

Optimization of Electrodeposition Parameters to Increase ^{99m}Tc Radioactive Concentration

M.B. Febrian*, Y. Setiadi and T.H.A. Wibawa

Center for Applied Nuclear Science and Technology, National Nuclear Energy Agency
Jl. Tamansari 71, Bandung 40132, Indonesia

ARTICLE INFO

Article history:

Received 2 November 2015

Received in revised form 14 July 2016

Accepted 3 October 2016

Keywords:

Electrochemical

Technetium-99m

NaNO_2

Radioactive concentration

ABSTRACT

The use of low activity concentration ^{99m}Tc would result in low-quality labeled compound for diagnostic purpose. The low activity concentration of labeled compound will alter biodistribution and lead to false imaging in diagnostic applications. Electrodeposition could be an alternative method for increasing the activity concentration of ^{99m}Tc solution. The influence of electrodeposition parameters such as electrolytes, concentration of electrolyte, and voltage and time of deposition were examined to find the optimum condition for electrodeposition. Electrolytes to be evaluated were NaNO_2 , Na-oxalate, NaOH , and NaCl . Concentration factor is defined by ratio of final against initial concentration of ^{99m}Tc . The quality assessment of ^{99m}Tc after electrodeposition was conducted by labeling test of methylene diphosphonate (MDP) and 1,4,8,11-tetraaza cyclotetradecyl-1,4,8,11-tetramethylene phosphonic acid (CTMP). The results showed that the addition of NaNO_2 electrolyte gave the highest electrodeposition yield in comparison with Na-oxalate, NaOH , and NaCl , while the optimum concentration of electrolytes was 0.67 M. The optimum deposition voltage and duration were 7 V and 90 minutes, respectively. The electrodeposition yield was 96 % under optimized condition with a concentration factor of up to 7.96. In the quality assessment, MDP and CTMP were successfully labeled by concentrated ^{99m}Tc to give ^{99m}Tc -MDP and ^{99m}Tc -CTMP labeled compounds with radiochemical purities of more than 95 %.

© 2017 Atom Indonesia. All rights reserved

INTRODUCTION

Technetium-99m (^{99m}Tc) is the most popular medical radioisotope, used in approximately 85 % of nuclear medicine diagnostic imaging procedures worldwide [1]. ^{99m}Tc is an ideal single-photon emitter, because of its favorable half-life, photon energy, and radiopharmaceutical chemistry [2]. The radioactive concentration and radiochemical purity of ^{99m}Tc are two important parameters in determining the quality of ^{99m}Tc -based radiopharmaceutical. The combination of sufficient dose and radioactive concentration is an important factor in good biodistribution and imaging quality [3]. A high radioactive concentration of labeled

compound is an important requirement for most of its application in biology and medicine [4]. Typical doses of some radiopharmaceuticals are in the 5-30 mCi/mL range, depending on the kind of radiopharmaceuticals [5].

Low radioactivity concentrations of ^{99m}Tc are usually produced by using neutron-activated ^{99}Mo as a parent radionuclide of ^{99m}Tc [6]. Presently, the use of neutron-activated ^{99}Mo tends to increase because of the policy that limits the use of highly enriched uranium (HEU) as a target material [7]. One of the fission products from HEU is ^{99}Mo , and most of its supply in the world is produced via HEU target material [1][8]. Increasing the concentration of ^{99m}Tc is an answer to the problem of the low activity concentration of ^{99m}Tc .

Solvent extraction by methyl ethyl ketone, column chromatography, and sublimation are

* Corresponding author.

E-mail address: mbasitf@batan.go.id

DOI: <http://dx.doi.org/10.17146/aij.2017.618>

examples of established methods for increasing the specific concentration of ^{99m}Tc [9]. However, those methods have several limitations such as requirement for personnel competency, moderate efficiency, and use of hazardous materials. In the sublimation method, attempts to concentrate ^{99m}Tc along to separate it from $^{99}\text{MoO}_3$ have met with limited success [10].

