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Isolation of high purity ^{73}Se using solid phase extraction after selective 4,5-[^{73}Se]benzopiazselenol formation with aminonaphthalene

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Abstract: A fast and efficient process for the production of the PET radionuclide ^{73}Se was developed using ^{75}Se as a surrogate. ^{75}Se was separated from proton irradiated arsenic trioxide by reaction with 2,3-diaminonaphthalene to 4,5-[^{75}Se]benzopiazelenol. This compound was purified using SPE column chromatography and subsequently decomposed with hydrogen peroxide. For further chemical conversions [^{75}Se]selenite was reduced to elemental [^{75}Se]selenium by either using thiosulfate or sulfur dioxide. The recovery yield of ^{75}Se from the target amounted to 43 %. The utility of the isolated ^{75}Se for radiosyntheses was demonstrated by the successful preparation of [^{75}Se]-selenomethionine. The methodology developed using ^{75}Se was successfully transformed to ^{73}Se.

Keywords: ^{73}Se/^{75}Se, production, radiochemical separation, speciation, synthesis of [$^{73/75}$Se]selenomethionine.

1 Introduction

Over the last few decades the significance of diagnostic studies in nuclear medicine using positron emission tomography (PET) has drastically increased. Usually standard short-lived positron emitters like ^{11}C, ^{13}N and ^{18}F are used. However, some novel longer lived positron emitters, termed as non-standard PET radionuclides, have become increasingly important. Therefore, the production of non-standard positron emitters represents an important field of modern radiochemical research [1]. ^{73}Se is a radionuclide which exhibits suitable decay properties for PET applications. The half-life of 7.1 h is short enough to keep the radiation exposure to the patient as low as possible, but it is, on the other side, compatible with slow physiological processes [1, 2]. Selenium is an essential element of the human body. It is incorporated into proteins and thus plays an important role in many biological functions like fertility and reproduction, DNA synthesis, formation of thyroid hormones and antioxidant defense [3]. Therefore, its isotopes can be applied to radiolabel physiological selenium compounds. Additionally, selenium as the heavier homologue of sulfur can serve as a surrogate in sulfur containing compounds since sulfur itself has no suitable PET isotope for imaging. This is particularly important because sulfur is one of the main constituents of pharmacologically relevant molecules.

Two radionuclides of selenium, namely ^{75}Se and ^{73}Se, are of special interest. The positron emitted by ^{73}Se ($t_{1/2}$ = 7.1 h) has a maximum energy of 1.3 MeV. It decays to ^{73}As ($t_{1/2}$ = 80.3 days) which subsequently decays by electron capture to stable ^{73}Ge. Although the intermediate product ^{73}As is radioactive too, in case of an application it does not add significantly to the dose of the patient, since only low γ-photons are emitted and the biological half-life of arsenic in the human body is only about 4 h [4]. The longer lived ^{75}Se ($t_{1/2}$ = 120 days) decays to ^{75}As by electron capture and emits two main γ-rays of 136 keV (59.0 %) and 265 keV (59.2 %) suitable for single photon emission computed tomography (SPECT). However, the long half-life of this radionuclide leading to inacceptable high radiation doses prevents its utilization in clinical practice. Nonetheless, due to the long half-life and γ-ray emission it is ideally suited as a surrogate for short-lived ^{73}Se for the radiochemical development of novel processes and separation techniques [5].

For the production of ^{73}Se and ^{75}Se a variety of production routes are established (see Table 1) [6–10]. Recently the nuclear data have been critically analyzed and yields calculated [11, 12].

Whereas ^{75}Se can be easily obtained at a small cyclotron, for the production of ^{73}Se higher proton or deuteron energies or α-particle induced nuclear reactions are required. Small amounts of $^{73/75}$Se have also been produced using intermediate energy protons on ^{nat}Br [13]. The isolation of radioselenium from the target material remains still challenging although several methods have been described in the literature. They comprise different

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Table 1: Possible nuclear reactions to produce ^{73}Se and ^{75}Se.

