Original Article

Comparative studies of extraction chromatography and electro-amalgamation separation to produce no-carrier added ^{177}Lu by Tehran research reactor

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ABSTRACT

Introduction: Owing to its favorable radionuclidic characteristics, such as $t_{1/2}$ = 6.73 day and $E_{\beta\ (max)}$ = 497 keV and ease of its large-scale production using medium flux research reactors, lutetium-177 (^{177}Lu) is an attractive radionuclide for various therapeutic applications. No carrier added (NCA) ^{177}Lu was obtained by thermal neutron bombardment (4×10^{13}n/cm^2.s) of ^{176}Yb target through ^{176}Yb(n, γ)^{177}Yb $\longrightarrow$ ^{177}Lu process have the advantage of preparing radiopharmaceuticals with high specific activity. So the existence of an effective Lu/Yb separation method is critical.

Methods: Many researchers illustrated no-carrier added ^{177}Lu production. However, the present study is based on comparison between two potential separation methods, namely extraction chromatography and electro-amalgamation separation with respect to separation yield and radiochemical characteristics.

Results: The no carrier added ^{177}Lu separated from ^{176}Yb target by two extraction chromatography and electro-amalgamation separation methods. The effective parameters on separation Lu/Yb were investigated in two procedures. The ^{177}Lu production yield by extraction chromatography and electro-amalgamation procedures were 82% and 88.83% respectively. The no carrier added ^{177}Lu was obtained with radionuclidic purity of 99.99% in two separation methods.

Conclusion: Although both separation methods have exhibited promising feature, the study reveals that electro-amalgamation separation offers the advantages of higher yield of ^{177}Lu, simplicity and easier to operate for large amount of target and less overall processing time.

Key words: ^{177}Lu; No carrier added; Extraction chromatography separation; Electro-amalgamation separation

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INTRODUCTION

Over the last several years, lutetium-177 has been one of the most promising radionuclides in nuclear medicine [1, 2]. Increasing the use of ^{177}Lu in nuclear medicine has been notable and a wide range of ^{177}Lu radiopharmaceuticals for a variety of therapeutic purposes including peptide receptor radionuclide therapy, bone pain palliation, radiation synovectomy and radioimmonuthrapy has been successfully developed and investigated [3]. Because of successful applications in targeted therapy and brachytherapy, the demand for ^{177}Lu is growing worldwide. The major criteria for the choice of a radionuclide for a radiotherapy are suitable nuclear decay characteristics, possibility of production with high radionuclidic purity and specific activity, ease of production and amenable chemistry [4, 5]. ^{177}Lu decays with a half-life of 6.71 d by emission of β-particles with $E_{\beta(max)}$ of 497 keV (78.6%), 384keV (9.1%) and 176 keV (12.2%) to stable ^{177}Hf. Because of the low energy of the emitted β^- and mean penetration range of 670μm, the ^{177}Lu is an ideal radionuclide for delivering energy to small tumors and metastatic lesions with minimum radiation exposure to non-targeted tissue. It also emits gamma photons of 113 keV (6.4%) and 208 keV (11%) which is ideally suited for imaging the in vivo localization [6]. The emission of low-energy photons is one of the important feature of ^{177}Lu that is used for therapeutic as well as diagnostic purposes. The optimal half-life of ^{177}Lu makes it useful for long distance shipments from the reactors and also provides extended time periods which may be required for chemical processing of separation, production of ^{177}Lu-based radiopharmaceuticals, quality control and finally administration to the patients [7].

There are two alternative production methods for ^{177}Lu:

(1) ^{176}Lu (n, γ) ^{177}Lu

(2) ^{176}Yb(n, γ) ^{177}Yb $\xrightarrow{\beta}$ ^{177}Lu

Route (1) namely the direct route based on neutron capture reaction on the isotope ^{176}Lu which is activated to Carrier added (CA) ^{177}Lu. Route (2) namely the indirect route based on neutron irradiation of ^{176}Yb target leading to the production of ^{177}Yb which undergoes β^- particle emission ($T_{1/2}$ =1.9 h) to produce no carrier added (NCA) ^{177}Lu. A long lived ($T_{1/2}$=160.5 days) metastable radionuclide of lutetium (^{177m}Lu) was produced in the direct method. The presence ^{177m}Lu in a radiopharmaceutical preparation is one of the drawbacks in the direct method that significantly lowers the radionuclidic purity and specific activity of ^{177}Lu as well as causing serious problems with the radioactive waste disposal after the process of labeling and treatment [8]. Also in this method, the specific activity has been significantly decreased due to macroquantities of nonradioactive isotopes of Lu in the product. In indirect process, it is feasible to separate ^{177}Lu from ^{176}Yb due to the chemical differences between Yb and Lu [9]. Therefore, it is possible to produce NCA therapeutic radioisotope ^{177}Lu that does not contain the non-radioactive isotope. Since no ^{177m}Lu is formed by the decay of ^{177}Yb, ^{177}Lu is produced with a very high radionuclidic purity. The use of high specific activity ^{177}Lu is preferred to minimize Lu cation competition (between ^{176}Lu and ^{177}Lu) for the finite binding sites of the biolocalization agent. So ^{177}Lu production by indirect process is preferred. As a consequence of obtaining NCA ^{177}Lu with maximum specific activity, micro quantities of ^{177}Lu must be separated from the macro amount of ytterbium target [10]. Therefore, research on the indirect process and the related chemical separation of Yb and Lu are ongoing world-wide [11]. There are a number of separation methods described in the literature for the separation of individual lanthanides which are based mostly on ion-exchange chromatography, solvent extraction, extraction chromatography (EXC), cementation and electrochemical process.

