



Isolation of Gadolinium/Terbium using Extraction chromatography approach for therapeutic issues

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Abstract

¹⁶¹Tb is a promising radionuclide owing to its favorable properties for treatment small size of cancer. NCA ¹⁶¹Tb can be produced by indirect method through ¹⁶⁰Gd(n,γ) ¹⁶¹Gd→¹⁶¹Tb nuclear reaction. To obtain the NCA radionuclides, the existence of an effective Gd/Tb separation method is critical. In this study isolation of Tb from Gd/Tb matrix using Ln resin column based on extraction chromatography method has been carried out. Fractions eluted from the column containing Gd/Tb matrix were identified and quantified using ICP. The optimization of different experimental parameters for the effective separation of Gd/Tb such as concentration of eluting solutions and flow rate of load and elution was investigated. The results showed that optimum condition on Gd/Tb isolation was obtained using HNO₃ solution with concentration of 0.8 and 3 N to separate gadolinium and terbium isotope, respectively. The separation yield of Tb and Gd were obtained 83.51 % and 81.8% respectively.

Keywords: No Carrier Added, Extractin chromatography, Terbium-161, Targeted therapy

Introduction

Theranostic radio-lanthanides like ¹⁵³Sm, ¹⁷⁷Lu, ¹⁶⁶Ho and ¹⁶¹Tb, have recently drawn great attentions in the targeted radionuclide therapy [1-3]. Among the theranostic radio-lanthanides, auger-electron emitters especially in non-carrier added form have a great impact on the treatment of tumors because of the relatively short range in the tissue, high local damage, high cytotoxicity effects and high specific activity which required in carrier molecules radiolabeling for therapy [4-5].

Terbium-161 (¹⁶¹Tb) with favorable nuclear properties like beta irradiation with energy 0.55 keV, γ-rays with energy 26-55 keV (63%) which is suitable for imaging, proper half-life 6.88 days and emission of a larger number of conversion and Auger electrons with energies 40-49 keV(54%), 17-26 keV(51%) and 1.5-8 keV (259%) can be considered as a good candidate for treatment small size of cancer. The direct method is not preferred to produce ¹⁶¹Tb, because the only stable isotope of terbium is ¹⁵⁹Tb. The NCA ¹⁶¹Tb can be produced by indirect method through ¹⁶⁰Gd(n,γ) ¹⁶¹Gd→¹⁶¹Tb nuclear reaction. Due to differences between Gd and Tb nuclides, the separation of them is achievable which make it feasible to produce NCA ¹⁶¹Tb radionuclide without including of cold isotopes[6-7]. In this study, isolation of Tb and Gd elements by Extraction Chromatography (EXC) was investigated to achieve a

successful method which can also be used for active nuclides.

Experimental

Materials

Natural Gd₂O₃ and Tb₂O₃ were purchased from sigma-Aldrich chemical Company, UK. LN2 resin (25-53μm particle size) was obtained from Eichrom Company. HNO₃(65%) and other chemical materials were obtained from Merck Company. All chemical reagents were of analytical grade.

Extraction Chromatography of Gd/Tb

This system consists of a glass column with an inner diameter of 8 mm and a bed height of 18 cm that a layer of glass wool was inserted as a top bed support. A peristaltic pump and a polyethylene tube are used to pass the solutions through the column. To obtain optimal conditions for this separation, about 10 g of LN-resin (particle size: 25-53 μm) was wetted in 0.1 N nitric acid for one week and then column was filled with it. The column was preconditioned by 50 ml of distilled water, 50 ml of 0.1 N nitric acid and again 50 ml of distilled water, respectively. 5 mg of Gd₂O₃ and 1 mg of Tb₂O₃ were dissolved in 5 mL of 0.1 M HNO₃ and were loaded on the column at a flow rate of 2 ml/min.

Optimization of experimental parameters

Among the experimental parameters such as concentration of eluting solutions and flow rate of load and elution, which influence the selective separation of Tb/Gd, the main separation parameter is the

concentration of eluting solutions as the mobile phase of the column.

Results and discussion

The effect of elution concentration on Tb/Gd EXC

A continuous sequence of elution concentrations of HNO₃ solutions (0.3M to 4M) were selected to evaluate the isolation of Gd/Tb elements. The eluted solutions was collected in 2.5mL bed volume and analyzed by ICP analysis. Fig. 1 shows the separation profile of Tb and Gd on the Ln resin Column.

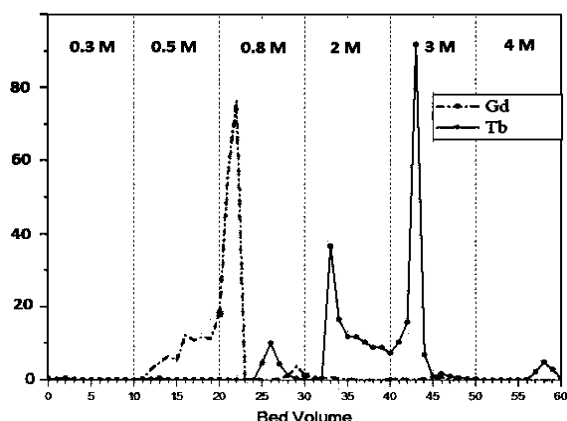


Fig. 1. Separation profile of Tb and Gd on the Ln resin based on ICP analysis

It can be concluded that in the ranges of 0.5-0.8 M, and 2-3 M HNO₃ concentrations the highest separation were observed for gadolinium nuclei and terbium nuclei respectively. With increasing of acidity concentration up to 4 M, no significant change in the separation process occurred. In the range of 0.8 M, a small peak of terbium is probably related to the continuous trend of increasing concentrations.

Also, in this study, various combinations of HNO₃ concentrations were used to obtain the optimum conditions on separation. The EXC column was eluted with each 50 mL of 0.3-4 N; 0.5-2 N; 0.8-3 N, and 2-3 N HNO₃ solutions. The separation yields of Tb and Gd that were obtained from the separation with various combinations of HNO₃ concentrations are summarized in Table 1.

Table 1. The separation yield of Tb and Gd eluted from the column using various combination of HNO₃ concentrations

The combination of HNO ₃ concentrations (N)	Tb yield (%)	Gd yield(%)
0.3-4	44.12	22.16
0.5-2	61.4	58.7
0.8-3	83.51	81.8
2-3	82.62	21.97

The results show that considering all the conditions, the concentrations of 0.8-3 M is the best choice for the separation of terbium and gadolinium.

The effect of flow rate of load and elution on Tb/Gd EXC

The effect of flow rate of loading and elution on separation of Gd and Tb was shown in Table 2. A peristaltic pump was used to adjust the flow rate to obtain the optimized conditions for loading and eluting.

Table 2. The effect of flow rate of load and elution.

Flow rate of loading (ml/min)	Flow rate of eluting (ml/min)	Time of separation (minute)	Separation yield (%)
1	1	110	75.6
1	1.5	77	83
1	1.7	70	79

Conclusions

In summary, the separation of Gd/Tb has been done by extraction chromatography method using Ln resin as a stationary phase and nitric acid solution as a mobile phase. The results showed that in order to achieve efficient separation, some factors such as elution concentration must be considered and optimized. In this study, the concentrations of 0.8-3 M are considered by the best separation yield to isolate gadolinium and terbium isotopes.

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