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STUDY OF THE PRODUCTION OF ^{177}Lu THROUGH ^{176} Yb (n, γ) ^{177}Yb → ^{177}Lu NUCLEAR REACTION

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ABSTRACT

The β^- emitter ^{177}Lu is a promising therapeutic radioisotope for the curative treatment of cancer using labelled proteins. It has a half – life of $T_{1/2}$ = 6.71 day and maximum and average β^- energies of 421 and 133 keV, resulting in a short range of radiation in tissue. The decay is accompanied by the emission of low energy γ-radiation with 208.3 keV (11%) and 113 keV (6.4%) suitable for simultaneous imaging, ^{177}Lu can be produced by two different routes, namely, by irradiation of natural Lu_2O_3 target (^{176}Lu, 2.6%) or enriched (in ^{176}Lu) Lu_2O_3 target, as also by irradiation of Yb target (Yb_2O_3) followed by radiochemical separation of ^{177}Lu from Yb isotopes. The objective of this work is to study the production of ^{177}Lu through the indirect ^{176}Yb(n,γ)^{177}Yb ⟶ ^{177}Lu nuclear reaction. The results of the production yield of ^{177}Lu will be shown and compared with the direct reaction. The method of choice for the chemical separation between Lu and Yb was the ion exchange, using an cation exchange resin in Cl^- form and α-HIBA as eluent. Preliminary results showed a good separation of ^{177}Lu from Yb_2O_3 indirect targets.

1. INTRODUCTION

Radioisotopes are essential to a variety of applications in medicine, where they are utilized in the radiodiagnosis and treatment of various diseases. The last years have witnessed a rapid growth in the demand of radioisotopes for treatment of cancer in nuclear medicine due to the advent of improved means of targeting tumors or other disease tissues with radiolabeled agents, primarily by chemical, immunochemical or mechanical means[1].

The radiolanthanides are particularly attractive and advantageous in the development of radiotherapeutic agents in that they share very similar chemistry, but have various nuclear properties. Researchers can develop the chemistry necessary to incorporate a lanthanide into a carrier which will target the diseased tissue, then choose the radiolanthanide with the appropriate half-life and/or beta energy for the specific treatment [1].

A promising radiolanthanide is the β^- emitter ^{177}Lu because of its favorable decay characteristics. ^{177}Lu decays with a half-life of 6.71 days by emission of β^- particles with E_{max} of 421 keV and 133 keV to stable ^{177}Hf. It also emits γ photons of 113 keV (6.4%) and 208 keV (11%), which are ideally suited for in vivo imaging with a gamma camera. The physical half-life of ^{177}Lu is comparable to that of ^{131}I, one of the most commonly used radioisotopes for radionuclide therapy. The long half-life of ^{177}Lu provides logistic advantage for facilitating supply to places far away from the reactors [2].

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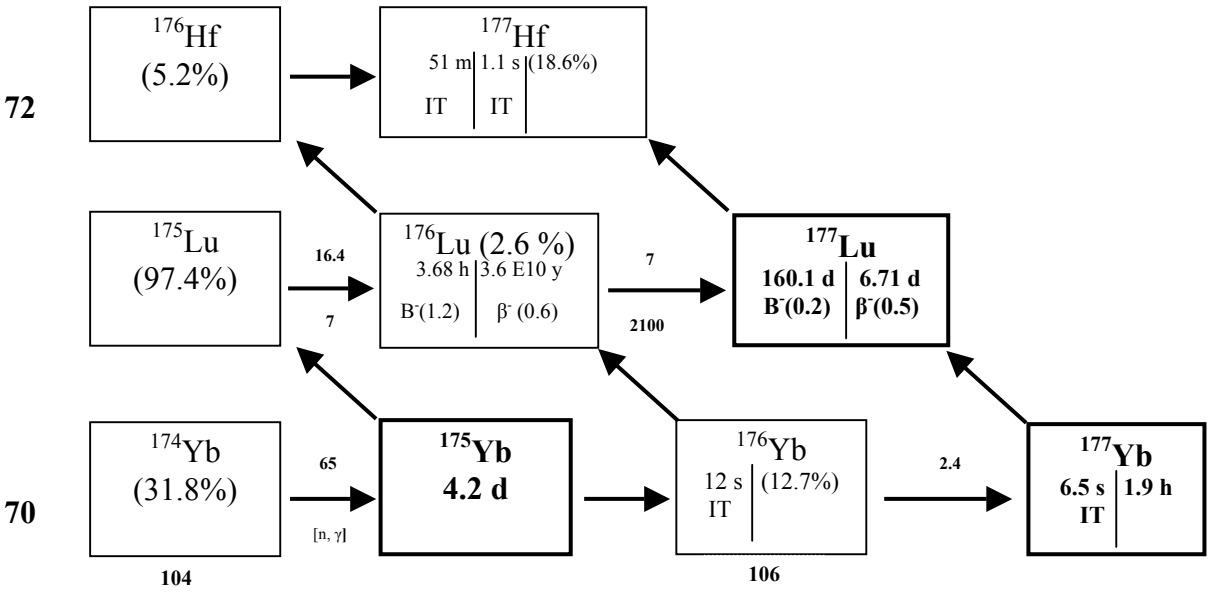

