

## INFLUENCE OF DRYING TIME AND TEMPERATURE ON ZIRCONIUM-BASED MATERIAL (ZBM) PROPERTIES FOR $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ GENERATOR DEVELOPMENT

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### ABSTRACT

**INFLUENCE OF DRYING TIME AND TEMPERATURE ON ZIRCONIUM-BASED MATERIAL (ZBM) PROPERTIES FOR  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  GENERATOR DEVELOPMENT.** Zirconium-based material (ZBM) has an important role in producing Technetium-99m ( $^{99\text{m}}\text{Tc}$ ) due to its high adsorption capacity to Molybdenum-99 ( $^{99}\text{Mo}$ ). The adsorption capacity of the ZBM depends on the specific surface area which is influenced by several parameters in the synthesis process. This study aims to investigate the influence of drying time and temperature on the structure and specific surface area of the ZBM. Synthesis of the ZBM was carried out using zirconium chloride, 2-propanol, water and tetrahydrofuran at 75 °C, 90 °C and 120 °C and for 3 hr, 5 hr and 7 hr, respectively. Functional group and specific surface area of the ZBM was analyzed by FTIR and BET method, respectively. At the variation of drying time, the functional group pattern showed by FTIR spectra was not significantly different. The O-H group of the ZBM increased as the drying temperature decreases. At 75 and 90°C, the specific surface area increased as the function of time was increased but was decreased at 120°C. The highest surface area of the synthesized ZBM had a poor performance as a  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator material, whereas the eluate met the required standard.

Keywords : ZBM, Sol-gel, Time, Temperature, Drying

### ABSTRAK

**PENGARUH SUHU DAN WAKTU PENGERINGAN TERHADAP KARAKTERISTIK MATERIAL BERBASIS ZIRKONIUM (MBZ) UNTUK PENGEMBANGAN GENERATOR  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ .** Zirconium-Based Material (ZBM) mempunyai peran penting dalam produksi teknesium-99m ( $^{99\text{m}}\text{Tc}$ ) karena kapasitas serapnya yang tinggi terhadap Molybdenum-99 ( $^{99}\text{Mo}$ ), yaitu radionuklida induk dari  $^{99\text{m}}\text{Tc}$ . Kapasitas serap ZBM bergantung pada luas permukaan spesifik yang dipengaruhi oleh berbagai parameter dalam proses sintesisnya. Tujuan penelitian ini adalah mengetahui pengaruh suhu dan waktu pengeringan terhadap struktur dan luas permukaan spesifik ZBM. ZBM disintesis dengan proses sol-gel menggunakan zirconium klorida, 2-propanol, air, dan tetrahidrofurana masing-masing pada 75 °C, 90 °C dan 120°C selama 3 jam, 5 jam dan 7 jam. Gugus fungsi dan luas permukaan spesifik ZBM dianalisis masing-masing menggunakan FTIR dan BET. Pada berbagai variasi waktu pengeringan, pola gugus fungsi ZBM yang ditampilkan oleh pola spektra FTIR tidak berbeda secara signifikan. Gugus O-H meningkat seiring dengan penurunan suhu. Pada 75 dan 90°C, luas permukaan spesifik meningkat seiring dengan lamanya waktu pengeringan, sedangkan pada 120°C, luas permukaan spesifik makin kecil seiring dengan lamanya waktu pengeringan. Hasil sintesis ZBM dengan luas permukaan spesifik paling tinggi memiliki kinerja yang rendah sebagai material generator  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ , sedangkan eluat yang dihasilkan memenuhi standard yang dipersyaratkan.

