Determination of Optimum Pressure for Gd^{3+} Separation from Gd-DTPA with Nanofiltration Membrane

Rahayu Iman*, Winanti Anti, Juliandri, Noviyanti Atiek Rostika, Eddy Diana Rakhmawaty, Anggraeni Anni and Bahti Husein H.
Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Jln. Raya Bandung-Sumedang km. 21 Jatinangor, Sumedang, West Java 45363, INDONESIA
*iman.rahayu@unpad.ac.id

Abstract
Nowadays, many studies on separation of rare earth elements have been conducted due to its diverse utilization. One of its applications in medical area is the utilization of gadolinium in the form of Gd-DTPA complex for contrast agent in magnetic resonance imaging (MRI). In the preparation of Gd-DTPA, there is a possibility of residual Gd^{3+} which is toxic in nature and therefore requires separation process before it can be applied. The separation of Gd^{3+} from Gd-DTPA complex can be performed by nanofiltration-complexation method.

In the present study, Gd-DTPA complex was prepared by reacting Gd_2O_3 with DTPA ligand with reflux followed by separation of Gd^{3+} from Gd-DTPA with nanofiltration membrane with varying pressure (5.8, 6.0, 6.2 and 6.4 bars) at 40°C followed by determination of flux and rejection coefficient of the membrane. The results of the present study indicate that flux of the permeate increased with increasing pressure up to 339.94 $L.m^{-2}.\ hour^{-1}$ while rejection decreased down to 9.02% at 6.4 bars. The concentration of Gd^{3+} presence in the Gd-DTPA after the filtration process was 0.201 ppm.

Keywords: Gadolinium, complex, Gd-DTPA, nanofiltration membrane.

Introduction
Exploitation of rare earth elements (REE) is very broad and highly related to development of science and technology and support in the manufacture of high-tech innovative inventions. One of application of REE in medical area is the utilization of gadolinium (Gd) in the fabrication of contrast agent to detect abnormal tissue using magnetic resonance imaging (MRI)[1]. The most common ligand used in the fabrication of Gd complex is diethylenetriaminepentaacetic acid (DTPA) which will form Gd-DTPA complex. The complex is proven to be safe and only has light side effect, such as headache and nausea[2].

The wide use of Gd-DTPA complex in medical area makes it as one of important compounds for diagnostic purpose[2]. However, in the preparation of the complex, there is possibility that the reaction does not go into completion and therefore there will be free Gd or DTPA in the reaction product. Free Gd is very toxic and therefore many efforts have been conducted to separate it from the reaction[1].

Membrane technology has been used in the separation process because it is fast and efficient. Furthermore, driving force in the form pressure difference (ΔP), concentration difference (ΔC), potential difference (ΔE) and temperature difference (ΔT) lead to capability of the membrane to transfer components based on physical and chemical properties of membrane and the separated components[4]. Nanofiltration is a relatively new method which has molecular weight cut off at 200-1000 Da and therefore capable of separating small molecules[3].

Sorin et al[5] performed separation of Gd^{3+} from Gd-DTPA and found 95% rejection at 3 bars, 15°C and 0.4 mM concentration. In addition, NF membrane can also separate Gd^{3+} through complexation using selective ligand such as DTPA with controlled operating parameters including pressure, ligand concentration, pH and temperature which can generate rejection of Gd-DTPA above 90%.

In the present study, separation was performed at varying higher pressure compared to previously reported condition i.e. 5.8, 6.0, 6.2 and 6.4 bars at 40°C which is expected to reduce Gd^{3+} in the Gd-DTPA product.

Material and Methods
Material: MilliQ water, glacial acetic acid, sodium acetate, diethylenetriaminepentaacetic acid, gadolinium chloride hexahydrate, gadolinium oxide, sodium hydroxide and xylenol orange.

Synthesis of Gd-DTPA: As much as 1,8150 g of gadolinium oxide and 2.1625 g DTPA were added to a reaction vessel followed by addition of 180 mL MilliQ water and refluxed for 1 hour until the solution becomes clear. After cooling, pH was measured and if the solution is still acid, 3 N sodium hydroxide was added dropwise until pH of 7-7.5 was reached. The solution was then filtered.