Figure 1: Reactor production of ^{177}Lu [3]

The usual method of preparation of ^{177}Lu is to irradiate Lu target in the nuclear reactor. However, small quantities of carrier free ^{177}Lu can be produced in a neutron irradiated Yb target, even though ^{169}Yb and ^{175}Yb are also produced by the neutron activation of ^{176}Yb present in the target. The carrier-free ^{177}Lu formed in the irradiated Yb target can be recovered either by preferential removal of the Yb target after its reduction to Yb^{2+} (since Lu^{3*} is not reduced) or by ion-exchange chromatography [4].

The separation factor for Lu/Yb pair is very small and it is difficult to separate them in good yield and in high purity when a trace amount of one is present with carrier amount of the other. An excellent eluent used, for this purpose, in ion-exchange chromatography is the α-hydroxyisobutiric acid (α-HIBA), that showed a good separation of carrier-free amounts of ^{177}Lu from carrier amounts of Yb irradiated [4].

The objective of this work was to study the production of ^{177}Lu through the alternative production route, the ^{176}Yb (half-life 1.9 h) $\longrightarrow$ ^{177}Lu process (thermal neutron cross sections [^{176}Yb] = 2.85 b). Natural targets of Yb_2O_3 were irradiated to produce no-carrier-added (nca) ^{177}Lu in the present work. An ion-exchange chromatography system with α-HIBA as eluent was used in order to separate nca ^{177}Lu from Yb targets

2. MATERIALS AND METHODS

2.1 Reagents

High purity Yb_2O_3 and α – HIBA were purchased from Aldrich chemical and used in all experiments. Dowex – 50X8 cation exchange resin in the H^+, 200-400 mesh, was purchased from Dow chemical.

2.2 Irradiations

Samples of Yb_2O_3 were irradiated inside sealed quartz tubes that were also put inside sealed aluminum containers in selected positions of the nuclear reactor IEA-R1 at IPEN/CNEN-SP. The neutron flux was 1.0 $x10^{13}$ n $.s^{-1}.cm^{-2}$ for 1 hour. After some cooling time the samples were sent to the Radiopharmacy Center, opened and processed.

2.2 Resin and column preparation

The Dowex – 50X8 cation exchange resin was first activated with successive washing with hydrochloric acid, water and sodium hydroxide. The resin was then poured inside a glass column (35 cm resin height and 1 cm diameter), the flow in this condition was 5 drops for minutes. This resin was percolated with 50ml of the proper eluent before the chemical processing. The eluents used for this separation were 0.1M HCl and 0.25 M α – HIBA, with the pH adjusted to 3.2 with ammonium hydroxide.

2.3 Ion exchange process

The irradiated target was dissolved with 0.1 M HCl and loaded in the column. After the loading, the solvent 0.25 M α-HIBA was percolated through the column. Aliquots were taken from the loading samples and the elution samples, after passing through the resin. These samples were then analysed by gamma ray spectroscopy using a HP Ge detector, from Canberra, using the energies of 208 keV for ^{177}Lu and 396 keV for ^{175}Yb.

3. RESULTS AND DISCUSSION

Table 1 and Figure 1 show the results of the first experiment using 0.25 M α-HIBA. In this experiment the column was percolated with 0.1 M HCl.

Table 1. Results of the first experiment of the chemical separation of ^{177}Lu from ^{175}Yb.

Sample Volume (mL)	% (^{177}Lu) (sum)	% (^{175}Yb) (sum)
Load	0	0
1	1.24	0.02
2	4.26	0.22
3	5.76	0.48
4	7.04	0.62
5	7.60	0.75

6	7.75	0.72
7	8.02	0.81
8	8.03	1.02
9	8.18	1.18
10	8.18	1.41
11	8.35	1.57
12	8.78	1.83
13	8.85	1.90
14	9.06	1.57

