

Isolation of ^{117m}Sn from Proton-irradiated Titanium–Antimony Intermetallic Compound

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Abstract—Various methods have been developed for the extraction of a promising medical radionuclide ^{117m}Sn from proton-irradiated TiSb intermetallic compound, a target material suitable for irradiation with an intense beam of accelerated protons. To separate radiotin from Ti, Sb, and radionuclides of other elements, methods of ion-exchange chromatography and liquid extraction were used, in particular, the anion-exchange separation of tin and titanium in the form of a peroxide complex in HCl solution, extraction of tin with benzene from iodide solutions, and chromatographic purification on silica gel from citrate solutions. As a result, ^{117m}Sn of high purity, which meets the requirements for nuclear medicine, was obtained.

Keywords: ^{117m}Sn , TiSb intermetallic compound, proton irradiation, separation of radiotin and titanium, ion exchange, extraction.

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In recent decades, the therapy of oncological and other human diseases with the use of radiopharmaceuticals (RP) has developed significantly. More than 80% of cancer patients suffer from bone metastases [1]. Interstitial radionuclide therapy using RP based on radionuclides releasing electrons is one of the effective methods of treating patients with widespread bone metastases. RP based on the ^{117m}Sn radionuclide (in particular, $^{117m}\text{Sn}^{4+}\text{DTPA}$) [2–5] have a number of advantages over other drugs. The decay of the metastable radionuclide ^{117m}Sn is accompanied by the release of monoenergetic conversion electrons (127, 129, and 152 keV) with a short and discrete range of 0.2–0.3 mm in biological tissue. Soft radiation leads to a local effect on tumor cells without damaging healthy tissues. The γ -radiation (159 keV) during the decay of ^{117m}Sn may be used to control the therapeutic effect (theranostics). Clinical trials of drugs $^{117m}\text{Sn}^{4+}\text{DTPA}$ for the relief of bone pain, $^{117m}\text{Sn}^{4+}\text{DOTA}$ -annexin for the treatment of cardiovascular diseases, and the ^{117m}Sn colloid for the relief of pain in osteoarthritis and rheumatoid arthritis are being successfully carried out [1, 6].

Until recently, ^{117m}Sn was produced mainly from the reactions of stable tin isotopes, $^{116}\text{Sn}(n,\gamma)^{117m}\text{Sn}$ or $^{117}\text{Sn}(n,n'\gamma)^{117m}\text{Sn}$, with neutrons. In this case, the

specific activity of ^{117m}Sn did not exceed 740 GBq/g (20 Ci/g) [2, 7]. The presence of stable tin seriously limits the possibilities of medical application of the reactor-produced ^{117m}Sn . A product with a high specific activity can be obtained via reactions with accelerated charged particles, of which two approaches are the most promising and demonstrate comparable production rates of ^{117m}Sn : $^{nat,121,123}\text{Sb}(p,x)^{117m}\text{Sn}$ [8, 9] and $^{116}\text{Cd}(\alpha,3n)^{117m}\text{Sn}$ [10,11]. Nowadays, powerful and compact cyclotrons of the Cyclone 70-type, developed and manufactured by the IBA Company (Belgium), are becoming more widespread, capable of accelerating proton beams with an intensity of more than 300 μA to an energy of 70 MeV. Such cyclotrons are successfully applied for large-scale production of radioisotopes, mainly for medical purposes [12, 13]. On the basis of experimentally determined cross sections, it was shown [14] that the ^{117m}Sn radionuclide can be produced by proton irradiation of an antimony target with an initial energy of 145 MeV and below. Irradiation of natural antimony or antimony enriched with ^{123}Sb with the proton energy 55 or 70 MeV, respectively, leads to the formation of ^{117m}Sn , which contains a trace amount of the undesirable long-lived radioisotope ^{113}Sn . The presence of another long-lived radioisotope ^{119m}Sn ($T_{1/2} = 293$ days), as impurity, which releases soft

gamma radiation during decay into stable ^{119}Sn , does not interfere with medical use of ^{117m}Sn . Therefore, the implementation of the $^{\text{nat},123}\text{Sb}(p,x)^{117m}\text{Sn}$ approach on cyclotrons of the Cyclone 70-type for producing large amounts of ^{117m}Sn of medical quality seems especially promising. In [15], we proposed a method for obtaining no-carrier-added ^{117m}Sn from a thick target of metallic antimony irradiated with protons. After dissolution of the antimony target, the radiotin was isolated by liquid-liquid extraction (LLE) with dibutyl ether, followed by exhaustive purification on silica gel. The method provides production of up to 3 Ci (100 GBq) ^{117m}Sn of high radionuclidic purity with a specific activity of about 1000 Ci/g (more than 40 GBq/mg).

However, since metallic antimony has low thermal conductivity, low melting point and high vapor pressure, antimony targets cannot withstand prolonged exposure to high-intensity proton currents. In addition, antimony actively interacts with many materials that are usually used for the manufacture of the target shell, which leads to its radiation damage. Instead of metallic antimony, intermetallic compounds, such as TiSb , NiSb , and AlSb , were considered as a target material, of which TiSb turned out to be the most promising [16]. The TiSb properties, unique in many respects, have been studied since the 1950s [17]. The compound combines high stability (the enthalpy of formation is estimated as -167 kJ/mol [18]), and a high melting point of 1160°C with pronounced metallic properties, including high electrical and thermal conductivity. According to our estimate, the value of the latter is twice the thermal conductivity of titanium and antimony taken separately.

In the chemical separation of ^{117m}Sn from irradiated TiSb , it is necessary to remove not only macro-quantities of antimony, but also macroquantities of titanium. Previously, removal of antimony was studied in [15]. Removal of titanium is difficult due to the similarity of its chemical behavior with that of tin; in the few studies described in the literature, extraction and chromatographic separation methods are used.

Sn(IV) can be extracted with methyl isobutyl ketone from 7 M HCl solutions, while Ti(IV) remains in the aqueous phase [19]. Then, the tin is reextracted with dilute solutions of hydrochloric or sulfuric acid [20].

In analytical practice, tin is also extracted with benzene from HI solutions. The extraction of tin with

benzene proceeds most efficiently at a perchloric acid content of 4.66 M, sulfuric acid content of 1 M (total acidity 6.6 M), and a potassium iodide content of 0.5 M. In this case, titanium and antimony, as well as I–III metals, including indium and scandium, are not extracted [21]. Tin is reextracted with a 1–2 M HCl solution. However, this technique was developed only for the analytical determination of milligram amounts of tin [22]; its applicability for isolation of no-carrier-added radiotin has not been studied.