Lanthanides separation by elution of their complexes from a cation-exchange column with α-hydroxyisobutyric acid (α-HIB, 2-hydroxy-2-methylpropanoic acid), advantages, disadvantages and improvement of separation has been studied by many researchers. [12-16]. The separation ^{177}Lu/Yb using Dowex 50WX8, a cation exchanger in Zn^{2+} form, has been reported by Balasubramanian [17]. Also, Hashimoto et al utilized reversed – phase ion-pair chromatography using a reverse C18 column [18]. The liquid–liquid extraction method using 1 % HDEHP [di-(2-ethylhexyl) orthophosphoric acid] in cyclohexane has been used by Lahiri et al. [19]. Kumric et al. used supported liquid membrane extraction (SLM) that has its roots in the solvent extraction method for Lu/Yb separation with DEHPA [20]. Recently Satoshi Watanabe et al. used reversed-phase ion-pair liquid chromatography to separate NCA ^{177}Lu from the macroscopic amounts of the Yb target [21]. The extraction chromatography (EXC) method has been established by Knapp et al, that one step extraction chromatography using LN Resin commercially available from Eichrom technologies [22]. Horwitz et al. reported ^{177}Lu/^{176}Yb separation using two different EXC resin, a resin containing HEH[EHP] (LN2) and a resin containing tetraoctyldiglycolamide (DGA) sorbed on Amberchrom CG-71 substrate [23]. Le Van So et al. developed a multi-column solid phase extraction (SPE) chromatography technique using di-(2-ethylhexyl) orthophosphoric acid (HDEHP) impregnated OASIS-HLB sorbent based SPE resins (OASIS-HDEHP) [24, 25].

To standardize the separation process of the radiolanthanides based on extraction chromatography, a radiolanthanide separation device (DISER) was designed and built by Monroy-Guzman et al. [26]. A cementation method that based on selective extraction of Yb by Na(Hg) amalgam from Cl-/CH3COO- electrolytes, followed by a final cation exchange purification, has been developed by Lebedev et al. [27]. An electrochemical separation based on reduction of Yb(III) to Yb(II) with sodium amalgam by formation of insoluble $YbSO_4$ has been reported by Bilewicz et al. [28]. Chakravarty et al. used the electro-amalgamation (ELM) separation based on electrolytic reduction of Yb^{3+} to Yb^{2+} in lithium citrate medium [29].

In this experiment the EXC and ELM separation methods were used for production of NCA ^{177}Lu and advantages and disadvantages of two separation methods were compared as far as radionuclidic purity, yield of ^{177}Lu production, recovery target, cost and other related factors are concerned.

METHODS

Material and instruments

Isotopically enriched $^{176}Yb_2O_3$ (^{176}Yb: 96.40%) was supplied by TRACE sciences international.LN2 resin (25-53µm particle size) and DGA resin (50-100µm particle size) were purchased from Eichrom, hydrochloric acid nitric acid, mercury was obtained from Merck Company, lithium citrate, whatman filter and pure water were obtained from Sigma-Aldrich chemical Company, UK. All chemical reagents were of analytical grade. A p-type coaxial HPGe detector (Eurasis Measure Company, France), with 80% relative efficiency, a standard NIM, and resolution 1.8 keV at gamma-ray energy 1332.5 keV of ^{60}Co was used in this research. Length and diameter of the crystal are about 69 cm and 65cm, respectively. The software Gamma-2000 was also utilized for data acquisition and analysis, as well as MATLAB and Table Curve software, versions R2011b (7.13.0.564) and 5.01, respectively.

Irradiation

NCA ^{177}Lu was produced by neutron irradiation of enriched ^{176}Yb target (the characteristics are shown in Table 1) in a quartz ampule with a thermal neutron flux of 4×10^{13} $ncm^{-2}s^{-1}$ for 14 days at the Research Reactor of Tehran. ^{175}Yb ($T_{1/2}$ = 4.185 days) was also produced due to the ^{174}Yb content in the target and was used as a tracer for Ytterbium. The irradiated target was cooled for two days to allow the decay of ^{177}Yb ($T_{1/2}$ =1.9 h). Then, the irradiated target was dissolved in 0.05N HCl and 0.1N HNO_3 for ELM separation and EXC separation, respectively.