Separation of Gd-DTPA Complex with Nanofiltration Membrane: Laboratory scale nanofiltration membrane was prepared. The membrane used in this study was Dow FilmTec TW30-1812-50 nanofiltration membrane made from polyamide material with a pore size of 0.1 nm and a surface area of 150 cm^2. The synthesized Gd-DTPA complex was diluted to 2000 mL using MilliQ water in a volumetric flask. MilliQ water was then passed through the membrane and nanofiltration process was performed for 60 minutes until it is stabilized. The Gd-DTPA solution was then passed through as feed solution and the separation process was performed with different pressure i.e. 5.8, 6.0, 6.2 and 6.4 at 40°C for 15 minutes with cross-flow system. Permeate and retentate were collected and flux of permeate was calculated for each pressure.

Determination of Permeate Flux and Rejection Coefficient of Gd^{3+}: Permeate flux was calculated by measuring volume of permeate that passed through membrane divided by area of membrane multiplied by time for each of the pressure variation as presented by equation (1):

$$J = \frac{V}{A \times t} \tag{1}$$

where J is flux of permeate, V is the volume of permeate, A is the area of membrane and t is time.

Rejection was calculated by measuring concentration of Gd^{3+} in feed and permeate with visible spectrophotometer and calculated using equation (2):

$$R = \left(1 - \frac{Cp}{Cf}\right) \times 100\% \tag{2}$$

where R is rejection coefficient, Cp is concentration of Gd^{3+} in permeate and Cf is concentration of Gd^{3+} in feed.

Results and Discussion

Separation process with nanofiltration method is based on difference in molecular size. Particle with smaller molecular size than the pores of the membrane will enter the pores while bigger molecules will be seized at the surface of the membrane. Feed solution with Gd-DTPA and Gd^{3+} will experience filtration mechanisms based on the difference in molecular weight.

Table 1 shows concentration of Gd^{3+} in feed, permeate and retentate solutions with varying pressure operation. Concentration of Gd in the retentate is lower than in the permeate. This result indicates that Gd^{3+} was seized on the membrane surface. The nanofiltration membrane used in the present study has molecular weight cut off of 200-1000 g/mole, however not all Gd^{3+} (157.25 g/mole) can pass through pores of the membrane due to polarization of concentration on the membrane surface which can cause blocking by Gd-DTPA (MW = 509.6 g/mole).

The Effect of Pressure on Permeate Flux and Rejection Coefficient of Gd^{3+}: Optimal performance condition of membrane is confirmed by permeate flux and rejection coefficient of feed. Higher flux and rejection values indicate better membrane performance. However, in reality, in a separation process using nanofiltration membrane, usually a phenomenon is found where flux is conversely related with rejection when flux increased, the rejection will decrease.

Figure 1 shows relationship between pressure with flux and rejection. The flux value at 5.8, 6.0, 6.2 and 6.4 bars were 61.22, 179.31, 187.32 and 339.94 $L.m^{-2}.h^{-1}$ respectively. Flux of permeate increased linearly with increasing pressure. This phenomenon is caused by driving force of pressure on the membrane where higher pressure applied the driving force will be higher and more molecules in the feed solution will pass through the pores of membrane and exit as permeate. Higher pressure is also affected by high diffusion speed of feed so that the interaction between feed solution and membrane surface becomes fast and leads for membrane to hold the feed solution and more Gd^{3+} can pass through membrane pores.

Rejection values at pressure of 5.8, 6.0, 6.3 and 6.4 bars were 28.35, 23.06, 15.77 and 9.02% respectively. In the present study, percentage of rejection shows the capability of membrane to retain Gd^{3+} that can pass through the membrane. Rejection of Gd^{3+} was found decreased with higher pressure. This phenomenon was caused by higher Gd^{3+} ion that passes through the pores of the membrane due to higher driving force on feed solution while Gd-DTPA complex which has higher molecular size, will be retained on the membrane. This, in consequence, will reduce the capability of the membrane to retain Gd^{3+} ion. According to equation (2), concentration of permeate affects rejection coefficient value. The coefficient of rejection is inversely related with concentration of permeate where higher permeate concentration will cause lower rejection coefficient. This is proved in the present study where lower rejection coefficient was obtained when higher pressure was applied.

Pressure at 6.4 bars was found as the best pressure for separation of Gd^{3+} from Gd-DTPA, because at this pressure the rejection was found to be the lowest (9.02%) compared to the other condition. When converted to ppm value, it is equal to 0.201 ppm. This value shows that 0.201 ppm of Gd^{3+} was still retained on the membrane surface and therefore the Gd-DTPA complex still contains 0.201 ppm of Gd^{3+}.