Chromatographic separation of Ti(IV) from ions of other metals is possible by sorption of titanium in the presence of hydrogen peroxide on a weakly basic anion exchanger Amberlite CG-4B [23]. A similar behavior of Ti(IV) is observed on AG 50W-X8 and Dowex 50W cation exchangers in 0.05 M H_2SO_4 solutions with the addition of 1% H_2O_2 [24]. Ti(IV) is not adsorbed on strongly basic anion-exchange resins (Dowex 1×8 and AG 1×8) [25]. As known, Ti forms peroxide complexes $[\text{TiO}(\text{H}_2\text{O}_2)]^{2+}$, positively charged and stable in strongly acidic solutions. At the same time, Sn forms the anionic complex $[\text{SnCl}_6]^{2-}$ in strong hydrochloric acid solutions; therefore, the separation of oppositely charged Sn and Ti complexes can be carried out both on cation-exchange and anion-exchange resins. For example, when a hydrochloric acid solution of Sn and Ti containing a minor excess of H_2O_2 , is passed through an anion-exchange resin, $[\text{SnCl}_6]^{2-}$ anions are adsorbed, whereas $[\text{TiO}(\text{H}_2\text{O}_2)]$ cations pass through the column. Then, tin is desorbed by passing through the column solutions that decompose the $[\text{SnCl}_6]^{2-}$ anionic complex. For separating trace amounts of tin from macroquantities of titanium, this method is preferable, since it does not require large volumes of sorbent.

Basically, the methods presented in the literature have been developed for the separation of macroquantities of Sn, Sb, and Ti, while the behavior of radionuclides in the “no-carrier-added” state can differ significantly. When producing ^{117m}Sn of high specific activity, it is necessary to separate the macroquantities of Sb and Ti from the ultramicroquantities of Sn. In addition, proton irradiation of antimony and titanium produces other radionuclides, capable of affecting purity of the target product, and they must also be separated from tin. In this study, we propose options for the extraction of ^{117m}Sn with a high specific activity from the proton-irradiated antimony–titanium intermetallic compound to prepare RP.

EXPERIMENTAL

Preparation and irradiation of experimental targets. The radionuclides ^{124}Sb (carrier-added), ^{113}Sn , $^{121\text{m}}\text{Te}$, $^{123\text{m}}\text{Te}$, and $^{114\text{m}}\text{In}$ (no-carrier-added) used in this study for model experiments were obtained from irradiated antimony targets by the method described in [9]. ^{44}Ti was supplied by CJSC Cyclotron (Obninsk).

Antimony–titanium intermetallic compound was formed by argon-arc melting of antimony and titanium powder in a molar ratio of 1: 1 [16]. To prepare the target, the crushed intermetallide was placed in an electron-beam welded titanium container 5 mm thick and was heated at a temperature of 910°C and a pressure of 150 MPa in argon for 1.5 h [26].

To produce radionuclides and study their chemical behavior, targets from the TiSb intermetallic compound and also from metallic antimony were irradiated. The activity of the used radionuclides was in the range of several μCi (~ 100 kBq). Irradiation was carried out at a high-precision accelerator of the Institute for Nuclear Research (Troitsk, Moscow) with the initial proton beam energy varied from 110 to 140 MeV and at the current 1–50 μA [27].

Materials and reagents. For preparing aqueous solutions, we used concentrated acids (HCl , HNO_3 , and H_2SO_4) and deionized water from a Millipore Simplicity water purification unit.

Antimony was extracted with dibutyl ether. For chromatographic separation of titanium, we used: (1) strongly basic monofunctional anionites AG 1 \times 8 (Bio Rad, USA) and Dowex 1 \times 8 (Dow, USA) based on a styrene copolymer with divinylbenzene containing $-\text{N}^+(\text{CH}_3)_3$ as the main functional group; (2) Dowex 50 \times 8 cation exchanger (Dow, USA) based on a styrene copolymer with divinylbenzene containing $-\text{SO}_3\text{H}$ as the main functional group. Particle size is 100 mesh, crosslinking, 8%, and bulk density of resins, 0.8 g/mL. Macroquantities of titanium were removed by extraction with methyl isobutyl ketone, benzene, and KI (all chemically pure grade). The final purification of the radiotin was carried out by chromatography on silica gel with a particle size of 100–160 μm . The reagents were of special purity or chemically pure grade.

Experimental technique. In model solutions used to develop the technique for separating radiotin from the titanium – antimony intermetallide, the maximum concentrations of the macrocomponents were 75 and

30 g/L for antimony and titanium, respectively. The above concentrations were chosen by assuming that the mass of the target for the production of large amounts of $^{117\text{m}}\text{Sn}$ is about 40 g, of which 29 g are antimony and 11 g, titanium. Most of the antimony in the presence of titanium was separated by extraction with dibutyl ether from a 10 M HCl solution [15].

Macroquantities of titanium were removed from radiotin by both chromatography and extraction.

For the chromatographic purification of radiotin from titanium, we prepared 10 mL of model solutions containing Ti, Sb, H_2O_2 , 6 M HCl , and a label (^{113}Sn , ^{124}Sb , $^{121\text{m}}\text{Te}$, $^{123\text{m}}\text{Te}$, and $^{114\text{m}}\text{In}$). The content of Ti varied from 1.5 to 30 g/L, the Sb content varied from $(2-5)\times 10^{-3}$ g/L, a value corresponding to the addition of the ^{124}Sb label, to 14.4 g/L, the H_2O_2 : Ti molar ratio was from 1 : 1 to 1.5 : 1. The label was obtained from an irradiated antimony target. The sorption and desorption of tin was performed under dynamic conditions by passing the solution through a column ($d = 0.6$ cm) with a sorbent layer 6 cm high.

Two anion-exchange resins were used as sorbents: Dowex 1 \times 8 and AG 1 \times 8. Before filling the column, the sorbents were kept in 6 M HCl for 12 h. First, 10 mL of the initial solution was passed through the filled column at a rate of 0.8 mL/min and then 40–50 mL of a 6 M HCl washing solution passed. For desorption of radiotin, 1–4 M HNO_3 solutions were used.