Nuclide	Nuclear reaction	Energy range (MeV)	Yield (MBq/μAh)
^{73}Se	^{75}As(p,3n)^{73}Se	40→30	1406
	^{75}As(d,4n)^{73}Se	40→33	700
	^{70}Ge(α,n)^{73}Se	26→13	300
^{75}Se	^{75}As(p,n)^{75}Se	17→6	2.8

separation techniques like thermochromatography, ion chromatography, extraction and solid phase extraction processes [6–10]. Nonetheless, these methods suffer from low recovery yields, poor reproducibility and time consuming and cumbersome methodologies. The aim of this work was to develop a fast and robust separation procedure to obtain ^{73}Se in high chemical and radiochemical purity for subsequent labeling reactions. The utility of the separated $^{73/75}$Se should be demonstrated by the preparation of [$^{73/75}$Se]selenomethionine as a model compound.

2 Experimental

2.1 Materials and methods

All chemicals were purchased from Sigma-Aldrich and used without further purification. In the case of 2-amino-4-bromobutyric acid hydrobromide (ABB · HBr) the purity was checked by NMR analysis and found to be in agreement with the reference data. LiChrolut® RP-18 E SPE cartridges (200 mg) were purchased from Merck (Weilheim). Strata-X-C® SPE cartridges (500 mg) were purchased from Phenomenex (Aschaffenburg). Argon (99.999 %) was purchased from Air Liquid. For irradiation As_2O_3 (99.995 % trace metal base, Sigma-Aldrich, Taufkirchen) was used.

Analytical high performance liquid chromatography (HPLC) was performed using a Hitachi L-6000 pump and a Sykam S3300 UV detector. The γ-trace was measured using a SCIONIX Holland 76B76 3″ NaI(Tl) scintillation detector mounted on an EG&G Ortec Model 276 photomultiplier base and a RG&G Ortec 925-SCINT ACE Mate amplifier and bias supply. Semipreparative HPLC was performed using a Phenomenex Synergy™ Hydro-RP 10 μm 80 A 250×10 mm and an eluent consisting of water with 1 % acetic acid and 3.425 g sodium acetate (pH = 5.7) at a flow rate of 4.9 mL/min. Radiochemical yield was determined by comparing the product peak to a second reference injection bypassing the column (corresponds to the total activity of the sample volume).

Analytical ion chromatography was perfomerd on a Metrohm 882 Compact IC plus using an A-Supp 5 150/4 column and an eluent consisting of 3 M Na_2CO_3 and 2.2 M $NaHCO_3$ at a flow rate of 0.7 mL/min. Detection of non-radioactive anions was based on conductivity after suppression. Radioactive compounds were detected offline by collecting fractions every 45 s and subsequent γ-ray spectroscopy (see below).

2.2 $^{73/75}$Se production

^{75}Se was produced by the ^{75}As(p,n)^{75}Se nuclear reaction by bombardment of an As_2O_3 pellet with 17 MeV protons for 10 h with 1 μA at the Baby Cyclotron (BC 1710) of the Forschungszentrum Jülich [14]. ^{73}Se was produced by the ^{75}As(p,3n)^{73}Se nuclear reaction by bombardment of the As_2O_3 target with 45 MeV protons for 1 h with 1 μA at the JULIC cyclotron of the Forschungszentrum Jülich [9, 15]. At both proton energies considerable amount of ^{74}As ($t_{1/2}$ = 17.8 days) was also formed via the ^{75}As(p,pn)-reaction. This radionuclide served as a good tracer for checking the removal of As from the separated radioselenium (see below).

The targets for both irradiations were prepared in the same way. About 250–500 mg of arsenic trioxide were pressed at 10 bar into a pellet (d = 13 mm) which was then transferred to an aluminum capsule (thickness of cap and bottom 200 μm). For the production of ^{73}Se the energy of the incident protons had to be reduced from 45 MeV to 40 MeV. This was achieved by using aluminum absorber foils (thickness of 10–50 μm) placed in front of the target.

2.3 Optimization of separation process

The irradiated As_2O_3 target was dissolved in 2 M NaOH solution (n ≥ 10). After dissolution the selenium was present in two oxidation states, namely selenite and selenate, which could be clearly identified by means of ion chromatography (Figure 1), followed by γ-ray spectroscopy of each fraction. In general, the selenate form was dominant.

