Optimization of the extraction process in the synthesis of high specific activity Molybdenum-99 by Szilard Chalmers reaction

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Abstract. Molybdenum-99 ($^{99}$Mo) is a parent radioisotope of technetium-99m ($^{99m}$Tc) which is widely used as diagnostic radiopharmaceutical because of its short half-life and ideal gamma-ray energy of 140 keV. Separation of $^{99m}$Tc and $^{99}$Mo is mainly carried out using a radioisotope generator of $^{99}$Mo / $^{99m}$Tc. Alumina column inside the generator has a low absorbency capacity of Mo (20 mg Mo / g alumina). Low alumina capacity requires $^{99}$Mo with high specific activity in order to minimize the amount of alumina so that the generator size could be kept as small and simple. High specific activity $^{99}$Mo alternatively can be obtained by Szilard Chalmers's reaction in irradiated molybdenum phthalocyanine (MoPc) target material. The purpose of this study was to optimize the extraction condition of $^{99}$Mo from irradiated MoPc. The study was conducted with stages consisting of the determination of the number of solvents, the effect of extraction time, and Physico-chemical characterization of $^{99m}$Mo solution. 5-gram MoPc was irradiated in TRIGA Reactor Bandung for 3 days with 5.10$^{12}$ n.s$^{-1}$.cm$^{-2}$ neutron flux. Extraction optimization was carried out using THF, DMSO and NaOH 3M solvents with a ratio of solvent : MoPc (v(ml):w(mg)) were 1: 5, 1:10, 1:25, 1:50, and 1:75. Extraction time was varied for 1, 2, 3, 4, and 5 hours. 3M NaOH with a volume ratio of 1: 5 with an extraction time of 1 hour was considered as an optimum condition to extract $^{99}$Mo from MoPc. This condition produced an extraction yield of 54.21% and an enrichment factor of 322.53 times with 95% radiochemical purity as ($^{99m}$MoO4)$^2$.

1. Introduction

Currently, $^{99}$Mo along with its daughter $^{99m}$Tc is considered as the most important radioisotopes in nuclear medicine because of its extremely high demand. The weekly demand for $^{99}$Mo is estimated to be 14,000 of 6 days curies by the Nuclear Energy Agency [1]. Most $^{99}$Mo used around the world is produced from the separation of uranium fission products. In order to create more secure and lowering fission product waste, some researchers have reinvestigated the neutron activation route $^{99}$Mo production.

The high specific activity of $^{99}$Mo is important in the fabrication of $^{99m}$Mo/$^{99m}$Tc radioisotope generator. With the fact that neutron activation route $^{99}$Mo production gives the low specific activity of $^{99}$Mo, researchers have to think of a way to immobilize high radioactivity of $^{99}$Mo in the limited size of separating columns inside the generator. Some researchers attempted to increase the absorption molybdenum capacity of separating column by using alternative sorbent rather than alumina [2][3]. Others considered enhancing $^{99}$Mo specific activity by recoil or Szilard Chalmers reaction.

Enhancing specific activity by Szilard Chalmers's reaction involves recoil energy from prompt gamma emission after capturing of neutron when bombardment occurred in the reactor [4]. This recoil energy breaks any chemical bond between $^{99}$Mo produced and its initial form of molybdenum
irradiation target whilst radioactive molybdenum still in its initial form because no recoil energy occurred. The most important step of the enhancement process of $^{99}$Mo specific activity by Szilard Chalmers's reaction is the extraction step of $^{99}$Mo from the target material.

Some researchers have investigated Szilard Chalmers's effect in some compounds including molybdenum hexacarbonyl and also from nanoparticle of molybdenum trioxide [4][5]. Molybdenum phthalocyanine considered as likely compounds in which recoil reactions could take place [6]. A preliminary study of Szilard Chalmers's reaction in molybdenum phthalocyanine has been carried out. The next stage of producing a high specific activity of $^{99}$Mo describe in this research that is the optimization of $^{99}$Mo extraction from irradiated molybdenum phthalocyanine. The optimization process consists of the determination of optimum solvent including its amount and time of extraction. The high specific activity of $^{99}$Mo is expected to be produced by optimizing the extraction step of $^{99}$Mo from irradiated molybdenum phthalocyanine.

