

Gram-Scale Yb/Lu Separation via Ion-Exchange Chromatography for No-Carrier-Added ^{177}Lu Production

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1. Introduction

Lutetium-177 (^{177}Lu) is a promising the therapeutic radionuclide widely used in targeted radionuclide therapy, and its demand has increased with the clinical application of radiopharmaceuticals such as Lutathra® and Pluvicto®. No-carrier-added (N.C.A) ^{177}Lu can be produced through the indirect $^{176}\text{Yb}(n,\gamma)^{177}\text{Yb} \rightarrow ^{177}\text{Lu}$ reaction. However, efficient separation of ^{177}Lu from a large excess of Yb remains a major challenge because of their similar chemical properties. In this study, an ion-exchange chromatographic separation process using α -hydroxyisobutyric acid(α -HIBA) was developed and scaled up to a 1 g Yb scale for the production of N.C.A ^{177}Lu .

2. Methods and Results

2.1 Preparation of Eluent

α -HIBA solutions of 0.07 M and 0.2 M were prepared as the eluent by dissolving the reagent in distilled water under continuous stirring until complete dissolution was achieved. The pH of the solution was adjusted to 4.2-4.5 using ethanalamine.

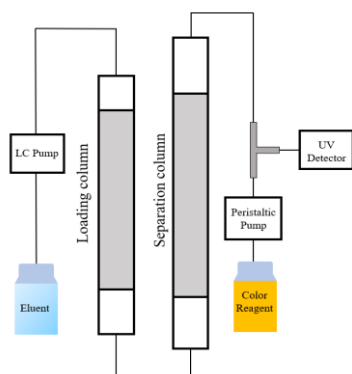


Fig. 1. Scheme of the Lu/Yb separation and detection system.

2.2 Analytical Method

The prepared solution was then passed through a membrane filter prior to use to remove any particulate impurities. PAR (4-(2-pyridylazo)resorcinol) was used as the chromogenic reagent for lanthanide detection. To ensure optimal color development, PAR was dissolved

in a pH 9.8 buffer solution prepared from acetic acid and ammonium hydroxide. The eluate from the separation column was continuously mixed with the PAR reagent using a mixing tee, and the absorbance was monitored in real time at 510 nm using UV/Vis detector.

2.3 Column Separation of Lu and Yb

Yb_2O_3 (1g) and Lu_2O_3 (5mg) were separately dissolved in nitric acid with heating to convert them into their nitrate forms. The resulting solutions were mixed and diluted with 30 ml of distilled water. A small amount of nitric acid was then added to adjust the pH to approximately 1-2. The prepared solution was passed through a loading column ($\Phi 15\text{ mm} \times 6.2\text{ cm}$) using a peristaltic pump to adsorb the metal ion onto the resin.

After loading, the column was connected to the separation column, and the separation was performed using 0.07 M α -HIBA at pH 4.2 with a flow of 15 ml/min under pressure below 250 psi. Lu was eluted between 152 and 214 min, whereas Yb eluted between 224 and 257 min. When Yb elution began, the eluent was switched to 0.2 M α -HIBA to accelerate Yb recovery. The separation was completed within 260 min using approximately 4 L of eluent. A resolution (R_s) of 1.69 was achieved, demonstrating successful separation of Lu from 1g Yb.

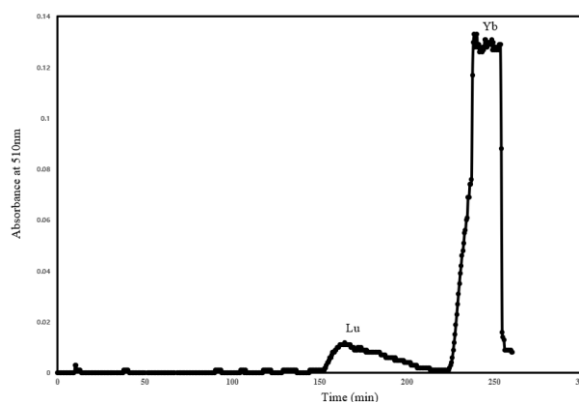


Fig. 2. Chromatographic separation of 1 g of Yb and 5 mg of Lu using 0.07 M α -HIBA (pH 4.2) as the eluent. The effluent was mixed with 0.2 mM PAR, and the absorbance was monitored at 510 nm using a UV/vis detector.

3. Conclusions

The proposed ion-exchange chromatographic process successfully achieved gram-scale separation of Lu from 1 g of Yb with a Rs of 1.69. The entire separation process was completed within 5 h, demonstrating that efficient Yb/Lu separation can be achieved at the gram scale within a practical processing time. Based on the target scale and expected ^{177}Lu production of up to approximately 10 Ci of N.C.A ^{177}Lu per batch. These results demonstrate the applicability of the proposed process to the large-scale production of N.C.A ^{177}Lu .

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