Model solutions used for extraction have a total acidity of 6.6 M and a volume of 30 mL and contain 4.66 M HClO_4 , 1 M H_2SO_4 , Ti (20 g/L), Sb in the form of antimony chloride with a concentration from $(2-5)\times 10^{-3}$ to 1 g/L, and 0.2–1 M KI. Also, (^{113}Sn , ^{124}Sb , $^{121\text{m}}\text{Te}$, $^{123\text{m}}\text{Te}$, and $^{114\text{m}}\text{In}$) produced from the irradiated antimony target was added to the model solution as label. To prepare a model solution, a weighed portion of KI was preliminarily dissolved in a minor amount of water and added, with vigorous stirring, to a mixture of HClO_4 and H_2SO_4 acids. Iodine was formed, and the larger the weight of KI sample, the darker the solution. However, even at low KI concentrations, when the solution was light yellow, a precipitate formed, presumably HIO . The solution was left for a day to reach equilibrium. Then, it was filtered, and the label and stable titanium and antimony were added, and after that, the extraction was performed. The prepared solution was stored for no more than a week. As the organic phase, we used benzene previously saturated with a solution of 4.66 M HClO_4 +

Table 1. Main radionuclides in the irradiated TiSb intermetallic compound [28]

Radionuclide	Half-life	E_γ , keV	γ -Line yield, %
^{114m}In	49.5 days	190.3	15.6
		558.4	4.4
		725.2	4.4
^{113}Sn	115.1 days	255.1	2.1
		391.7 (^{113m}In)	65.0
^{117m}Sn	14.0 days	156.0	2.1
		158.6	86.4
^{124}Sb	60.2 days	602.7	97.8
		1691.0	47.6
^{121m}Te	164.2 days	212.2	81.5
		1002.1	2.5
^{123m}Te	119.2 days	159.0	84.0
^{44}Ti	59.1 years	67.9	93.0
		78.3	96.4
^{46}Sc	83.8 days	889.3	99.98
		1120.5	99.99

1 M H_2SO_4 . Extraction from 30 mL of the working solution was carried out successively with two portions of benzene, 10 mL each. At each stage, the stirring time of the phases was 30–40 s, and separation time, 10 min. The radiotin was reextracted in 60 mL of 1.5 M HCl (stirring time 5–6 min, and separation time, 17–20 min).

At the final stage, exhaustive purification and concentration of radiotin on silica gel from a model solution of 2 M HNO_3 labeled with ^{113}Sn , ^{124}Sb , ^{121m}Te , and ^{44}Ti was performed, according to the procedure described in detail in [15].

To study the interaction of the TiSb intermetallic compound with acids, nonirradiated samples weighing from 0.5 to 20 g were dissolved by heating in concentrated HCl, to which H_2O_2 or concentrated HNO_3 were added, as oxidizing agent. The completeness of dissolution was controlled by weighing the undissolved residue. The content of titanium and antimony in the residue and the concentration of antimony in the solution were calculated from results of the spectrophotometric determination of the titanium concentration in the solution.

For testing the developed technique, we manufactured, irradiated, and processed an experimental target of titanium – antimony intermetallic compound.

An intermetallic compound with a mass of 16 g was dissolved according to the procedure worked out on nonirradiated samples. The concentration of antimony

and titanium in the working solution was 60 and 24 g/L, respectively. Most of the antimony was removed from the solution by extraction with dibutyl ether (three stages of extraction with dibutyl ether, previously saturated with 10 M HCl [15]).

One portion of the aqueous phase was purified from titanium by chromatography on anion exchangers, and the other, by extraction with benzene from iodide solutions using the optimal conditions found in model experiments. The final purification of radiotin on silica gel from citrate solutions was performed, as described in [15].

Analytical measurements. The radionuclides (Table 1) present in the solution and on the sorbent were determined by the γ -spectrometric method with a high purity ORTEC GEM15P4-70 Ge detector. The γ -spectra were interpreted using the Gamma Vision 32 software. To analyze the chemical behavior of the radiotin, we used not only the target radionuclide ^{117m}Sn , but also the longer-lived impurity ^{113}Sn .

Macroquantities of titanium were determined spectrophotometrically with hydrogen peroxide (absorption maximum 416 nm, $\epsilon_{416} = 810 \text{ L/mol cm}$) and diantipyrylmethane (DAM). Ti (IV) forms a strong complex compound with DAM in 0.5–4 M HCl with an absorption maximum at 389 nm. The absorption coefficient $\epsilon_{389} = 3.3 \cdot 10^4 \text{ L/mol cm}$ is much higher than that of H_2O_2 . The determination technique is described in [29].

Table 2. Extraction of antimony with dibutyl ether from a solution of the TiSb intermetallic compound containing ^{113}Sn , ^{124}Sb , and ^{44}Ti radioisotopes

Isotope	Component concentration, %					
	1 st stage of extraction		2 nd stage of extraction		3 rd stage of extraction	
	Aqueous phase	Organic phase	Aqueous phase	Organic phase	Aqueous phase	Organic phase
^{44}Ti	>99.8	<0.2	>99.8	<0.2	>99.8	<0.2
^{113}Sn	98.7	1.3	97.3	1.4	96.0	1.3
^{124}Sb	2.8	97.2	<0.4	2.8	<0.3	<0.3

RESULTS AND DISCUSSION

Isolation of no-carrier-added $^{117\text{m}}\text{Sn}$ from an irradiated antimony target is not an easy task, since these elements have similar chemical behavior. In the case of the separation of $^{117\text{m}}\text{Sn}$ from the TiSb intermetallic compound, the task is complicated by the need to purify also from titanium, which also exhibits chemical properties close to that of tin. Therefore, the main task of this study was the efficient separation, providing a high chemical yield, of radiotin from the macrocomponents of antimony and titanium.

For purification from the main amount of antimony in the presence of titanium, we used extraction with dibutyl ether, which was described previously in the absence of titanium in [15]. Extraction was performed from a model 10 M HCl solution containing 55 g/L Sb, 20 g/L Ti, and a label (^{113}Sn , ^{124}Sb , and ^{44}Ti) (Table 2). The study showed that following three successive extractions, more than 99.7% of antimony passes into dibutyl ether, while radiotin and titanium remain in the aqueous phase. After the first stage of extraction, the concentration of antimony decreases to 1.5 g/L. After three stages, it may be reduced to 0.1 g/L. More than 95% of titanium and radiotin remain in the aqueous phase. It was found that the extraction of antimony in the presence of titanium proceeds in the same way as in its absence.

