

Evaluating the effect of ammonium ions on the separation efficiency of two adjacent lanthanides

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1. Introduction

Radiolanthanides such as lutetium-177 (^{177}Lu) and holmium-166 (^{166}Ho) have received considerable attention as important therapeutic radionuclides in nuclear medicine [1,2]. It has attractive features for radioimmunotherapy due to its theranostic potential, which enables simultaneous diagnosis and therapy, and the complex formation with appropriate chelating agents. For these applications, it is preferable to use carrier-free radiolanthanides, which have high specific radioactivity and high radionuclidic purity without the long-lived radionuclidic impurity.

^{177}Lu emits β^- particles ($E_{\beta,\text{max}} = 498$ keV) with a soft tissue penetration range of less than 3 mm and γ -rays ($E_{\gamma} = 208$ keV (11.0%) and 113 keV (6.4%)) suitable for imaging with a detector [1]. The carrier-free ^{177}Lu can be produced *via* neutron capture (n, γ) of ^{176}Yb target as an indirect production and subsequent β^- decay of produced ^{177}Yb ($t_{1/2} = 1.91$ h), as follows: $^{176}\text{Yb}(n,\gamma)^{177}\text{Yb} \rightarrow ^{177}\text{Lu}$.

^{166}Ho ($T_{1/2} = 26.6$ h) emits a proper γ -energy (80 keV) for diagnosis and therapeutic β -energy ($E_{\beta} = 665.7$ keV). ^{166}Dy as parent nuclide can be produced by double neutron capture reaction of stable ^{164}Dy . ^{166}Ho produced by (n,γ) β reaction, $^{164}\text{Dy}(n,\gamma)^{165}\text{Dy}(n,\gamma)^{166}\text{Dy} \rightarrow ^{166}\text{Ho} + \beta^-$, from ^{166}Dy [$T_{1/2}=81.5$ h, $E_{\beta,\text{max}}=486.8$ keV, $E_{\beta,\text{av}}=130$ keV] is a carrier free state [3].

A critical process for obtaining carrier-free nuclides is the radiochemical separation of the desired nuclide from macroscopic amount of the target material with adjacent atomic number. As the demand for radiolanthanides increases, many researchers have devoted themselves to developing faster and more efficient separation techniques. In particular, the separation technology based on ion exchange to improve selectivity have been developed. Two adjacent lanthanides are separated by a small difference in their binding stability constant with a complexing agent. In addition, it can be eluted by effectively displacing the lanthanide bound to the resin with any other cation [4]. Thus, ion-exchange technology generally uses α -HIBA (α -hydroxyisobutyric acid) as a complexing agent and NH_4^+ (ammonium hydroxide) as a separating cation. However, P. S. Balasubramanian [5] reported that ^{177}Lu was separated from neutron-irradiated ytterbium target using a cation exchange resin (Dowex-50X8, 200-400 mesh) with α -HIBA and Zn^{2+} ion as a separating ion. The reason that the use of Zn^{2+} ion has better separation efficiency than the use of NH_4^+ ion was due to the large

particle size of the resin (37-74 μm) used. There are few papers evaluating the separation efficiency using other cations to replace NH_4^+ ion.

This study aims to evaluate the separation efficiency of two adjacent lanthanides (Yb/Lu and Dy/Ho) according to the types of ammonium ion (Fig.1; primary, secondary and tertiary ammonium ions in addition to NH_4^+ ion,) through separation experiments using stable isotopes. Separation experiments were performed using α -HIBA as eluent adjusted to pH with ammonium hydroxide, methylamine, ethylamine, diethylamine, pyridine, ethanolamine and ethylenediamine, respectively. The separation of stable isotopes was detected on-line by a post-column reaction system using PAR (4-(2-pyridylazo) resorcinol). The on-line system makes it easier and faster to perform many experiments in a variety of conditions.

2. Experiments

2.1. LC instrument with an on-line post-column system

The LC instrument was composed of a high-pressure pump and a six-port Rheodyne valve equipped with sample loop of 500 μl or 2,000 μl . The LC column was prepared by packing the cation exchange resin BP-OA into Eco Plus glass column. The lanthanide sample was injected into the mobile phase α -HIBA. The eluted metal ions were mixed in a mixing-tee with PAR solution, as the post-column reagent, added using a peristaltic pump. Then, the mixed solution was monitored using a UV-vis spectrophotometer through the flow cell.