After addition of the DAN-reagent (hydroxylammonium hydrochloride, glycine, Na_2-EDTA) and 200 μL of concentrated hydrochloric acid to a achieve a pH of about 2.5, a quantitative formation of [$^{73/75}$Se]benzopiazselenol was observed, as demonstrated by fixation of the entire Se activity on the RP cartridge. This was ascertained by comparing the ^{73}Se activity given to the cartridge with

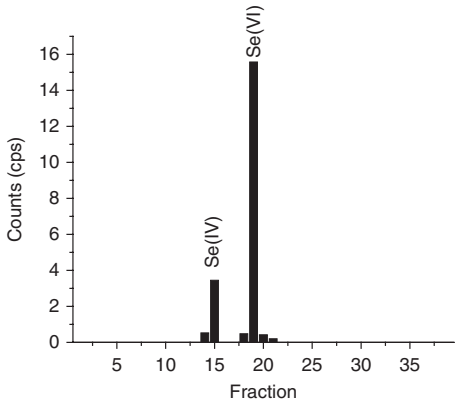

Figure 1: Selenium speciation after dissolution of irradiated As_2O_3 target in NaOH.
Fractions are collected from analytical ion chromatography (for conditions see text).

that adsorbed on the cartridge, which was determined by direct γ-ray spectrometry of the cartridge (see below). We estimate an uncertainty of about 5 % in the determination of the ratio of the two activities. The almost quantitative fixation can be tentatively attributed to the composition of the reagent mixture containing also reducing agents. The reaction was optimized, similar to the work of Cukor and Lott [16]. However, we worked with n.c.a ^{75}Se. Our studies dealt with the following reaction parameters: reaction time, temperature and pH. Furthermore, the shelf-life of the reagent and the influence of the solvent on the recovery yield from the cartridge were determined.

2.4 Se separation, purification and specification

The whole irradiated target was dissolved at 90 °C in 2 mL of 2 M sodium hydroxide solution in a 5 mL v-vial with a cap. Subsequently the pH was adjusted to about 2 using 6 M hydrochloric acid. One milliliter of a solution of 50 mg 2,3-diaminonaphthalene, 210 mg hydroxyl-ammonium chloride, 50 mg Na_2-EDTA, 188 mg glycine and 200 µL conc. HCl in 25 mL distilled water were added and the solution was heated at 80 °C for 10 min. After the reaction of Se with diaminonaphthalene was completed the solution was cooled down and immediately passed through a RP-18 E cartridge. The cartridge was washed with 1 mL of pure water, 1 mL of 0.01 M HCl and again 1 mL of pure water. Thereafter the compound formed was eluted with a suitable organic solvent (see Results and discussion) into another 5 mL v-vial with a cap. To convert the organoselenic compound back into an ionic species an oxidative digestion was done. For this, after the removal of the solvent at 80 °C under reduced pressure of 600–500 mbar, 1 mL hydrogen peroxide solution (35 %) was added and the mixture refluxed at 115–120 °C for 30–40 min. To remove organic components, the solution was cooled down and passed through another RP-18 E cartridge, which was subsequently washed with 1 mL of pure water. The collected solutions were combined in a v-vial and evaporated at 90 °C under reduced pressure below 100 mbar to dryness.

The residue was dissolved in a mixture of sodium hydrogencarbonate and sodium carbonate which was also used as mobile phase. The pH strongly influences the chemical form of Se in the solution. Selenium speciation was determined by ion chromatography (IC). After injection samples were drawn in intervals of 45 s, which were all measured afterwards by γ-ray spectroscopy. The elution times of the samples containing radioactive selenium were compared to those of selenite (t_R: 10.8 min k: 4.0) and selenate (t_R: 13.8 min k: 5.4) reference compounds to identify the chemical form of the separated selenium.

For detailed optimization information on the whole separation process refer to the results and discussion section.

2.5 Measurement of radioactivity

The radioactivity of each sample (mostly 0.5 mL of solution in a vial) was measured via γ-ray spectroscopy using a large-sized HPGe detector of EG&G Ortec (USA). The sample to detector distance was invariably 10 cm and the counting dead time <3 %.

In RP cartridge adsorption studies, the cartridge (9 mm I.D. × 4 mm) was counted in a calibrated geometry. The efficiency versus energy curve of the detector was determined using the γ-ray standard point sources of ^{57}Co, ^{60}Co, ^{54}Mn, ^{133}Ba and ^{152}Eu supplied by the Physikalisch-Technische Bundesanstalt Braunschweig. The resolution of the detector was 1.8 keV at the 1332 keV γ-ray of ^{60}Co. The investigated radionuclides were identified by their characteristic γ-rays: ^{73}Se (361 keV); ^{75}Se (136 and 265 keV); ^{74}As (596 and 635 keV). The γ-ray spectra were analyzed using the software GammaVision 6.01 (EG&G Ortec). We estimate that the uncertainty in the relative activity measurement was about 4 % and in the absolute measurement about 7 %.