For the subsequent purification of radiotin from titanium macroquantities, both chromatography on strong anion exchangers with the addition of hydrogen peroxide and extraction with benzene from iodide solutions were used.

Chromatographic separation of radiotin from titanium. According to the literature data [24], Ti (IV) is well sorbed on the Dowex 50W-X8 cation exchanger in the presence of hydrogen peroxide due to the formation

of positively charged complexes $[\text{TiO}(\text{H}_2\text{O}_2)]^{2+}$. These complexes are stable in acidic media, including HCl, in which tin forms the anionic complexes $[\text{SnCl}_6]^{2-}$. Our preliminary experiments showed that Ti macroquantities are not sorbed from 2 M HCl and are not completely sorbed from 1 M HCl. The ion-exchange separation of radiotin from titanium was carried out from 0.5 M HCl, while the titanium concentration was reduced by a factor of 20. However, this method is not entirely suitable for solving our problem, since large volumes of sorbent are required to remove macroamounts of titanium, which should be disposed and lead to the loss of radiotin.

The separation of radiotin from titanium on strongly basic anion exchangers turned out to be more promising approach. The above possibility was studied on model solutions. The chromatographic procedure consisted of passing a hydrochloric acid solution of radiotin and titanium, containing a small stoichiometric excess of H_2O_2 , through an anion exchange resin. In this case, $[\text{SnCl}_6]^{2-}$ anions were sorbed on the column, while $[\text{TiO}(\text{H}_2\text{O}_2)]^{2+}$ cations passed through the column. The column was washed with 6 M HCl to remove titanium. The titanium concentration in the washing solution and, as a consequence, in the target product depended on the degree of purification of the initial solution from macroamounts of antimony (Fig. 1).

Figure 1 shows that an increase in the antimony concentration has adverse effect on the purification from titanium. Next, we compared the efficiency of purification of radiotin from titanium, tellurium, and antimony residues on two strongly basic anion exchangers: Dowex 1×8 and AG 1×8 .

Both resins, similar in composition but differing in brands, have approximately the same effect in relation to tin, tellurium, and antimony radionuclides. At the same time, they differ in relation to titanium (Fig. 2). Figure 2 shows that titanium is more easily washed out of a

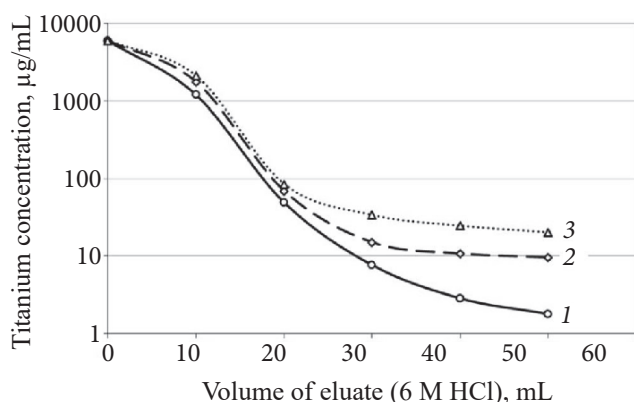


Fig. 1. Dependence of the titanium concentration in a 6 M HCl washing solution on the concentration of antimony in the initial solution. Sorbent AG 1×8 , column 0.6 cm in diameter and 6 cm in height, flow rate 0.8 mL/min. Antimony concentration, g/L: (1) $(2-5) \cdot 10^{-3}$, (2) 3.6, and (3) 14.4.

column filled with AG 1×8 , especially in the presence of macroamounts of antimony. Therefore, further experiments were performed with AG 1×8 resin.

After washing, part of tellurium remains on the column, in addition to radiotin. Radiotin was eluted with a nitric acid solution, which decomposes the anionic complex. Table 3 shows the dependence of the amount of radiotin remaining in the adsorbed state on the nitric acid concentration. With an increase in the HNO_3 concentration, the yield of radiotin increases, while tellurium radionuclides start to desorb simultaneously.

Optimal for elution is 2 M HNO_3 . In this case, a radiotin yield of about 90% is achieved, and the content of tellurium radionuclides is reduced by about 2-fold. Heating nitric acid to 40°C increases the radiotin yield up to 98%.

A high content of antimony in the initial solution not only has adverse effect on the removal of titanium, but also decreases the yield of radiotin, which can be seen from the integral curves of ^{113}Sn elution at various

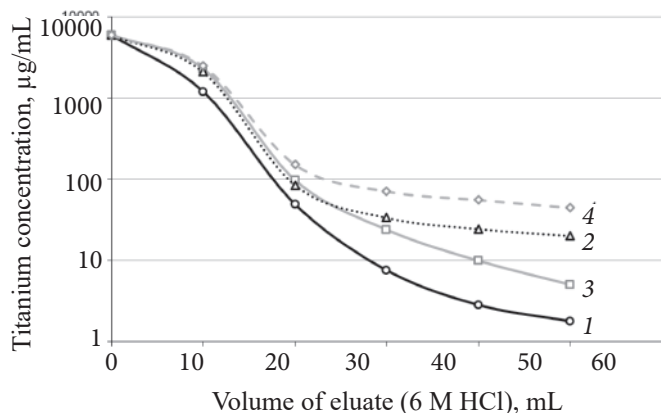


Fig. 2. Influence of the brand of anion-exchange resin and the concentration of antimony in the initial solution on the concentration of titanium in a 6 M HCl washing solution. Column 0.6 cm in diameter and 6 cm in height, flow rate 0.8 mL/min. Curve: (1) AG 1×8 , $c(\text{Sb}) = (2-5) \cdot 10^{-3}$ g/L; (2) AG 1×8 , $c(\text{Sb})$ 14.4 g/L; (3) Dowex 1×8 , $c(\text{Sb}) = (2-5) \cdot 10^{-3}$ g/L; (4) Dowex 1×8 , $c(\text{Sb})$ = 6.5 g/L.

concentrations of antimony in the initial solutions (Fig. 3). Increasing the antimony concentration in the solution to 3.6 g/L reduces the radiotin yield to 90%. Thus, the presence of antimony with a concentration on the order of 1 g/L will be quite acceptable for efficient separation of ^{117m}Sn and titanium at this stage.

