CHEMISTRY OF CINTICHEM PROCESS FOR ^{99}Mo PRODUCTION AND DEVELOPMENT OF ^{99m}Tc GENERATORS USING (n,γ) ^{99}Mo

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1. INTRODUCTION

Technetium-99m (^{99m}Tc), the daughter product of molybdenum-99 (^{99}Mo), is the most important radionuclide used in nuclear medicine practice. The importance of these radionuclides stems from the fact that ^{99m}Tc is used for well over 30 million medical diagnostic procedures annually and accounts for 80% of all diagnostic radiopharmaceutical injections each year. The majority of ^{99}Mo used worldwide has been produced by the irradiation of highly enriched uranium (HEU) targets. The amount of ^{235}U in the targets consumed in the production of ^{99}Mo is less than 5% of the total quantity of ^{235}U used, thus leaving behind a large amount of HEU in the ^{99}Mo producing facility. The recognition of the risks of nuclear proliferation and terrorism associated with the use of HEU for ^{99}Mo production has raised international concern [1]. In line with the objective of minimizing and eventually eliminating the use of HEU for ^{99}Mo production, efforts have been underway to transition from HEU to low enriched uranium (LEU) targets. Taking advantage of existing, domestic facilities and capabilities, there has been steady pursuit in India towards development of alternate non-HEU technologies for ^{99m}Tc generators. A variety of options for accessing ^{99m}Tc through (n,γ) ^{99}Mo (neutron activation of ^{99}Mo) have been explored to achieve the objective of the CRP. In parallel, chemistry of fission based ^{99}Mo using Cintichem process is being pursued for R&D purposes, but not for regular production.

2. CHEMISTRY OF CINTICHEM PROCESS

Since the Cintichem process for the separation of fission ^{99}Mo is well known, process refinement work has been performed in our laboratory. The use of simulated fission products solution spiked with appropriate tracers provided an opportunity to evaluate the efficiency of the individual separation steps of the Cintichem process. The main objectives of these experiments were to understand the processing variability, to identify potential problems, and to determine the optimum parameters to be used during processing of ^{99}Mo. This provided a mechanism not only to measure the efficiency of individual separation steps but also to evaluate the performance of the individual process steps. Of particular interest were the radionuclides ^{131}I, ^{103}Ru, ^{132}Te, ^{95}Zr and $^{85+89}$Sr. Our work mainly focused on the study of the chemistry of the Cintichem process using simulated fission products solution and neutron irradiated Mo-U alloy. Initially, our studies indicated that minor chemical modifications will be required to remove the fission products contamination. The composition of simulated fission product solution used is depicted in Table 1.

TABLE 1. COMPOSITION OF SIMULATED SOLUTION

Element	Isotope	Quantity
U	Nat U (^{238}U+ ^{235}U)	2 grams
Mo	^{99}Mo	2 mg
I	^{131}I	28μg
Te	^{132}Te	25μg
Ru	^{103}Ru	20μg
Zr	^{95}Zr	20μg
Nb	^{95}Nb	20μg
Sr	$^{85+89}Sr$	20μg

2.1. REMOVAL OF RADIOIODINE

The first part of the Cintichem process after the dissolution of target is the removal of radioiodine. The removal of radioiodine presents a challenge in the chemical processing of ^{99}Mo. We felt that the experimental parameters can be fine-tuned to arrive at the condition that facilitates optimum removal of radioiodine. In this process, 10 mL of NaI carrier (2-10 mg/mL) + 0.5 mL of 10% $AgNO_3$ in 0.1M HNO_3 were added to precipitate iodide. The effect of inactive carrier concentration of NaI in the feed solution on the percentage removal of iodine was examined and the result is depicted in Table 2. Ignoring some fluctuation, the percentage of iodine removal was nearly ~90% when the carrier concentration was between 6 to 10mg/mL. Hence, a 10mL of NaI solution of carrier concentration of 6mg/mL can be used.

TABLE 2. EFFECT OF AMOUNT OF NaI CARRIER

S.No.	Amount of NaI carrier (mg/mL)	% Removal of ^{131}I
1	2	67.06 ± 2.3
2	4	89.03 ± 2.5
3	6	90.12 ± 1.5
4	10	90.18 ± 2.1

The remaining amount of iodide was removed by the addition of 2.5% $KMnO_4$ solution slowly to the raw fission liquor until a deep pink color holds for ~30 seconds. Removal of iodine was accomplished as per the following chemical reactions:

$$MnO_4^{-} + 5 I^{-} + 8 H^{+} = I_2 + 5/2\ Mn^{2+} + 4H_2O$$
$$NO_2^{-} + I^{-} + 2H^{+} = ½I_2 + NO + H_2O$$
$$I_2 + H^{+} + NO_3^{-} = IO_3^{-} + NO_2 + H_2O$$
$$IO_3^{-} + I^{-} + H^{+} = I_2 + H_2O$$

2.2. REMOVAL OF ^{103}RU

During the dissolution of uranium in nitric acid, micro amounts of ruthenium are evidently present in the form of nitrosylruthenium ($RuNO^{3+}$) complexes, which can be expressed as the general formula $[RuNO(NO_2)_m(OH)_n]^{3-(m+n)}$. Nitrosylruthenates is a very stable compound which is destroyed only when the element is oxidized to the octavalent state (RuO_4). Experimentally it was observed that nitric acid is not strong enough to oxidize Ru to RuO_4 and therefore quantitative removal of ^{103}Ru was not possible. In order to remove ^{103}Ru completely from the mixture, higher oxidation potential of the oxidant were used and tested. Several series of experiments were conducted using higher oxidation potential of the oxidant. In these experiments, 2mL of Rh carrier (8 mg/mL) and 2mL of Ru carrier (5 mg/mL) were added to the raw fission liquor and 0.5 g of oxidant was used. The distillation was continued for 2 hrs. The influence of oxidants on the removal of Ru as RuO_4 is shown in Table 3.