Extraction chromatography (EXC) separation

EXC is a separation strategy that combines the selectivity of solvent extraction with the ease of operation and rapidity of a column chromatography. The system (Figure 1) used for separation is composed of two glass column (inner diameter of 11 mm and 22 cm bed height) that a layer of glass wool was inserted as a top bed support. The glass column number 1 was thermostated at 50 ºC using recirculating water. A peristaltic pump and a connected polyethylene tube were used for passing solutions through columns. To determine the optimum condition for this separation, about 10 g of LN2 resin (25-53µm particle size) and 10g DGA resin (50-100µm particle size) were wetted by 0.1N nitric acid for 24h. The column (1) and column (2) with glass wool end capped was filled with well-wetted LN2 resin and DGA resin, respectively. Columns were preconditioned with respectively 50 mL of distilled water, 50mL of 0.1N HNO_3 for column (1) and 0.05N HCl for column (2) and again 50 mL of distilled water. The irradiated target (in 0.1N HNO_3) was loaded on the column(1) at a flow rate of 2 ml/min, was washed with 0.1N HNO_3 and 1.5N HNO_3 and was eluted with 4N HNO_3. Column (2) was washed with 0.1N HNO_3 and was eluted with 0.05N HCl. The eluted solution was collected in 5mL bed volume and analyzed for Yb and Lu radionuclide using the HPGe detector.

Table 1: Characteristics of ytterbium isotope and radioisotopes from neutron reaction in reactor.

Isotope	Enriched (%)	(n, γ)	Half life	Cross section (barn)	Decay mode	Decay production
^{168}Yb	<0.12	^{169}Yb	32.026 d	2300	EC	^{169}Tm
^{170}Yb	<0.12	^{171}Yb	-	9.9	stable	-
^{171}Yb	0.41	^{172}Yb	-	58.3	stable	-
^{172}Yb	0.69	^{173}Yb	-	1.3	stable	-
^{173}Yb	0.51	^{174}Yb	-	15.5	stable	-
^{174}Yb	1.8	^{175}Yb	4.2 d	63	β^-, γ	^{175}Lu
^{176}Yb	96.4	^{177}Yb	1.9h	2.85	β^-, γ	^{177}Lu

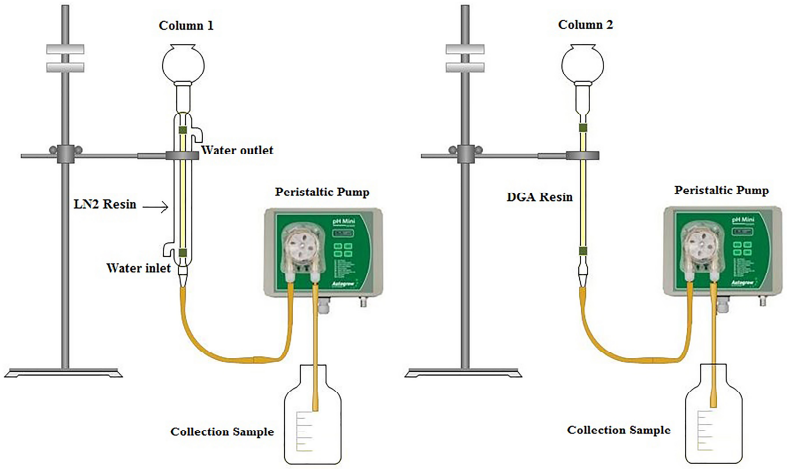

Fig 1. Extraction chromatography separation system.

Electro-amalgamation (ELM) separation

The formation of Yb amalgam by electrolysis reduction of Yb^{3+} to Yb^{2+} in lithium citrate medium is base of ELM separation method. In this work, electrochemical set-up of Chakravarty et al. [29] has been used (Figure 2).

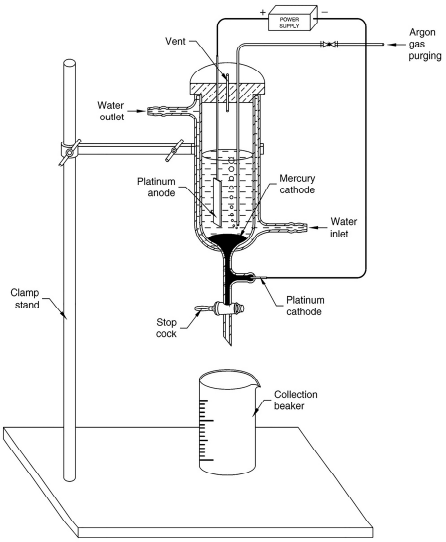

Fig 2. The setup of ELM separation [29].

A high pure platinum plate anode (1.5×6 Cm^2) and mercury-pool cathode (5mL) has been used. The mercury-pool cathode has been connected to the negative pole of power supply via a platinum wire. During the course of electrolysis, argon gas has been blown through the hole in the teflon stopper end-capping the cell. The irradiated target dissolved in 0.05N HCl and has been mixed with 15 mL lithium citrate (0.15M). At the end of process, the separated electrolyte from Yb amalgam has been analyzed by HPGe detector.

