Brief Communications

Photonuclear production of carrier-free radionuclides: ^{69m}Zn

R. A. Aliev,[a,b]★ G. S. Aleshin,[b] S. S. Belyshev,[c] B. S. Ishkhanov,[c,d] A. B. Priselkova,[d] V. Yu. Pozharskaya,[c] V. V. Khankin,[d] M. A. Orlova,[b,e] and S. N. Kalmykov[a,b]

[a]*National Research Center "Kurchatov Institute," 1 pl. Akad. Kurchatova, 123098 Moscow, Russian Federation. E-mail: ramiz.aliev@gmail.com*
[b]*Department of Chemistry, M. V. Lomonosov Moscow State University, Build. 3, 1 Leninskie Gory, 119992 Moscow, Russian Federation*
[c]*Department of Physics, M. V. Lomonosov Moscow State University, Build. 2, 1 Leninskie Gory, 119992 Moscow, Russian Federation*
[d]*D. V. Skobeltsyn Research Institute of Nuclear Physics of M. V. Lomonosov Moscow State University, Build. 2, 1 Leninskie Gory, 119992 Moscow, Russian Federation*
[e]*Dmitry Rogachev National Research Center of Pediatric Hematology, Oncology, and Immunology, 1 ul. Samory Mashela, 117997 Moscow, Russian Federation*

The yields of ^{66}Ga, ^{67}Ga, ^{68}Ga, ^{70}Ga, ^{65}Zn, and ^{69m}Zn upon irradiation of gallium with the natural isotopic composition by the bremsstrahlung photon beam with the energy up to 55 MeV were measured. The yield of ^{69m}Zn yield was 0.13 MBq μA^{-1} h^{-1} g^{-1}. A simple and rapid method for ^{69m}Zn separation based on the extraction of gallium followed by ion-exchange chromatography was proposed.

Key words: zinc, radionuclides, preparation of ^{69m}Zn, photonuclear reaction.

Zinc is a basically important microelement for the organism. On the one hand, at the physiological concentration zinc is a protector of cells and tissues. On the other hand, the violation of zinc homeostasis leading to its deficient or excess causes cell apoptosis. The active role of zinc during various diseases, including Alzheimer´s, Parkinson´s, and other diseases.[1,2]

The introduction of radioactive zinc into the organism can have a significant diagnostic function due to the dual effect of the action of zinc upon cells. In the case of the corresponding vector delivering zinc or its compound to a tumor tissue, the possibility of therapeutic effect appears for the treatment of cancer. Since there are many specific and non-specific zinc transporters in the human organism,[3] both functions of radioactive zinc can be successful under certain conditions. This is especially probable because zinc is widely able to complex formation[4]; *i.e.*, the probability to find an appropriate specific chelating vector is rather high. Attempts to use ^{69m}Zn and ^{71m}Zn for medical purposes have already been made pre-

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viously,[5,6] but were not properly developed. For example, it was proposed to apply ^{69m}Zn for the study of brain tumors.[7] However, these studies were not brought to clinical completion. This radionuclide can also be used as a radiotracer when studying the behavior of zinc in various living systems.[8]

The ^{69m}Zn isotope can be obtained by the irradiation of gallium by fast neutrons *via* the reaction ^{69}Ga(n,p)^{69m}Zn (the reaction cross section in a range of 7.5—14.5 MeV were obtained earlier[9]). Another method is irradiation of ^{71}Ga by protons *via* the reaction ^{71}Ga(p,2pn)^{69m}Zn. The yield of this process is about 36 MBq μA^{-1} h^{-1} at the energy of protons 60 MeV.[10—12] The irradiation of gallium by deuterons[12] also results in the formation of ^{69m}Zn in the reaction ^{nat}Ga(d,x)^{69m}Zn. The possibility of the photonuclear production of ^{69m}Zn *via* the reaction ^{71}Ga(γ,pn)^{69m}Zn was studied.[13] An analysis of literature data shows that experimental works concerning ^{69m}Zn preparation are fairly few. The purpose of the present work is the further study of the photonuclear method for the preparation of ^{69m}Zn and separation of this radionuclide for subsequent biochemical assays.

Experimental

The gallium target of the natural isotopic composition was irradiated at the Research Institute of Nuclear Physics of the M. V. Lomonosov Moscow State University on a racetrack microtron with the bremsstrahlung photon beam obtained by the retardation of electrons with an energy of 55 MeV in a tungsten converter with a thickness of 2.1 mm. An aluminum electron absorber (3 cm) was placed behind the converter, and a target of liquid metallic gallium in a cylindrical polystyrene container (diameter 16 mm, thickness 2.8 mm) was placed directly behind the absorber. The target weight was 3.43±0.01 g. A copper foil-monitor with a diameter of 16 mm and a thickness of 0.1 mm was used to control the irradiation parameters. The average accelerator current was 84 nA. The current was monitored using Faraday´s cylinder. In addition, activation monitoring based on measurements of radionuclide ^{64}Cu formed in copper foil-monitors *via* the reaction ^{65}Cu(γ,n)^{64}Cu was used. The current values determined by the copper monitors were used in all calculations of the yields. Faraday´s cylinder was applied only to control the stability of current during irradiation.