Electrochemical deposition is an alternative method to increase the concentration of ^{99m}Tc . In a previous study by Chakravarty *et al.* [11], ^{99m}Tc was electrodeposited on platinum (Pt) electrode using oxalate as supporting electrolyte. Afterward, the deposited ^{99m}Tc was removed and transferred into a small volume of normal saline. The result of the study was suitable to concentrate ^{99m}Tc obtained from zirconium molybdate gel generator. They used 5 M sodium oxalate bulk solution, but there were some discrepancies with other works. According to Rozaini [12], the solubility of sodium oxalate in aqueous solution is 2.1 M at 25 °C, and because of this low solubility in water, it is impossible to use 5 M sodium oxalate bulk solution as Chakravarty did. Khorsand *et al.* [13] found that the addition of oxalate anion would reduce the nuclei density of metal deposition, although they studied different metal from ^{99m}Tc . Reducing nuclei density means reducing deposited metal in electrodeposition.

In another work, Ignatova *et al.* [14] suggested that the use of sodium nitrite in Ag-Cu deposition could enhance the quality of deposited Ag-Cu. Another previous work [10] suggested the use of sodium hydroxide in electrochemical separation ^{99m}Tc from ^{99}Mo . The use of electrolytes other than oxalate in electrodeposition probably result in shifting other parameters, so optimization of electrodeposition parameters is required if oxalate is replaced by any other electrolytes.

In this study, optimization of electrodeposition parameters has been carried out. Parameters to be optimized were electrolyte type, concentration of electrolyte, and voltage and time of deposition. Those optimized parameters will be used to increase the activity concentration of ^{99m}Tc . Electrolytes to be evaluated were NaNO_2 , Na-oxalate, NaOH , and NaCl . The concentration factor is defined as the ratio of the final concentration of ^{99m}Tc to its initial concentration. The quality assessment of the concentrated ^{99m}Tc will be performed by labeling methylene diphosphonate (MDP) and 1,4,8,11-tetraaza cyclotetradecyl-1,4,8,11-tetramethylene phosphonic acid (CTMP) as labeled compounds for bone imaging purpose.

EXPERIMENTAL METHODS

Preparation of ^{99m}Tc radioisotope

Low-activity ^{99m}Tc (up to 6 mCi) was obtained from used $^{99}\text{Mo}/^{99m}\text{Tc}$ generator (Polatom and Gentech). High-activity ^{99m}Tc (up to 25 mCi) was obtained from the irradiation of 2 g of MoO_3 (nat) in the G.A. Siwabessy multipurpose reactor for five days. The irradiated Mo target was processed to obtain separated ^{99m}Tc using electrochemical separation described by Chakravarty [10]. The processing of irradiated Mo was carried out in the Labeled Compound and Radiometry Laboratory, Center for Applied Nuclear Science and Technology, BATAN Bandung.

Electrochemical cell and electrodeposition procedure

The electrochemical cell used in this work consisted of two platinum electrodes (Sigma-Aldrich) connected to a power supply (BK Precision 1785B, 0-18 Volt range, 10 mV voltage programming resolution, and 3 mV offset). A 10-mL quartz vial was used as electrolytic chamber. A polyethylene cap with two holes 5 mm apart for electrodes and one small hole for gas ventilation was fitted on the mouth of the vial. Four 50-mm thick lead bricks were laid around the vial as a radiation shield. The cathode and the anode were connected to power supply via test cables. After filling with 1.5 mL to 7 mL of $^{99m}\text{TcO}_4^-$ in desired radioactivity, the cap together with electrodes were fitted to vial, and the electrodes were connected to power supply. After the power supply operation reached a constant voltage, electrolysis reaction occurred in the electrochemical cell.

After the electrolysis had proceeded for the desired duration, the cap along with both electrodes were lifted up from the solution and the power supply was switched off. The electrodeposited ^{99m}Tc was brought into normal saline (0.9 % NaCl) by placing the electrodes into narrow glass tube (7 mm diameter) containing 500-1000 μL of normal saline [10,11]. The electrodes were connected to power supply in reverse potential to deposition process. By this method, almost all electrodeposited ^{99m}Tc could be brought into saline with smaller volume than the initial volume of ^{99m}Tc .

Optimization of electrodeposition parameters

The variables of voltage, time of deposition (t), and selection of Na-oxalate and NaOH

electrolyte is referred to Chakravarty *et al.* [10,11] and subjected to be optimized in this study. A schematic diagram of this study is provided in Fig. 1.

