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Simultaneous production and quality control of ^{73}Se and ^{75}Se radioisotopes in a 30 MeV cyclotron

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ABSTRACT

Background: Selenium-73 ($T_{1/2}$=7.1h) and Selenium-75 ($T_{1/2}$=119.8d) are useful radioisotopes in many research fields. The wide ranges of applications of these radioisotopes arose great interest for their production. Simultaneous production of ^{73}Se and ^{75}Se is more cost-effective and less time-consuming.
Materials and Methods: ^{73}As (p, 3n) ^{73}Se and ^{75}As (p,n)^{75}Se reactions were determined as the best choices for the production of ^{73}Se and ^{75}Se radioisotopes, according to the present facilities and conditions. The bombardment was performed by 30 MeV protons in Cyclone 30-IBA accelerator. ALICE and SRIM nuclear codes were used to determine the best energy and target thicknesses. Targets were specifically designed for simultaneous production of the radioisotopes as two consecutive pellets. Chemical processing was performed by no carrier added solvent extraction method. Radio-TLC was performed on polymer backed silica gel. A colorimetric method was used for chemical quality control. Radionuclidic quality control of the final products was carried out by gamma spectroscopy with HPGe detector.
Results: The production yield was 5.3 mCi/μAh for ^{73}Se and 50 μCi/μAh and 678 μCi/μAh for ^{75}Se in the first and second pellets respectively. The specific activity of ^{73}Se was 1.06 mCi/ml and that of ^{75}Se was 135.6 μCi/ml after one hour of proton bombardment with a current of 5μA. The isotopic purity of ^{73}Se was 99% in the first pellet and that of ^{75}Se was 100% in the second, just after the end of bombardment. A 0.04 ppm colorimetric method showed no traces of arsenic in the final product.
Conclusion: The quick and inexpensive procedure used in this research, resulted in high yields, high chemical and high isotopic purity for both radioisotopes. It can be considered as the method of choice for simultaneous production of ^{73}Se and ^{75}Se.

Key words: *Selenium-75, Selenium-73, cyclotron, simultaneous production, quality control.*

INTRODUCTION

^{73}Se and ^{75}Se radioisotopes are widely used in medicine, industry and agriculture. ^{75}Se is used in high activity brachytherapy (Weeks and Schulz 1986), assessment of pancreatic exocrine function (Goriya *et al.* 1974, Denisov 1986), study of bile acids and evaluation of illeal function (Ferraris *et al.* 1986, Soundy 1982, Amaral 1985), industrial radiography (Thiele 1995, NAC Annual Report 1991) and as a tracer in the assessment of chemical, biochemical, biophysical processes, metabolic researches and agricultural studies.^{73}Se is used in pancreas scanning (Agnew 1976), hyperthyroidism diagnosis (Amersham International PLC 1990), adrenal scanning (Hawkins *et al.* 1980), tumor detection (Hara *et al.* 1973, Jereb 1975, Paterson 1976), detection of brain dopamine receptors (Sadek *et al.* 1988), parathyroid tumor

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detection (Amersham International PLC 1990) and detection of brain blood flow (Kung and Blau 1980).

These radioisotopes were selected to be produced in the country according to their wide range of applications. The aim of this study was to find the best physical and chemical conditions for the production of ^{73}Se and ^{75}Se. The idea of simultaneous production of these radioisotopes arouses after the completion of primary studies and development of new targetry techniques. The simultaneously produced radioactive nuclei had equal chemical characteristics and they had to be kept as separately as possible. This was performed by making some modifications in the bombardment conditions and targetry techniques. Important physical characteristics of ^{73}Se and ^{75}Se are given in table 1.

Table 1. Physical characteristics of ^{73}Se and ^{75}Se radioisotopes.

Radioisotopes	Half Life	Disintegration Mode (%)	Gamma Energy (keV)
^{73}Se	7.1 h	E.C.(35%), β^+ (65%, $E_{\beta+}$=1300, 1700)	67(65%),361(98%), 511(β^+)
^{75}Se	119.8 d	E.C. (100%)	120.8(17.2%), 136(58.5%), 265(58.6%), 279.5(24.9%)

MATERIALS AND METHODS

Chemicals were purchased from Merck Company (Germany). The arsenic powder with 99.5% purity and ultra high purity benzene were used in this research. Radio thin layer chromatography (RTLC) was performed on polymer-backed silica gel (F 1500/LS 254, 20 ´ 20 cm, TLC Ready Foil, Schleicher & Schuell$^{\hat{a}}$- Germany). Radio-chromatography was performed by counting different 5 mm slices of polymer-backed silica gel paper using a Canberraä high purity germanium (HPGe) detector (model GC1020-7500SL). All calculations and RTLC counting were based on 361 and 136 keV peaks for ^{73}Se and ^{75}Se respectively.

