Removal of Tc from Neutron-Capture ^{99}Mo using Eichrom's ABEC Resin

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ABSTRACT

NorthStar Medical Radioisotopes is pursuing a neutron capture [^{98}Mo(n,γ)^{99}Mo] route for ^{99}Mo production at the University of Missouri Research Reactor (MURR). Argonne is assisting NorthStar in the development of some aspects of the operation. Once the molybdenum targets are removed from the reactor, they will undergo dissolution. The output of the dissolution results in ~1500 mL of a 5 M KOH solution containing ~400 Ci of ^{99}Mo, as well as a few byproducts (compared to fission) including Tc. This solution is pumped from a shielded cask through a chromatography column containing ABEC to remove Tc present from the target irradiation. This polishing step will allow radiopharmacies to use the first aliquot of Tc they elute from their generators. Currently, radiopharmacies discard the first aliquot from the generator, as it contains unacceptable levels of ^{99g}Tc. Various ABEC cartridge sizes and flow rates through these cartridges have been investigated, and a method for processing the 1500 mL of 5 M KOH solution has been established.

1. Introduction

More than 80% of nuclear medicine diagnostic tests or approximately 70,000 medical imaging procedures throughout the world daily use metastable technetium-99 (^{99m}Tc), [1]. In 2009, it was reported that Canada's Chalk River research reactor and the Netherlands' High Flux reactor produce approximately 85% of Europe's and North America's ^{99}Mo supply [2]. It was recently announced that the Chalk River reactor will cease ^{99}Mo production after 2016, creating a worldwide shortage of ^{99}Mo unless reliable, alternative production methods are developed. ^{99m}Tc cannot be stockpiled because its parent isotope is

molybdenum-99 (^{99}Mo), which has a 66-hour half-life [3].[3]. One possible production method is based on the [^{98}Mo(n,γ)^{99}Mo] reaction pathway.

The typical reaction pathway for the production of ^{99}Mo is neutron-induced fission of high-enriched uranium (HEU; ≥20% ^{235}U) in a nuclear reactor. After irradiation of the HEU target, the ^{99}Mo is isolated from the uranium and other fission products, purified, and loaded onto a generator for delivery to radiopharmacies. The radiopharmacies then use the generator to separate the decay product or daughter, ^{99m}Tc, from the ^{99}Mo. The ^{99m}Tc has a 6-hour half-life and can be administered to patients on-site [4]. The production of ^{99}Mo with HEU is a nuclear proliferation concern, because HEU can be weaponized. It is far more desirable to produce ^{99}Mo from either non-uranium-based sources, such as Mo irradiation, or using low enriched uranium (LEU ≤ 20% ^{235}U) [4]. The major downside of ^{99}Mo production using non-HEU is that much more target material is needed, regardless of if the reaction pathway uses Mo or non-HEU uranium, in order to synthesize an equal amount of Mo as with HEU. Production using non-HEU methods, whether with a reactor or an accelerator, are greatly preferred because nuclear proliferation concerns are greatly reduced [5].

The reaction [^{98}Mo(n,γ)^{99}Mo] is of interest, as it uses no uranium targets and presents no proliferation concern. After irradiation in the University of Missouri Research Reactor (MURR) the Mo target is undergoes dissolution that results in the reaction products being in a final solution of 5 M KOH and a volume of 1500 mL. Upon receipt of the dissolution solution, it is desired to further remove the Tc that has built up during irradiation from the solution so that it can be aliquoted and delivered to the radiopharmacies for immediate use. Eichrom Technologies, LLC has developed ABEC, an extraction chromatographic resin specific for Tc which is being used to purify the final dissolution solution.