TABLE 3. EFFECT OF AMOUNT OF OXIDENTS ON THE OXIDATION OF Ru TO RuO_4

	Oxidant	**% of ^{103}Ru removal**
1.	KIO_4	99.3 ± 0.2
2.	$(NH_4)_2S_2O_8$	98.9 ± 0.3
3.	$NaBiO_3$	95.7 ± 0.3
4.	$KMnO_4$	90.2 ± 0.5
5.	PbO_2	94.8 ± 0.8
6.	$NaBrO_3$	51.8 ± 2.5

It was seen that KIO_4 and $(NH_4)_2S_2O_8$ gave almost quantitative removal of radioruthenium. This may be due to the fast kinetic of the oxidation reactions of ruthenium with the oxidants. When KIO_4, $(NH_4)_2S_2O_8$ and $NaBiO_3$ were used, 30 min of distillation was long enough to result quantitative removal of radioruthenium; however, when $KMnO_4$ was used, this reaction time was too short to remove radioruthenium completely. These data show that KIO_4 is preferable as the oxidant for the quantitative removal of radioruthenium. It has been observed that by passing air through the solution at a rate of 100mL/min and heating the reaction mixture at 70-90°C for 30 min, quantitative removal of ^{103}Ru is possible. Radioruthenium was collected in a trap containing 6M HCl or 3M HCl containing 15% H_2O_2.

2.3. PRECIPITATION OF ^{99}Mo BY ABO

Alpha-benzoin oxime is a compound containing OH group linked to the nitrogen atom which can be easily dissolved in alcohol and dilute NaOH solution. About 2% alpha-benzoin oxime solution dissolved in both ethyl alcohol and 0.4 M NaOH solution was used for the precipitation of ^{99}Mo from the raw fission liquor. The efficacy of both the solutions was evaluated and the result is shown in Table 4.

Experimentally it was observed that solution prepared from ethyl alcohol gives near quantitative precipitation of ^{99}Mo. Further, the effect of molybdenum concentration in the feed solution on the precipitation of ^{99}Mo was studied and the results are depicted in Table 5. It is seen that alpha-benzoin oxime is effective for the precipitation of ^{99}Mo when the Mo concentration was between 10 to 50 mg. This shows the selective nature of the precipitate.

TABLE 4. EFFECT OF SOLVENT OF ALPHA-BENZOINE OXIME

S.No	**Solution of α-benzoin oxime**	**% of ^{99}Mo Recovery**
1	0.4 M NaOH	78.28 ± 1.5
2	Ethyl alcohol	98.3 ± 0.9

TABLE 5. EFFECT OF Mo CONCENTRATION ON PRECIPITATION

S.No	**Amount of ^{99}Mo (mg) in the feed**	**% Recovery**
1	10	98.5 ± 0.25
2	15	98.18 ± 0.5
3	25	98.6 ± 0.5
4	50	99.8 ± 0.1

In an attempt to understand the selective nature of alpha-benzoin oxime to precipitate ^{99}Mo in the presence of U, the concentration of U in the feed was varied from 10 mg to 500 mg and percentage of ^{99}Mo recovered were estimated. The result is depicted in Table 6.

TABLE 6. EFFECT OF U ON THE PRECIPITATION OF ^{99}Mo

	Amount of U added	**Amount of ^{99}Mo added**	**% of ^{99}Mo Recovery**
1	10 mg	10mg	98.53 ± 0.25
2	100mg	10mg	99.21 ± 0.2
3	500 mg	10mg	99.38 ± 0.2
4	1000 mg	10mg	98.51 ± 0.5

2.4. RECOVERY OF ^{99}Mo FROM ^{99}Mo-ABO PRECIPITATE

The ^{99}Mo-ABO precipitate was washed several times with 0.1 M HNO_3 and ethanol to remove contaminants trapped in the precipitate**.** The dissolution behavior of precipitate was studied using organic as well as inorganic reagents and the results are illustrated in Table 7.

It is also critical to estimate the level of radio-contaminants adsorbed on the ^{99}Mo-ABO precipitate. We have thoroughly investigated the percentage of radionuclides associated with the precipitate by gamma spectrometric study and the result is shown in Table 8.

TABLE 7. DISSOLUTION OF ^{99}Mo-ABO PRECIPITATE

	Reagent	% of ^{99}Mo in the solution
1	0.4M NaOH + 1% H_2O_2	98.8 ± 0.5
2	Ethyl acetate	98.5 ± 0.5

TABLE 8. RETENTION OF FISSION PRODUCTS IN THE PRECIPITATE (DURING PRECIPITATION)

	Isotope	% present in the PPt
1.	^{95}Zr	10.3 ± 1.5
2.	^{103}Ru	8.4 ± 2.1
3.	^{131}I	12.4 ± 3.5
4.	$^{85+89}$Sr	11.4 ± 1.8

2.5. REMOVAL OF RADIO-CONTAMINANTS BY CARRIER PRECIPITATION

The inability to remove these radionuclidic impurities efficiently during the precipitation step was resolved by carrier precipitation method. At first, radioiodine was removed from the solution (obtained by the dissolution of ^{99}Mo-ABO precipitate) by the addition of 5 mL of KI (conc=10mg/mL) followed by 0.5 mL of 10% $AgNO_3$ in 0.1M HNO_3. The solution was decanted and AgI precipitated was discarded as radioactive waste. The pH of the solution was brought to alkaline and Fe^{3+} & Zr^{4+} carrier solution (5 mL, 10mg/mL) was added to precipitated ^{95}Zr as zirconium hydroxide. In order to remove ^{90}Sr and ^{89}Sr impurities, 5 mL of $Sr(NO_3)_2$ (10mg/mL) and 10 mL of $(NH_4)_2CO_3$ were added. This precipitated $SrCO_3$. The solution was filtered to remove the precipitate [$Fe(OH)_3$,$ZrO(OH)_2$,$SrCO_3$]. The extent of decontamination achieved during the carrier precipitation step is shown in Table 9.