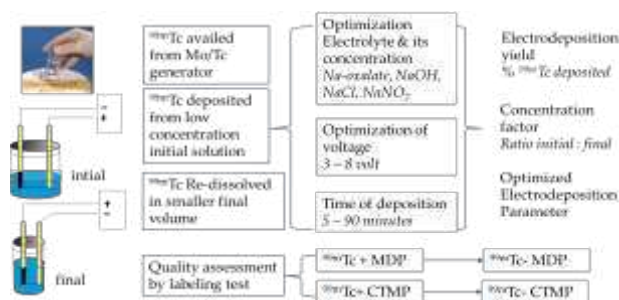


Fig. 1. Schematic diagram in optimization of electrodeposition parameter to increase radioactive concentration of ^{99m}Tc .

Optimization of electrolyte

To evaluate the effects of electrolyte on electrodeposition efficiency, four types of electrolytes (NaCl, Na-oxalate, NaOH and NaNO_2 , Merck p. a) were investigated. Two hundred μL of each electrolyte bulk solution (5 M NaCl, 5 M NaOH, and 5 M NaNO_2) and 670 μL of 1.5 M Na-oxalate were transferred to four separated vials containing 0.5 mL of 0.5-1 mCi $^{99m}\text{TcO}_4^-$ in 0.9 % NaCl obtained from $^{99}\text{Mo}/^{99m}\text{Tc}$ generator (Polatom and Gentech) for each vial. The final volume of electrolytic solution was set to 1.5 mL by adding 0.9 % NaCl solution (IPHA).

In order to find the optimum concentration of electrolytes for electrodeposition of ^{99m}Tc , several microliter portions of 5 M NaNO_2 were added gradually to several vials containing 0.5 mL of 0.5 mCi-1 mCi ^{99m}Tc in 0.9 % NaCl solution. The final volume of electrolytic solution was 1.5 mL with variation in electrolyte concentrations from blank solution to 0.83 M of NaNO_2 .

Optimization of voltage

The effects of the applied voltage on the electrodeposition of ^{99m}Tc were investigated by varying the voltage applied to the electrolytic cell from 1 V to 8 V in 30 minutes for each variation. Electrolytic cell contains 0.5 mL of 0.5-1 mCi $^{99m}\text{TcO}_4^-$ in 0.9 % NaCl solution and supporting electrolyte 0.67 M NaNO_2 with a total volume of 1.5 mL.

Optimization of time

According to Chakravarty [11], the optimum duration for the electrodeposition of ^{99m}Tc was 25

minutes. To optimize this time parameter, 0.5-1 mL of 3-5 mCi $^{99m}\text{TcO}_4^-$ in 0.9 % NaCl solution and a supporting electrolyte of 0.67 M NaNO_2 of 5 mL total volume were subjected to electrodeposited under optimized voltage in variants of duration.

Electrodeposition yield and concentration factor

The electrodeposition yield or percentage of ^{99m}Tc deposited was determined from the ratio of initial radioactivity of ^{99m}Tc before electrodeposition to the final radioactivity of concentrated ^{99m}Tc after electrodeposition. These radioactivities were determined by measuring the ^{99m}Tc solution in a dose calibrator at the ^{99m}Tc channel. The concentration factor is defined as the ratio of final concentration of ^{99m}Tc to its initial concentration. The effects of radioactivity on electrodeposition yield were determined by varying ^{99m}Tc activity p to 25 mCi.

Quality assessment

To ensure the labeling effectiveness of the concentrated ^{99m}Tc , several tests of the labeling were carried out. ^{99m}Tc obtained from electrodeposition process was used to prepare ^{99m}Tc -MDP and ^{99m}Tc -CTMP. One mL of 1 mCi $\text{Na}^{99m}\text{TcO}_4^-$ was injected into a sealed vial of methylene diphosphonate (MDP) kit and then mixed with vortex mixer for one minutes and incubated at room temperature for 30 minutes. The same procedure was used to obtain ^{99m}Tc -CTMP by labeling a sealed vial of 1,4,8, 11-tetraaza cyclotetradecyl-1,4,8,11-tetramethylene phosphonic acid (CTMP) dry kit with ^{99m}Tc [15,16].

The radiochemical purities of $^{99m}\text{TcO}_4^-$, ^{99m}Tc -MDP, and ^{99m}Tc -CTMP were determined by paper chromatography method. Two kinds of mobile phase, acetone and 0.9 % NaCl, were used. Acetone was used to determine non-complexed $^{99m}\text{TcO}_4^-$ whereas 0.9 % NaCl was used to determine reduced and hydrolyzed ^{99m}Tc as $^{99m}\text{TcO}_2$. An aliquot (5 μL) of sample was spotted on the origin in a strip of instant thin layer chromatography silica gel or ITLC-SG (0.5 cm \times 10 cm) and it was allowed to dry. The strip was placed into chromatographic chamber for development by 0.9 % NaCl eluent until final point. The strip was removed from the chamber and dried at microwave oven at 60 $^\circ\text{C}$ for 10 minutes. The retardation factors (R_f) of radiochemical species in the chromatographic paper were determined by radio-TLC scanner. The radiochemical purity of labeled compound calculated by the equation $100\% - (\% ^{99m}\text{TcO}_4^-) - (\% ^{99m}\text{TcO}_2)$ [17].