Kata kunci : ZBM, Sol-gel, Waktu, Suhu, Pengeringan

### INTRODUCTION

Development of new material for Molybdenum-99 ( $^{99}\text{Mo}$ )/ Technetium-99m ( $^{99\text{m}}\text{Tc}$ ) generator is very important due to the shortage

of fission  $^{99}\text{Mo}$  in the future, which encourages the world to use non-fission  $^{99}\text{Mo}$  (Mahesh and Madsen 2017). The shortage is caused by

several issues including the safety issue regarding the uranium usage, the high activity of radioactive waste and the aging of the main research reactors supplying fission  $^{99}\text{Mo}$  in the world (Cutler and Schwarz 2014; Dash, Knapp, and Pillai 2013; M. R. A. Pillai, Dash, and Knapp 2013). Non-fission  $^{99}\text{Mo}$  is obtained from natural Molybdenum ( $\text{MoO}_3$ ) irradiated by either cyclotron or research reactor (M. R. a Pillai, Dash, and Knapp 2015; Selivanova et al. 2016; Amin et al. 2014). The advantages of non-fission  $^{99}\text{Mo}$  compared to fission  $^{99}\text{Mo}$  are the easy handling of the waste, the low radioactivity waste, and the simple post-irradiation method. On the other hand, the drawback is the low specific activity compared to fission  $^{99}\text{Mo}$  (Blaauw et al. 2017; Marlina et al. 2017).

Currently, the  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator based on fission  $^{99}\text{Mo}$  contains alumina as an adsorbent material which has an adsorption capacity of  $\pm 20$  mg molybdenum/g alumina. The  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator based on non-fission  $^{99}\text{Mo}$  which has a lower specific activity needs an adsorbent material which has a higher adsorption capacity than alumina. The Zirconium-Based Material (ZBM) which has a higher adsorption capacity to molybdenum is an alternative solution for development of  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator based on non-fission  $^{99}\text{Mo}$  (I Saptiama et al. 2016; Munir et al. 2017; Indra Saptiama et al. 2014). The ZBM is an inorganic polymer of zirconium which contains chlorine on its surface and synthesized from zirconium chloride ( $\text{ZrCl}_4$ ) as the main starting material. The ZBM has enough hardness and radiation resistance during  $^{99}\text{Mo}$  adsorption and Technetium-99m ( $^{99\text{m}}\text{Tc}$ ) elution (Indra Saptiama et al. 2014). So et al. (2007) developed poly zirconium compound (PZC), which has a similar function, properties and synthesis route with the ZBM. This material has an adsorption capacity to molybdenum up to 240 mg/g PZC and  $^{99\text{m}}\text{Tc}$  yield up to 98.8%. A tandem column of PZC and alumina was applied in generator system to reduce the  $^{99}\text{Mo}$  breakthrough.

The ZBM has been developed by sol-gel process using tetraethyl ortho silicate (TEOS) coating to increase its hardness as well as using sodium hypochlorite to increase the  $^{99\text{m}}\text{Tc}$  yield (Awaludin et al. 2015; Marlina et al. 2016). The resulting  $^{99\text{m}}\text{Tc}$  had been tested for methylene diphosphonate (MDP) radiopharmaceuticals kit (I Saptiama et al. 2016). Further development of the ZBM was carried out to increase the adsorption capacity to molybdenum and  $^{99\text{m}}\text{Tc}$  yield. Zhao et al. reported, generally, a specific surface area has an important role to increase the adsorption capacity of an adsorbent material due to the availability of surface sites (Zhao et al. 2016). The surface area of a material produced by the sol-gel process is influenced by the characteristic of the reagents and solvent, the

molar ratio of the reactants, the use of a modifying agent, pH, and the drying condition (Danks, Hall, and Schnepf 2016). The reagents composition in the ZBM synthesis has been well established, though the influence of temperature and drying time is not clearly understood yet. These parameters might play an important role as well. The study aims to determine the influence of drying time and temperature on the properties of the ZBM for  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator development. The material which has the highest surface area was chosen and evaluated its adsorption capacity,  $^{99\text{m}}\text{Tc}$  yield, and the other generator parameters.

## MATERIAL AND METHOD

### Material

All chemicals were used as received without any further purification. Zirconium chloride ( $\text{ZrCl}_4$ ), 2-propanol, tetrahydrofuran (THF), NaOH, and HCl were purchased from Merck. Purified water was obtained from IPHA Laboratory.