TABLE 9. EFFICIENCY OF CARRIER PRECIPITATION STEP

	Radionuclides	% Removal
1.	^{99}Mo	< 1 %
2.	^{95}Zr-^{95}Nb	90.2 ± 1.2
3.	$^{85+89}$Sr	89.1 ± 1.8
4.	^{131}I	88.3 ± 2.3
5.	^{132}Te	85.4 ± 2.8
6.	^{103}Ru	81.4 ± 2.5

The results of the carrier precipitation process revealed that quantitative removal of radio-contaminants was not possible and prompted us to purify the filtrate further. The filtrate was then acidified and ^{99}Mo was reprecipitated with alpha-benzoin oxime. The precipitate was then dissolved in 0.4M NaOH with ~1% H_2O_2. This solution was then passed through a series of ion exchange columns having frit at the bottom and packed with adsorbent. The first column contains silver coated charcoal, the second hydrous zirconium oxide and the third charcoal column. Prior to the passage of solution, these columns were preconditioned at pH 12-13. The column pH is critical and should be kept basic to preclude the formation of polymeric crystals of polymolybdate ions.

The effluent from these columns was collected; the pH was adjusted to 2-3 by the addition of 0.1M HNO_3 and passed through an ion exchange column containing alumina wherein ^{99}Mo gets adsorbed. The column was washed with 25 mL of 0.01MHNO_3 solution. The adsorbed ^{99}Mo from the column was eluted with 10 mL of 0.1M NaOH solution. The purity of the ^{99}Mo isolated from the above process was evaluated by taking the gamma spectra which shows photo peaks pertaining to ^{99}Mo/^{99m}Tc only.

Based on the above observation, a modified Cintichem procedure was developed. The flow diagram of the modified process is shown in Fig.1.

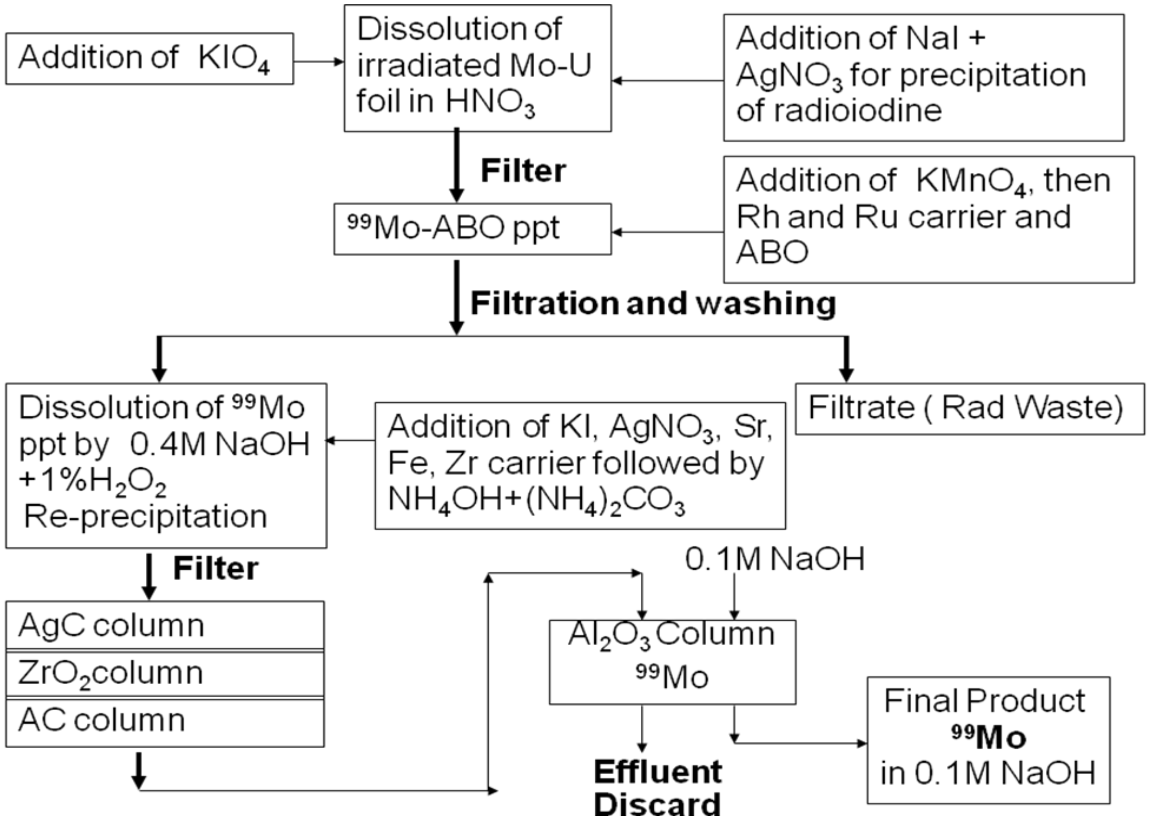


FIG. 1. Flow sheet of modified Cintichem Process.