Selection of the best reaction

Various nuclear reactions which might be used for the production of ^{73}Se and ^{75}Se are shown in table 2 (Firestone 1996, Nozaki *et al.* 1979, Mushtaq *et al.* 1988).

Among the reactions given in table 2, those which use α and ^{3}He as the projectile particles were discarded since high energy and high intensity beams of α and ^{3}He are not available in Iran at present. Those reactions which apply ^{74}Se and ^{76}Se as the target material could not be used, because of their low isotopic values (0.87% and 9.02% respectively), and their chemical separation processes are difficult, expensive and time-taking, due to the equal chemical properties of the product and the target

Table 2. Nuclear reactions for the production of 73Se and 75Se radioisotopes.

^{73}Se	^{75}Se
^{70}Ge(α,nγ)^{73}Se	^{72}Ge(α,nγ)^{75}Se
^{72}Ge(α,3nγ)^{73}Se	^{73}Ge(α,2nγ)^{75}Se
^{73}Ge(α,4nγ)^{73}Se	^{74}Ge(^{3}He,2nγ)^{75}Se
^{74}Ge(α,5nγ)^{73}Se	^{76}Se(^{3}He,4nγ)^{75}Se
^{70}Ge(^{3}He,γ)^{73}Se	^{76}Se(p,d)^{75}Se
^{72}Ge(^{3}He,2nγ)^{73}Se	^{76}Se(d,t)^{75}Se
^{73}Ge(^{3}He,3nγ)^{73}Se	^{74}Se(n,γ)^{75}Se
^{74}Ge(^{3}He,4nγ)^{73}Se	^{75}As(p,n)^{75}Se
^{76}Ge(^{3}He,5nγ)^{73}Se	
^{75}As(d,4n)^{73}Se	
^{75}As(p,3n)^{73}Se	

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material (Sandler 1996).

Therefore ^{75}As (p,n)^{75}Se seemed to be the most appropriate reaction for the production of ^{75}Se. The ^{75}As(d,4n)^{73}Se reaction was not as suitable as ^{75}As(p,3n)^{73}Se, because of the lower radionuclidic purity of the product (Nozaki *et al.* 1979).Thus the best reaction for the production of ^{73}Se was determined to be ^{75}As(p,3n)^{73}Se .

There was no need for an isotopic enrichment process, due to the presence of arsenic as ^{75}As (100%) in nature. On the other hand, chemical separation could be carried out in simple, inexpensive methods in a short time, due to the difference between target materials and the products. So the above reactions were taken to be the best choices according to the present conditions and facilities.

Cross section calculations for ^{75}As reactions with protons

Characterization of excitation function is a very important step for the determination of the projectile beam energy range. Excitation function can be determined by using computer codes such as ALICE (Blann and Bislinghoff 1991) or experimental methods. In the present research, performed in the cyclotron department of Atomic Energy Organization of Iran (IBA, Cyclone-30), ^{75}As reaction cross-sections with protons were calculated for beam energy range of 3-30 MeV (this cyclotron can accelerate protons to 30 MeV energy) using ALICE code and the results were compared with previous experimental data given in the literature (Mushtaq *et al.* 1988, Johnson *et al.* 1958, Levkovskij 1991). The results of this comparison are shown in figure 1.

Figure 1 shows a good agreement between the results of ALICE code and the experimental data. The three main reactions were ^{75}As (p, n)^{75}Se, ^{75}As(p,pn)^{74}Se and ^{75}As(p,3n)^{73}Se. Production of ^{75}Se began at about 2 MeV and reached its maximum around 12 MeV, where the reaction cross section was about 840 mb. Production of ^{74}As began around 13 MeV and reached its maximum at about 26 MeV, where the reaction cross section was about 170 mb. ^{74}As (which was considered as impurity) has a half life of 17.8 days, so it could be easily separated from the product by efficient chemical methods and it was not taken into account while energy selection. Production of ^{73}Se began at around 22 MeV proton energy and continued to increase while beam energy increased to 30 MeV, where the