RESULTS AND DISCUSSION

The results of this work were mainly about the optimization of other studies of electrochemical step to concentrate ^{99m}Tc . Almost all concepts of this work were similar to those in previous studies [10,11] except for several conditions such as the absence of inert gas in the electrolysis step and the use of 0.9 % NaCl blank instead of pure H_2O blank.

Optimization of electrodeposition parameters

Optimization of electrolyte

There was a discrepancy between this work and other studies as mentioned in Table 1. The highest electrodeposited yield of ^{99m}Tc was achieved when NaNO_2 was added as supporting electrolyte instead of Na-oxalate. In this study, a problem appeared in the dissolution process of Na-oxalate in water to a 5 M concentration as Chakavarty *et al.* [11] reported. According to M. Rozaini *et al.* [12], the solubility of Na-oxalate in water at 298 K was 2.11 mol kg^{-1} , thus, unless Na-oxalate was dissolved in H_2O at a different temperature, it was impossible to provide a 5 M Na-oxalate solution in room temperature.

The effects of NaNO_2 were different from those of other electrolytes even at the same concentration of electrolyte. There was a similarity between NaCl, Na-oxalate, and NaOH results in the deposition of ^{99m}Tc . Zhang *et al.* [18] found that the addition of NaNO_2 in electrodeposition of lithium reduces the hydrogen evolution.

Table 1. Electrodeposition yield of ^{99m}Tc in several electrolytes. $t = 30 \text{ min.}$, 5 V, Pt electrodes, electrolyte concentration 0.67 M except NaCl 0.9 % (blank), number of replication (n)=5

| Electrolytes | ^{99m}Tc deposited (%) |
|-----------------|---------------------------------|
| NaCl 0,9 % | $27.4 \pm 0,9$ |
| NaCl | $34.7 \pm 0,4$ |
| Na-Oxalate | 34.8 ± 0.8 |
| NaOH | $36.8 \pm 0,1$ |
| NaNO_2 | $53.7 \pm 0,9$ |

The formation of hydrogen bubbles on the surface of electrode will prevent the deposition of reduced metal, thus reducing the electrodeposition yield. Ignatova *et al.* [14] studied the effects of NaNO_2 addition on Ag-Cu electrodeposition and found that the addition of NaNO_2 caused the dispersed Ag-Cu powder to be finer. NaNO_2 acts as anodic inhibitors, reducing oxidation currents which

means suppressing oxygen formation from electrolysis of water [19]. The low oxygen concentration in the electrolytic solution would prevent reoxidation of deposited $^{99m}\text{TcO}_2$ or ^{99m}Tc metal and increase ^{99m}Tc electrodeposition yield.

The optimum concentration of NaNO_2 as supporting electrolyte was 0.67 M according to Fig. 2. There is a linear relation between the increase of electrolyte concentration and electrodeposition yield for concentrations below the optimum concentration. Above this concentration, the yield of electrodeposition remains constant. The stagnant yield and high standard deviation above the optimum concentration are caused by high hydrogen gas evolution preventing deposition of ^{99m}Tc on cathode surface.

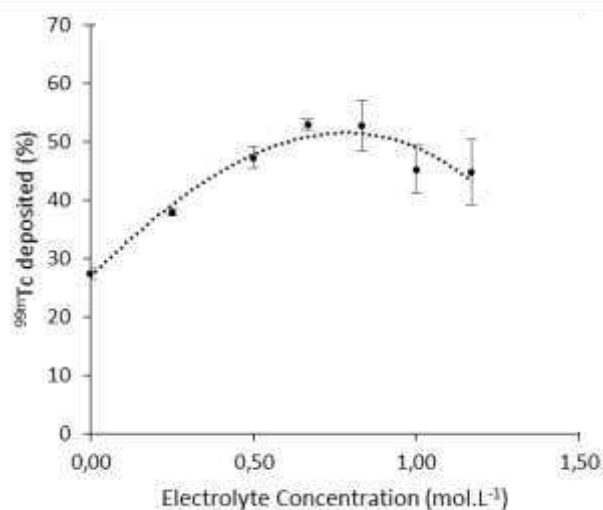


Fig. 2. Effect of NaNO_2 electrolyte concentration on ^{99m}Tc electrodeposition, $t = 30 \text{ min.}$, 5 V, Pt electrodes, n=5.