2.6. PROCESS DEMONSTRATION USING NEUTRON IRRADIATED U-Mo ALLOY

Hot test is essential with the goal of demonstrating that the process could be successfully used and for the validation of the process in terms of product purity and process efficiency. The process begins with the irradiation of U-Mo alloy (100mg). To generate fission isotopes, the target was placed at a flux of 6 × 10^{13} in Dhruva reactor for a period of 1 week. This was used to demonstrate the Cintichem process for the separation ^{99}Mo within the target.

After irradiation, the target was removed from the reactor and kept in a 100mm thick lead shielded facility. The irradiation can was opened and uranium turning/foil from the irradiated can was removed and verified that all the pieces are present and intact. The irradiated uranium turning/foil was transferred into a dissolver flask. Care was taken to ensure complete transfer of target. The reaction vessel was closed. The stop cock connecting the iodine trap was opened. The stop cock connecting the vacuum pump the dissolver was open to evacuate the air from the dissolver. When evacuation was complete (evident by the vacuum-pump gauge reaching a constant value), the stop cock was closed and the vacuum pump was disconnected from the dissolver. The dissolver solution (Conc HNO_3) was then transferred into the dissolver through the glass tubes. The position of the dissolver flask in the heating mantle was verified, and the heating was turned on. When dissolution was complete, the heating mantle was put off and allowed the dissolver to cool for 10 minutes. All stop cocks were closed and iodine trap was detached. The gamma spectra of the dissolver solution are shown in Fig. 2. Following the modified procedure as described above, separation of ^{99}Mo was carried out. The gamma spectra of the isolated ^{99}Mo are shown in Fig. 3 and decontamination factor different fission products at different steps are depicted in Table 10.

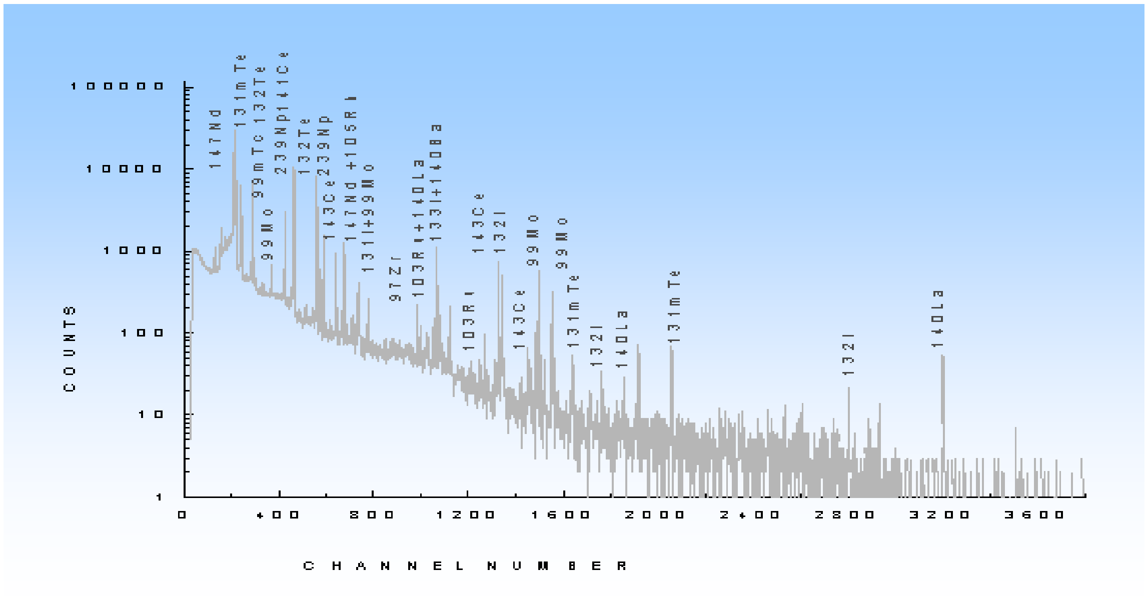


FIG. 2. Gamma spectra of fission products solution.

