Simultaneous Direct Determination of Stable Isotope Yb/Lu Separated by Liquid Chromatography

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1. Introduction

Lutetium-177 (^{177}Lu, $t_{1/2}$ = 6.7 d) has been utilized as therapeutic radionuclides in nuclear medicine for very specific diagnosis and treatment of various diseases due to its high theranostic potential [1]. ^{177}Lu emits β^- particles ($E_{\beta,max}$ = 498 keV), which has soft tissue penetration range of several millimeters, and γ-rays (E_γ = 208 keV (11.0%) and 113 keV (6.4%)), which is suitable for imaging [2].

The indirect production route produces the no-carrier added (nca) radiolanthanides with high specific radioactivity and high radionuclidic purity, which involving a neutron capture of an enriched target and subsequent decay followed by radiochemical separation and purification from the target material. The nca ^{177}Lu can be produced *via* neutron capture (n, γ) of ^{176}Yb target and subsequent β^- decay of produced ^{177}Yb ($t_{1/2}$ = 1.91 h), as follows: ^{176}Yb(n,γ)^{177}Yb → ^{177}Lu [3,4].

To find the optimal conditions for the separation of nca ^{177}Lu, this study was carried out sufficient separation tests using stable isotopes Yb and Lu. After separating process was performed, it is difficult to find out when lanthanides were separated due to their colorless states. Generally, AAS and ICP-AES are used to find out lanthanide ions although it takes long time. To circumvent this difficulty and identify it immediately, the process for confirmation of the separated stable isotopes was introduced by post-column reaction after the sample is eluted from the column. Post-column reaction is based on spectrophotometric measurement for the chemical reaction between the appropriate chromogenic complexing agents, so-called post-column reagent. Furthermore, effects of the concentrations and pH of α-HIBA (α-hydroxyisobutyric acid) as eluent, the type and size of resin on the separation efficiency were examined in this study.

2. Experiments

2.1. Materials

Ytterbium oxide (Yb_2O_3) and lutetium oxide (Lu_2O_3) were obtained from Sigma-Aldrich. α-HIBA (α-hydroxyisobutyric acid) and PAR (4-(2-pyridylazo) resorcinol), were purchased from TCI. Ammonium hydroxide and glacial acetic acid were purchased from Daejung Chemicals and Merck, respectively. Cation exchange resin in the H^+ form, BP-OA-10 (about 10 μm in diameter, cross-linkage 8%), BP-OA-20 (about 20 μm in diameter, cross-linkage 8%) and BP-100 (about 10 μm in diameter, cross-linkage 6%), were purchased from Benson Polymeric Inc.

2.2. LC system with the post-column reaction detection

The LC instrument was consisted of a high pressure pump and a six-port Rheodyne valve equipped with sample loop of 500 μl. The LC column was prepared by packing a 75 mm length of the cation exchange resins into Eco Plus glass column (YMC, i.d. 10 mm). The lanthanide sample was injected into the mobile phase HIBA delivered at a flow rate of 1.5 ml/min. The eluted metal ions were mixed in a mixing-tee with the post-column reagent added using a pump with a flow rate of 0.5 ml/min. Then, the mixed solution was monitored using a UV-vis spectrophotometer (Agilent 8453) through the flow cell. (Fig. 1)

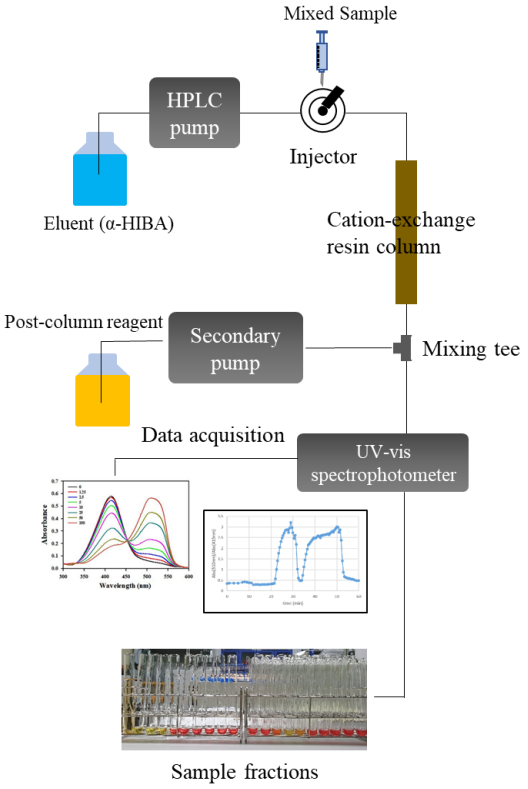

Fig. 1. Photographs for LC system with the post-column detection.

2.3. Separation of stable isotopes Yb and Lu

0.5 ml of sample, including 3 mg of Yb and 1 mg of Lu, was injected into the prepared column under isocratic condition in which the eluent α-HIBA is flowing at 1.5 ml/min. At the same time, post column

reagent was eluted to the mixing-tees by operating pump at the rate of 0.5 ml/min. Then, the mixed solution was measured using a UV-vis spectrophotometer at an interval of 30 s or 1 min.

3. Results and Discussion

Simultaneous detection with post-column reagent makes it possible to find the optimum separation conditions in a short time. Although not many attempts have been tried to prepare the nca radio metal ions, this research will give much information such as column efficiency, reproducibility and durability. The more detail process will be discussed in this presentation.

REFERENCES

[1] S. Banerjee, M. R. A. Pillai, and F. F. (Russ) Knapp, Lutetium-177 Therapeutic Radiopharmaceuticals: Linking Chemistry, Radiochemistry, and Practical Applications, Chem. Rev., Vol. 115, pp. 2934−2974, 2015.
[2] M. Van de Voorde, K. Van Hecke, T. Cardinaels, and K. Binnemans, Radiochemical Processing of Nuclear-Reactor-Produced Radiolanthanides for Medical Applications, Coord. Chem. Rev., Vol. 382, pp. 103-125, 2019.
[3] K. Hashimoto, H. Matsuoka, and S. Uchida, Production of no-carrier-added ^{177}Lu via the ^{176}Yb(n,γ)^{177}Yb → ^{177}Lu process, J. Radioanal. Nucl. Chem., Vol. 255, pp. 575-579, 2003.
[4] S. Watanabe, K. Hashimoto, S. Watanabe, Y. Iida, H. Hanaoka, K. Endo, and N. S. Ishioka, Production of Highly Purified no-carrier-added ^{177}Lu for Radioimmunotherapy, J. Radioanal. Nucl. Chem., Vol. 303, pp. 935–940, 2015.
[5] M. R. Buchmeiser, G. Seeber, and R. Tessadri, Quantification of Lanthanides in Rocks Using Succinic Acid-Derivatized Sorbents for On-Line SPE-RP-Ion-Pair HPLC, Anal. Chem., Vol. 72, pp. 2595-2602, 2000.