Optimization of applied voltage

The effect of applied voltage to electrodeposition yield is shown in Fig. 3. Under the optimized electrolyte condition, the optimum voltage for electrodeposition of ^{99m}Tc was 7 V. As mentioned in other studies [10,11], increasing the voltage would result in a higher electrodeposition current that then increases the yield of electrodeposition of ^{99m}Tc . According to Faraday's law, the mass of an element, such as ^{99m}Tc , deposited on the electrodes has a positive linear correlation to the current transferred to the electrode in the electrolysis process [20].

In a previous study [11], it was found that the electrodeposition yield remained constant beyond the optimum voltage. In this study we found that above the optimum voltage, the electrodeposition yield tends to decrease. This condition was caused

by an increase in the rate of hydrogen gas evolution, preventing deposition of ^{99m}Tc on the cathode surface.

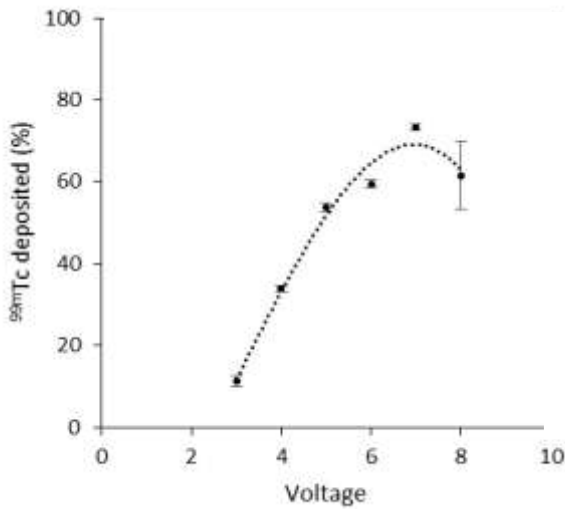


Fig. 3. Effect of applied voltage on ^{99m}Tc electrodeposition, (·) this study, electrolyte NaNO_2 0.67 M, $t = 30$ min, Pt electrodes, $n=5$.

Optimization of time and concentration factor

Investigations of the duration of electrodeposition were carried out in order to achieve adequate electrodeposition yield. The relation between electrodeposition yield and time of deposition is shown in Fig. 4. In this study, electrodeposition yield was likely a logarithmic function of time, whereas in other studies [10,11], the electrodeposition yield vs. time curve resembled a titration “S” curve.

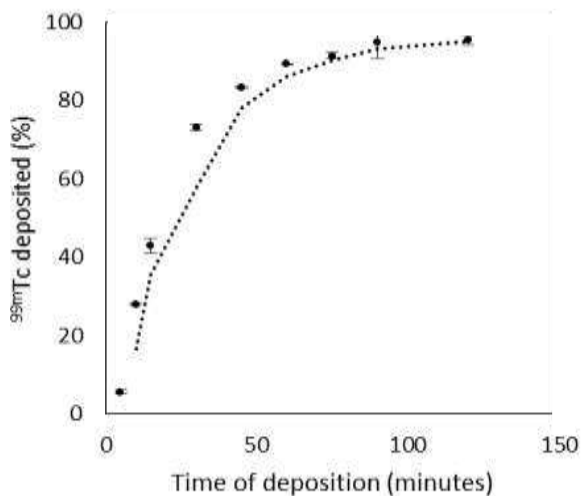


Fig. 4. ^{99m}Tc electrodeposition yield as a logarithmic function of time, (·) this work, electrolyte NaNO_2 0.67 M, 7 V, Pt electrodes.

Peiro *et al.* [21] found that at the beginning of electrodeposition, the cathodic current tends to be high, but drops drastically after thin film of metal deposit covers the cathode; further, if the deposition process continues, the cathodic current continues to decrease but the decrease is not as drastic as in the beginning of the electrodeposition process. If cathodic current is directly related to the yield of electrodeposition, the trend of electrodeposition will likely be a logarithmic function of time, having high slope in the beginning then becomes steady afterwards.