According to Rahayu et al[1], maximum concentration of Gd^{3+} that still can be tolerated for MRI application is 0.150 ppm. If the concentration is higher, it will be toxic for the body and can have bad effect on functions of organs. The present study shows that separation of Gd^{3+} from Gd-DTPA complex can be achieved with nanofiltration-complexation. However, the separation was not good enough because it still retains Gd^{3+} and therefore the Gd-DTPA complex still contains higher Gd^{3+} then the allowed concentration.

Table 1
Concentration of Gd^{3+} in feed, permeate and retentate solution with varying pressure conditions

Pressure (bar)	Concentration of Gd^{3+} (ppm)		
	Feed	Permeate	Retentate
5.8	0.5485	0.393	0.255
6.0		0.422	0.242
6.2		0.462	0.216
6.4		0.499	0.201

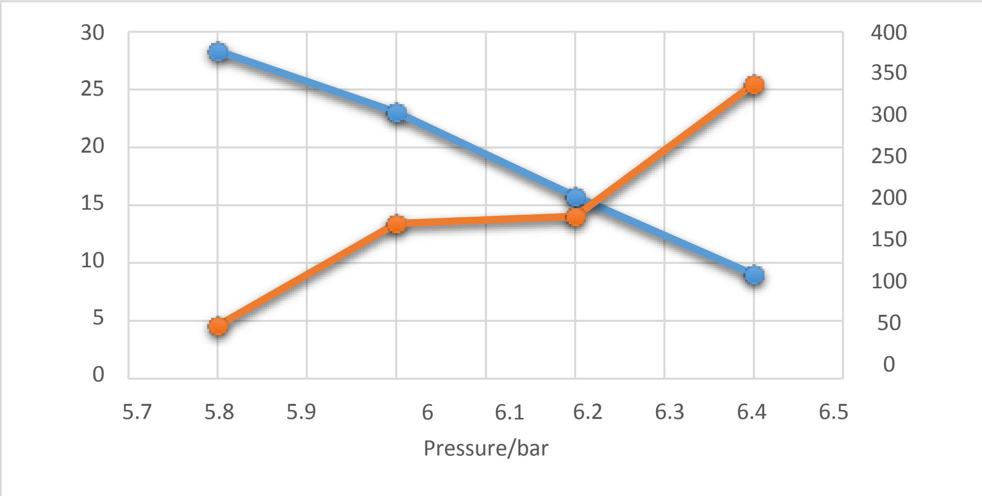

Figure 1: The effect of pressure on rejection coefficient and permeate flux

Conclusion

The present study shows that pressure has effect on Gd^{3+} separation from Gd-DTPA, higher pressure increases permeate flux and decreases Gd^{3+} rejection. The best condition for separation was achieved at 6.4 bars with rejection coefficient of 9.02%, or 0.201 ppm.

Acknowledgement

Authors gratefully acknowledge financial support from Universitas Padjadjaran through Academic Leadership Grant 2017.

References

1. Rahayu I., Anggraeni A., Soedjanaatmadja U.M.S. and Bahti H.H., The effect of pressure and temperature on separation of free gadolinium (III) from Gd-DTPA complex by nanofiltration-complexation method, IOP Conference Series: Material Science and Engineering, **196**, 012040 **(2017)**

2. Chitry F., Garcia R., Nicod L., Gass J.L. and Madic C., Separation of Gd^{3+} by nanofiltration-complexation in aqueous medium, *Journal of Radioanalytical and Nuclear Chemistry*, **240**, 931-934 **(2001)**

3. Murthy Z.V.P. and Choudhary A., Application of nanofiltration to treat rare earth element (neodymium) containing water, *Journal of Rare Earths*, **29(10)**, 974-978 **(2011)**

4. Mulder M., Basic Principles of Membrane Technology, 2nd ed., Kluwer Academic Publisher, London **(1996)**

5. Sorin A., Favre-Réguillon A., Pellet-Rostaing S., Sbaï M., Szymczyk A., Fievet P. and Lemaire M., Rejection of Gd (III) by nanofiltration assisted by complexation on charged organic membrane: Influences of pH, pressure, flux, ionic strength and temperature, *Journal of Membrane Science*, **267(1-2)**, 41-49 **(2005)**.