2.6 Synthesis of [$^{73/75}$Se]selenomethionine

Pure selenate, which was present after separation and purification, was dissolved and simultaneously reduced

to selenite by addition of 9 M HCl (150 µL). In a 2 mL Eppendorf tube the selenite was reduced to elemental selenium by addition of 65–100 µL of a 1.2 M sodium thiosulfate pentahydrate solution. The mixture was centrifuged at 14,000 rpm for 15 min to separate the aqueous phase from the precipitated sulfur matrix which was subsequently washed and centrifuged three times with dry THF [5]. In a 25 mL two neck flask with magnetic stirring bar the residue was heated two times under an atmosphere of argon and reduced pressure. After cooling down, 4 mL of dry THF and the yellow sulfur precipitate containing also elemental selenium were added. The matrix was transformed into a mixture of methyl sulfide and [$^{73/75}$Se]methylselenide, by dropwise addition of 400 µL of a methyl lithium solution (1.6 M in diethyl ether). Immediately after addition of the first drops the solution turned slightly yellow and then became clear again. After 5 min 887 µL of a 0.22 mM ethanoic (absolute) 2-amino-4-bromobutyric acid hydrobromide (ABB · HBr, 40 mg) solution was added dropwise. Slight foaming appeared due to the reaction of excess methyl lithium with ethanol. The argon flow was increased and the solution was stirred for 30 min. The residual solution was acidified by addition of 5–7 mL of a 0.1 M HCl (slight turbidity). The whole solution was then passed through a Strata-X-C cation exchange cartridge which had been earlier conditioned with 1 mL of methanol and 1 mL of water. After washing with 1 mL acidic water solution the product was eluted with 3–4 mL of a 5 % ammonia solution in methanol/water 5 % (v/v).

The resulting solution was concentrated. Thereby volatile ammonia was removed. Thereafter, [^{75}Se]selenomethionine was isolated using HPLC [17].

Alternatively selenite could be reduced to elemental selenium by bubbling sulfur dioxide through the solution for 1 min. The aqueous solution was evaporated at 85 °C under reduced pressure. To enhance recovery yields, Se(VI) carrier (1.5 mg $Na_2SeO_4 \times 10\ H_2O$) was added before the reduction step. The subsequent steps of the reaction procedure remain the same.

3 Results and discussion

The process development was based on a former work which dealt with the determination of trace quantities of selenium in analytical chemistry [18]. That work exploited the reaction of selenous acid with aromatic ortho diamines to produce compounds containing a five membered selenodiazol ring system. These fluorimetric reagents exhibit a high fluorescence efficiency and extinction coefficient allowing the determination of exceedingly low concentrations of selenium [19]. Furthermore, selenodiazol derivatives are extractable from acid solution. Therefore, these kind of compounds should enable solid phase extraction of the organic bound selenium from the inorganic matrix. Transferred to our situation, Se should be fixed on a solid reversed phase cartridge after transformation with 2,3-diaminonaphtalene (DAN) to the aromatic compound. Since the target material As does not react with aromatic ortho diamines, this should enable a quantitative separation of Se from As. However, this separation technique is only applicable if Se is present as selenous acid since the reaction is selective for Se(IV). Therefore, the chemical form of radioselenium had to be determined before establishment of this process.

3.1 Optimization results

The results of the optimization studies are compiled in Figures 2–5. Product formation is equated with the adsorption of the Se activity on the RP cartridge. The error bars indicate the standard deviation of the triple experiments.

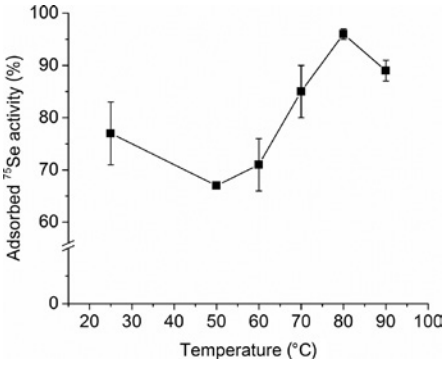

Figure 2: Formation of [^{75}Se]benzopiazselenol obtained from the adsorbed Se activity on a Lichrolut RP-18 E cartridge; n = 3.