RESULTS

Extraction chromatography (EXC) separation

In EXC separation, the irradiated target was dissolved in 1mL 0.1N HNO_3. This solution containing ^{175}Yb,^{169}Yb and ^{177}Lu was passed through the preconditioned column 1 (LN2 resin). The column was then washed with 30mL 0.1N HNO_3 and 30 mL 1.5N HNO_3 for removing ytterbium impurities. ^{175}Yb radionuclide as major radionuclide impurities was washed with 50 mL 4N HNO_3. The NCA ^{177}Lu was eluted with 50 mL 4N HNO_3. For adjusting the acidity of the solution and purification of ^{177}Lu from other metal ions in the periodic table, DGA resin was used in the next step. The collected solution in pervious step (^{177}Lu in 50 mL 4N HNO_3) was loaded on to column 2 (DGA resin) and washed with 30 mL 0.1N HNO_3. The purificated ^{177}Lu was eluted with 50 mL 0.05N HCl. The gamma ray spectra of irradiated target and the final product were shown in Figure 3. No radiotracer of ytterbium radionuclide (^{169}Yb, ^{177}Yb, ^{175}Yb) was observed in the γ-spectrum of ^{177}Lu eluted portion. Various steps of isolation of radionuclides were shown in flowsheet of Figure 4. Activity and the elution yield of each radionuclide in two separation steps on LN2 resin and DGA resin columns are given in Table 2. The elution's profile of ^{177}Lu was shown in Figure 5. The overall yield of 82% ^{177}Lu was obtained. To determine the optimum condition, some effective factors on separation Lu/Yb by EXC, like an initial mass of ytterbium target, flow rate of loading and elution as well as temperature were examined.

The effect of the initial mass of the ytterbium loaded on the column was studied for amounts of 5, 10, and 20 mg.

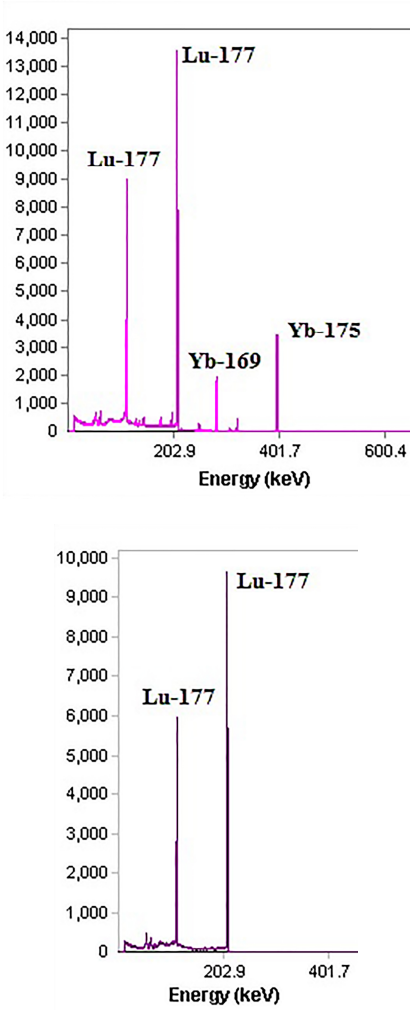

Fig 3. The gamma ray spectra of irradiated $^{176}Yb(NO_3)_3$ target (above) and the final product after separation (EXC separation method) (below).

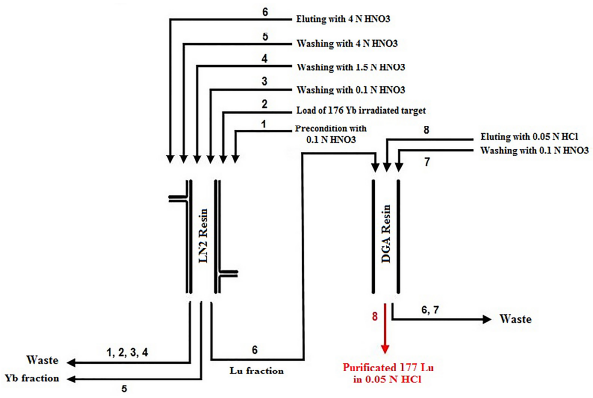

Fig 4. The flowsheet of EXC separation.

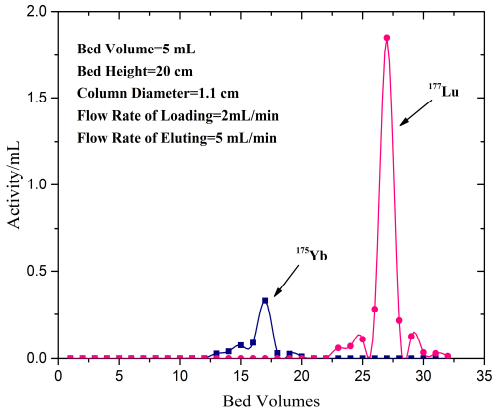

Fig 5. The resultant profile for the elution of ^{177}Lu in EXC separation method.