### Method

The ZBM synthesis procedure was conducted by the modification procedure similar to PZC as described previously (I Saptiama et al. 2016; Awaludin et al. 2015). A zirconium (IV) chloride ( $\text{ZrCl}_4$ ) was added to the mixture of THF and 2-propanol followed by another addition of water and THF. The solution was then stirred at room temperature for 24 hr, and heated. The temperature was varied at 75 °C, 90 °C, and 120 °C, whereas the time was varied at 3 hr, 5 hr and 7 hr. The functional groups of the resulted ZBM were analyzed using Fourier Transform Infrared (FTIR) using Alpha FTIR Spectrometer Bruker at 4000-400  $\text{cm}^{-1}$ . Its specific surface area was tested by BET method using Quadrasorb SI - QuantachromeQuadrawin.

A  $^{99}\text{Mo}$  adsorption capacity and  $^{99\text{m}}\text{Tc}$  elution test of the selected ZBM variation were conducted by the procedure described by Saptiama et al (2016).

## RESULT AND DISCUSSION

The PZC spectra were used as a reference for the FTIR analysis of the ZBM due to their structural similarity. The overlapping spectra between the PZC and the synthesized ZBM are shown in Figure 1. These show that the structure of the ZBM, represented by the treatment of 75°C, 3 hr, has similar spectra with the PZC. The PZC and the ZBM have an identical function as a material for  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator system as well as the starting material. Awaludin et al. (2015) developed the ZBM synthesis process from PZC with several modifications.

Spectra of the ZBM and the PZC have 3 main peaks at  $\sim 3300$ ,  $\sim 1600$ , and  $\sim 600$   $\text{cm}^{-1}$ . The peak at  $\sim 3300$   $\text{cm}^{-1}$  corresponds to vibrational O–H from  $\text{H}_3\text{O}^+$ , CH–OH and Zr–OH. The peak at  $\sim 1600$   $\text{cm}^{-1}$  corresponds to O–H from  $\text{H}_2\text{O}$ , whereas the peak at  $\sim 600$   $\text{cm}^{-1}$  corresponds to Zr–O (So et al. 2007).

The presence of  $\text{H}_3\text{O}^+$  and Zr–OH in the ZBM was caused by the hydrolysis of Zr–Cl (Le 2014; So et al. 2007). Zr–Cl bond was not observed in FTIR spectra, however, its presence was observed by So et al. (2017) using thermal analysis and Awaludin et al. (2015) using X-ray. The presence of  $\text{H}_2\text{O}$  was from both moisture content and water crystal. The water crystal was from the reagent during the synthesis process, which was trapped in the ZBM, whereas the presence of moisture content was caused by the hygroscopicity of the ZBM (So et al. 2007).

Figure 2 illustrates the infrared spectra of the ZBM at  $3600 - 2000$   $\text{cm}^{-1}$  and  $2000 - 1000$   $\text{cm}^{-1}$ . The figure shows that the spectra of

various drying temperature the ZBM are similar in its pattern. The similarity of the spectra indicates that the structural bonds in variations of the ZBM are similar, without significant differences as a function of temperature. On the other hand, the spectra as a variety of drying time were similar in its pattern and overlapping each other. The ZBM spectra were not influenced by the drying time.

Figure 2 shows that the lower the temperature, the higher the peak intensity. At the lowest temperature, the drying process was not completed and retained the amount of water in the ZBM. On the other hand, at the highest temperature, the retained water concentration was the lowest, because the evaporation was more effective.

The specific surface areas of the ZBM at 3 levels of temperature and time are presented in Table 1, while the data distribution is presented in Figure 3.