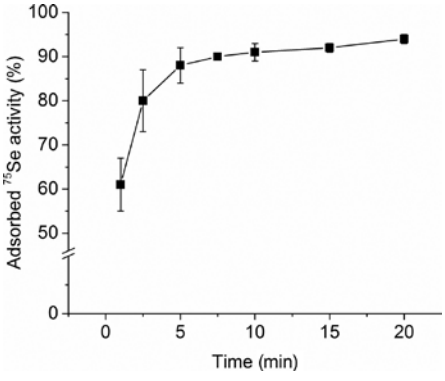

Figure 3: Reaction kinetics of [^{75}Se]benzopiazselenol formation between selenium(IV) and DAN; n = 3 (T = 80 °C, pH = 2.4).

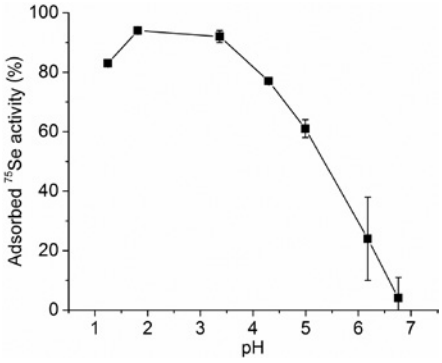

Figure 4: pH-value dependence of the formation of [$^{73/75}$Se]benzopiazselenol under optimal conditions; n = 3.

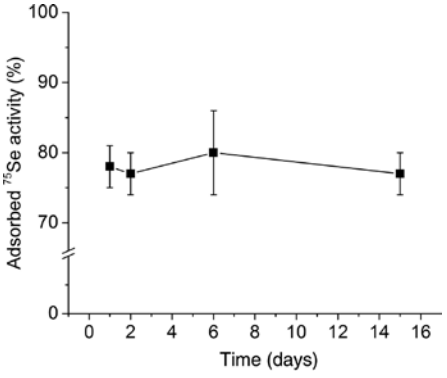

Figure 5: Alteration of the coloring reagent with time; n = 3.

The temperature dependency is shown in Figure 2. From room temperature until 60 °C the formation yield amounts to only 70–80 %. At 60 °C the formation yield starts increasing, reaching a maximum at 80 °C.

The reaction kinetics for the formation of 4,5-[^{75}Se]-benzopiazselenol from Se(IV) and diaminonaphtalene is shown in Figure 3. The product formation is practically completed after 5 min and a plateau is reached at 90 %.

As can be seen from Figure 4, product formation takes place quantitatively in the acid range of pH 2–4. Below and above this range the product forming tendency is less pronounced. Above pH 4 a major drop is observed showing that no product formation takes place in the neutral region.

In Figure 5 the shelf-life of the DAN reagent is depicted. The graph shows that the reagent is stable for more than 14 days. The stability and shelf-life of the reagent is not significantly altered during this time period. The resulting optimized reaction conditions are summarized in Table 2.

Using these parameters the radiochemical yield of [^{75}Se]benzopiazselenol from the arsenic trioxide matrix was on average 75.5 % compared to the initial activity of

Table 2: Optimized reaction parameters for the product formation between selenium(IV) and 2,3 diaminonaphthalene to [^{75}Se]benzopiazselenol.

Temperature (°C)	pH	Time (min)	Eluent (mL)
80	2.4	15–20	MeCN:DCM 2:1

Table 3: Total yields of the elution of [$^{73/75}$Se]benzopiazselenol with different solvents.

Eluent	Yield of 1st elution (%)	Yield combining 1st and 2nd elution (%)
MeCN	72.2	–
Acetone	75.5	84.5
Diethyl ether	82.9	–
Chloroform	80.8	87.6
DCM	82.2	94.2

^{75}Se. Finally the retained compound had to be eluted. Different solvents were examined. The recovery in dependence of solvent is summarized in Table 3.

The highest recovery was obtained using diethyl ether or dichloromethane (DCM). Elution of the product with acetonitrile (MeCN) or acetone delivered recovery yields of around 75 %. However, with highly efficient DCM a second elution step had to be carried out to obtain overall recovery yields of 94 %. ^{75}Se losses can be mainly attributed to partial adsorption losses in the reactor (≈1 %), to unconverted selenium (≈7 %) and [$^{73/75}$Se]benzopiazselenol which can not be eluted from the SPE cartridge.