The effect of the initial mass of Yb on the resolutions of Lu and Yb was shown in Figure 6. By increasing the amount of Yb from 5 to 20 mg, a significant reduction in resolution was observed because of consuming a larger fraction of the column capacity and broadening of Lu peak considerably. So for separation in large quantities, using column with larger dimension and repeating the purification steps is necessary.

Temperature: The effect of temperature on separation of Yb and Lu on column 1 containing LN2 resin for 30ºC and 50ºC was shown in Figure 7. Although separation factor is higher at the lower temperature, but the elution curves are broader, therefore the column 1 was thermostated at 50 ºC using recirculating water.

Flow rate of load and elution: The effect of flow rate of loading and elution on separation of Yb and Lu was shown in Table 3. A peristaltic pump was used to adjust the flow rate to obtain the optimized condition for loading of irradiated target on a column and eluting of NCA ^{177}Lu.

Electro-amalgamation (ELM) separation

In ELM separation method, the irradiated target was dissolved in1mL 0.05N HNO_3. This solution contains ^{175}Yb, ^{169}Yb and ^{177}Lu (the gamma ray spectra of the irradiated target and electrolyte solution at the end of step2 were shown in Figure 8) was mixed with 15mL lithium citrate (0.15M) as an electrolyte. By using a constant potential of 10V and adjusting the pH of electrolyte to 6-7 for 45 minutes, electrolysis was done. After doing electrolysis, amalgam was separated from the cell through the stop-cock. In order to remove residual impurity of mercury in the electrolyte solution, Whatman filter paper was used. For removing any trace amount of Yb from the ^{177}Lu electrolyte, ELM separation was repeated using a fresh mercury cathode and platinum anode.

Table 2: Activities and elution yield of separation processes on LN2 resin column-1 and DGA resin column-2.

Loading of 15.4 mCi ^{177}Lu and 2.7 mCi ^{175}Yb on to the column 1 containing LN2 resin				
Separation processes	**Eluted Activity (mCi)**		**Eluted yield (%)**	
	^{177}Lu	^{175}Yb	^{177}Lu	^{175}Yb
Washing the column-1 with HNO_3 0.1N	N.D*	N.D	-	-
Washing the column-1 with HNO_3 1.5N	N.D	4.07×10^{-4}	-	0.015
Washing the column-1 with HNO_3 4N	6.32×10^{-3}	2.34	0.04	86
Elution the column-1 with HNO_3 4N	13.96	N.D	90	-
Washing the column-2 with HNO_3 0.1N	3.41×10^{-5}	N.D	0.002	-
Elution the column-2 with HCl 0.05 N	12.73	N.D	82	-

*N.D: Not Detected

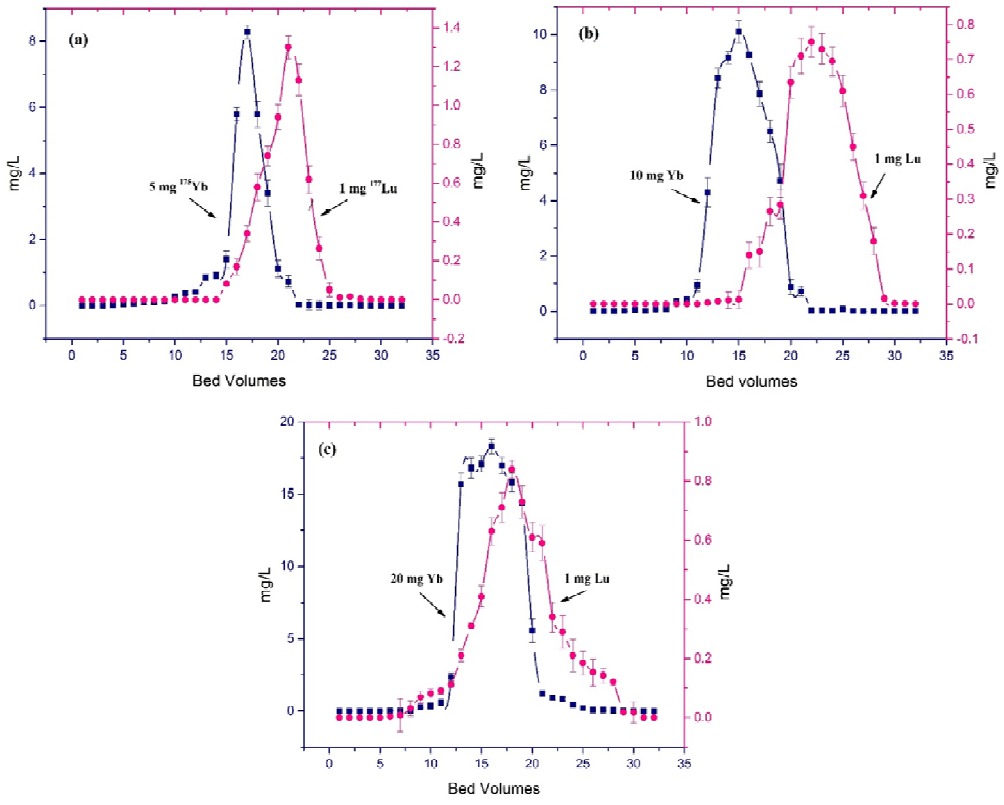

Fig 6. The effect of the initial mass of ytterbium: **a**) 5 mg, **b**) 10mg **c**) 20 mg (EXC separation method).