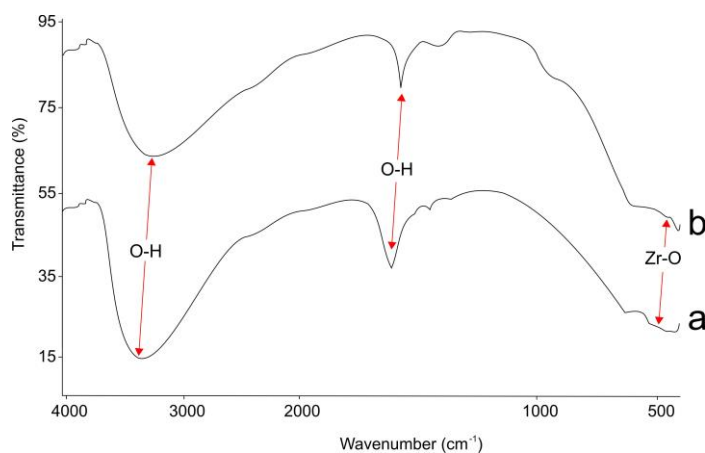


Figure 1. Infrared spectra of the PZC (a) (So et al. 2007) and (b) spectra of the ZBM (75°C, 3 hr)

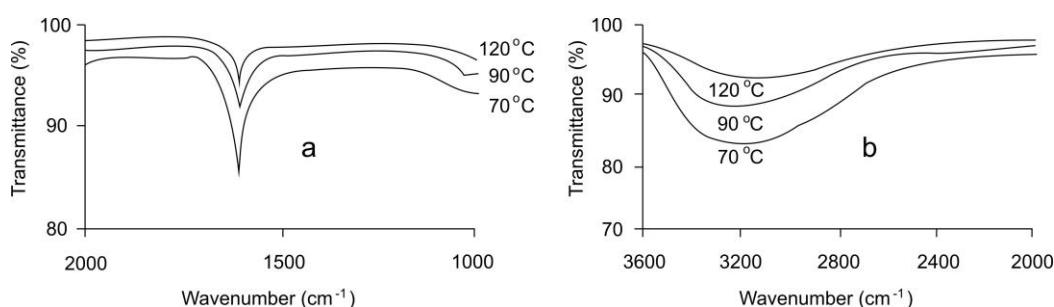


Figure 2. The infrared spectra of the ZBM at  $3600 - 2000$   $\text{cm}^{-1}$  (a) and  $2000 - 1000$   $\text{cm}^{-1}$  (b)

Table 1. Specific surface area of the ZBM synthesized at various temperature and time

Temperature (°C)	Surface area ( $\text{m}^2/\text{g}$ )		
	3 hr	5 hr	7 hr
75	25.1	40.8	56.6
90	56.3	48.0	86.8
120	76.0	42.1	22.4