2. Material and Methods

2.1. Synthesis of Molybdenum Phthalocyanine and Target Irradiation
Molybdenum Phthalocyanine (Mo-Pc) as target material for irradiation was synthesized by the reaction of ammonium heptamolybdate ((NH$_4$)$_6$M$_{7}$O$_{24}$·4H$_2$O) and phthalonitrile (C$_6$H$_4$(CN)$_2$) in closed reflux system with heating at 300°C for 3 hours. Mo-Pc solids were purified by washing with water, ethanol and potassium hydroxide [7]. 5 gr of Mo-Pc was weighed and irradiated in TRIGA 2000 Research Reactor Bandung for 72 hours at 5.10$^{12}$ n.cm$^{-2}$.s$^{-1}$ neutron flux.

2.2. Solvent optimization for extraction
The solvents used for extraction of $^{99}$Mo from Mo-Pc were tetrahydrofuran (THF), Dimethyl Sulfoxide (DMSO), and 3M Sodium Hydroxide (NaOH). THF and DMSO solvents are organic solvents while NaOH is inorganic solvents. The selection of these three solvents is based on the results of previous research studies conducted in 2017 [8]. Irradiated Mo-Pc was weighed into 1.5 mL PE tube so the volume of solvents would not exceed 1.5 mL. The ratio between Mo-Pc weight and solvent volume was 1: 5, 1:10, 1:25, 1:50, and 1:75. Radioactivity of $^{99}$Mo in each sample was measured using dose calibrator and NaI(Tl) radioactivity counter in the $^{99}$Mo energy window.

Samples and solvent in PE tubes were shaken by a vortex mixer for an hour and followed by centrifugation for 5 minutes at 5000 rpm speed. Solvent and solids were separated and radioactivity of each part was measured. Total molybdenum content in each sample was measured by the spectrophotometric method [6].

2.3. Time optimization for extraction
One optimized solvent from 3 kinds of solvents in the solvent optimization section was selected for the time of extraction optimization. Irradiated Mo-Pc was weighed into 1.5 mL PE tube so the volume of solvents would not exceed 1.5 mL. The ratio between Mo-Pc weight and solvent volume was the optimum ratio found insolvent optimization section. Samples and solvent in PE tubes were shaken by a vortex mixer for the various time (1,2,3,4 and 5 hours) and followed by centrifugation for 5 minutes in 5000 rpm speed. Solvent and solids were separated and radioactivity of each part was measured. Total molybdenum content in each sample was measured by the spectrophotometric method [6].

2.4. Determination of Enrichment Factor
Enrichment factor is defined as the ratio of the irradiation target-specific activity after washing to the target-specific activity after washing [1], the term of washing means the separation process of expected radionuclide from target matrix after irradiation of target. Safavi-Tehrani et al measured the enrichment factor of lanthanide after Szilard Chalmers's reaction by re-irradiating the target material with the same condition of first irradiation to determine the leftover amount of non-activated stable isotope [9]. The simple method of determination of enrichment factor was used in this research.
2.5 XRD characterization of irradiated Molybdenum Phthalocyanine

XRD patterns of solids were recorded by PANalytical X’Pert Pro XRD with the setup of the equipment as shown in Table 1. Pre-irradiated and post-extraction of Mo-Pc samples were subjected to be analyzed by XRD. Before measured, post extraction of Mo-Pc samples was decayed until the dose rate at the sample surface below 1 µSv·h⁻¹.

Table 1. Setup parameters of XRD measurement

| XRD properties (X’Pert Pro) |   |
|-----------------------------|--|
| λ of the X-ray source       | 1.540598 Å (Cu Kα) |
| Scan range (2θ)             | 5° to 90° |
| Step angle                  | 0.01° |
| Time of step                | 1 second |
| Detector                    | PW3011 (sealed proportional gas) |

3. Result and Discussion

After the irradiation and cooling process, Mo-Pc was divided for weighing. All experiment process was carried out inside shielded gloves box with proper air circulation and negative pressure. The optimization process only used a small amount of Mo-Pc in a 1.5 mL PE tube with the consideration that the waste generated from the results of the process is not so much and to minimize the occurrence of contamination when weighing the target material that is radioactive.