Activity and separation yield in three separation steps are given in Table 4. In order to optimize the condition of the ELM separation, the effects of the initial mass, potential, pH and time of electro-amalgamation process as well as number of cycles of electrolysis were investigated.

Initial mass of ytterbium target: The effect of the initial mass of the ytterbium on the efficiency of separation was shown in Figure 9. The experimental results showed that with increasing the mass of ytterbium up to 5-20mg, the efficiency of separation is increased.

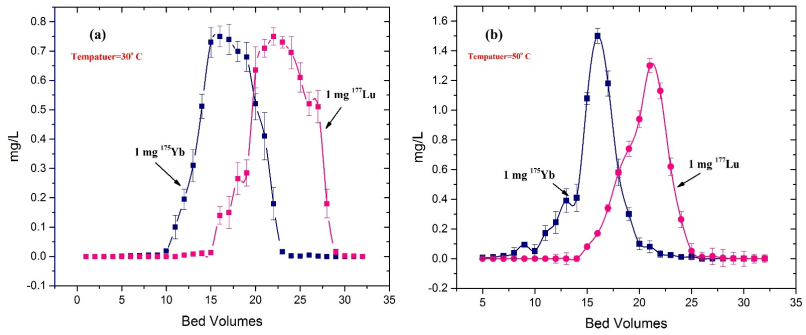

Fig 7. The effect of varying the temperature on separation of Yb and Lu on column 1: **a**) 30 ^{0}C, **b**) 50 ^{0}C mg (EXC separation method).

Table 3: The effect of flow rate of load and elution.

Flow rate of loading (ml/min)	Flow rate of eluting (ml/min)	Time of separation (hour)	Separation yield (%)
1	2	5	74
2	5	3.5	85
5	5	3	68.4
7	7	2.75	73

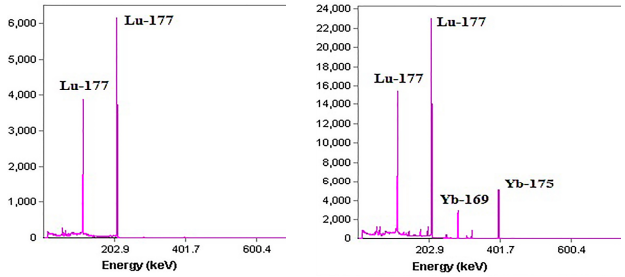

Fig 8. The gamma ray spectra of the irradiated $^{176}Yb(NO_3)_3$ target (right) and electrolyte solution at the end of step2 (ELM separation method) (left).

Table 4: Activity and separation yield in two separation steps.

Radionuclide	Activity (mCi)	Activity at the end of step 1 (mCi)	^{177}Lu yield at the end of step 1 (%)	Activity at the end of step 2 (mCi)	^{177}Lu yield at the end of step 2 (%)	Activity at the end of step 3 (mCi)	^{177}Lu yield at the end of step 3 (%)
^{177}Lu	7.3	6.7	91.78	5.93	81.23	4.83	66.16
^{175}Yb	2.9	0.03		N.D*		N.D.	
^{177}Lu	21.5	20.1	93.48	19.1	88.83	17.63	82
^{175}Yb	11.49	0.6		N.D		N.D	
^{177}Lu	27.60	26.21	94.96	23.21	84.09	21.65	78.49
^{175}Yb	13.3	0.4		N.D		N.D	

*N.D: Not Detected

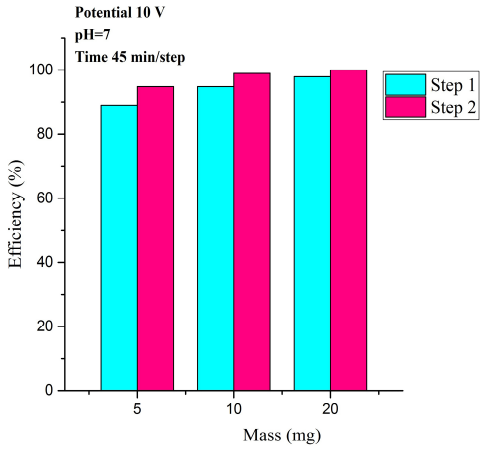

Fig 9. The effect of the initial mass of ytterbium on step 1: first purification, step 2: second purification in ELM separation method.