Change in the chromatographic behavior can be followed in Fig.4, demonstrating curves of elution of antimony from the column upon washing with a 6 M HCl and desorption of radiotin in a 2 M HNO_3 on the antimony concentration in the initial solution. As seen, with an increase in the concentration of antimony in the initial solution, it is less retained by the sorbent upon passage of 6 M HCl and is desorbed with 2 M HNO_3 by a broader peak.

Based on the above dependences, the following optimal parameters of the anion-exchange separation of radiotin and titanium were determined:

– AG 1×8 is the most preferred anion-exchange resin for separation;

Table 3. Activity of ^{113}Sn and ^{121m}Te remained on the column ($d = 0.6$ cm, sorbent layer 6cm) after passing 50 mL of 6 M HCl and 25 mL of HNO_3 of various concentrations. Sorbent AG 1×8 , $c(\text{Sb}) = (2-5) \cdot 10^{-3}$ g/L

Radionuclide	Radionuclide activity remained on the column, %, at indicated HNO_3 concentration, M		
	1	2	4
^{113}Sn	9.2	1.3	0.87
^{121m}Te	72.5	56.5	30.4

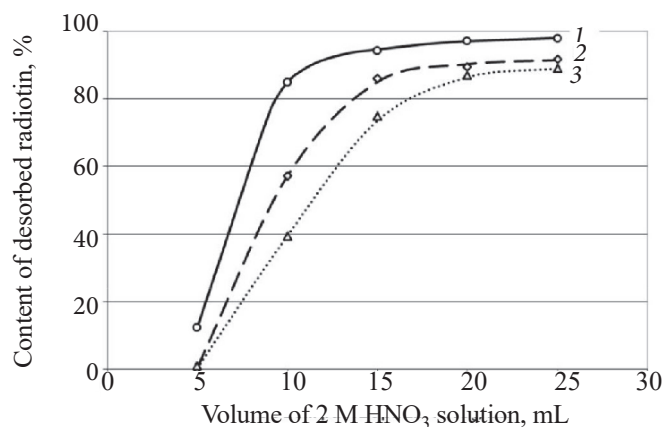


Fig. 3. Integral curves of ^{113}Sn elution at various concentrations of antimony in the initial solution. Sorbent AG 1 \times 8, column 0.6 cm in diameter and 6 cm in height, flow rate 0.8 mL/min. Antimony concentration, g/L: (1) $(2-5) \times 10^{-3}$, (2) 3.6, and (3) 14.4.

– the concentration of antimony in the initial solution should be on the order of 1 g/L, i.e. most of the antimony should be previously removed, by extraction with dibutyl ether in particular;

– sorption of radiotin should be performed from a 6 M HCl solution;

– selective elution of titanium with respect to radiotin should be carried out in a 6 M HCl (for a chromatographic column volume of 2.5–3 mL and a sorbent layer height of 6–7 cm, 50 mL of 6 M HCl is sufficient).

For desorption of radiotin, a 2 M HNO_3 solution heated to 40°C should be used; with the above column parameters, 25 mL of 2 M HNO_3 is sufficient to extract 98–99% of the radiotin.

The purification factor from Ti depends on its concentration in the initial solution and reaches 10^4 at a titanium concentration of 25 g/L; a purification factor of up to 10^6 may be achieved after two stages of chromatographic purification.

Extraction separation of radiotin from titanium. Along with the chromatographic method, extraction methods are also used to separate radiotin from titanium macroquantities. One of these methods is extraction with methyl isobutyl ketone [19].

Our model experiments showed that methyl isobutyl ketone extracts up to 80% of radiotin from 7 M HCl, while the titanium concentration decreases 200 times. The extraction of radiotin from a solution of 7 M

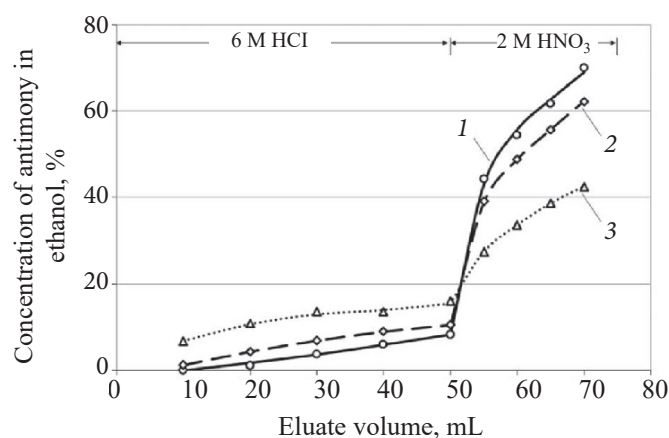


Fig. 4. Integral curves of antimony elution at various concentrations of antimony in the initial solution. Sorbent AG 1 \times 8, column 0.6 cm in diameter and 6 cm in height, flow rate 0.8 mL/min. Antimony concentration, g/L: (1) $(2-5) \times 10^{-3}$, (2) 3.6, and (3) 14.4.

HCl + 7 M LiCl reaches 96%, whereas the titanium concentration decreases only 60 times. Thus, this method does not allow for complete purification of the radiotin from titanium macroquantities in a high yield.

Another extraction method of separation from titanium, providing up to 99% yield, is the extraction of tin with benzene from iodide solutions. This method was studied for the separation of milligram amounts of tin from titanium and antimony in [21]. The behavior of a no-carrier-added tin may differ from the behavior of macroscopic amounts of tin. The difference in the extraction behavior of tin is mainly influenced by the concentration of stable antimony and iodide ions.

It was shown in [15] that after the removal of antimony by extraction with dibutyl ether, a minor amount of it nevertheless remains in the solution. At the first stage, the effect of the concentration of antimony in the initial solution on the extraction of radiotin with benzene was studied. In this case, the KI concentration was kept constant (0.5 M). In the studied range of antimony concentrations $(2-5) \times 10^{-3}$ –1 g/L, at least 98% of radiotin is extracted with two 10-mL portions of benzene. The dependence of the extraction of antimony on its concentration in the initial solution is demonstrated in Fig. 5. As seen, the more antimony in the initial solution, the more it is extracted into the organic phase (salting out effect). Therefore, the antimony concentration should be minimal.