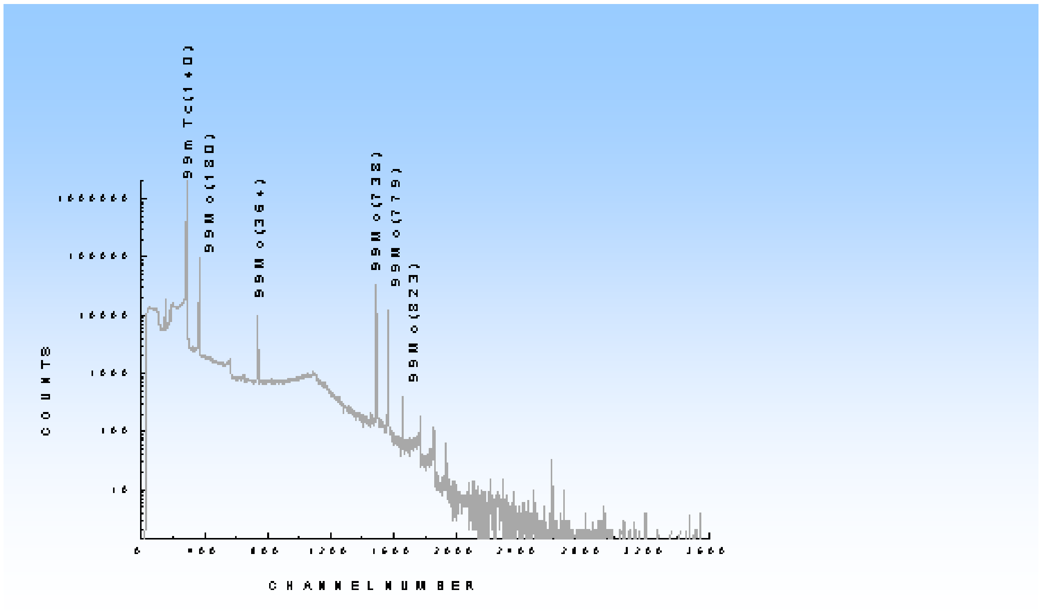


FIG. 3. Gamma spectra of separated ^{99}*Mo*

TABLE 10. DECONTAMINATION FACTOR DIFFERENT FISSION PRODUCTS

Step	**α ABO Pptn.**	**Purifn. Step-I Activated Charcoal (AC)**	**Purifn. Step-II AC + Ag coated AC + HZrO**	**Purifn. Step-III Acidic alumina**
% ^{99}Mo Recovery	84.72	80.1	76.3	72.7
% decontamination				
^{95}Zr	75.2	99.65	100	100
^{95}Nb	50	75.4	100	100
^{103}Ru	75.2	75.6	94.4	99.9
^{127}Sb	84.8	88.2	100	100
^{131}I	98.1	99.95	100	100
^{132}Te	87.1	99.08	100	100
^{137}Cs	96.8	87.5	100	100
^{140}Ba	98.58	100	100	100
^{140}La	76	99.7	100	100
^{141}Ce	98.64	100	100	100
^{143}Ce	86.7	100	100	100
^{147}Nd	86.6	100	100	100
^{153}Sm	98.5	100	100	100
^{239}Np	98.5	99.4	100	100

Although the demonstrations were highly successful, a series of tests using grams quantity of U-Al alloy are required to evaluate the efficiency of the process, effect of reagent in the presence of ionizing radiation from the time of processing to use, performance of the chromatographic columns and the radiation effects on the glassware. Such tests are essential to identify potential problems that could be encountered at the plant scale. Additional tests are required with process hardware, glassware, and chemicals to demonstrate the Cintichem process and isolation of ^{99}Mo, which met radiopharmaceuticals specifications.

3. DEVELOPMENT OF AN ELECTROCHEMICAL PROCESS TO AVAIL ^{99m}Tc USING (n,γ)^{99}Mo

A mixture of metal ions having adequate difference in their formal potential values in an electrolytic medium can be mutually separated by selective electrodeposition of one metal on an electrode surface under the influence of controlled applied potential [2-8]. Exploring the potential of electrochemical technique in the field of radionuclide generators, we are the first to report the electrochemical separation of ^{90}Y from ^{90}Sr [9] and thereafter separation of ^{188}Re from ^{188}W [10] for their utility in the preparation of radionuclidic generators. As a logical extension, here we have attempted to use this technique in the preparation of ^{99}Mo/^{99m}Tc generator.

Separation of ^{99m}Tc from Na$_2$ [^{99}Mo]MoO$_4$ solution (alkaline medium) appeared to be the most attractive alternative pathway due to the existence of hexavalent state of ^{99}Mo in the electrolyte as soluble Na_2MoO_4. Technetium has various oxidation states from +7 to -1, and shows the tendency for hydrolysis, disproportionation and formation of complexes. Heptavalent state has a low tendency to reduction. Technetium is soluble when in the form of pertechnate (TcO_4^- i.e. Tc (VII) valency) or in the form of Tc (V) but under normal conditions is insoluble as Tc (IV) or Tc (0). Therefore, Tc in the electrolyte should remain in the form of Tc (VII) or Tc (V), of which Tc (VII) is the most common and convenient. On electrolysis, Tc(VII) gets reduced to Tc(IV) or below and gets deposited on the surface of the platinum electrode [11]. The reduction of TcO_4^- takes place as per the reaction

$$TcO_4^- + 3e^- + 4H^+ \rightarrow TcO_2 + 2H_2O \qquad E_o = 0.738\ V\ [12]$$

where E_o is the potential in volts with respect to a normal hydrogen electrode.

The separation potential must be set to a value more cathodic than the redox half-cell potential of Tc. The need to achieve quantitative deposition of ^{99m}Tc within a reasonable period of time, prompted us to apply a potential much higher than the standard reduction potential (E_o) required for depositing ^{99m}Tc. The evolution of hydrogen gas at that high potential paves the way for a non-adherent deposit of ^{99m}Tc on the electrode surface. Although a satisfactory explanation for the mechanism of electrodeposition has still not been identified, the deposited ^{99m}Tc is expected to be a mixture of Tc(0) and oxide/hydroxide of Tc(IV) [11] . The ^{99m}Tc deposit could be easily detached from the electrode surface for pharmaceutical applications.

The electrochemical cell consisted of a quartz vial (24 × 40 mm, 20 mm ID) and a teflon cap with a small hole (~2.5 mm) for venting off any gases. The electrodes used were made of high purity platinum plates (5 cm × 1 cm) which were fitted on the mouth of the quartz vial, parallel to each other, 5 mm apart and connected to the power supply. Electrolysis was performed by applying a constant potential difference of 5 volts (current 450 mA, current density 328 mA/cm^2), for 50 minutes. After the electrolysis, the electrodes were moved up from the cell along with the lead cap while maintaining the potential and turned off after removal. An identical lead cap with acrylic lining but without electrodes was placed on the quartz cell for radiation shielding (Fig. 4). The electrodeposited ^{99m}Tc could be brought into saline solution by placing the electrode in a narrow (1 mL) glass vial (0.5 cm diameter) containing 500 μL of saline solution. A new Pt electrode was also dipped in the solution and the polarity of the cathode was reversed. A high voltage (10 V) was applied for few seconds (~20 s) and both the electrodes were taken out from the solution after switching off the current. Schematic diagram of the electrochemical cell is portrayed in Fig. 4. The salient aspects and the details of the experimental procedure on this generator are available in our published articles [13-14].

