

Cyclotron Production and Radiochemical Isolation of the Therapeutical Radionuclide ^{186}Re

I. E. Alekseev and V. V. Lazarev

St. Petersburg State University, St. Petersburg, Russia

Received June 10, 2005

Abstract—The reaction cross sections and the energy dependences of the yields of ^{186}Re in the reactions $^{\text{nat}}\text{W}(d, 2n)$ and $^{186}\text{W}(d, 2n)$ in the range of low deuteron energies (<14 MeV) were determined. The specific features of the physicochemical behavior of impurity ^{186}Re atoms in irradiated tungsten cyclotron targets were studied in relation to the gas medium composition. The yield of the desired product increases with an increase in the oxygen content in the course of heat treatment of the targets. A simple “dry” procedure was developed for isolation of ^{186}Re with a yield no less than 85% and radiochemical purity no worse than 99.99%. A prototype of a cyclotron target for commercial production of the therapeutical radionuclide ^{186}Re was suggested.

PACS numbers: 25.45.-z

DOI: 10.1134/S1066362206050171

Radioactive isotopes and ionizing radiation sources are widely used in science, industry, engineering, and medicine. In the past two decades, two major trends were steadily observed on the world market of radioisotopes: decline in the use of fissile radioactive materials and increase in the production of radionuclides for nuclear medicine [1].

Radionuclide therapy is an actively developing field of nuclear medicine. It has doubtless advantages over other kinds of radiation therapy because of low side effects, minimal damage of normal tissues, and possibility of treating metastases and disseminated tumors.

Presently the annual volume of sells of radionuclides for medicine and of radiopharmaceuticals in the United States (45% of the world market in this field) is about \$700 mln. American marketing companies expect that by 2015 the annual volume of sells of radionuclides for medicine will increase to \$4.5 bln, primarily due to increased production of therapeutical radioisotopes [1].

In the past 3–4 years, the efforts of the leading research laboratories and medical centers (Brookhaven National Laboratory, BNL; Los Alamos National Laboratory, LANL; Paul Scherrer Institute, PSI; Oak Ridge National Laboratory, ORNL, etc.) are focused on the development of processes for production of certain radionuclides (^{47}Sc , ^{89}Sr , ^{131}I , ^{153}Sm , ^{186}Re , ^{188}Re , ^{213}Bi , ^{211}At), among which ^{186}Re occupies a prominent place. The following factors are responsible for the increased interest in ^{186}Re .

This is a short-lived radionuclide ($T_{1/2} = 3.78$ days) undergoing β^- -decay with an “impurity” of electron capture (7.47%) [2]. Short path length of the electrons (their maximal energy is 359.2 keV) in living tissues allows destruction of tumors up to 1 mm in diameter. The intrinsic γ -radiation of the radionuclide (the energy of its main transition, 137.2 keV with an intensity of 9.47%, is approximately the same as that of $^{99\text{m}}\text{Tc}$ widely used in SPECT, 140.5 keV) is well detected with a commercial scintillation γ -ray camera and allows efficient monitoring of the behavior of the labeled preparation in patient’s body.

The main goals of this study are as follows: determination of the reaction cross sections and energy dependences of the yields of ^{186}Re in the reactions $^{\text{nat}}\text{W}(d, 2n)$ and $^{186}\text{W}(d, 2n)$ in the range of low deuteron energies (<14 MeV); study of the specific features of the physicochemical behavior of impurity ^{186}Re atoms in irradiated tungsten cyclotron targets in relation to the gas medium composition; development of a diffusion-thermal procedure for isolating ^{186}Re ; mastering of procedures for preparing cyclotron targets from isotopically enriched (^{186}W) powder materials; and preliminary radiation and materials-science studies of the new types of the targets.

EXPERIMENTAL

Determination of the reaction cross sections and energy dependences of the yields of ^{186}Re in the reactions $^{\text{nat}}\text{W}(d, 2n)$ and $^{186}\text{W}(d, 2n)$ in the range of low deuteron energies (<14 MeV). Cyclotron tar-

gets were prepared from pieces of 20- μm foil (surface density 38.6 mg cm^{-2}) of W metal of natural isotope composition (chemical purity 99.95%) and from powders of isotopically enriched ^{186}W (99.78% enrichment) or of naturally abundant W (chemical purity no less than 99.91%).