2.2. Separation of lanthanides using stable isotopes

The column was pre-saturated with an appropriate α -HIBA eluent prior to sample injection. A sample containing two adjacent lanthanides (1 mg/3 mg of Yb/Lu or Dy/Ho) was injected into the prepared column under isocratic condition. Herein, the pH 4.2 of α -HIBA (0.07 M – 0.1 M) is adjusted by each ammonium hydroxide, methylamine, ethylamine, diethylamine, pyridine, ethanolamine and ethylenediamine. At the same time, post column reagent was eluted to the mixing-tees by a peristaltic pump. Then, the absorbance of the mixed solution was measured at 510 nm using a UV-vis spectrophotometer at intervals of 30 s or 1 min.

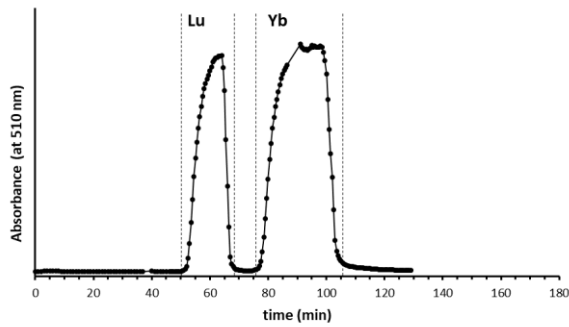


Fig.1. Chromatogram of separation of Yb and Lu by α -HIBA (pH adjusted with NH_4OH).

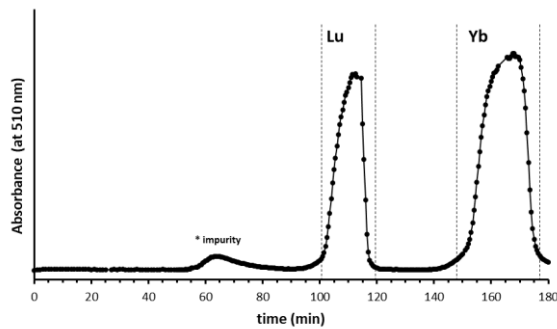


Fig.2. Chromatogram of separation of Yb and Lu by α -HIBA (pH adjusted with CH_3NH_2).

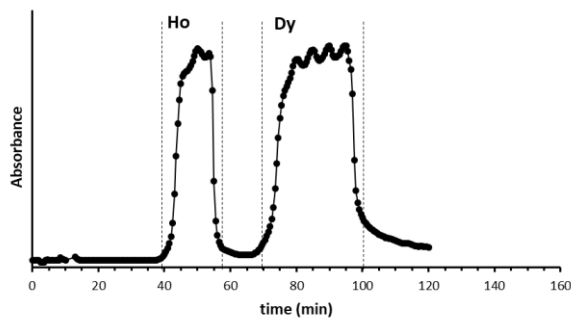


Fig.3. Chromatogram of separation of Dy and Ho by α -HIBA (pH adjusted with NH_4OH).

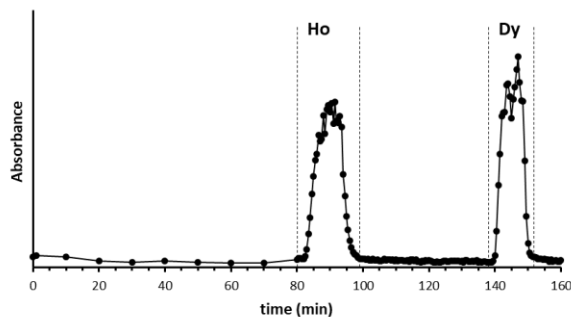


Fig.4. Chromatogram of separation of Dy and Ho by α -HIBA (pH adjusted with CH_3NH_2).

3. Results and Discussion

In this study, the separation efficiency of two adjacent lanthanides (Yb/Lu and Dy/Ho) was evaluated according to the types of ammonium ions such as primary, secondary and tertiary ammonium ions. It was found that the use of higher order amines results in longer column retention times and elution times. For example, when the ions contained in the eluent are methylamine (primary amine), the retention time is longer than that of NH_4^+ ion, and separation efficiency is improved (Fig. 1, 3 and 2, 4). The eluent containing amines of the second or higher order could not elute lanthanide ions. In order to effectively and selectively separate two adjacent lanthanides, it is important to select an appropriate the ammonium ion. The more detail process will be discussed in this presentation.

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