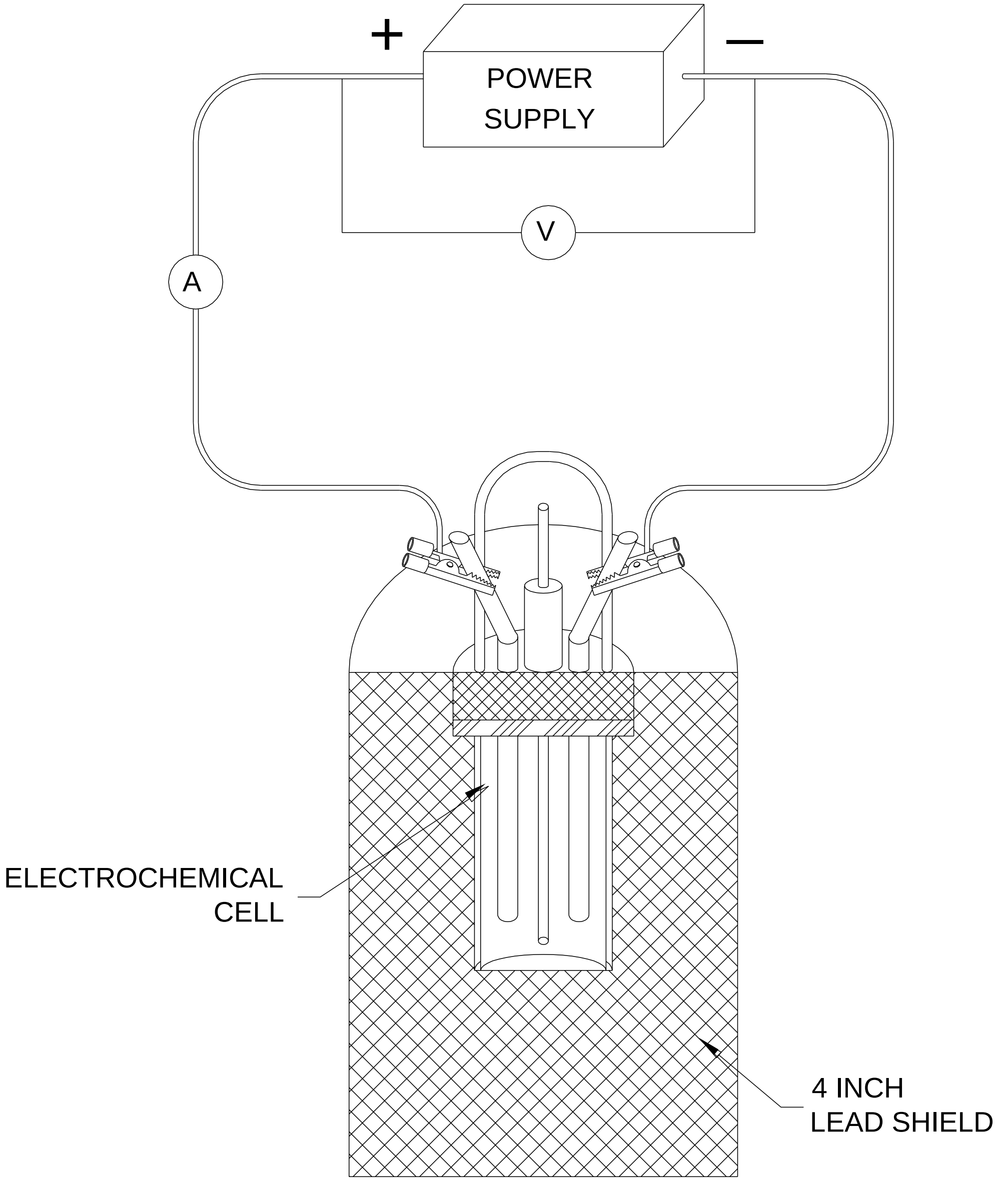


FIG. 4. Electrochemical cell in a lead shielded container.

Several high activity generators 22.2- 29.6 GBq (600-800 mCi) were prepared and ^{99m}Tc was separated under the optimized operation conditions. The overall performance of the generator remained consistent in all the batches over a period of 10 days, which is normally the shelf-life of a ^{99}Mo/^{99m}Tc generator. In the electrochemical cell, platinum was used as the electrode material as it is inert and hence suitable for repeated effective removal of deposited ^{99m}Tc. The electrolysis was carried out in a single "reaction" vessel, in order to reduce the radiation exposure and to maintain the inventory of ^{99}Mo. In order to minimize the radiation exposure to the operating personnel, the whole system was shielded. Due to loose adhesion of ^{99m}Tc on the inert surface of Pt electrode, the deposited ^{99m}Tc activity could be dissolved in small volumes of 0.9% NaCl.