Potential: One of the effective factors to perform an electrochemical separation is applied potential. The separation efficiency as a function of applied potential was illustrated in Figure 10. It is shown that the efficiency of separation for 8, 9, 10 V is similar and it can be seen that the efficiency of separation increases with increasing potential.

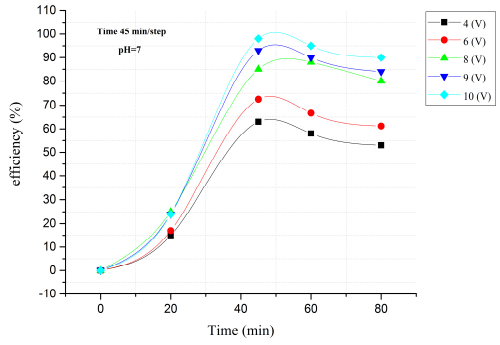

Fig 10. The efficiency of separation as a function of applied potential (ELM separation method).

pH: One of the most important factors of electrochemical separation is pH of aqueous electrolyte. Figure 11 shows the efficiency of separation as a function of the electrolyte pH. It can be observed that the efficiency percentage reaches a maximum at pH 7. Since the pH of the electrolyte tends to increase due to loss of H^+ ion during the electrolyze, a value between 6 and 7 for PH was adjusted. At higher pH, formation of ytterbium hydroxide prevents the transport of the ytterbium to the amalgam and at lower pH of the electrolyte, the amalgam started to decompose.

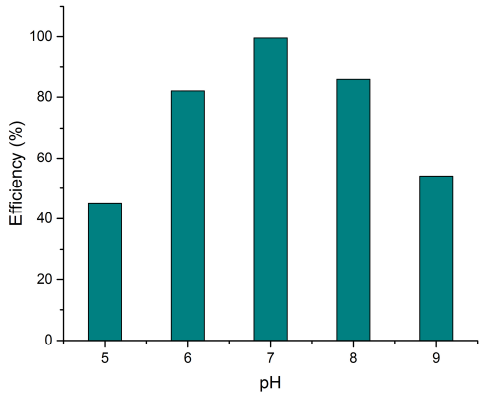

Fig 11. The efficiency of separation as a function of the electrolyte pH (ELM separation method).

Time between end of Yb amalgamation and Yb separation from the electrolyte solution: At the end of one separation stage, for reduction of the evolution of gaseous product on the platinum anode and clarify the electrolyte solution, before the separation of amalgam from electrolyte solution, 10-20 minutes of break were kept. The clarification of the electrolyte solution leads to oxidation of Yb^{2+} to the more stable Yb^{3+} and decomposition of Yb amalgam, as Yb^{3+} does not form an amalgam [30].

As can be seen in Figure 12, the separation efficiency was increased by removing of the amalgam from the electrolytic system immediately.

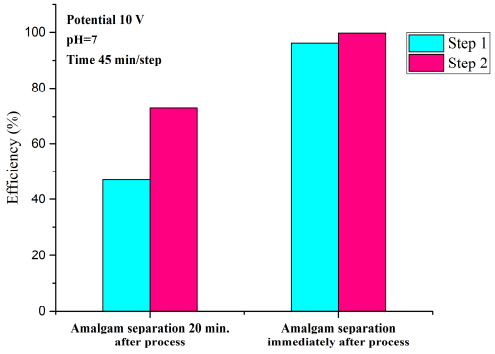

Fig 12. The effect of varying the period of time between end of Yb amalgamation and Yb separation from the electrolyte solution (ELM separation method).

Time: The separation efficiency as a function of time for a two-step process were illustrated in Figure 13. Results showed that among the three options of running the electrochemical separation, the optimum time was 45 minutes. As increasing of amalgamation step to 60 minutes contributed to decreasing of pH the electrolyte solution and decomposition of the amalgam and for the time 30 min/step the yield of production was less than the expected value.

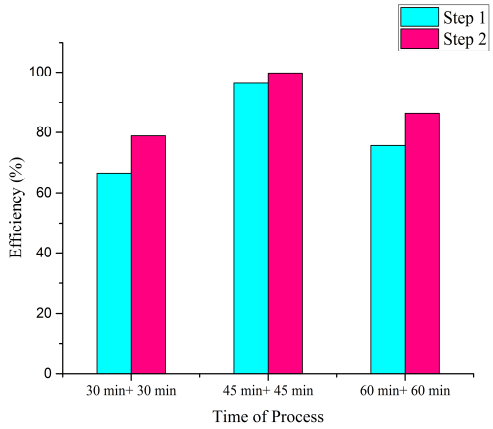

Fig 13. The efficiency of separation as a function of time of process (ELM separation method).

Numbers of steps: The results for two and three step of separation were presented in Figure 14. As can be seen, for two and three step of separation, the results are basically similar and adding a third step of separation had no effect on increasing the separation yield.