3.2 Conversion of separated selenium into a suitable chemical form

3.2.1 Decomposition studies

After the separation of selenium from arsenic, [$^{73/75}$Se]benzopiazselenol had to be decomposed to obtain selenium in a chemical form suitable for further labeling reactions. Therefore, first the solvent which was used to elute the [$^{73/75}$Se]-benzopiazselenol from the cartridge had to be removed by evaporation. Afterwards residual [$^{73/75}$Se]benzopiazselenol was treated in different ways aiming at decomposition of the organic compound and release of selenium.

When the decomposition reaction was completed the whole solution was loaded onto a LiChrolut RP-18 E cartridge to remove organic residues and undisintegrated [$^{73/75}$Se]benzopiazselenol. To determine the decomposition efficiency the amount of free radioactive selenium in the

run-through solution and the amount of retained radioselenium on the cartridge were measured.

First, the residue of [^{75}Se]benzopiazselenol was treated with a mixture of hydrogen peroxide and hydrochloric acid [ratio of 1:4 (v/v)]. The reaction was stopped after 5, 10 and 15 min and the respective yield was calculated. Immediately after addition of reagents and heating, the solution changed its color to yellow and gas formation occurred. Already after 10 min the [$^{73/75}$Se]benzopiazselenol had been decomposed to almost 90 % (determined by adsorption of intact piazselenol on the LiChrolut RP-18 E cartridge). The temperature should not be elevated above 100 °C since volatile selenium chlorides are formed.

As the oxidative decomposition of [$^{73/75}$Se]benzopiazselenol was very effective using H_2O_2 and HCl, the next step was to achieve the same results by using only hydrogen peroxide. Avoiding hydrochloric acid has three major advantages. First, the temperature necessary to evaporate the solution is much lower; second, there is no excess of chloride which can interfere with the determination of selenium species via IC, and third, there is no liquid/solid residue besides H_2O (and unreacted H_2O_2). The disadvantage of using only hydrogen peroxide is that the reaction is much slower, as the oxidative potential of hydrogen peroxide is catalyzed by an acidic milieu. Hence, the time needed to decompose the organic compound is significantly longer, compared to the HCl catalyzed reaction. Nevertheless, due to the above mentioned disadvantages associated with the use of HCl the application of H_2O_2 alone is advantageous. Therefore, H_2O_2 supported decomposition was used for further applications. A flow sheet of the separation process is depicted in Figure 6.

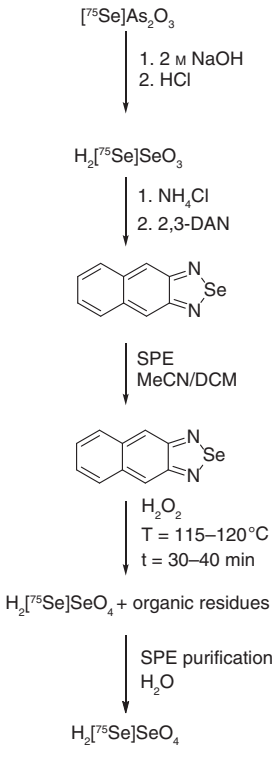

Figure 6: Scheme of selenium separation.

Since labeling of organic molecules with radioselenium requires usually elemental selenium a reductive method for decomposition of [$^{73/75}$Se]benzopiazselenol would be advantageous. Reductive decomposition would avoid a further reduction step. Therefore, hydrazine was selected for decomposition of the compound under reductive conditions. However, reductive decomposition of [^{75}Se]benzopiazselenol by addition of hydrazine took much longer, mainly due to the application of lower temperatures (danger of explosive decomposition). After 40 min at a maximum temperature of 100 °C only 43 % of the [$^{73/75}$Se]benzopiazselenol was decomposed. Since the reaction time was too long and the reaction yield too low this method was not further pursued. The results of all decomposition studies are summarized in Table 4.

3.2.2 Purity of converted selenium

After release from the organic compound, again the chemical form of selenium had to be determined. Speciation was carried out using ion chromatography. The retention time of the eluted ^{75}Se activity corresponded to the retention time of the corresponding selenate standard. Thus, only Se(VI) was present after decomposition. In addition, the inevitably coproduced ^{74}As (see Section 2.2) could not be detected in any fraction collected from the analytical ionchromatography. Moreover, 24 h γ-ray measurement of the final product solution showed that no trace of ^{74}As was present. Consequently, arsenic was quantitatively removed from the n.c.a. radioselenium. Considering an upper limit of the intensity of the 596 keV γ-ray of ^{74}As in the spectrum, we place a limit of <0.2 µg of inactive As in the separated ^{75}Se.

