The Production of n.c.a Radiolanthanides (Lu-177 and Ho-166) and its Purification for Medical Application

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1. Introduction

Radiolanthanides are important therapeutic radionuclides in nuclear medicine due to its high theranostic potential. The no-carrier added (n.c.a.) radiolanthanides have high specific radioactivity and high radionuclidic purity without the long-lived radionuclidic impurity.

The nca ^{177}Lu, for example, can be produced via neutron capture (n, γ) of ^{176}Yb target as an indirect production and subsequent β- decay of produced ^{177}Yb (t1/2 = 1.91 h), as follows: ^{176}Yb(n,γ)^{177}Yb → ^{177}Lu [1,2]. ^{166}Ho (T1/2 = 26.6 h) emits a proper γ-energy (80keV) for diagnosis and therapeutic β-energy (Eβ = 665.7keV).

^{166}Dy as parent nuclide can be produced by double neutron capture reaction of stable ^{164}Dy. ^{166}Ho produced by (n,) reaction, ^{164}Dy(n,γ)^{165}Dy(n,γ)^{166}Dy → ^{166}Ho + β-, from ^{166}Dy [T1/2=81.5 h, Emax=486.8 keV, Eav=130 keV] is a carrier free state.

Many researchers have devoted themselves to finding the optimal method for separating n.c.a. radionuclides. Some researchers have studied the production of carrier-free radiolanthanides using electrochemical fusion methods or cation exchange chromatography. By the 2010s, most researchers agreed that chromatography was the most suitable method for producing n.c.a. radiolanthanides. Ion exchange techniques typically use α-HIBA (hydroxyisobutyric acid) as a complexing agent and NH_4OH(ammonium hydroxide) as the separating cation.

This study aimed to evaluate the separation efficiency of two adjacent lanthanides (eg, Yb/Lu and Dy/Ho) depending on the type of ammonium ion, through stable isotope separation experiments. Five amines were selected, each pH-adjusted, and α-HIBA was used as the eluent. Furthermore, stable isotope separation was confirmed online using a post-column reaction system using PAR (4-(2-pyridylazol) resorcinol).

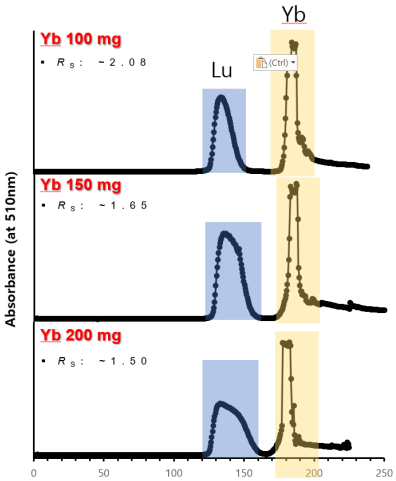
2. LC system for metal identification

The configuration of the LC instrument equipped with an online column system is as follows.

It consists of a six-port rheodyne valve with a 1,000 μl sample loop, an LC pump, and a separation column. A T-type valve was attached downstream to induce a color reaction by injecting a colorimetric reagent. The LC column contained a cation exchange resin, and the eluent for separation used a solution of varying compositions of α-HIBA. The downstream mixed solution was monitored through a flow cell using a UV-vis spectrophotometer (Genesys 150, Thermoscientific).

3. Separation & Purification

A stable isotope was used as the material used in the separation purification experiment. First, Lu_2O_3, Yb_2O_3, Dy_2O_3, and Ho_2O_3 were dissolved in acid to determine the concentration between adjacent lanthanide groups, and then separation was performed by mixing. For separation, the real-time separation analysis confirmation device introduced earlier was used. As a result of the separation, the separation ability (RS) was about 1.5 to 2.0, and it was confirmed that the separation ability slightly decreased as the concentration of the target increased.



<Chromatogram of Lu separation>

A cation exchange resin (50W-X8) and concentrated hydrochloric acid were used in the purification process. The yield according to purification after separation was 95% or more.

3. Production of n.c.a Lu-177 & Ho-166

Targets were irradiated into one for the production of carrier Lu and Ho. Mainly, IP 5 irradiation holes and IP 15 irradiation holes were used. The irradiation capsule recovered the target after cooling for 1 day and dissolved in concentrated HCl to prepare a sample for separation. The equipment for separation is shown in

the following figure. The final yield after separation is about 80% or more, and the discussion will be conducted in the presentation.

4. Results and discussion

The production of carrier isotopes is one of the most important factors in the development of radioactive drugs. It has been supplied free of charge to nine domestic institutions through the separation and purification technology developed by KAERI, and the discussion will be conducted through this presentation.

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