK) solvent extraction method [6]. The method has the merits of early adaptability in India, compatibility with the low specific activity of ^{99}Mo produced via the (n,γ) process in our research reactors and relatively low cost. The inherent drawbacks of this system include daily handling of radiation hazardous ^{99}Mo solution, manual separation of organic and aqueous layer, evaporation of inflammable solvent like MEK by heating (chances of contamination with aldol impurities due to overheating) and, furthermore, the necessity of terminal sterilization.

There have been concerted efforts in our laboratory to develop user-friendly ^{99m}Tc delivery systems using ^{99}Mo of

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low–medium specific activity, typically 7.4–14.8 GBq/g (200–400 mCi/g), obtained by neutron activation of natural MoO_3 targets, denoted as $(n,\gamma)^{99}Mo$ [4,5,7,8]. The main features being pursued are ease and simplicity of operation and safety-cum-reliability from both radiological and pharmaceutical points of view.

In this report, we describe a simple, improved method of recovery of ^{99m}Tc from alkaline molybdate solution based on column extraction of ^{99m}Tc with MEK [9] from sodium [^{99}Mo] molybdate solution immobilized on alumina column and on online purification of ^{99m}Tc using column chromatography technique.

2. Experimental

2.1. Materials

All chemicals were from commercial sources and were mostly of AR/GR grade. Aluminium oxides, active basic and active acidic (100–200 mesh, Brockman grade 1) (Prabhat Chemicals, Mumbai, India), were used in preparing the purification columns. Molybdenum-99 produced by the $^{98}Mo(n,\gamma)^{99}Mo$ reaction was obtained as [^{99}Mo]Na_2MoO_4 in 5N NaOH [150 mg Mo/ml: 1.11–2.22 GBq/ml (30–60 mCi/ml)] from the Radiochemicals Section, Radiopharmaceutical Division, BARC and BRIT, Mumbai, India. The three-way Mediflex stopcock (nonpyrogenic and sterile) was purchased from Eastern Medikit, Ltd., India.

2.2. Radionuclide analyses

Radionuclide activities were determined using a calibrated HPGe detector (Eurisys M, Caen, France) coupled to a PC-based multichannel analyzer (ORTEC, Oak Ridge, TN, USA). The detector has a 30% efficiency relative to a 3×3-in. NaI (Tl) detector and an energy resolution of 1.74 keV at the 1332-keV photopeak of ^{60}Co. The levels of ^{99}Mo and ^{99m}Tc were determined by quantification of the different γ-lines of the respective radioisotopes at 739.6 keV (12.1%) and 140.5 keV (89%). The recovery of the separated ^{99m}Tc was determined by using a calibrated dose calibrator (ISOMED 50, Hans Walischmiller GmbH, Dresden, Germany).

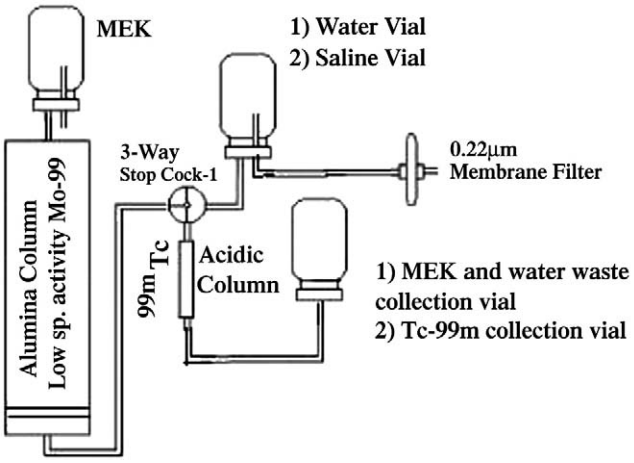

Fig. 1. Schematic illustration of the elution of ^{99m}Tc.

Fig. 2. A prototype technetium-99m generator using the solid–liquid extraction technique.

2.3. Quality control tests of $Na[^{99m}Tc]TcO_4$

The Al^{3+} content in the final Na[^{99m}Tc]TcO_4 solution was determined by a spot test, based on the reaction of Al^{3+} ions with alizarin S (sodium salt of the 1,2-dioxyanthaquinone sulphonic acid). The typical level of organic solvent (MEK) in the Na[^{99m}Tc]TcO_4 solution was determined with the iodoform test.

The pertechnetate obtained as above was checked for clarity, pH, radiochemical purity of pertechnetate and for ^{99}Mo breakthrough. The efficacy in labeling specific compounds was assessed using locally produced standard radiopharmaceutical kits, such as ^{99m}Tc-methylene diphosphonate (^{99m}Tc-MDP), ^{99m}Tc-ethylene-di-cysteine (^{99m}Tc-EC), ^{99m}Tc-L,L-ethylene cysteinate dimer (^{99m}Tc-ECD) and ^{99m}Tc-sestamibi (^{99m}Tc-MIBI).

2.4. Preparation of column

2.4.1. Preparation of basic alumina column

Commercially available basic alumina (100–200 mesh, 16 g) was used directly without any further treatment for preparing basic alumina column (6 cm×2.8 cm, height×diameter).

2.4.2. Preparation of acidic alumina column

Commercially available acidic alumina (100–200 mesh) was soaked overnight in dilute nitric acid (0.1 M) and washed with sufficient double-distilled water till the pH of the final washing reached a 3–4 range. The conditioned and wet alumina was dried under an IR lamp to get free-flowing particles. The dried acidic alumina (5 g) was used to prepare the acidic alumina column (6 cm×1.2 cm, height×diameter).