The overall yield of ^{99m}Tc was >90%, with >99.99% radionuclidic purity and >99% radiochemical purity. The compatibility of the product in the preparation of ^{99m}Tc labeled formulations such as ^{99m}Tc-DMSA and ^{99m}Tc-EC was found to be satisfactory in terms of high labeling yields (>98%). The radioactive concentration (RAC) is adequate for labeling with current generation of radiopharmaceuticals kits. The major advantages of this technique are:

1. Possible to access ^{99m}Tc of acceptable quality using low specific activity ^{99}Mo availed by (n,γ) process.
2. There is no restriction on the specific activity of (n,γ)^{99}Mo.
3. Cost effectiveness: Cell constructions and peripheral equipment are simple, portable and inexpensive.
4. Clean process: The process is basically an oxidation reduction reaction that takes place at the surface of conductive electrodes in a chemical medium under the influence of an applied potential. Electron brings about separation with minimum consumption of reagents and produces negligible radioactive waste. The process can be carried out at ambient temperature and pressure.
5. Extended life: Owing to the sensitivity of the process, ^{99m}Tc of acceptable radioactive concentration can be availed from the system up to 10-12 days.
6. Versatility: It has flexibility in terms of the sample size required and applicability from mCi to multi curies level. The process permits a great flexibility in the use of (n,γ)^{99}Mo obtained from different sources.
7. Amenability to automation: The inherent variables of electrochemical processes such as electrode potential, cell current, electrode positioning and inert gas purging, are amenable for process automation and can be computer-controlled.

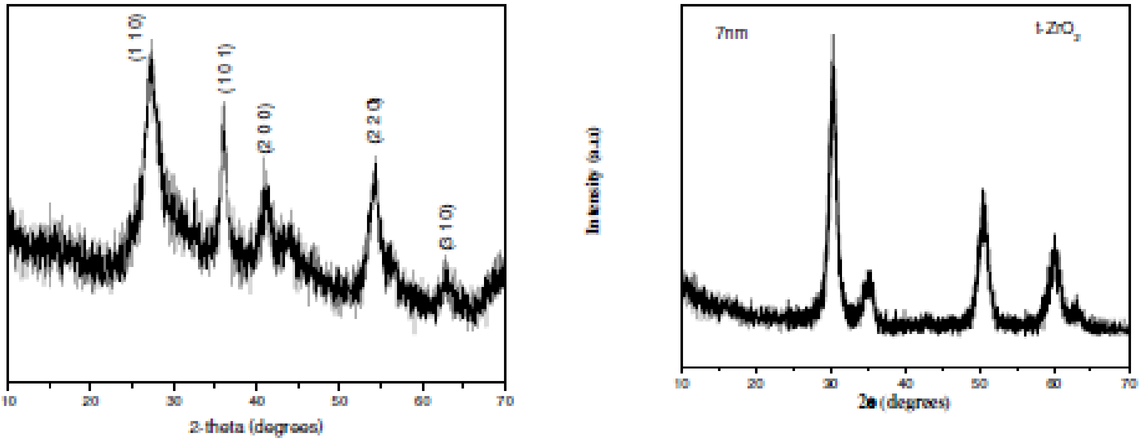
The findings of this study suggest that the electrochemical separation is very effective for isolating ^{99m}Tc from the aqueous solutions of ^{99}Mo/^{99m}Tc equilibrium mixture and a fully integrated electrochemical separation system is an achievable objective that could be used to access ^{99m}Tc from ^{99}Mo produced by (n,γ) method. The system is suitable for the routine daily production of ^{99m}Tc with minimum radiation dose to the operator, since it can be left unattended during the electrodeposition process. The pertechnetate can be dissolved in any required volume of physiological saline so that small volumes can be used for radiopharmaceuticals studies. The system could be easily modified for automatic operation. Having successfully completed the feasibility demonstration studies, technology development of a compact, portable and automated generator assembly concurrent to the process has been undertaken with the help of a multidisciplinary team comprising of chemists and engineers. It is envisaged that the electrochemical technology would serve in good stead for ensuring the availability of ^{99m}Tc using (n,γ)^{99}Mo, although alumina column chromatographic generators based on the use of fission ^{99}Mo might continue to remain the main source of ^{99m}Tc for most of the large-scale production needs. This alternative strategy may not be enough to fill the shortage of fission ^{99}Mo, but can serve as an option for accessing ^{99m}Tc, particularly in countries with research reactors for radioisotope production.

4. NANOMATERIALS AS A NEW GENERATION SORBENT FOR THE DEVELOPMENT OF ^{99}Mo/^{99m}Tc GENERATOR USING (n,γ)^{99}Mo

In recent years, the field of nano sized materials has had the attention, imagination, and close scrutiny of scientists owing to their extremely small size, large specific surface area and distributions of reactive surface sites [15]. The ^{99}Mo/^{99m}Tc generator literature contains numerous reports on the development of novel sorbents; however, to date only small percentages have focused on the nano enabled sorbents. Although today the use of nanomaterial based sorbent in radiochemical separation has a fairly young approach; our group has recognized the utility of such materials.