Eichrom's ABEC resin consists of polyethylene glycols (PEGs) physisorbed onto an inert support. Eichrom has previously characterized the behavior of the pertechnetate ion (TcO$_4^-$) on ABEC resin in both batch and low flow rate (<4 mL/min) column studies [6-9]. Due to restrictions for commercial production-scale, flow rates of >10 mL/min are necessary. In addition to this requirement, it is also necessary that all 1500 mL of solution are processed with the same ABEC cartridge. A successful process is defined as all post-ABEC cartridge aliquots (29 mL) containing < 30 % of the possible Tc per pre-ABEC cartridge (the stock solution) aliquot (29 mL). The possible Tc per aliquot is defined as the total amount of Tc in 1500 mL divided by 1500 mL multiplied by the aliquot volume (29 mL). The performance of ABEC cartridges at flow rates ranging from 2 to 30 mL/min has been investigated.

2. **Experimental**

ABEC resin, available from Eichrom Technologies, LLC, in the form of pre-packed 2 cc cartridges, was used during this study. In addition to these, 25 cc ABEC cartridges

were wet- packed at NorthStar Medical Radioisotopes. American Chemical Society (ACS) reagent-grade potassium hydroxide pellets, potassium nitrate were used. American Chemical Society (ACS) reagent-grade molybdenum trioxide available from Acros Organics was used. Ultima Gold XR liquid scintillation cocktail was obtained from Perkin Elmer. The ^{99}Tc was original in the ammonium pertechnetate chemical form and was obtained from Oak Ridge National Laboratory.

A stock solution of ~200 g/L Mo, 5 M KOH, 0.1 M KNO$_3$ was made using 18 MΩ deionized distilled water and filtered through a 0.22 μm polyethersulfone (PES) filter available through Fisher Scientific). After the filtration, ~170 ug of ^{99}Tc was added to 1500 mL of the stock solution. It is expected that 170 ug of total Tc is the upper limit of Tc at the End of Irradiation (EoI) of a natural molybdenum target.

The ABEC resin was slurry packed into a column. The column was then attached to a dispensing unit developed by NorthStar Medical Radioisotopes. The dispensing unit uses pressure to push eluents through the ABEC column. The column was conditioned with ~10 bed volumes of 5 M KOH. After conditioning, an aliquot of 29 mL of the stock solution, containing ^{99}Tc, was passed through the ABEC cartridge and a sample collected for Liquid Scintillation Counting (LSC). In order to evaluate the performance of the ABEC cartridge a total of 5 aliquots were passed through a single ABEC cartridge, instead of a total of 50 aliquots. Each data set presented is an average of 3 individual experiments.

3. Results and Discussion

3.1 2 cc ABEC cartridge

Figure 1 shows the breakthrough curves for 2 cc ABEC cartridges at flow rates ranging from 2 to 30 mL/minute. It is clear that at flow rates >10 mL/minute breakthrough increases by more than 10 %. As flow rate increases, it is expected that breakthrough will increase due to the mobile phase having less residence time and thus less interaction with the stationary phase. However, it is interesting that at flow rates of 15, 20, 25 and 30 mL/minute, the breakthrough of Tc is experimentally consistent. This indicates that for applications where less Tc is present or smaller aliquot volumes are required ABEC is extremely robust and can be used at high flow rates. Despite this, based on the upward trend of breakthrough with increased flow rate, as shown in Figure 1, a large cartridge will be necessary to accommodate flow rates > 10 mL/ minute in order to meet the requirements for the intended application.

Although, ABEC appears to be robust with respect to flow rate, a 2 cc ABEC cartridge will not purify a full 1500 mL stock solution to the required specifications (See Section 1). A full 1500 mL stock solution, dispensed in 29 mL aliquots, results in a total of 51 aliquots. Figure 1 indicates that a 2 cc ABEC cartridge fails to me the required specifications at aliquot #5 for flow rates ≤ 10 mL/min, and at aliquot #4 for ≥ 10 mL/minute. This indicates that a much larger