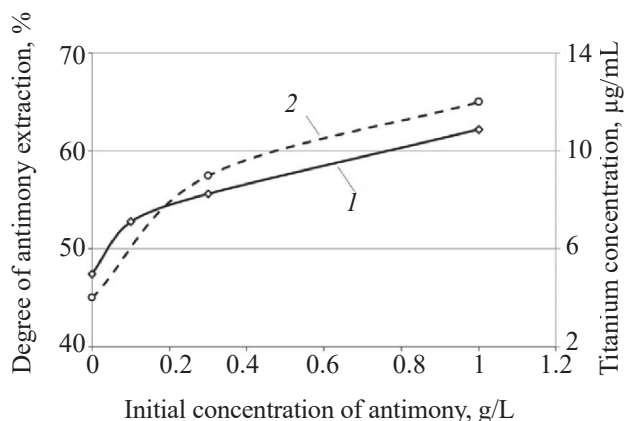


Fig. 5. Dependences of the fraction of extracted antimony (1) and the concentration of titanium in the reextract (2) on the concentration of antimony in the initial solution.

For reextraction of radiotin from the organic phase, we used 1.5 M HCl and 0.25 M H_2SO_4 solutions proposed in the literature [22]. The efficiencies of reextraction with solutions of both acids were found to be close. Since further purification was performed in hydrochloric acid solutions, 1.5 M HCl was used for reextraction. The influence of the initial concentration of antimony on the reextraction was investigated. In particular, it was shown that with an increase in the concentration of antimony in the initial solution, the purification degree of radiotin, reextracted from benzene, from titanium also decreases (Fig. 5).

It was found that after a certain time (within an hour) elapsed after extraction, a white precipitate formed in the organic phase.

For tin reextraction, the organic phase was decanted, with some radiotin remaining on the sediment and on the surface of the chemical glassware (Fig. 6).

The influence of the concentration of antimony and iodide ions in the initial solution on the loss of radionuclides in the sediment was studied. As seen, the loss of radiotin in the sediment increases with increasing antimony concentration (Fig. 6). To minimize the loss, it is necessary to limit the interval between extraction and reextraction, and also to reduce the concentration of antimony in the initial solution to 0.1 g/L. But even at this minimum concentration the amount of precipitate increases with an increase in the KI concentration. The loss of radiotin in the KI concentration range studied, 0.2–1 M, was within 10–15%, and the content of antimony in the precipitate increased with KI concentration. Since titanium is not

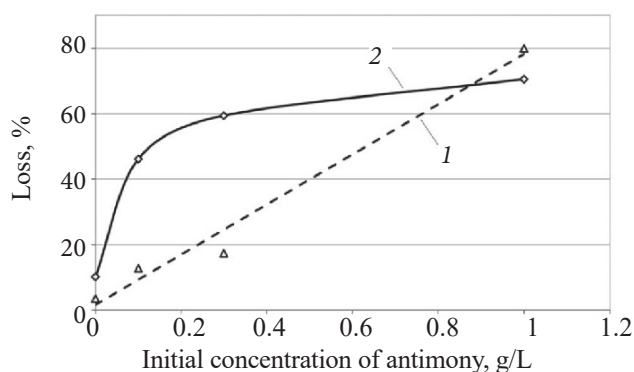


Fig. 6. Loss on the sediment formed in the organic phase after extraction and on the surface of chemical glassware. Curve: (1) antimony (^{124}Sb) and (2) ^{113}Sn .

extracted in significant quantities, antimony remains the only macrocomponent that can lead to insoluble compounds. Based on the fact that the content of antimony in the precipitate increases with concentrations of both antimony and KI, it can be assumed that the precipitate is Sb(V) iodide or its derivatives.

The effect of the concentration of iodide ions on the course of extraction was studied at the constant concentration of antimony in the initial solution equal to 0.1 g/L.

It was found that, in the concentration range studied, 0.2–1 M, the KI concentration dramatically affects the extraction of radiotin and antimony: at low concentrations, antimony is extracted, while up to 70% of radiotin remains in the aqueous phase. With an increase in the KI concentration, the behavior of the elements changes: the radiotin quantitatively leaves the aqueous phase, while the antimony remains (Fig. 7). Analysis of the obtained experimental data showed that more than 98% of titanium and tellurium radionuclides remained in the aqueous phase after extraction with benzene. In addition, iodide ions contribute to a more complete separation of radiotin from titanium. With KI concentration increased from 0.2 to 1 mol/L, the degree of purification from titanium is increased by a factor of 4–5.

Based on the above dependences, the optimal parameters of the extraction separation of radiotin and titanium were selected:

- the concentration of antimony in the initial solution should be below 0.1 g/L, i.e. it must first be removed, for example, by extraction with dibutyl ether;

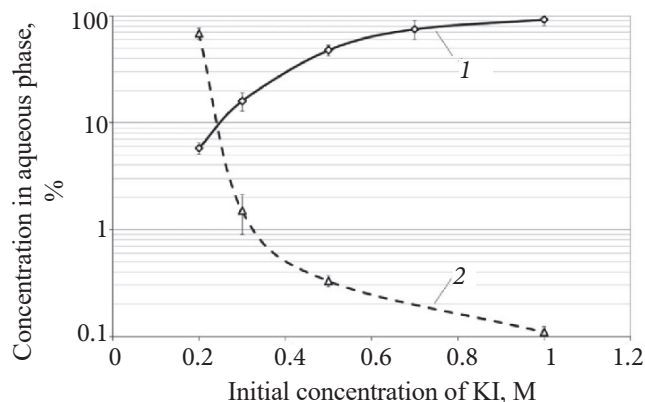


Fig. 7. Fraction of antimony (1) and radiotin (2) remained in the aqueous phase after extraction, depending on the concentration of KI in the initial solution.

– the optimal composition of the aqueous phase is 4.66 M HClO_4 + 1 M H_2SO_4 + (0.5–1) M KI, the the organic phase is benzene, previously saturated with a solution of 4.66 M HClO_4 + 1 M H_2SO_4 ;

– the time between extraction and reextraction should be minimal and not exceed 45 min.;

– the concentration of the solution for reextraction of radiotin should be about 1.5 M HCl.

Thus, titanium can be almost completely removed from radiotin by extraction with benzene, whereas trace amounts of antimony and tellurium present in the product may be removed by chromatographic purification on silica gel.

On processing an irradiated antimony target, such a final purification was performed in a solution containing 0.5 M sodium citrate (pH 5.5), which, in turn, was prepared from a 10 M HCl solution, which is determined by the previous stage of processing described in [15]. In the case of the extraction separation of radiotin and titanium, a sodium citrate solution was prepared from a 1.5 M HCl solution, and in the case of chromatographic separation on AG 1 × 8 resin, the preceding solution was 2 M HNO_3 , not HCl.