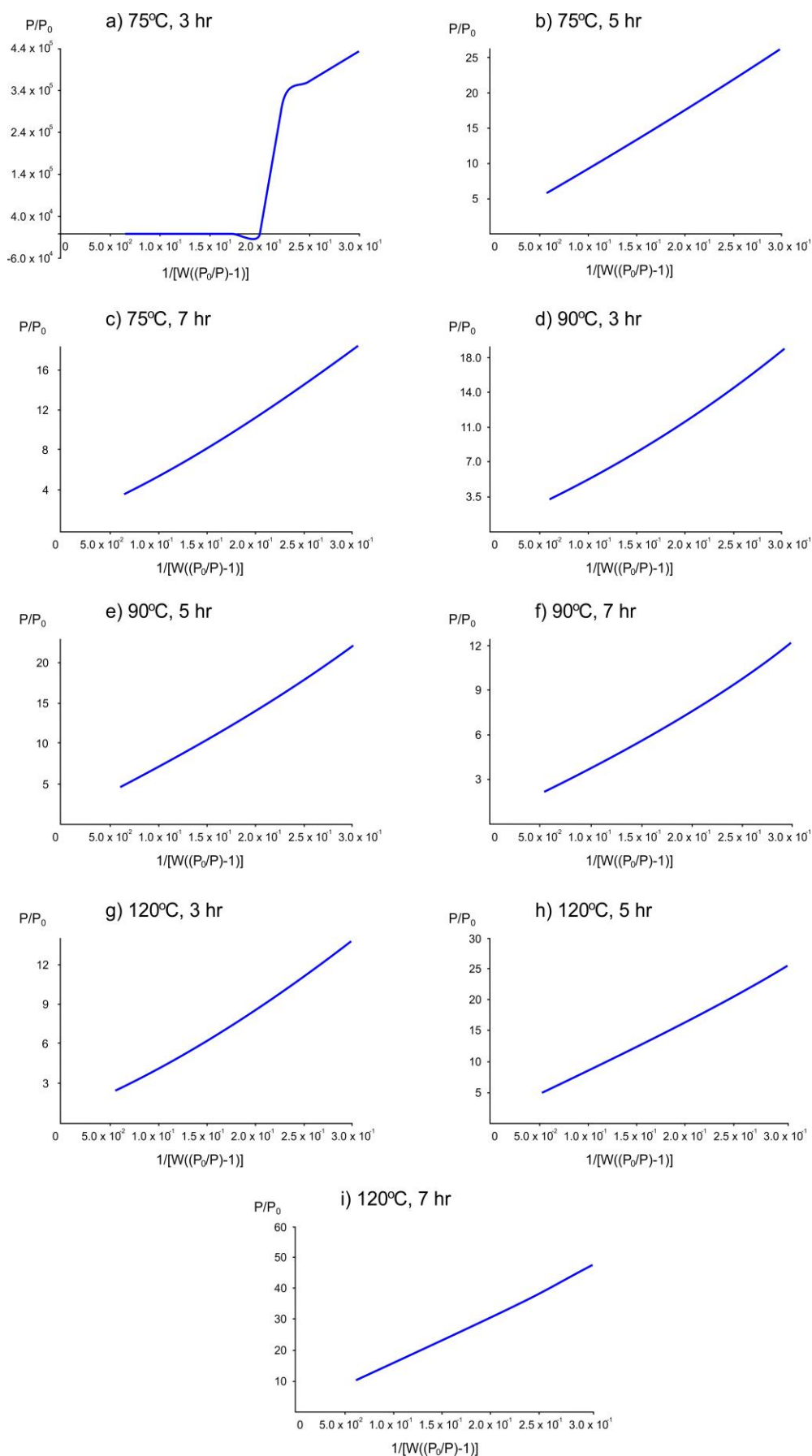


Figure 3. The data distribution the specific surface areas of the ZBM

The specific surface area at the temperature of 75 °C and 90 °C increased as the drying time increases. This was caused by the aging process of gel in the sol-gel process. Iswar et al. 2017 reported the identical phenomenon on the silica sol-gel process. The aging process strengthens the gel network which can withstand the material shrinkage during the drying process. The phenomenon explained by Iswar et al (2017) might also happen in the sol-gel process of the ZBM. The aging process was conducted at room temperature, but it was continued at 75 °C and 90 °C due to the presence of excess water in the mixture. The similar phenomenon at 75 °C and 90°C was occurred because both temperatures were below the boiling point of water. Hence, the presence of water was retained.

On the other hand, at the temperature of 120°C, specific surface area decreased as the function of drying time. The aging process at this temperature was not occurred because of the absence of excess water in the mixture. This temperature was higher than a boiling point of the water so the solvent was completely evaporated. Without the aging process, the gel network was not adequate to withstand the shrinkage. The drying step in the sol-gel process at ambient pressure drying (APD) usually causes the shrinkage of the synthesized material. The shrinkage in silica sol-gel process can be used to explain the phenomenon in the ZBM. The factor which encourages the shrinkage during the APD process was the polar OH groups on the material surface. The OH group causes the capillary and tension effect which pull the surface material during the APD step. The shrinkage was also caused by the generating of a new crosslink among near surfaces (Seraji, Seifi, and Bahramian 2015; Seraji et al. 2017).

The proposed illustration of the drying process is shown in figure 4.

Figure 4 illustrates the material structure growth from the initial process to final drying. At 75 °C and 90 °C, the aging process was occurred in presence of water, therefore a strong material structure was formed, and a shrinkage possibility was reduced. These resulting surface areas that getting higher by time increasing at 75 °C and 90°C, as shown in table 1. On the other hand, as shown in figure 4, the aging process at 120 °C was not occurred due to the absence of water, therefore it increased the shrinkage. As the result, the surface areas was getting lower by time increasing as shown in table 1.

