Separation of Lutetium from Ytterbium for carrier-free Lu-177 Large-Scale Production Processes

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1. Introduction

Lu-177 is interested in the field of nuclear medicine as a radionuclide for targeted radiotherapy. Lu-177 has a half-life of 6.65 days, making it suitable for use as a medicine, and it releases low-energy beta rays (E_{β},max = 0.5MeV) that can eliminate only tumors without affecting surrounding normal tissue. In addition, Lu-177 releases ramma rays (E_{γ}=208 keV (11.0%) and 113 keV (6.4%)), which can be used for diagnostics. [1, 4]

The production methods of Lu-177 can be accomplished in two ways: the 'direct' method is neutron irradiation of target Lu-176 to generate Lu-177 through reaction $^{176}Lu(n,\gamma)^{177}Lu$. The other method is 'indirect'. The 'indirect' method is neutron irradiation of target Yb-176 to generate Yb-177 throuth reaction $^{176}Yb(n,\gamma)^{177}Yb$, that decays to Lu-177.[2] The direct method is unsuitable because it produces Lu-177m as a byproduct. On the other hand, the indirect method produce only Lu-177 without a carrier. However, the Yb-176 target is mixed with Lu-177, which requires separation.

Lutetium and ytterbium are neighboring elements on the periodic table, and their chemical behaviors are so similar that it is difficult to separate them. Various separation method have been reported in the past, which are mostly based on electrochmical separation, solvent extraction, extration chromatography and ion exchange chromatography. [3-6] Of these methods, ion exchange chromatography has the simplest procedure, but the separation factor decreases with the higher amount of ytterbium.[7] In this experiment, the separation conditions were compared by increasing the amount of ytterbium. The separation efficiency can be increased by changing the eluent and column conditions. Finally, Lu was separated from 500mg of Yb and the results and conditions are discribed in this paper.

2. Methods and Results

In these experiments, the natural state of lutetium and ytterbium were used instead of radioisotopes. Lanthanide ions are colorless in aqueous solution, thus requiring analysis by ICP-OES or AAS to confirm the presence of Lu and Yb. Instead, chelators that form complexes with lanthanum metals to create color can be used for easily detecting these metals. 4-(2-pyridylazo)resonocinol(PAR) is yellow under conditions pH 9.8, which turns red when it form a complex with lanthanum metal.[8] The results were analyzed by measuring the absorbance of the PAR and lanthanied concentration with a UV detector.

2.1 Separation

The ion-exchange chromatography separates Lu/Yb using α-hydroxyisobutyric acid (α-HIBA) at pH4.2 (0.07M) as the eluent. The resin used in column was a BP-OA cation exchange resin composed of solfonyl group.

The separtion ability of primary amines used to adjuest the pH of α-HIBA was compared [Fig.1]. The α-HIBA with NH_4OH had a Rs value of 1.32 showing non-separation. The α-HIBA with methylamine had a Rs value of 2.09 and the α-HIBA with ethanolamine had a Rs value of 2.11, which were completely separated.

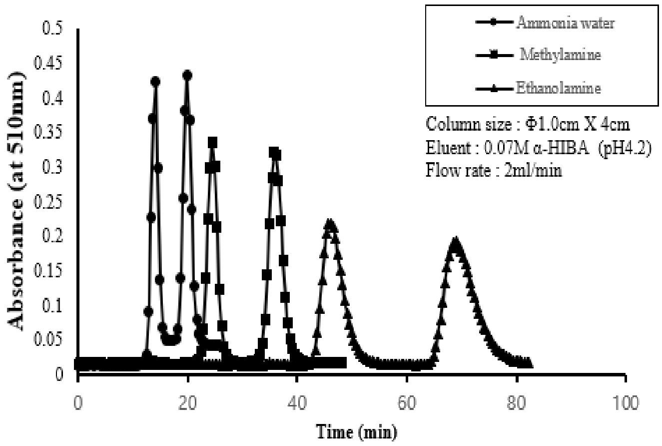

Fig.1. Separated 0.15 mg of Lu and 0.15 mg of Yb. The leading peak is Lu and the trailing peak is Yb.

The separation tendency of α-HIBA with methylamine and ethanolamine by changing column conditions is shown in Fig. 2, 3. At the Yb peak, α-HIBA of 0.15M was used for rapid elution of Yb. Under the same column conditions of methylamine and ethanolamine, ethanolamine can separate a larger amount of Yb. Therefore ethanolamine is more suitable for large-scale production of Lu-177.