We checked how traces of nitrate ions affect the chromatography efficiency on silica gel, the formation of antimony complexes with citrate ions in particular. To do this, a citrate solution containing ^{113}Sn , ^{124}Sb , $^{121\text{m}}\text{Te}$, and ^{44}Ti was prepared starting from a 2 M HNO_3 . The solution was passed through a column filled with SiO_2 ,

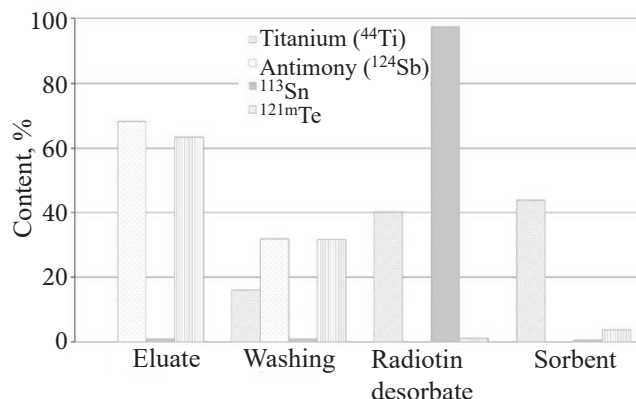


Fig. 8. Results of chromatographic purification of radiotin on silica gel from a 0.5 M Na_3Cit solution (pH 5.5) containing traces of nitrate ions. Column 0.6 cm in diameter and 6 cm in height, flow rate 0.6 mL/min.

then the column was washed, and radiotin was eluted with 6 M HCl according to the method described in [15]. The results are demonstrated in Fig. 8. It follows from Fig. 5 that the radionuclides Sn, Sb, and Te behave in the same way, as in the absence of nitrate aions. In this case, about 45% of ^{44}Ti remains on the column.

Isolation of radiotin from an irradiated TiSb sample. After the process of radiotin separation was studied in model experiments, an experimental target of titanium – antimony intermetallic compound was fabricated and irradiated.

The chemical and physical properties of TiSb have been little studied. To study the interaction of TiSb with acids, nonirradiated samples weighing from 0.5 to 20 g were successively dissolved in concentrated HCl and then in concentrated HCl with the addition of HNO_3 . Heating TiSb in concentrated hydrochloric acid caused solution to turn violet (owing to the formation of Ti^{3+} ions). As the sample dissolved, the reaction rate decreased. The addition of H_2O_2 or concentrated HNO_3 leads to the resumption of dissolution. However, in this case, Ti^{3+} transforms into Ti^{4+} , causing precipitation and passivation of the TiSb surface.

We succeeded in performing complete dissolution as follows. The bead of the compound was placed in a flask, and a concentrated HCl was added. The flask was heated for 12 h at reflux temperature. Solution (no. 1) turned deep violet, indicating the formation of Ti^{3+} ions. Then, the insoluble residue was transferred into a flask with a fresh portion of concentrated HCl, and

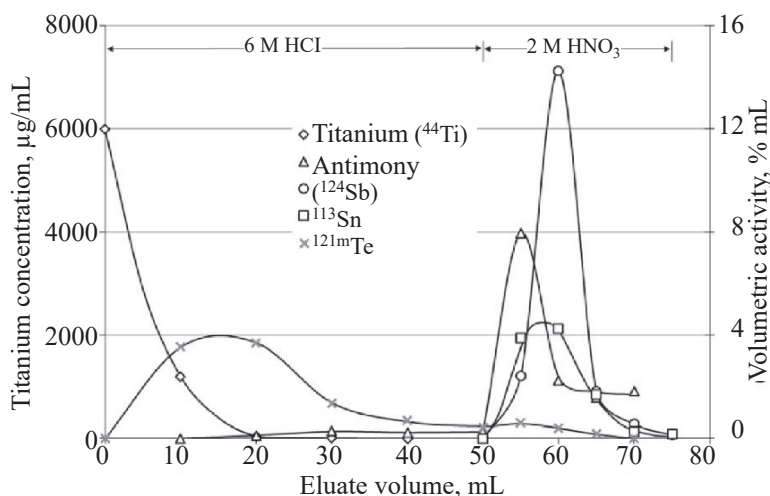


Fig. 9. Chromatographic isolation of titanium during the separation of radiotin from an irradiated TiSb target. Sorbent AG 1×8. Column 0.8 cm in diameter and 8 cm in height, flow rate 0.8 mL/min.

a concentrated HNO_3 was added dropwise on heating. Violent dissolution and formation of a white suspension was observed. After 4 h, dissolution was complete. After cooling the thus obtained solution (no. 2), the precipitate was filtered off. To the solution (no. 1) a filtered solution (no. 2) was added.

This method was used to dissolve an experimental TiSb sample irradiated in an accelerator. It was shown that radiotin is not adsorbed on the formed sediment at the acidity above 3 M HCl. The composite solution was transferred into a 10 M HCl solution, and macroquantities of antimony were removed by extraction with dibutyl ether. Since model experiments demonstrated the possibility of purification from titanium macroquantities both by extraction and by chromatography, the solution obtained after removing antimony was divided into two portions to test both methods. The first portion was

purified from titanium on a chromatographic column, and the second portion, by extraction with benzene from iodide solutions.

For chromatographic purification on an AG 1 × 8 column, the solution was diluted to 6 M HCl. Results of the anion-exchange separation of radiotin and Ti are demonstrated in Fig. 9. Passing the initial solution and subsequent washing the column with a 6 M HCl caused titanium to wash out of the column in the form of a positively charged complex $[\text{TiO}(\text{H}_2\text{O}_2)]^{2+}$ and as trivalent cations of indium and scandium radioisotopes, while radiotin and antimony in the form of anionic complexes $[\text{SbCl}_6]^-$ and $[\text{SnCl}_6]^{2-}$ retained by the sorbent together with tellurium radioisotopes.