3.1. Solvent optimization for extraction

This optimization section was carried out to find the optimum solvent for the extraction of ⁹⁹Mo from irradiated Mo-Pc. Optimum solvent was defined as a solvent that gave the highest percentage of extracted ⁹⁹Mo and lowest total molybdenum content. That optimum solvent would produce a high enrichment factor of ⁹⁹Mo from irradiation of natural molybdenum target.

![Figure 1. Solvent and solvent ratio optimization of ⁹⁹Mo extraction from irradiated Mo-Pc](image)

Figure 1 depicts the result of solvent optimization. 3M NaOH extracted ⁹⁹Mo more than DMSO and THF. Molybdenum is known to dissolve easily in NaOH rather than an organic solvent [10]. Molybdenum phthalocyanine has low solubility in any kind of solvent [11]. This low solubility of molybdenum phthalocyanine prevented the optimum extraction process of ⁹⁹Mo from irradiated Mo-Pc. In this work, there was a trend that ⁹⁹Mo extraction percentage inversely proportional to the amount of solvent. The cause of this phenomenon still needs to be studied. In conclusion, 3M NaOH and 1:5 Mo-Pc : the solvent ratio was considered as an optimum solvent for ⁹⁹Mo extraction from
irradiated Mo-Pc.

**Figure 2.** The enrichment factor of $^{99}$Mo extracted from Mo-Pc by 3M NaOH

Figure 2 shows the enrichment factor calculation result of $^{99}$Mo solution extracted from irradiated Mo-Pc by 3M NaOH. High enrichment factor means the final $^{99}$Mo solution contains less total molybdenum content compared to initial condition before the irradiation and extraction process have taken place. The specific radioactivity of $^{99}$Mo was multiplied by the enrichment factor after Szilard Chalmers's reaction and extraction process.

3.2. **Time optimization for extraction**

The ratio of the amount of solvent that gave optimum results for the extraction of $^{99}$Mo from Mo-Pc was NaOH at a ratio of 1: 5. The ratio of the amount of NaOH 1: 5 is then used to optimize the extraction time, which is 1, 2, 3, 4 and 5 hours.

The time of shaking in the extraction process has an important effect on the percentage of extraction. The longer time of extraction does not always result in a higher percentage of extraction. Figure 3 shows that an hour of shaking time results in the highest percentage of extraction.

**Figure 3.** Effect of shaking time in percentage of $^{99}$Mo extraction, extracted by 3M NaOH

Most $^{99}$Mo was extracted in the early time of extraction (first hour) with the 54.21% percentage of extraction. Shaking time addition did not yield a higher extraction percentage significantly compared to one hour of shaking time. A similar phenomenon was discovered in $^{99}$Mo extraction by ionic liquids from seaborgium [12]. Unfortunately, this research did not study the shaking process in under an hour.
Further examination should be carried out for the extraction process under an hour.

![Figure 4](image-url)

**Figure 4.** The enrichment factor of $^{99}$Mo extracted from Mo-Pc by 3M NaOH in the various shaking time.

Figure 4 depicts the enrichment factor after the extraction process by 3M NaOH in various shaking time. Data for sample 1 was an outlier compared to other data. The average enrichment factor of $^{99}$Mo was calculated as 322.53. The result shows that shaking time did not affect the percentage of $^{99}$Mo extracted significantly thus an hour of shaking was concluded as optimum shaking time by consideration of time efficiency.

4. **Conclusion**

3M NaOH and Mo-Pc : NaOH ratio of 1:5 were considered as an optimum solvent in the extraction of $^{99}$Mo from irradiated Mo-Pc. $^{99}$Mo solution extracted has a higher specific activity compared to its initial condition. The high specific activity of $^{99}$Mo is important in the fabrication of $^{99}$Mo/$^{99m}$Tc radioisotope generator. By this work, the fabrication of $^{99}$Mo/$^{99m}$Tc radioisotope generator by non fission product of $^{99}$Mo could be materialized soon.

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