Samples were irradiated on a U-120 cyclotron with deuterons (initial energy 13.5 MeV).

The energy dependences of the reaction cross section and yield of ^{186}Re in the energy range 12.84/5.85 MeV (energy threshold of the reaction 3.58 MeV) were measured using foil stacks.

To determine the integral deuteron beam current, we used iron monitors (surface density 16.5 mg cm^{-2} , chemical purity no less than 99.9%) which were arranged along the deuteron beam before and after the tungsten samples [4].

Radiation materials-science studies of cyclotron targets based on isotopically enriched powdered ^{186}W . Preliminary radiation materials-science tests of cyclotron targets were performed on a U-120 cyclotron using deuteron beams (initial energy 13 MeV) of various intensities (maximal beam current 8 μA , beam power up to 40 W).

The cyclotron targets were W/C composites compacted under a pressure of 340–370 atm. Graphite was added as an inert weakly activated (its proton or deuteron irradiation yields only ultra-short-lived radionuclides ^{11}C , ^{13}N) binder having high thermal conductivity. The W/C ratio was varied from 1 : 1 to 1.5 : 1; the surface density with respect to $^{\text{nat}}\text{W}$ was 290–300 mg cm^{-2} , and the bulk density, 1.5–2.0 g cm^{-3} .

The integral deuteron beam current was also determined with iron monitors [4].

Radioisotope composition of irradiated targets and beam monitors was determined by precision γ -ray spectrometry (GX1018 semiconductor HPGe detector). To calibrate the spectrometer scale with respect to energy and determine the efficiency of γ -radiation detection in the energy range 0.120–1.500 MeV, we used a ^{152}Eu reference source (45 kBq) from an OSGI kit.

The activity of the forming radionuclides was determined from the following photopeaks (MeV; in parentheses, intensity, %) [2]: ^{56}Co (beam monitor) 0.8468 (99.93), 1.2383 (66.95); ^{65}Zn (beam monitor) 1.1155 (50.74); ^{186}Re 0.1372 (9.47). The activity of radionuclides in the targets and beam monitors after the irradiation was measured with an accuracy of 2%.

Specific features of physicochemical behavior of impurity ^{186}Re atoms in irradiated tungsten cyclotron targets; development of a procedure for isolating the desired product. We studied the emanation of impurity ^{186}Re atoms from irradiated tungsten cyclotron targets (these experiments were performed with powders of both enriched ^{186}W and naturally abundant W) in relation to the gas medium composition. Samples were annealed at 530–1200 K in a vacuum (residual pressure 10^{-5} – 10^{-4} or 10^{-3} – 10^{-2} torr) or in air (in the latter case, the irradiated tungsten was mixed with a powder of spectrally pure graphite).

The optimal annealing time, 3600 s, was chosen taking into account the results of previous experiments with the generator couple $^{188}\text{W}/^{188}\text{Re}$.

The ^{186}Re egress from the metal was determined from the ratio of the counting rates of the samples before and after etching, using the photopeak at 0.1372 MeV.

The possible loss of W metal during annealing of the foils was determined using similar comparative γ -ray spectrometric measurements of the intensities of the photopeaks at 0.6858 (intensity 31.6%) and 0.4795 MeV (25.3%) of ^{187}W formed by the reaction $^{186}\text{W}(d,p)^{187}\text{W}$, reaction threshold 0 MeV.

RESULTS AND DISCUSSION

Determination of the reaction cross sections and energy dependences of the yields of ^{186}Re in the reactions $^{\text{nat}}\text{W}(d,2n)$ and $^{186}\text{W}(d,2n)$ in the range of low deuteron energies (<14 MeV). The energy dependence of the ^{186}Re yield (recalculated to the end of irradiation) is given below.

Deuteron energy, MeV	Yield of ^{186}Re , $\text{MBq } \mu\text{A}^{-1} \text{ h}^{-1}$
12.84/11.86	0.917
11.86/10.82	0.874
10.82/9.71	0.726
9.71/8.53	0.447
8.53/7.26	0.175
7.26/5.85	0.033

From these data, we calculated the energy dependence of the cross section of the ^{186}Re formation in the examined range of deuteron energies. The results are shown in the figure together with certain published data [5, 6].