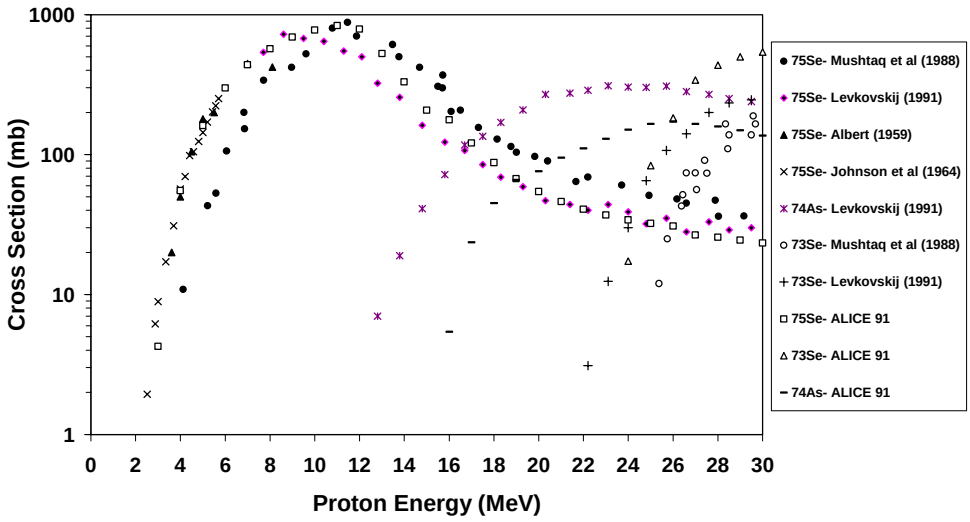


Figure 1. Comparison of ALICE code results with previous experimental data.

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reaction cross section was about 550 mb.

Therefore, if the target thickness were enough to reduce the proton energy from 22 MeV to 0, then the only product would be ^{75}Se, but if it reduced the proton energy from 30 to 22 MeV, then it would result in the production of a considerable amount of ^{73}Se and some ^{75}Se.

Targetry

According to the results of calculation of cross section variations with energy, an appropriately designed target could result in the production of optimal amounts of both ^{73}Se and ^{75}Se radioisotopes.

For this purpose a two-ply target was designed. A considerable amount of ^{73}Se and some ^{75}Se was produced as a result of 30MeV proton bombardment of the first layer. The first layer was thick enough to reduce the proton energy to 22 MeV, so that when protons reached the second layer, only ^{75}Se could be produced. SRIM nuclear program was used for the determination of the proper thicknesses (Ziegler *et al.* 2002). The first and second layer thicknesses were calculated as 1230 μ and 1730 μ respectively. Figure 2 shows the proton beam range variations with proton energy in arsenic targets. Arsenic powder with a purity of 99.5% (Merck Co.) was compressed as 2 pellets of 13 mm radii with a density of 5.02 gr/cm^3 and masses of 4.6 gr and 3.3 gr. They were fitted in the target holder, ready for the bombardment.

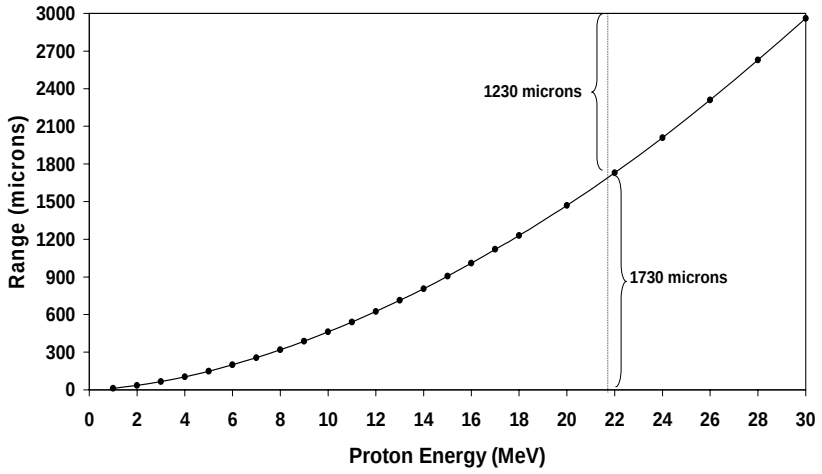


Figure 2. Proton range variations in arsenic target.

Chemical Processing

The irradiated targets were transferred to the radiochemistry laboratory. Many methods were considered for the separation of selenium-73, 75 from the starting arsenic pellets. Mushtaq *et al.* used a pressure accelerated anion exchange resin with 25% loss of radioactivity after ion exchange chromatography (Mushtaq *et al.* 1988). Thermo-chromatography did not yield good results due to reported technical problems (Blessing *et al.* 1994). Solvent extraction could give good results under carrier-added conditions but toxicity of the products was high due to the presence of carrier selenium in high concentrations (Nozaki *et al.* 1979, Plenevaux and Guillaume 1990). By solvent extraction using ultra pure benzene (Nozaki *et al.* 1979) under no carrier added (NCA) conditions, ^{73}Se was reported to obtain in high radiochemical yields.