The highest electrodeposition yield of ^{99m}Tc in this study was attained at 90 minutes, at which more than 96 % of ^{99m}Tc was deposited onto electrode, after a relative slow increment of electrodeposition yield occurred from 60 minutes to 90 minutes. When thin films of metal already covers immersed electrode, the electrodeposition of the metal will continue only at a low rate [21]. By considering this slow rate of electrodeposition, 60 minutes of electrodeposition was enough to obtain a suitable activity concentration of ^{99m}Tc . The same result of slow increment happened when the concentration factor was calculated (Table 2).

The concentration factor is defined as the ratio of final radioactive concentration after electrodeposition to initial radioactive concentration. As shown in Table 2, ^{99m}Tc concentration could be increased up to 7.93 times for 60 minutes of electrodeposition.

Table 2. Concentration factor in ^{99m}Tc electrodeposition, initial volume 5 mL, final volume 0.5 mL, electrolyte NaNO_2 0.67 M, applied voltage 7 V, $n=5$

| Time (minutes) | Electrodeposition yield (%) | Concentration Factor |
|----------------|-----------------------------|----------------------|
| 60 | 89.4±0.2 | 7.93±0.09 |
| 75 | 91.6±0.7 | 7.88±0.09 |
| 90 | 96.0±0.5 | 7.96±0.13 |

The concentration factor was determined not only by ratio of initial volume against final volume of ^{99m}Tc , but also duration of electrodeposition. Decay of radioisotopes will occur during the electrodeposition. As seen in Table 2, the concentration factors from 60 to 90 minutes were not significantly different from each another. By consideration of time efficient and decay process of ^{99m}Tc , 60 minutes of electrodeposition was sufficient to get optimum deposition yield.

Table 3 shows electrodeposition yield vs. ^{99m}Tc activity. From that table it can be concluded

that increasing the activity of ^{99m}Tc did not reduce electrodeposition yield. Almost all (~90 %) of ^{99m}Tc could be deposited in Pt electrode. The highest ^{99m}Tc radioactivity used in this experiment was limited to 25 mCi. However, further experiments could be conducted to confirm there would be no significant decrease of electrodeposition yield for activities of more than 25 mCi.

Table 3. Effect of Radioactivity in Electrodeposition Yield in Optimum Condition

| Radioactivity (mCi) | Electrodeposition yield (%) |
|---------------------|-----------------------------|
| 1.80 | 92.2 |
| 2.98 | 95.7 |
| 5.70 | 91.3 |
| 16.44 | 90.8 |
| 20.90 | 89.6 |
| 25.00 | 91.0 |

Quality assessment

The radiochemical purity (RCP) of $^{99m}\text{TcO}_4^-$ as a quality parameter was examined after the concentration process. The RCP of $^{99m}\text{TcO}_4^-$ is defined as percentage ^{99m}Tc in the form of $^{99m}\text{TcO}_4^-$ versus whole form of ^{99m}Tc . Figure 5 shows a chromatogram of $^{99m}\text{TcO}_4^-$ peak in 0.9 % NaCl mobile phase. It appears that there was no significant peak of reduced $^{99m}\text{TcO}_2$ in the origin of the chromatogram. The RCP of $^{99m}\text{TcO}_4^-$ obtained from the electrodeposition was 99.75 ± 0.36 % in five replications.

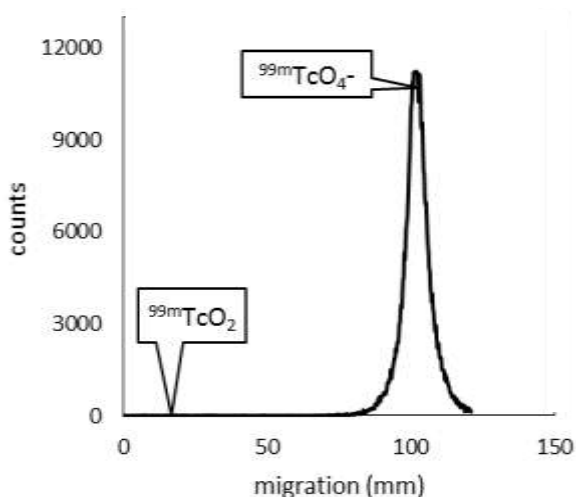
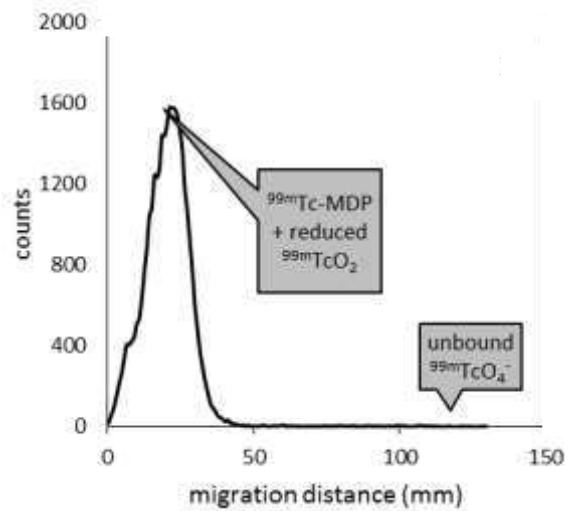