The prediction of the polymerization mechanism of the ZBM can be constructed by general sol-gel reaction scheme presented by C. Jeffrey and George W (1990). As shown in figure 5, the reactions produce water, however, the presence of a solvent, such as water, is prerequisite for the reaction. The aging process requires a solvent to bring the monomer to the existing polymer and strengthen the network as shown in figure 6. Without a solvent, the strengthening process was not occurred.

The undesirable shrinkage in the drying process can be avoided by supercritical drying. However, either a high temperature-pressure drying or freeze-drying process is difficult to be applied in the ZBM synthesis due to its susceptibility to high temperature and the presence of acid vapour from the material. In the attempt to reduce the shrinkage of the ZBM, solvent modification, as reported by Omranpour and Motahari, might be applied (Omranpour and Motahari 2013).

An evaluation of the highest surface area the ZBM as an adsorbent for <sup>99</sup>Mo/<sup>99m</sup>Tc generator is presented in Table 2.

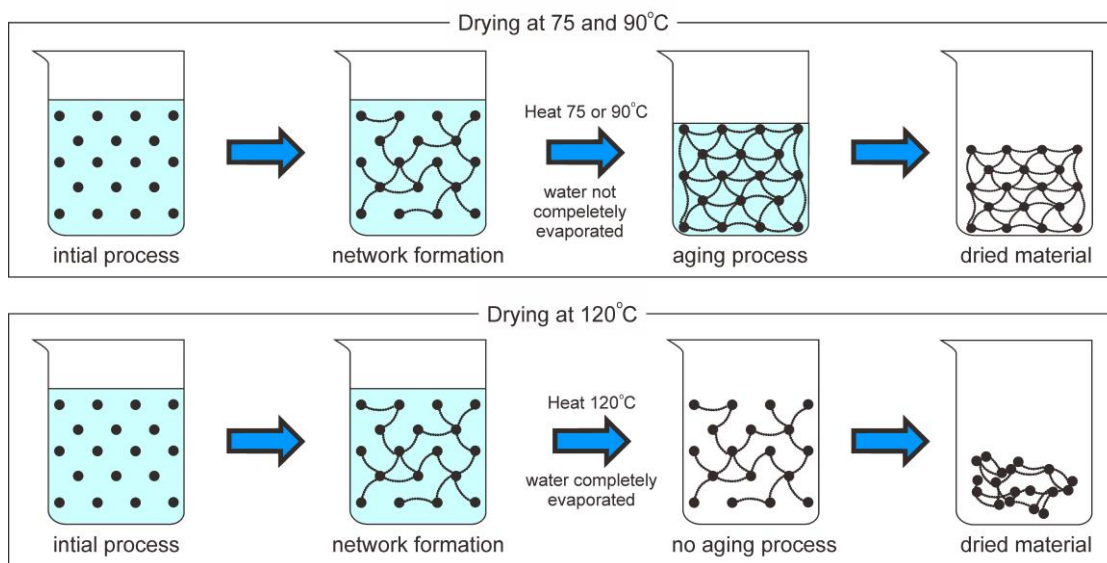
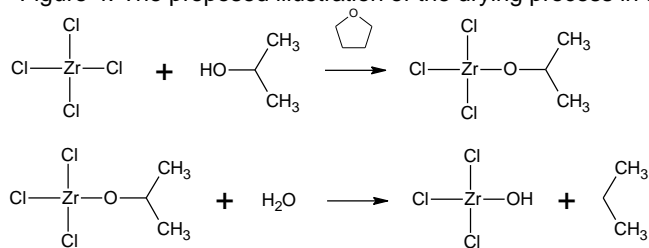
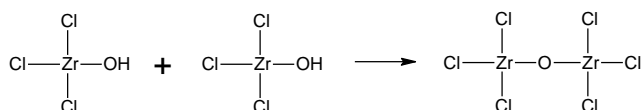


