PASTA project: optimization of a radiochemical separation of Sc from Ti

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INTRODUCTION

Scandium-47 ($T_{1/2}$ = 3.35 d), due to its β- emission ($E_{\beta av}$=162.0 keV) and by exploiting its γ-emission at 159 keV (68.3%), is one of the few radionuclides that are intrinsically suitable for both therapeutic and diagnostic purposes. It thus can be used as single theranostic radionuclide delivering cytotoxic dose to small-medium sized tumors and performing SPECT/CT imaging studies [1]. Moreover, ^{47}Sc together with the β+ emitters ^{44}Sc or ^{43}Sc ($T_{1/2}$= 3.97 h and 3.891 h respectively) represents some examples of ideal matched pair for theranostic applications [2]. From the chemical point of view, Sc(III) has similar coordination chemistry to Lu(III) and Y(III), allowing the use of ligands already developed for the two well-established therapeutic radionuclides, ^{177}Lu ($T_{1/2}$=6.647, $E_{\beta av}$ =134.2 keV) and ^{90}Y ($T_{1/2}$=64.0 h, $E_{\beta av}$ =933.6 keV). The main advantage of ^{47}Sc-labelled compounds, and theranostic radionuclides in general, is the possibility to perform low-dose imaging studies prior therapy with the same radiopharmaceutical, allowing the selection of patients with a significant chance of responding to the specific treatment. The critical issue in the use of ^{47}Sc is the lack of availability in sufficient amount and at a reasonable cost. Aiming at answering to the increasing request of ^{47}Sc production for clinical applications the PASTA project (Production with Accelerator of Sc-47 for Theranostic Applications), funded by CSN5 with the Bando Giovani Ricercatrici e Ricercatori N. 18203 (2017-2018) and developed in the framework of LARAMED at INFN-LNL, was thus focused on the measurement of the most promising proton-induced nuclear reactions cross section, contaminant radionuclides evaluation (such as ^{46}Sc, half-life 83.79 d) and the study of a radiochemical procedure to extract ^{47}Sc from the irradiated target.

Aiming to the clinical application, after the ^{47}Sc cyclotron production, the desired product has to be separated and purified from the target and contaminants. In designing and optimizing a separation and purification radiochemical method, the chemical form of the product, that should be suitable for radiolabeling various molecules, should be taken into account. A variety of ^{47}Sc separation methods from metallic Ti, TiO_2 and $CaCO_3$ targets based on solvent extraction by tri-n-butyl phosphate (TBP), extraction chromatography or cation and anion exchange processes have been reported in literature [3, 5-7].

In the case of calcium targets, all proposed methods are simple, fast and allow to recover high percentage of the desired radionuclide and to apply a simple chemical procedure for the target recovery [8]. In the case of titanium targets, the proposed procedures are longer and sometimes requiring time-consuming dissolution and evaporation steps because of the difficulties in dissolving the target, in particular in the TiO_2 form. Moreover, in the majority of the proposed procedures, the use of hydrofluoric acid is required and accordingly, the employment of proper and resistant materials to this hazardous acid is mandatory [9].

Recently some procedures have been developed to dissolve titanium in metallic form using hot HCl solution (8M), thus avoiding the use of hydrofluoric acid, and the separation of ^{43}Sc from ^{46}Ti was performed using a DGA extraction chromatographic resin [7]. This resin selectively retains Sc, while Ti is eluted off, from a HCl 4M solution. Pourmant et al. [10] also reported the strong retention of Sc(III) on DGA resin and the negligible retention of Ti(III) at HCl molarities below 6 M. We have also investigated a similar procedure that allows obtaining scandium in a water solution using only DGA resin.

EXPERIMENTAL

Starting from the literature outcomes we have investigated a separation and purification procedure based on DGA-N extraction chromatographic resin (normal, particle size 50-100µm, TrisKem International, Bruz, France).

The radiochemical separation has been developed with cold materials (non-radioactive) by simulating the real experimental conditions of a titanium metal target after the irradiation. The efficiency of the procedure has been evaluated by ICP-OES analysis by quantifying element trace in all the solutions. To perform our tests, we have always prepared a mock solution by dissolving 10 mg of natural metallic titanium (thickness=20µm, purity=99.6%) in 3ml of HCl 4M and adding 2µl of a 1000 mg/l scandium standard solution in HNO3 (5%).

The steps of the separation procedure are hereafter briefly described. 85mg of DGA resin were packed in a 1 ml column and conditioned with 5ml of HCl 4M. The mock solution, containing Ti and Sc, was loaded on the resin, the Sc was retained while the Ti was eluted off and collected in the first sample called LOAD. The resin was then washed with 5ml of HCl 4M to ensure complete removal of Ti(III) and collected in the sample called WASH. Finally, the Sc (III) was eluted from the resin with 4ml of HCl 0.1M and collected in the sample called ELUTION (Figure 1).