The integral yield of ^{186}Re in the energy range 12.84/5.85 MeV was 3.17 $\text{MBq } \mu\text{A}^{-1} \text{ h}^{-1}$, which is in good agreement with published data [5–9].

With enriched W samples, the yield of the desired product can be increased to $11.1 \text{ MBq } \mu\text{A}^{-1} \text{ h}^{-1}$; with 99.78%-enriched ^{186}W , we measured the ^{186}Re yield in the energy range 12.8/10.8 MeV. The yield of the desired product was $6.29 \text{ MBq } \mu\text{A}^{-1} \text{ h}^{-1}$, which is fully consistent with the results of previous studies made with foil stacks.

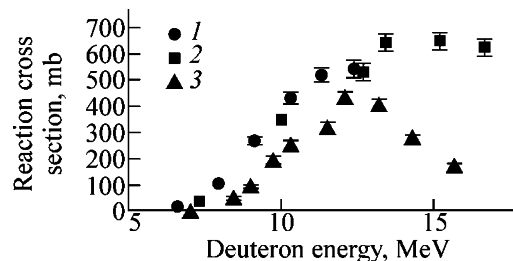
Specific features of physicochemical behavior of impurity ^{186}Re atoms in irradiated tungsten cyclotron targets; procedures for isolating the desired product. In some systems (e.g., Mo: ^{99m}Tc , Sn: ^{113m}In , W: ^{188}Re), a polymorphous transition is accompanied not only by accelerated diffusion associated with the radiation damage of the metal upon irradiation, but also by emanation into the gas phase of impurity atoms that diffused to the metal surface [10–13]. Below we give as example data on the emanation of ^{113m}In from Sn metal to the gas phase above the point of the polymorphous transition of the metal from tetragonal to hexagonal modification (Sn, $\beta \rightarrow \gamma$, 446 K) [11, 12].

Annealing temperature, K, ± 2	463	473	483	493	500
Release into gas phase, %	6.0	8.7	12	15	20

The discovered phenomenon formally resembles the classical emanation of inert gases from crystalline salts [14] and release of volatile fission products from UO_2 [15].

It should be emphasized that such processes are observed only in systems with polymorphism. In particular, in the Sn: ^{113m}In system the release of the ^{113m}In atoms into the gas phase starts in the temperature range of the $\beta \rightarrow \gamma$ polymorphous transition (from 453 K), and in the Cd: ^{111}In system no “volatilization” of impurities is observed even at temperatures approaching the melting point (575–585 K) [16]. Studies of the emanation in the Sn: ^{113m}In system also showed that the release of the impurity atoms into the gas phase depends on the nuclear and physicochemical history of the sample, conditions of foil annealing, and composition of the gas medium [10, 11].

As in the case of the Sn: ^{113m}In system, in the W: ^{186}Re system we also observed the release of daughter atoms into the gas phase, taking place only in a combination with a polymorphous transition. Annealing of the irradiated metal at temperatures below the phase transition point (<1000 K) was not accompanied by the egress of ^{186}Re from the bulk of the metal (these experiments were performed only with



Cross section of the $^{186}\text{W}(d, 2n)^{186}\text{Re}$ reaction as a function of deuteron energy: (1) this study, (2) data of [5], and (3) data of [6].

irradiated W powders, because a polymorphous transition in W was discovered only in finely dispersed samples [17]).

Heating of irradiated W above the polymorphous transition point (>1000 K) was accompanied by the release of ^{186}Re into the gas phase; the release of the impurity atoms from the bulk of the metal became more active with an increase in the oxygen content in the medium in the course of heat treatment of the targets. In particular, when the irradiated cyclotron targets were annealed at 10^{-5} – 10^{-4} torr, the release of ^{186}Re did not exceed 3%, at 10^{-3} – 10^{-2} torr it did not exceed 15%, and when the samples (W/C composites) were heated in air, the release increased to 65% (typical value for the majority of our experiments). This fact strongly suggests that, along with the emanation occurring at polymorphous transitions, there is some other process facilitating the release of radioactive microimpurities (in the form of volatile rhenium species ReO_3 , Re_2O_7) into the gas phase, e.g., their release in the course of cyclic gas transport reactions of the following type: oxidation of irradiated W metal with atmospheric oxygen \rightarrow sublimation of WO_3 with the release of impurity ^{186}Re atoms into the gas phase \rightarrow condensation of WO_3 on graphite powder followed by its reduction to metal \rightarrow reoxidation of W metal, etc.