When the mobile phase is changed for a 2 M HNO_3 solution, the complexes of tin and antimony decompose, and desorption of these elements and also a part of

Table 4. Results of titanium extraction with benzene from a 4.66 M HClO_4 + 1 M H_2SO_4 + 1 M KI solution containing 30 mg/mL Ti and ^{113}Sn , ^{124}Sb , ^{121m}Te , ^{123m}Te , ^{114m}In , and ^{46}Sc radioisotopes

Radionuclide	Aqueous phase after 2nd stage of extraction, %	Organic phase 1, %	Organic phase 2, %	Reextraction (aqueous phase), %	Reextraction (organic phase), %
^{113}Sn	2.4	92.7	4.9	91.4	6.2
^{121m}Te	98.7	0.9	0.4	0.7	0.6
^{123m}Te	98.4	1.3	0.3	0.8	0.8
^{124}Sb	47.0	32.0	21.0	45.0	8.0
^{114m}In	>99.99	<0.01	<0.01	<0.01	<0.01
^{46}Sc	>99.99	<0.01	<0.01	<0.01	<0.01
Ti	>99.99	<0.01	<0.01	<0.01	<0.01

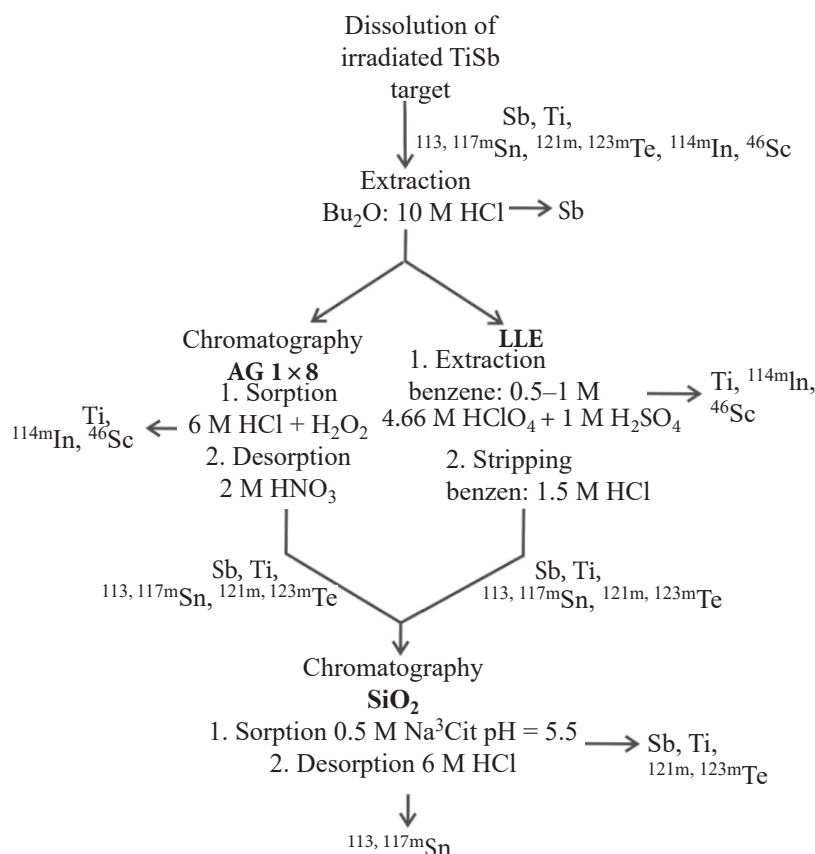


Fig. 10. Scheme of processing an irradiated TiSb target.

tellurium occurs. For the final purification of the radiotin, chromatographic separation on silica gel was carried out as described above. As a result, the total yield of $^{117\text{m}}\text{Sn}$ was 75–82%, the purification factors for Sb and Ti were about 106, and the radionuclidic purity of $^{117\text{m}}\text{Sn}$ was no less than 99.9% (excluding the ^{113}Sn isotopic impurity, which is not chemically separated).

Second portion of the solution prepared by dissolving TiSb was transferred into a solution containing 4.66 M HClO_4 , 1 M H_2SO_4 , and 1 M KI, and the radiotin was extracted twice with benzene. Then, radiotin was reextracted from benzene with 1.5 M HCl. Like chromatography, this method provided purification of radiotin from titanium, indium, and scandium radionuclides. Trace amounts of antimony and tellurium impurities (Table 4) remained after the extraction were removed by further adsorption on silica gel from citrate solutions.

In the given case, the total yield of $^{117\text{m}}\text{Sn}$ was 80–85%, the purification factor for Sb and Ti, about 106, and the radionuclidic purity was no less than 99.7%

(excluding the ^{113}Sn isotopic impurity, which is not chemically separated).

CONCLUSION

Two developed methods for processing an irradiated TiSb target are schematically shown in Fig. 10.

To conclude, the processes of separation of no-carrier-added $^{117\text{m}}\text{Sn}$ from the TiSb intermetallic compound irradiated with protons have been investigated. The dissolution of TiSb in the HCl and HNO_3 acids with the addition of HNO_3 and H_2O_2 has been studied. It was shown that the presence of titanium in the resulting solutions does not impede the effective extraction of most of the antimony with dibutyl ether. For further separation of radiotin from macroquantities of titanium, both chromatography and extraction can be used.

Using the chromatography method, we studied the possibility of separating radiotin in the form of $[\text{SnCl}_6]^{2-}$ from titanium in the form of an oppositely charged complex $[\text{TiO}(\text{H}_2\text{O}_2)]^{2+}$ on strong AG 1×8 and

Dowex 1×8 anion exchangers from a 6 M HCl solution in the presence of H_2O_2 . It was shown that AG-1 $\times 8$ provides higher purification efficiency.

In the extraction separation of radiotin and titanium, the best results were achieved for the extraction of radiotin with benzene from a solution containing a mixture of perchloric and sulfuric acids and iodide ions with a concentration of 0.5–1 M.

Each of the methods used has its own advantages and disadvantages [30]. In our case, the advantage of extraction in comparison with chromatography is the short time of the process, and the disadvantage is a slightly lower yield of radiotin and worsening of its purification from titanium at a residual concentration of antimony in the initial solution above 0.1 g/L.

In our opinion, the method of titanium separation on the AG 1×8 anion exchanger is most preferable, since it, although being more time-consuming, is less sensitive to the antimony content in the initial solution (about 1 g/L), and is also easier-to-implement in hot chambers.

In both methods, the separation of radiotin was terminated by chromatographic purification on silica gel from a solution containing 0.5 M sodium citrate at pH 5.5. As a result, the ^{117m}Sn product with high radionuclidic purity and high specific activity was obtained in at least 75-% yield, which is promising for the development of production technology of ^{117m}Sn in large quantities in the future.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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