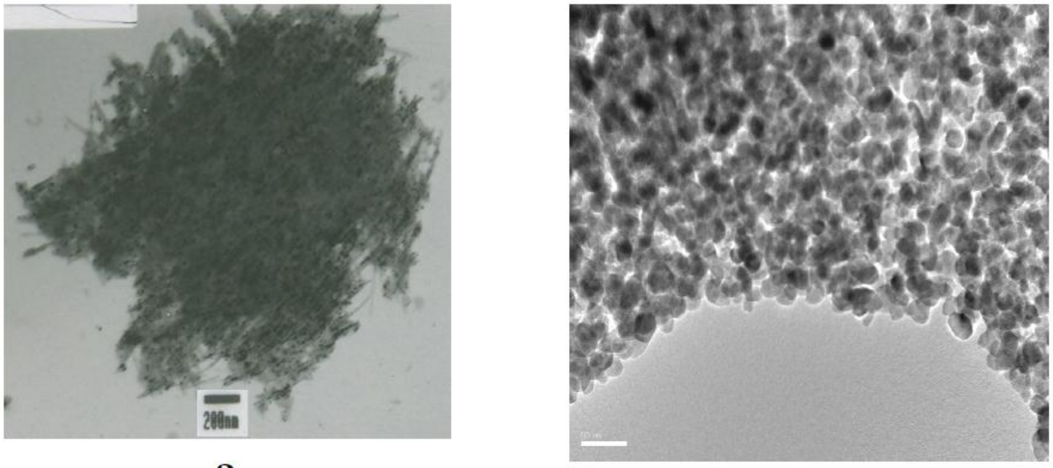
One of the specific properties of nanomaterials is that a high percent of the atoms are on the surface. These lead to peculiar properties that cannot be found in corresponding bulk materials. The surface atoms of nanoparticulate metal oxides are unsaturated, exhibit intrinsic surface reactivity and can strongly adsorb metal ions in solution. The potential of this new generation of sorbents in the chromatographic separation of metal ions [16-18] has been exploited. However, research about the preparation of radionuclidic generators using nanoparticles is seldom reported. The development of nanomaterial based sorbents for radionuclidic generators represents a dynamic and rapidly growing research area that requires dedicated and collaborative efforts of material chemists, radiochemists, analytical chemists and radiopharmaceutical chemists. In order to tap the potential of nanomaterials as a viable sorbent in the relatively unexplored field, we have explored the synthesis and characterization of two noble sorbents, polymer embedded nanocrystalline titania (TiP) and nanocrystalline zirconia and their possible application in the preparation of ^{99}Mo/^{99m}Tc generator [19-20]. Such efforts have potential impact both for the utilization of (n,γ)^{99}Mo and reducing the dependence on fission ^{99}Mo.

Details of the synthesis procedures, structural characterization, determination of distribution Ratio (K_d) for ^{99}Mo/^{99m}Tc ions, zeta-potential determination, evaluation of sorption capacity and process demonstration studies are available in our published articles [19-20]. X-ray diffraction and TEM micrograph of these nanomaterial based sorbent materials are depicted in Fig. 5 and Fig. 6, respectively.



a **b**

FIG. 5. XRD pattern of (a) polymer embedded nanocrystalline titania(TiP), (b) nanocrystalline zirconia.



a **b**

FIG. 6. TEM micrograph of (a) polymer embedded nanocrystalline titania (TiP), (b) nanocrystalline zirconia.

The surface acid-base properties of nanocrystalline metal oxides are inherent and are primarily responsible for the retention of ^{99}Mo. Interfacial chemistry of nanocrystalline metal oxides has allowed the selective sequester of negatively charged poly molybdate ions. Apart from improving sorption capacity, the rigid, open pore structure of these nanomaterial based sorbents facilitate poly molybdate ions anions to reach binding sites of sorbent for rapid and efficient sorption kinetics. The decay of ^{99}Mo to ^{99m}Tc is not accompanied by any serious disruption of chemical bonds. As these molybdate ions start transforming into pertechnate ion ($^{99m}TcO_4^-$), which has only -1 charge, the binding would get weaker and an easy displacement of $^{99m}TcO_4^-$ is expected and gets eluted easily with normal 0.9% saline.

From the perspective of the end-user, the reported procedure retains the simple-to-operate qualities of the chromatographic generator. The ^{99m}Tc availed from these nanomaterial based generators is indistinguishable in quality and applicability from that produced by the traditional alumina based generator containing fission ^{99}Mo. The radioactive concentration (RAC) of ^{99m}Tc availed from this generator is adequate for labeling with current generation of radiopharmaceuticals kits. Additionally, it was possible to recover the adsorbed ^{99}Mo from the spent generator prior to disposal, leading to economic advantage. The materials are capable of preserving its physicochemical and sorption properties in long use.

The major benefits in the use of nanomaterial based sorbent are

(1) High capacity of the sorbent owing to small size and high specific surface area.
(2) Rapid packing due to the high density of the sorbent that settles in a few minutes.
(3) Rigidity which allows the use of high flow rates.
(4) Enhanced chromatographic efficiency due to large surface to volume ratio.
(5) Negligible ^{99}Mo bleeding due to the stable chemical link of the ^{99}Mo species to the matrix.
(6) Chemical and radiation stability of the nanomaterial based sorbent matrix.

Although the use of nanomaterials in the preparation of ^{99}Mo/^{99m}Tc radionuclide generators using $(n,\gamma)^{99}$Mo is still in its infancy, these studies have demonstrated the long awaited potential of nanomaterials. The volume of production possible by this route may be limited but could still be of interest in meeting local need.

5. CONCLUSION

During the CRP, we have studied the chemistry of the Cintichem process to understand the processing variability, to identify potential problems, and to determine the parameters to be used during production of fission ^{99}Mo. This report also provides a brief overview of the alternate strategy developed in the authors' laboratory to use $(n,\gamma)^{99}$Mo for the preparation of ^{99}Mo/^{99m}Tc generator system. These recent developments not only offer alternative resources to meet the expanding demand of ^{99m}Tc using $(n,\gamma)^{99}$Mo, but also represent state-of-the-art separation chemistry for ^{99}Mo/^{99m}Tc generator development. Recent results of the electrochemical generators and use of nanomaterial based sorbents can be considered as a springboard and spur not only further development but also continued searches for other paths to utilize $(n,\gamma)^{99}$Mo in the foreseeable future. Success in this new paradigm will not only provide great intellectual and scientific satisfaction, but will also have a significant and beneficial impact upon the availability of ^{99m}Tc.

ACKNOWLEDGEMENTS

The authors are grateful to Prof. M. R. A. Pillai, Head, Radiopharmaceuticals Division for his helpful suggestions, scientific discussions, and patiently editing the manuscript. The authors thank all their co-workers. The authors would like to express their sincere thanks to Dr. A.K. Tyagi and his colleagues from Chemistry Division for their collaboration in nanomaterial based science.

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