We took this separation scheme as a basis for a “dry” process for ^{186}Re production. Further experiments showed that the yield of the desired product can be increased to 85%, with its radiochemical purity being no worse than 99.99%.

Radiation materials-science studies of cyclotron targets based on isotopically enriched powdered ^{186}W . In view of the above facts, it seemed appropriate to take pressed $^{186}\text{W/C}$ composites as cyclotron targets for preparing ^{186}Re .

Radiation tests of such targets in charged particle beams with a power of up to 40 W (at mean deuteron

beam currents of 4–8 μA) confirmed that these targets can be used as prototypes of cyclotron targets for commercial production of the therapeutical radionuclide ^{186}Re .

ACKNOWLEDGMENTS

The study was financially supported by the Russian Foundation for Basic Research (project no. 06-02-16772) and by the International Science and Technology Center (project no. 1795).

REFERENCES

1. Radionuclide Production, *Report of American Business Linkage Enterprise*, 1997, no. A3157.
2. Magill, J., *Nuclides 2000: An Electronic Chart of the Nuclides on the CD-ROM*, Karlsruhe (Germany): European Commission, Inst. for Transuranium Elements, 1999, 1st ed.
3. Mausner, L.F., Kolsdky, K.L., Joshi, V., et al., *Appl. Radiat. Isot.*, 1998, vol. 49, no. 4, pp. 285–294.
4. Charged Particle Cross-Section Database for Medical Radioisotope Production: Diagnostic Radioisotopes and Monitor Reactions, *IAEA-TECDOC-1211*, Vienna: IAEA, 2001.
5. Nassiff, S.J. and Munzel, H., *Radiochim. Acta*, 1973, vol. 19, p. 97.
6. Zhenlan, T., Fuying, Z., Huiyuan, Q., and Gongqing, W., *Chin. J. Nucl. Phys.*, 1981, vol. 3, p. 242.
7. Szelescsenyi, F., Takacs, S., Tarkanyi, F., et al., *J. Label. Comp. Radiopharm.*, 1999, vol. 42, pp. 912–914.
8. Scharzbach, R., Blauenstein, P., Jegge, J., and Schubiger, P.A., *J. Label. Comp. Radiopharm.*, 1995, vol. 37, p. 816.
9. Ishioka, N.S., Watanabe, S., Osa, A., et al., *J. Nucl. Sci. Technol.*, 2002, suppl. 2, pp. 1334–1337.
10. Alekseev, I.E., Bondarevskii, S.I., and Eremin, V.V., *Radiokhimiya*, 1991, vol. 33, no. 6, pp. 138–139.
11. Alekseev, I.E., Bondarevskii, S.I., and Eremin, V.V., *Radiokhimiya*, 1998, vol. 40, no. 5, pp. 427–443.
12. Alekseev, I.E. and Antropov, A.E., *Radioact. Radiochem.*, 2000, vol. 11, no. 2, pp. 38–43.
13. Alekseev, I.E. and Antropov, A.E., *Radiokhimiya*, 2002, vol. 44, no. 4, pp. 334–336.
14. Nesmeyanov, A.N., *Radiokhimiya* (Radiochemistry), Moscow, 1972.
15. Matzke, H. and Ronchi, C., Program and Abstracts, *IUPAC Conf. on Chemical Thermodynamics and 39th Calorimetry Conf. Joint Meet.*, Hamilton, 1984, sect. 1, p. 155.
16. Alekseev, I.E., Antropov, A.E., Darmograi, V.V., and Maslennikov, D.E., *Radiokhimiya*, 2001, vol. 43, no. 6, pp. 515–520.
17. Morokhov, N.D., Chizhin, S.P., Gladkikh, N.T., and Grigor'eva, L.K., *Dokl. Akad. Nauk SSSR*, 1978, vol. 243, no. 4, pp. 917–920.