column is necessary, in order to use a single column to separate the Tc from the entire 1500 mL stock solution.
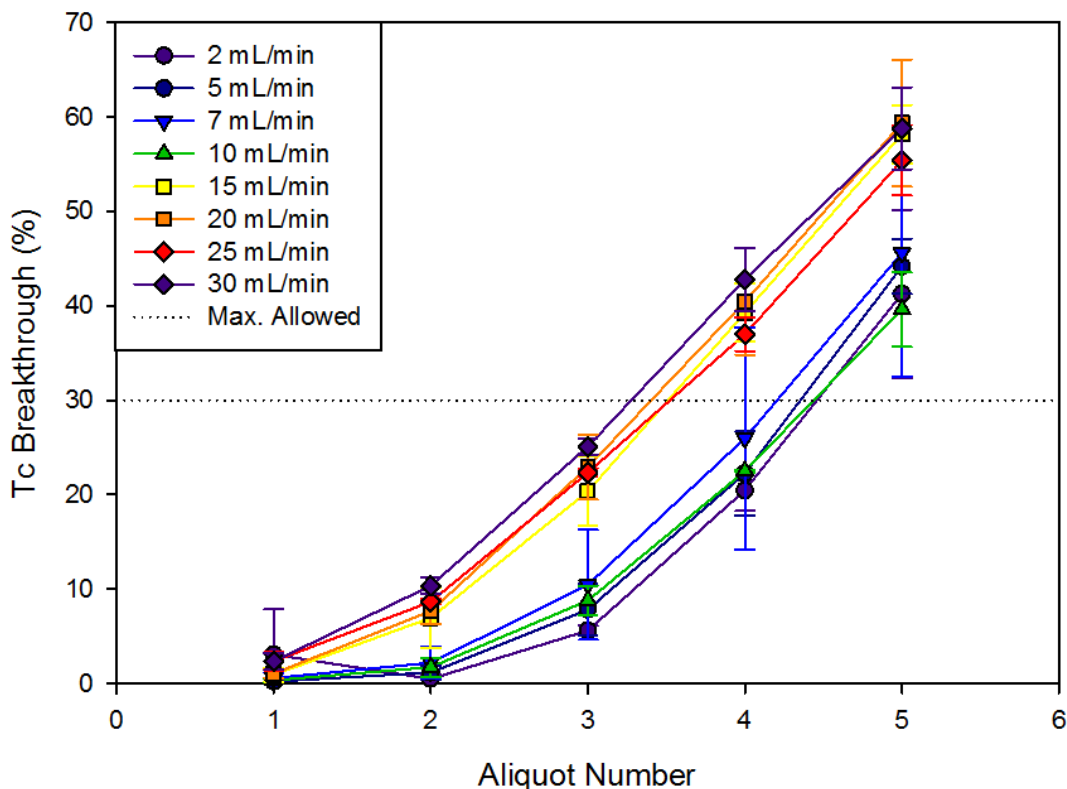

Figure 1. Breakthrough curves for ^{99}Tc on 2 cc ABEC cartridges for flow rates ranging from 2 to 30 mL/min. It can clearly be seen that flow rates of > 10 mL/minute there is increased breakthrough of [99]Tc. It should also be noted that at aliquot 5 for flow rates ≤10 mL/min, and at aliquot 4 for flow rates ≥ 15 mL/min the required specification fail to be met.