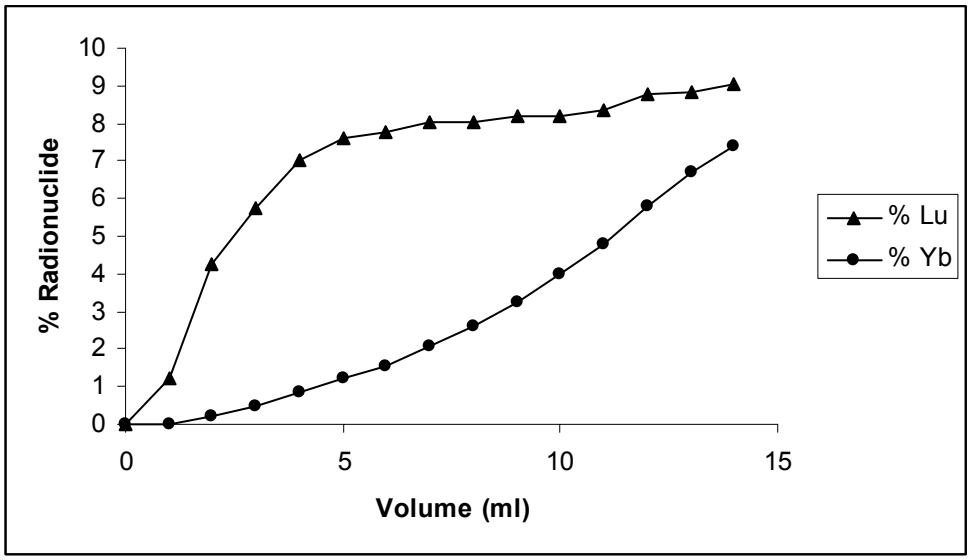

Fig. 2. Elution curve for the separation of Lu and Yb - HCl

From these results it can be seen some separation between Lu and Yb, but not with a good separation factor. Then the eluent solvent was changed to 0.25 M α-HIBA and the results can be seen in Table 2 and Figure 3.

Table 2. Results of separations of ^{177}Lu for ^{175}Yb using 0.25 M α-HIBA

Sample Volume (mL)	% (^{177}Lu) Sum	% (^{175}Yb) Sum	Sample	% (^{177}Lu) Sum	% (^{175}Yb) Sum	Sample	% (^{177}Lu) Sum	% (^{175}Yb) Sum
Load	0	0	19	43.12	3.35	38	67.44	8.95
1	1.97	0.03	20	46.68	3.64	39	67.44	9.09
2	5.17	0.11	21	48.69	3.81	40	67.44	9.27
3	7.84	0.22	22	51.26	4.05	41	67.44	9.57
4	10.51	0.55	23	53.17	4.30	42	67.44	10.09
5	13.12	0.70	24	55.06	4.61	43	67.44	10.70
6	15.42	0.87	25	56.76	4.88	38	67.44	8.95
7	17.55	1.02	26	58.23	5.21	39	67.44	9.09

8	20.52	1.24	27	59.70	5.55	40	67.44	9.27
9	23.03	1.42	28	60.51	5.87	41	67.44	9.57
10	26.12	1.70	29	61.34	6.19	42	67.44	10.09
11	27.03	1.78	30	62.54	6.55	43	67.44	10.70
12	27.71	1.86	31	63.12	6.89			
13	27.84	1.87	32	63.88	7.20			
14	28.52	2.03	33	64.98	7.51			
15	30.35	2.26	34	65.67	7.85			
16	32.79	2.47	35	66.42	8.18			
17	35.80	2.72	36	67.08	8.52			
18	39.25	3.02	37	67.44	8.76			

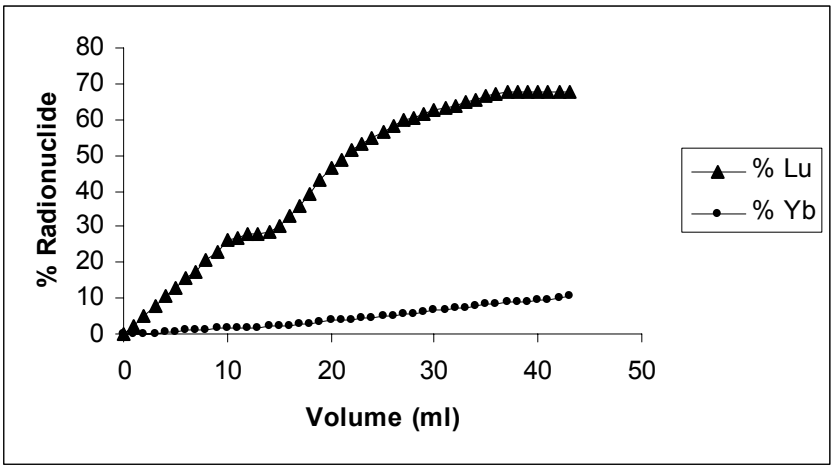

Fig. 3 Elution curve for the separation of Lu and Yb - HIBA

The results show a big improvement in the separation between Lu and Yb when 0.25 M α-HIBA is used as the solvent. A higher amount of ^{177}Lu is eluted in smaller volumes and lesser impurities of ^{175}Yb when 0.25 M HIBA is used as eluent.

3. CONCLUSIONS

The α-HIBA was more efficient as eluent for the separation between ^{177}Lu and ^{175}Yb, and is more promising for establishing a process of indirect production of ^{177}Lu than HCl. Further work must be done to improve the separation, giving a minimum level of ^{175}Yb impurity.

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