Table 4: Time dependence of the decomposition of [^{75}Se]benzopiazselenol using different reagents.

Reagent	Reaction time (min)	Decomposition (%)
H_2O_2/HCl	5	59.1
	10	89.2
	15	89.1
H_2O_2	25	76.5
	30	90.7
	35	92.3
N_2H_4	40	43

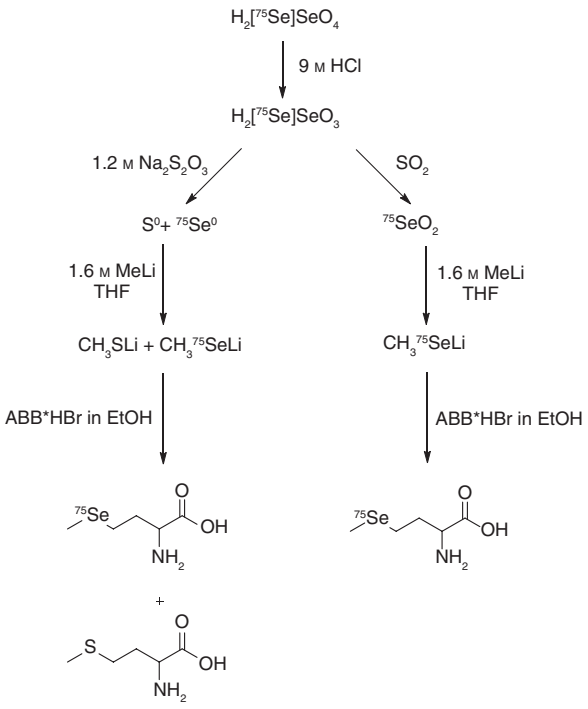

Figure 7: Reaction scheme of the [$^{73/75}$Se]selenomethionine synthesis.

3.3 Radiosynthesis of selenomethionine

Finally, to demonstrate the suitability of separated ^{75}Se for further labeling reactions the radiosynthesis of [^{75}Se]selenomethionine was performed (see Figure 7). The purified selenate could be transformed into a chemical form applicable for labeling reactions by first reduction to selenite, then elemental selenium and finally selenide [5, 17]. In a substitution reaction with 2-amino-4-bromobutyric acid c.a as well as n.c.a [^{75}Se]selenomethionine was successfully prepared. The respective RCY of c.a. [^{75}Se]selenomethionine was 30–50 % in relation to the initial amount of ^{75}Se activity. In case of n.c.a. synthesis the yield was lower (10–20 %).

3.4 Transformation of developed methodology to ^{73}Se

The methodology of separation of radioselenium from an irradiated As_2O_3 target, followed by radiosynthesis of selenomethionine, developed by using the γ-ray emitter ^{75}Se as a surrogate nuclide, was transformed to the PET radionuclide ^{73}Se. The target irradiated with intermediate energy protons was processed as described above and ^{73}Se in the form of [^{73}Se]benzopiazselenol was obtained 5 h after end of bombardment (EOB) in a quantity of about 220 MBq (n = 2). This value corresponds to about 40 % of the theoretically expected ^{73}Se activity at the end of separation. After conversion of the organic compound to a suitable chemical form (see above) the activity was used in the radiosynthesis of selenomethionine. The HPLC chromatograms of n.c.a. and c.a. [^{73}Se]selenomethionine are shown in Figures 8 and 9, respectively. The amount of the finally purified n.c.a. product