Several tests have been conducted to select the proper eluent (water, saline, HCl) and volume.

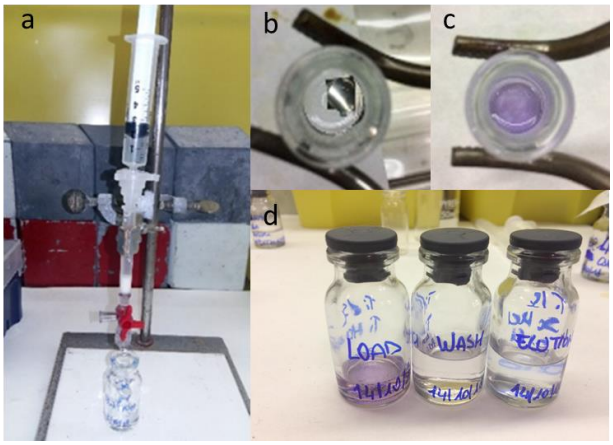

Fig. 1. Pictures of (a) the experimental setup (DGA resin), a titanium metal target before (b) and after (c) the dissolution and (d) the three samples (load, wash, elution) collected from the resin.

Aiming to maximize the scandium/titanium separation yield and concentrate the final product in a compatible solution with radiolabeling procedures, the scandium solution (4ml of HCl 0.1M), eluted from the first resin, was rinsed with 1.5 mL of concentrated HCl to get a final HCl molarity around 2.5-3. The solution was loaded onto a second 1 mL column cartridge, containing ~30 mg DGA-N and after washing with 5.0 mL of 2.5M HCl, Sc(III) was eluted with 0.7 mL of water. All eluted fractions were analyzed by ICP-OES (Optima 3100 XL, Perkin Elmer, wavelengths: Ti = 336.121 nm; Sc = 361.383 nm).

A summary of the experiments and separation efficiency achieved by analysing ICP-OES results is reported in table 1.

Table 1. Summary of the separation tests performed and their efficiency. (DL) detection limit: DL (Sc) = 40 ppb; DL* (Ti) = 0.2 ppm.

test#	sample	eluent	Vol (ml)	Ti ppm	Sc µg
#1	LOAD	HCl 4M	5		< DL
	WASH	HCl 4M	5		< DL
	ELUITION	HCl 0.1M	4	1.06	2.144
#2	LOAD	HCl 4M	2		< DL
	WASH	HCl 4M	5		< DL
	ELUITION	HCl 0.1M	4	0.69	2.376
#3	LOAD	HCl 4M	1.5		< DL
	WASH	HCl 4M	6		< DL
	ELUITION	HCl 0.1M	4	2.81	2.88
#4	LOAD	HCl 4M	1.5		< DL
	WASH	HCl 4M	6		< DL
	ELUITION	water	4	3.44	2.7
#5	LOAD	HCl 4M	1.5		< DL
	WASH	HCl 4M	6		< DL
	ELUITION	saline	4	9.1	2.18
#6	LOAD1	HCl 4M	1.5		< DL
	WASH 1	HCl 4M	6		< DL
	LOAD2	HCl 2.5-3M	5		< DL
	WASH 2	HCl 2.5M	5		<DL
	ELUITION2	water	0.7	<DL*	2.184

RESULT AND DISCUSSION

The Sc recovery yield is considered to be quantitative since all the amount of Sc in the mock solution is completely recovered in the ELUTION sample.

The two DGA resins procedure (#6) (Figure 2) has turned to be the best separation/purification keeping Ti below the ICP-OES detection limit (<0.2ppm). This procedure lasts approximately 20 minutes and is easily automatable.

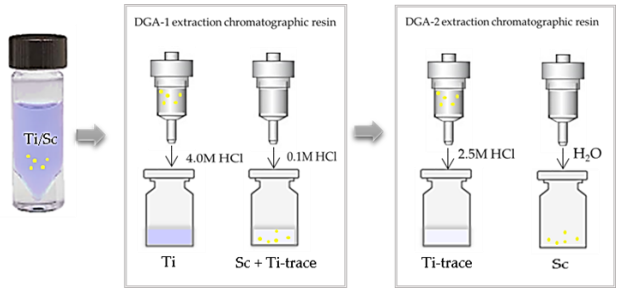

Fig. 2. Schematic representation of the separation of scandium is from titanium using DGA-extraction chromatographic resin (test #6).

CONCLUSION

This work describes the experimental tests and results achieved within the PASTA project on the separation and purification of Sc from the target of metallic Ti. The radiochemical procedure selected can be easily automated in view of an effective clinical application.

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