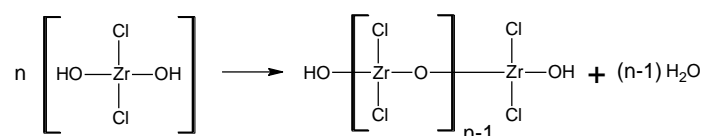
Figure 4. The proposed illustration of the drying process in the ZBM synthesis



Dimer :



Chain :



Ring :

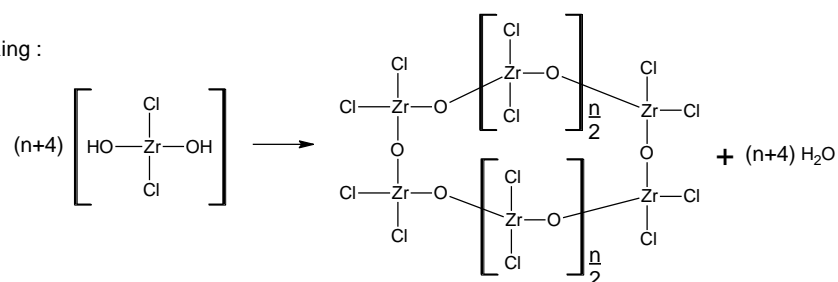


Figure 5. The prediction of the mechanism of the ZBM synthesis

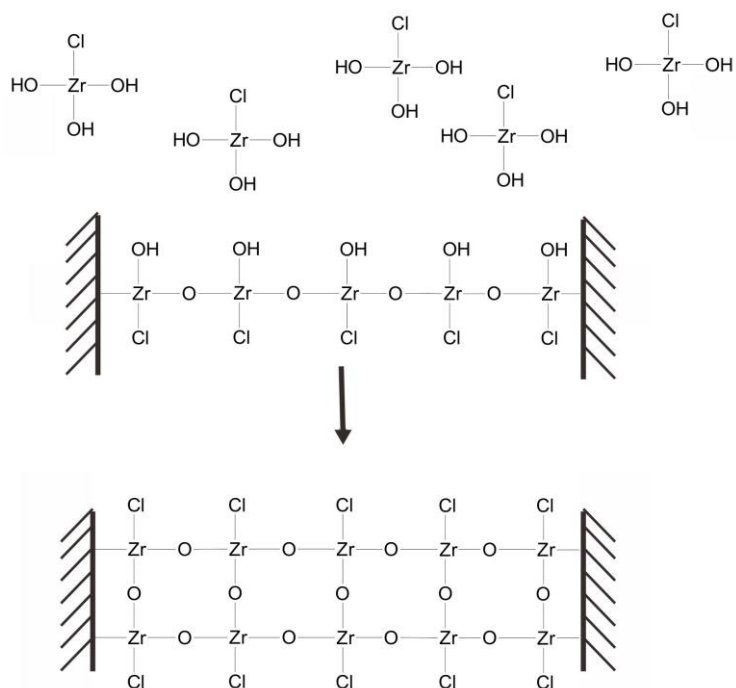


Figure 6. The prediction of the mechanism of the ZBM synthesis

The  $^{99}\text{Mo}$  adsorption test shows the adequate result for  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator material, though it is lower than the PZC which has the adsorption capacity more than 240 mg Mo/gram PZC. The ZBM synthesized by Saptiama which has a surface area of 13.2  $\text{m}^2/\text{g}$ , also generated similar  $^{99}\text{Mo}$  adsorption capacity. The similarity of  $^{99}\text{Mo}$  adsorption capacity between the ZBM which have different surface area indicates that the capacity does not only depend on surface area. The  $^{99}\text{Mo}$  adsorption mechanism on the ZBM was occurred through ion exchange between  $\text{MoO}_4^-$  and  $\text{Cl}^-$  ions on the material surface. The presence of  $\text{Cl}^-$  ions on the ZBM can be the key of  $^{99}\text{Mo}$  adsorption capacity.