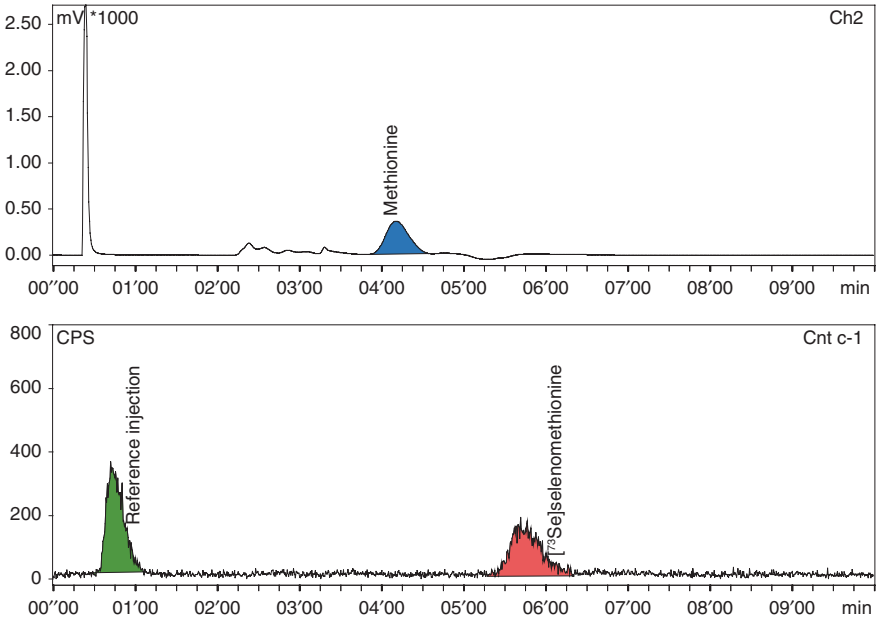

Figure 8: HPLC chromatogram of the synthesis of n.c.a. [^{73}Se]selenomethionine.

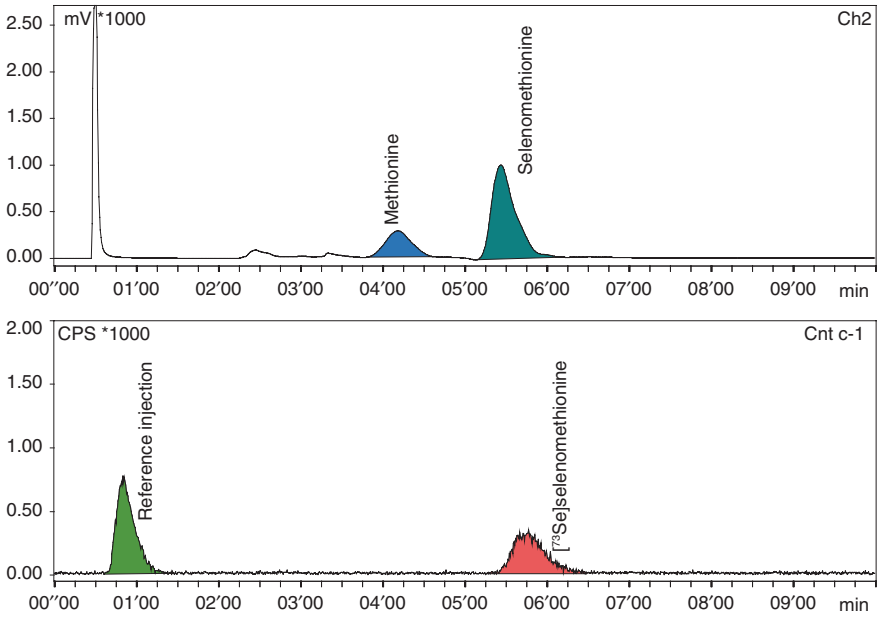

Figure 9: HPLC chromatogram of the synthesis of c.a. [^{73}Se]selenomethionine using 1.5 mg elemental selenium as carrier.

[^{73}Se]selenomethionine was about 50 MBq. These investigations served as a proof of principle. Larger quantities of the radiopharmaceutical could be obtained by performing the proton irradiation at a higher current and for a longer period. It should be pointed out that because of its toxic nature a careful analysis of the arsenic impurity (possibly via ICP-MS) may be necessary in real clinical production runs.

4 Conclusions

A fast and robust separation procedure was developed which enabled to obtain radioselenium in high chemical and radiochemical purity from irradiated As_2O_3 targets. The novelty of the separation process is based on the selectivity of 2,3-diaminonaphthalene to form a lipophilic organoselenic compound with selenous acid. 4,5-[$^{73/75}$Se] benzo-piazselenol was fixed on a RP-18 SPE cartridge and isolated from water soluble AsO_3^{3-}. After elution with acetonitrile the organic compound was decomposed with a solution of hydrogen peroxide. Elemental selenium was obtained after addition of either hydrazine or sulfur dioxide. The recovery of $^{73/75}$Se amounted to 75 %. The effective radiochemical yield of the procedure was 43 % at the end of separation. The utility of the isolated ^{75}Se was proven by the radiosynthesis of [^{75}Se]selenomethionine as a model compound. The developed methodology using ^{75}Se was successfully transformed to the PET radionuclide ^{73}Se.

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