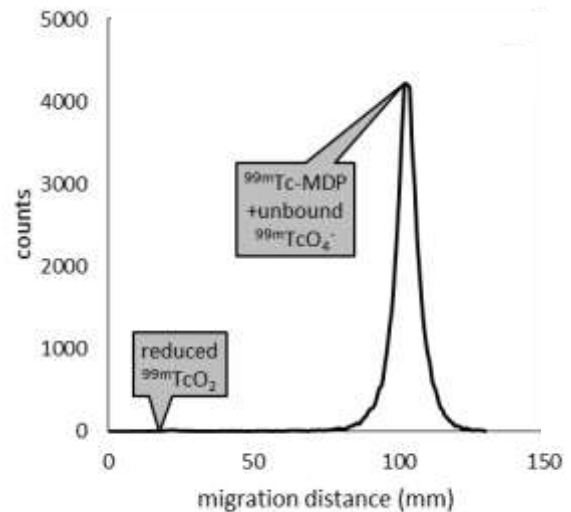
Fig. 5. Chromatogram of $^{99m}\text{TcO}_4^-$ in 0.9 % NaCl mobile phase.

The labeling efficacy of the electrochemically concentrated ^{99m}Tc was investigated by carrying out a labeling process of MDP and CTMP. Both of them are used as radiopharmaceuticals in bone imaging.

The quality of a radioactive-labeled compound is determined by how much impurities is present. The determination of $^{99m}\text{TcO}_2$ and $^{99m}\text{TcO}_4^-$ as impurities was carried out using paper chromatography. Along with the determination of labeling yield, the quality of $^{99m}\text{TcO}_4^-$ used in this labeling process was determined using the same paper chromatography system. Chromatograms of labeled MDP in two kind of mobile phase (acetone and 0.9 % NaCl) are shown in Fig. 6. ^{99m}Tc -MDP and reduced $^{99m}\text{TcO}_2$ were retained at origin whereas unbound $^{99m}\text{TcO}_4^-$ was carried by acetone as mobile phase to the end of chromatogram (Fig. 6.(a)).



(a)



(b)

Fig. 6. Chromatogram of ^{99m}Tc -MDP (a) dry acetone mobile phase (b) 0.9 % NaCl mobile phase.

An 0.9 % NaCl mobile phase was used to determine $^{99m}\text{TcO}_2$ impurities. ^{99m}Tc -MDP and unbound $^{99m}\text{TcO}_4^-$ were carried by 0.9 % NaCl mobile phase, found at $R_f = 0.9-1$ (Fig. 6.(b)) and $^{99m}\text{TcO}_2$ could be analyzed by counts of peak at

origin point or $R_f = 0-0.2$. Similar pattern of chromatogram was found on ^{99m}Tc -CTMP.

Table 4. Radiochemical purity (RCP) of ^{99m}Tc -MDP and ^{99m}Tc -CTMP using concentrated $^{99m}\text{TcO}_4^-$

| Labeled compounds | $^{99m}\text{TcO}_2$ (%) | $^{99m}\text{TcO}_4^-$ (%) | RCP (%) |
|-------------------------|--------------------------|----------------------------|-----------|
| ^{99m}Tc -MDP | 0.59±1.2 | 0.38±0.2 | 99.03±0.9 |
| ^{99m}Tc -CTMP | 1.42±0.6 | 1.28±0.7 | 96.30±0.5 |

Table 4 shows the radiochemical purity calculation from chromatogram results in Fig. 5. The radiochemical purities of ^{99m}Tc -MDP and ^{99m}Tc -CTMP were 99.03 % and 96.30 %, respectively. By this result, both labeled compounds pass the qualification as radiopharmaceuticals for bone imaging [15,16].