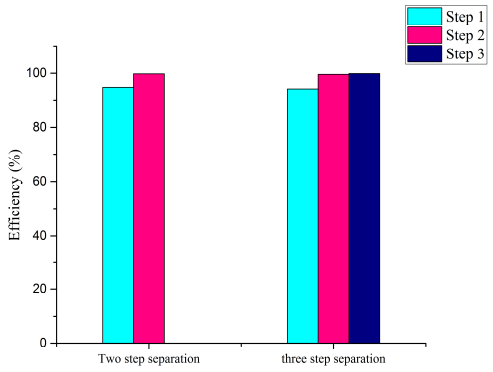

Fig 14. The effect of number of steps (ELM separation method).

Temperature: During the course of electrolysis, the electrolyte bath temperature should be maintained well below its boiling point. In this work, to maintain the temperature of the electrolyte at 25 ºC, a water-jacketed glass cell by circulation of cold water was used.

DISCUSSION

The specific activity of radionuclides is a very important factor for radiopharmaceutical applications. NCA radionuclides have the advantage of preparing radiopharmaceuticals with high specific activity. When the radionuclide is formed in such case will be NCA, the atomic number of isotope changes because of using the indirect production route. Radiochemical separation will be essential to separate the radionuclide from the target. As it was previously mentioned, several papers have reported the production of NCA ^{177}Lu [12-30]. But the methods reported by Horwitz et al. [23] and Chakravarty et al. [29] were found to be more efficient in separating of NCA ^{177}Lu from Yb target. Table 5 shows a comparison between EXC and ELM separation. One important parameter for separation of radionuclides is the length of the processing time. Many reactor or accelerator-based radioisotope products might miss its End of Cycle (EOC) activity during time interval consumed for adequate radioisotope production. Whereas, ^{177}Lu with a half-life of 6.7 days, demonstrates favorable characteristics to obtain an economic and a fast radioisotope purification procedure to deliver high specific activity of the purified radioisotope to nuclear medicine centers, for which a fast separation process is needed. Among different separation procedures, ELM separation is suitable for ^{177}Lu recovery from the other associated impurities. To produce ^{177}Lu, an enriched ytterbium target is used. The economic target material recovery is another important aim in a selected separation procedure. Experimental data has shown that ytterbium could easily be extracted using an EXC column by washing the column followed by decreasing the acidity of solution. It could be reused as the target material after converting to ytterbium salt. ELM separation ytterbium recovery from amalgam, however, needs some chemical processes and is time-consuming. EXC is robust to separate different radiolanthanides and due to required material and equipment is cost-effective separation method. The EXC process is more preferred for routine remote operation as well as for automation in shielded systems. However, the ELM separation is known as a fast procedure, simple in the operation, user friendly leading to less radiation exposure to the during the radionuclide separation. In comparison with ELM separation, the EXC procedure is time-consuming and HPGe detector could analyze many extracts (wash and eluent in any step) to achieve desired radionuclidic purity in any step while the ELM separation would deliver final two electrolyte solutions.

Table 5: The comparison between EXC and ELM separation method.

Method	Time (h)	Radionuclide purity (%)	^{177}Lu Yield (%)	Recovery of Yb target	Simplicity	Production in large quantities	Radioactive waste	Automation
EXC	3.5	99.99	82	Easy	Feasible but a lot of steps to perform and analyze	Feasible but limited	More waste	Preferred
ELM	2	99.99	88.83	Radiochemical processing	Easy	Preferred	Minimum waste	-

More factors should be optimized in EXC procedure to keep suitable resolution in Yb and Lu peaks in comparison with ELM separation. The stability of the optimized factors is higher in an electrochemical process. Evidently, Lu does not form any amalgam with mercury, which enhances surpass of ELM than EXC while in the EXC procedure if the conditions is not optimized, Lu and Yb peaks could overlap. To separate high amount of the Yb target, electrochemical procedure is preferable due to the fact that high amount of Yb (200 mg) could be isolated in one step separation. The EXC procedures for separation of a large amount of Yb target need three step separation, six chromatography columns, data analysis of any step and high amount of resin is required. The ELM method is unsusceptible to radiolytic damage and generates minimum radioactive waste.

CONCLUSION

The results showed that under appropriate condition and procedures, NCA ^{177}Lu can be produced in a moderate flux reactor and can act as an effective agent in the growth of ^{177}Lu-based radiopharmaceutical. In this study, two separation methods: EXC and ELM were applied for production of NCA ^{177}Lu by TRR. The NCA ^{177}Lu was produced by EXC and ELM separation methods with a radionuclide purity of 99.99%. The ^{177}Lu production yield by EXC and ELM procedures were 82% and 88.83% respectively. In addition, a comparison between two separation methods was carried out. The EXC separation method is more appealing in term of target recovery, inexpensive method, and automation. However, ELM separation method has some advantages by considering the factors such as separation time, minimum generation of waste, simplicity and ease of performance. In general, apart from being more costing, ELM separation is preferred over EXC method.

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