3.2 25 cc ABEC Cartridges

Based on the data presented in Figure 1, it was determined that a larger ABEC cartridge needed to be employed to ensure that no sample contained > 30 % of the allowed Tc over the course of 51 samples. A 25 cc ABEC cartridge was tested at 10 mL/minute to evaluate the size of cartridge necessary for processing 1500 mL of solution containing 170 μg of [99]Tc. The data are shown in Figure 2. It is clear that the 25 cc ABEC cartridge at a flow rate of 10 mL/min retains enough Tc, such that, each aliquot of 29 mL meets the specification requirements of the dispensed aliquot containing <30 % of the allowed Tc. A 25 cc ABEC cartridge would be suitable for the intended use of removing < 30 % of the possible Tc per pre-ABEC cartridge aliquot.
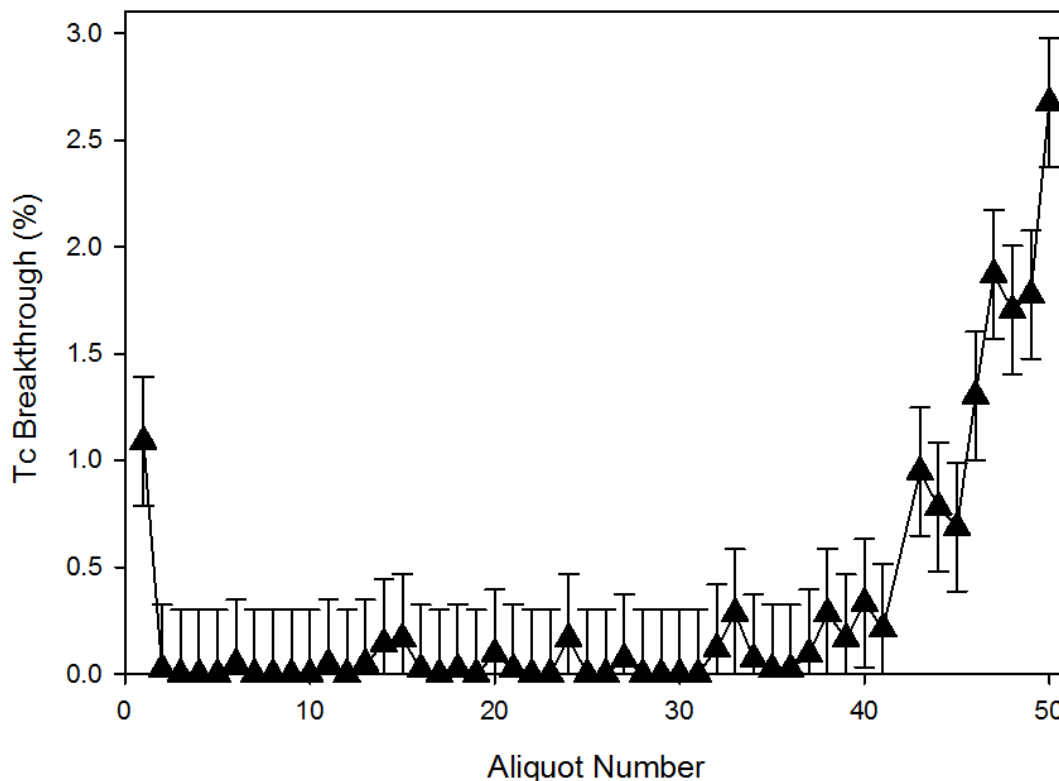
Figure 2. The breakthrough curves for ^{99}Tc on a 25 cc ABEC cartridges for a flow rate of 10 mL/min. Over the course of 50 samples, or ~ 1500 mL, all samples meet the requirement of < 30 % Tc in each aliquot.

4. Conclusions

Flow rate studies on 2 cc ABEC cartridges has been conducted, and it was determined that at flow rates > 10 mL/minute there is increased breakthrough of ^{99}Tc of ~ 10% compared to flow rates of ≤10 mL/minute. However, at flow rates between 15 and 30 mL/min ABEC performed virtually the same, indicating that the ABEC resin and cartridge is robust and has a large affinity for Tc. Despite this; however, the 2 cc ABEC cartridges cannot be used in the desired process, as a successful process is defined as the use of a single ABEC cartridge, at a flow rate of ≥10 mL/min, in which all post-ABEC cartridge aliquots containing < 30 % of the possible Tc per pre-ABEC cartridge aliquot. Because of this, a larger, 25 cc ABEC cartridge was investigated.

A 25 cc ABEC cartridge at a flow rate of 10 mL/minute was investigated for use in the desired process. It was determined that under these conditions, this cartridge was successful, as defined by the use of a single ABEC cartridge, at a flow rate of ≥10 mL/min, in which, all post-ABEC cartridge aliquots containing significantly < 30 % of the possible Tc per pre-ABEC cartridge aliquot.

5. REFERENCES

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