CONCLUSION

In the optimization of electrochemical concentration of ^{99m}Tc , it was found that the addition of NaNO_2 electrolyte at 0.67 M significantly increased the electrodeposition yield of $^{99m}\text{TcO}_4^-$. By adjusting voltage to 7 V and electrodeposition duration to 90 minutes, an electrodeposition yield of 96 % can be achieved. The concentrated $^{99m}\text{TcO}_4^-$ was successfully applied in the labeling of MDP and CTMP with radiochemical purities of more than 95 %. Future improvements of this study may include investigations to attain a deeper understanding of the mechanism of electrodeposition of ^{99m}Tc in NaNO_2 electrolyte.

ACKNOWLEDGMENT

This work was financially supported by DIPA 2015 in the Center for Nuclear Science and Applied Technology, National Nuclear Energy Agency (PSTNT BATAN). The authors would like to express their gratitude to Mr. Epy Isabela and Ms. Eva Maria from the Labeled Compounds Group of PSTNT BATAN for supporting us in use of $^{99}\text{Mo}/^{99m}\text{Tc}$ generator and to Prof. Dr. rer. nat. Evvy Kartini for improving this paper in DJFP 2015 Researcher's Training.

REFERENCES

1. Anonymous, *Non-HEU Production Technologies for Molybdenum-99 and Technetium-99m*, 1st ed., IAEA, Vienna (2013) 1.

2. F. Bernard, K.R. Buckley, T.J. Ruth *et al.*, *J. Nucl. Med.* **55** (2015) 1.
3. E.G.F. Núñez, E.A. de Oliveira, N.G. da Silva *et al.*, *Nucl. Med. Biol.* **39** (2012) 145.
4. T.H. Bokhari, S. Hina, M. Ahmad *et al.*, *J. Chem. Soc. Pak.* **35** (2013) 147.
5. N. Helal, *Int. J. Recent Res. Appl. Stud.* **11** (2012) 153.
6. M.R.A. Pillai, A. Dash and F.F.R. Knapp, *J. Nucl. Med.* **54** (2013) 313.
7. Kadarisman and H. Adang, *Urania* **17** (2011) 26. (In Indonesian).
8. V. Le, *Sci. Technol. Nucl. Install.* **2014** (2014) 1.
9. Sriyono, H. Lubis, Herlina *et al.*, *Concentration of ^{99m}Tc Solution from Eluate Based Polyzirconium Compound (n,γ) $^{99}\text{Mo}/^{99m}\text{Tc}$ Generator by Extraction*, Proceedings of the Conference on Research and Management of Nuclear Devices (2011) 156. (In Indonesian).
10. R. Chakravarty, A. Dash and M. Venkatesh, *Nucl. Med. Biol.* **37** (2010) 21.
11. R. Chakravarty, S.K. Sarkar, M. Venkatesh *et al.*, *Appl. Radiat. Isot.* **70** (2012) 375.
12. M.Z.H. Rozaini and P. Brimblecombe *J. Chem. Thermodyn.* **41** (2009) 980.
13. S. Khorsand, K. Raeissi and M.A. Golozar, *J. Electrochem. Soc.* **158** (2011) D377.
14. K. Ignatova and D. Stoykova, *Bulg. Chem. Commun.* **43** (2011) 48.
15. R. Amin M, A. Haque, A. Biswas *et al.*, *J. Chem. Eng. IEB* **27** (2012) 31.
16. H. Sadeghpour, M. Alavi, M. Shahedi *et al.*, *Trends Radiopharm. Sci.* **1** (2015) 15.
17. M.C. Borré, F.C. Tesán, N.M. Leonardi *et al.*, *Appl. Radiat. Isot.* **82** (2013) 322.
18. Z. Zhang, W. Chen, E. Ni *et al.*, *Electrochim. Acta* **81** (2012) 224.
19. M. Hayyan and S. Sameh, *Int. J. Electrochem. Sci* **7** (2012) 6941.
20. D. Topayung, *Scientific Journal of Science* **11** (2011) 97. (In Indonesian).
21. A.M. Peiro, E. Brillas, J. Peral, *et al.*, *J. Mater. Chem.* **12** (2002) 2769.