In this research, chemical processing was performed for the two target pellets separately. The arsenic pellets were dissolved in 25ml of concentrated aqua-regia (HNO_3, HCl; 1:3 v/v) and heated to dryness. The residue was dissolved in 25% HCl and heated indirectly (through a water bath) at various temperatures while a flow of

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sulfur dioxide gas bubbled into the active solution to reduce trace amounts of [^{73,75}Se]selenium(IV) oxide to elemental ^{73}Se and ^{75}Se, The latter process was necessary since only reduced selenium ions migrate from liquid to organic phase (benzene). Temperatures were precisely controlled by a digital thermometer-thermostat. The best temperature seemed to be 80°C (figure 3).

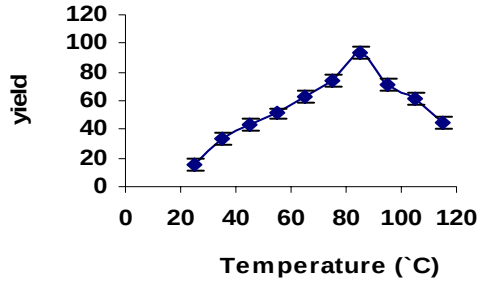


Figure 3. Effect of temperature on the radiochemical yield of selenium, n=5, SE<3%.

Lower temperatures gave lower radiochemical yields due to imperfect reduction process. Higher temperatures yielded lower radiochemical purity possibly due to the formation of volatile selenium chlorides. Surprisingly, sparging the dissolution container with sulfur dioxide, instead of stirring, enhanced the radiochemical yield. This was possibly because of the creation of a suitable thermal equilibrium and crushing of the irradiated pellets (up to 10%).

The elemental ^{73}Se and ^{75}Se were extracted from the acidic solution (25% HCl) by ultra-pure benzene (3´5 ml), followed by dehydration of the mixed organic extracts over anhydrous magnesium sulfate to absorb the possible residues of arsenic in aqueous phase and yield high purity ^{73}Se and ^{75}Se. The organic phase was then evaporated to dryness by a flow of nitrogen gas. Radio-thin layer chromatography (RTLC) (silica, $CHCl_3$-MeOH; 9: 1 v/v) showed the radiochemical and chemical purity of the elemental ^{73}Se and ^{75}Se (R_f= 0.7). To detect possible traces of the starting arsenic in the products, a 0.04 ppm sensitive colorimetric method (Nunn and Waters 1981) using iodinated starch reagent, was used which showed no arsenic in the final products. Gamma-Spectroscopy with HPGe detector and radio-chromatography were performed to check the radionuclide purity and chemical purity of the final solution respectively.

RESULTS

Arsenic targets were bombarded under the above conditions, with a proton current of 5 µA. The production yield for ^{73}Se in the first pellet was 5.3 (mCi/µAh) and the production yield for ^{75}Se was 50 (µCi/µAh) in the first and 678 (µCi/µAh) second pellets. The specific activity of ^{73}Se was 1.06 mCi/ml and that of ^{75}Se was 135.6 µCi/ml after one hour of proton bombardment with a current of 5µA. The results were in accordance with the previous data given in the literature (Mushtaq *et al.* 1988, Dimitriev *et al.* 1973). After a quick chemical separation, the isotopic purity of ^{73}Se was 99% in the first pellet and that of ^{75}Se was 100% in the second, almost just after the end of bombardment. A 0.04 ppm colorimetric method ultra high purity showed no traces of arsenic in the final product which shows a perfect chemical separation performed by no carrier added (NCA) solvent extraction.

Gamma-Spectroscopy of the product with HPGe detector showed high radionuclidic purity for selenium samples. Radio-chromatography of the final solution showed a high chemical purity for elemental ^{73}Se and ^{75}Se.

DISCUSSION

According to the importance of ^{73}Se and ^{75}Se in different fields of study, their production was of great interest. The method introduced in this paper was quite originative and used quick, inexpensive chemical separation processes with high yields, performed for both pellets simultaneously. The results were comparable with the data given in the literature (table 3). It must be noted that although Mushtaq's (1988) results

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seem to have higher thick target yields, their chemical separation method (ion exchange chromatography) resulted in a 25% loss of activity, while we had only lost about 3% of the activity during chemical processing.

Considering the optimal production yield and high isotopic and chemical purity obtained for both radioisotopes, the suggested process can be considered as the method of choice for simultaneous production of ^{73}Se and ^{75}Se radioisotopes.

Table 3. Comparison of the results of this study with the previous data given in the literature.

Research	Radioisotope	Proton Energy (MeV)	Thick Target Yield (μCi/μAh)
Mushtaq *et al.* (1988)	^{75}Se	22	~ 700
	^{73}Se	30	~ 6000
Dmitriev *et al.* (1973)	^{75}Se	6.5	4.5
		9.3	17.7
		11.4	29.5
		15.5	40
		21.8	52
This work	^{75}Se	22	678
	^{73}Se	30	5300

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