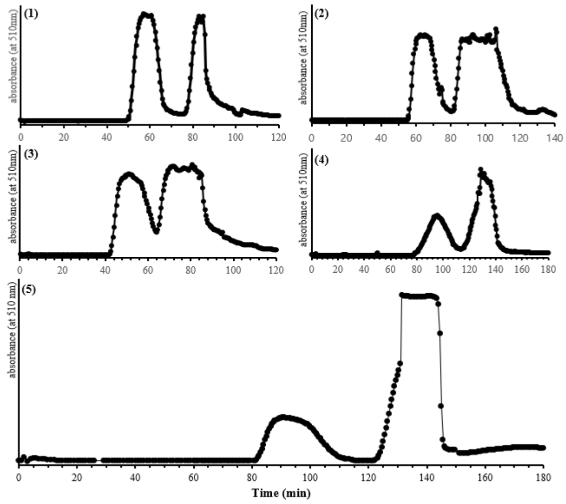

Fig. 2. Separated 0.5mg of Lu and chaning amounts of Yb with methlyamine. (1)3mg, (2)20mg, (3)30mg, (4)50mg. (5)200mg. The column size and flow rate for (1), (2) and (3) Φ1.0cm×5cm, 3ml/min, (4) Φ1.5cm×7cm, 3ml/min, (5) Φ2.5cm×5cm, 6ml/min.

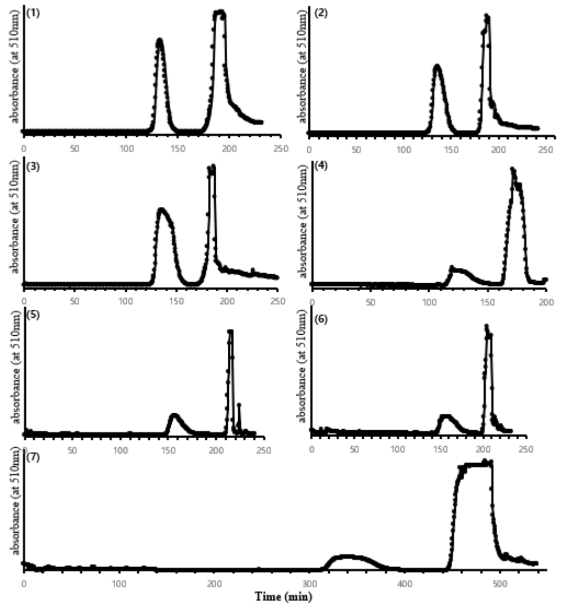

Fig. 3. Separated 0.5mg of Lu and chaning amounts of Yb with ethanolamine. (1) 50mg, (2) 100mg, (3) 150mg, (4),(5) 200mg, (6) 400mg, (7)500mg. The colium size and flow rate for (1), (2)and (3) Φ1.5cm×7cm , 3ml/min, (4) Φ2.5cm× 4cm, 4ml/min, (5) and (6) Φ2.5cm×5cm, 6ml/min, (7) Φ2.5cm×8cm, 4ml/min.

2.2 Purification

In order to utilize Lu-177, it is necessary to elimination the α-HIBA and amine used in the separation. The purification process used 50W-X8 resin. The Lu was completely absorbed on to the 50W-X8 resin at pH2 [9]. The absrobed resin with Lu can be washed with dilute hydrochloric acid to purify the impurities used in the sepatarion. The purified Lu was recovered using diffrents concentration of hydrochloric acid and the recovery the purification efficiency is shown in Fig.4. The highest recovery yield was 97% at 3M concentration when using 200-400mesh resin.

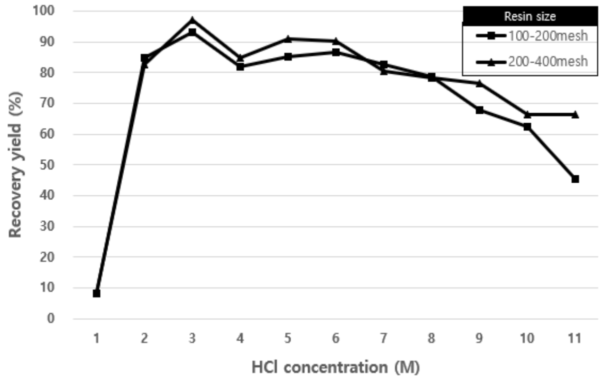

Fig. 4. Lu recovery yield by concentration in 10ml of hydrochloric acid.

3. Conclusions

This study provides conditions for efficient separation and purification using cation exchange chromatography in the production of Lu-177. α-HIBA with ethanolamine facilitated the separation, and 500 mg of Yb was successfully separated. 500 mg of Yb is enough to produce about 5 Ci of Lu-177. In addition, 50W-X8 and 3M HCl can be used to produce purified Lu-177 without loss.

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