The quality control results of the  $^{99\text{m}}\text{Tc}$  solution meet the required standard as shown in table 2. European Pharmacopeia (Ph. Eur.) 5.0 and United States Pharmacopeia 35/National Formulary 30 (USP 35/NF 30) have a similar requirement in  $^{99\text{m}}\text{Tc}$  solution. A slight difference of both pharmacopeias is found in the pH requirement (Zolle 2007; *United State Pharmacopeia/National Formulary* 2011).

The  $^{99\text{m}}\text{Tc}$  elution test from the ZBM column generated a low  $^{99\text{m}}\text{Tc}$  yield. The Ideal

$^{99\text{m}}\text{Tc}$  generator system generates  $^{99\text{m}}\text{Tc}$  yield of 80% – 90% (Saha 2018). The low amount of  $^{99\text{m}}\text{Tc}$  eluted from the ZBM column was caused by the solvated electron resulting from  $\beta$  emission of  $^{99}\text{Mo}$  which reduces  $\text{Tc(VII)O}_4^-$  to insoluble  $\text{Tc(IV)O}_2$ . The  $\text{Tc(IV)O}_2$  was retained in the ZBM. The addition of 3% NaOCl was proven to give the optimum results of  $^{99\text{m}}\text{Tc}$  yield by removing the solvated electron (I Saptiama et al. 2015a; Awaludin et al. 2015). However, the NaOCl residue in  $^{99\text{m}}\text{Tc}$  eluate inhibits a radiolabeling reaction of  $^{99\text{m}}\text{Tc}$  and radiopharmaceutical kit. NaOCl reduces the function of stannous chloride ( $\text{SnCl}_2$ ) in the kit. The  $^{99\text{m}}\text{Tc}$  elution profile is presented in figure 4.

The  $^{99\text{m}}\text{Tc}$  elution profile as shown in figure 7 was good for  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator system. The high yield in the first elution reduces the eluate volume.

The radiochemical purity and aluminium breakthrough are the quality parameter of  $^{99\text{m}}\text{Tc}$  eluate. Table 2 shows that these parameter quality meet the required standard of European Pharmacopeia.

Table 2. Evaluation of the highest surface area the ZBM as an adsorbent for  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator

Parameter	Result	Standard	
		Ph. Eur. 5.0	USP 35/NF 30
$^{99}\text{Mo}$ adsorbed in the ZBM (GBq)	2.77	NA	NA
$^{99}\text{Mo}$ adsorption capacity (mg Mo/g ZBM)	176.51	NA	NA
$^{99\text{m}}\text{Tc}$ yield (GBq)	0.17	NA	NA
$^{99\text{m}}\text{Tc}$ yield percentage (%)	6.62	NA	NA
Radiochemical Purity (%)	> 95	> 95	> 95
Aluminium breakthrough (ppm)	< 10	< 10	< 10
Clarity	Clear	Clear	Clear
pH	5	4-8	4,5-7,5

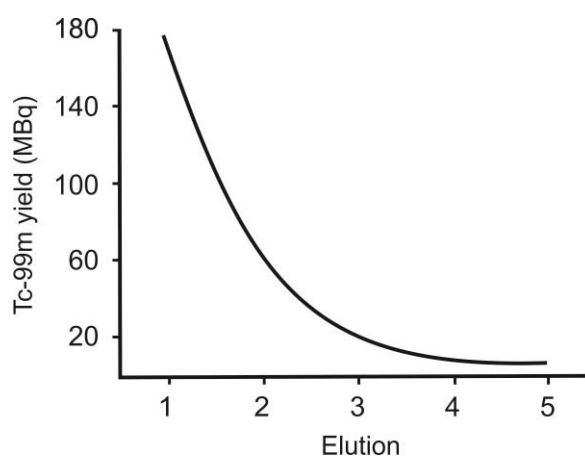


Figure 7.  $^{99\text{m}}\text{Tc}$  elution profile.



## CONCLUSION

The drying time and temperature have a significant influence on the specific surface area of the ZBM. The highest surface area the ZBM as the best-resulted material has a poor performance as a  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator material. Hence, there is a need to investigate another parameter, such as atmosphere, heat distribution and reagent composition, for a  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator development. The eluate of generator met the required quality based on USP/NF and Ph.Eur.

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