The radioactivity of the activation products was measured on a γ-spectrometer with a Canberra GC 3020 HPGe detector. The activity of ^{69m}Zn was determined by a γ-line of 438.6 keV (94.8%). The standard point sources "Standard Spectrometric γ-Emitters" were used for calibration. The irradiated samples were measured at a significant distance from the detector (15 cm), which made the geometry close to point. When measuring bulky samples, the efficiency of detection was modeled using the GEANT 4 program.[14]

The irradiated target was dissolved in a mixture of concentrated hydrochloric and nitric acids (3 : 1 vol/vol), evaporated to wet salts, and repeatedly dissolved in 6 *M* HCl. The bulk gallium was extracted two times by equal volumes of methyl isobutyl ketone. Then the aqueous phase was diluted to a concentration of 2 *M* with respect to HCl and passed through a column packed with the anion-exchange resin Dowex 1×8 (Cl^- form, length 9 cm, volume 3.5 cm^3), which was then washed with 2 *M* HCl. Under these conditions, zinc retained on the column, and other impurities (including gallium) passed freely through the column. After this, zinc was eluted from the column with distilled water. The completeness of separation was monitored using a γ-spectrometry.

Results and Discussion

The irradiation of the Ga target affords a series of gallium and zinc isotopes (Table 1). As should be expected, the major are the (γ,n)-reactions leading to gallium isotopes.

Only one series of literature data[13] on the yields of ^{69m}Zn at a maximum energy of bremsstrahlung photons of 30—60 MeV is available. According to these data, about 52 MBq of ^{69m}Zn can be obtained upon irradiation for 5 h on an accelerator with an average current of 150 μA at a maximum energy of bremsstrahlung photons of 60 MeV. These calculations result in the estimate of the yield of 0.078 MBq μA^{-1} h^{-1} and correspond to the target with a weight of 1 g.

The yield of photonuclear reactions depends on many factors, in particular, on the shape of the bremsstrahlung spectrum (which is determined, in turn, by the energy of the electron beam and material and thickness of the converter) and on the target geometry. Therefore, in most cases, it is difficult to directly compare the absolute yields obtained on different setups. Unlike absolute yields, relative results depends less on experimental conditions, especially when comparing the reactions with close thresholds. The ratio of activity yields ^{67}Ga/^{69m}Zn equal to 5.6 was obtained in this work, which is comparable with the earlier determined[13] value of 6.1.

Liquid extraction or ion-exchange chromatography can be used for the separation of gallium and zinc. The methods for gallium and zinc separation are well studied. Gallium can be separated by extraction[15] with diisopropyl ether from 7 *M* HCl, while zinc is not extracted

Table 1. Yields of radionuclides upon irradiation of gallium with the natural isotopic composition by bremsstrahlung photons with the energy up to 55 MeV

Radionuclide	$T_{1/2}$	Route of formation	Yield /MBq μA^{-1} h^{-1} g^{-1}
^{70}Ga	21.1 min	^{71}Ga(γ,n)^{70}Ga	205±20
^{68}Ga	67.6 min	^{69}Ga(γ,n)^{68}Ga ^{71}Ga(γ,3n)^{68}Ga	66±9
^{67}Ga	3.26 days	^{69}Ga(γ,2n)^{67}Ga	0.170±0.020
^{66}Ga	9.49 h	^{69}Ga(γ,3n)^{66}Ga	0.077±0.010
^{69m}Zn	13.76 h	^{71}Ga(γ,pn)^{69m}Zn	0.030±0.003
^{65}Zn	244.26 days	^{69}Ga(γ,p3n)^{65}Zn	(3.5±0.6)·10^{-5}

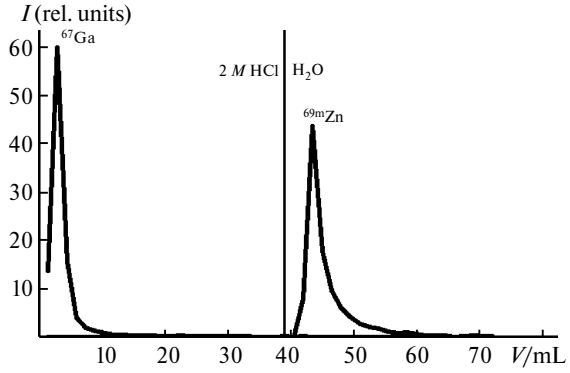

Fig. 1. Chromatogram of ^{69m}Zn separation. Sorbent Dowex 1×8, column with a length of 9 cm and a volume of 3.5 cm^3.

under these conditions. Zinc and gallium can be separated on a cation-exchange column in a hydrochloric medium. Unlike gallium, zinc is not retained in a medium of 10 *M* HCl, and gallium can then be eluted with 4 *M* HCl. In this case, copper is eluted along with zinc.[16] The separation can also be carried out in an ammonia medium where gallium is presented as a $[Ga(OH)_4]^-$ anion and is not retained on a chromatographic column packed with the cation-exchange resin,[17] unlike zinc and copper giving positively charged ammoniates $[M(NH_3)_4]^{2+}$.

In this work, we used the method of anion-exchange separation in hydrochloric media (the chromatogram is presented in Fig. 1). The yield of ^{69m}Zn was 92%. When targets with a higher weight (more than 0.5 g) are irradiated, it seems reasonable to preliminarily separate the major mass of gallium by extraction with methyl isobutyl ketone from 6 *M* HCl. The results of our experiments showed that more than 90% gallium were removed within two stages of extraction.

To conclude, we studied the possibility of photonuclear preparation of ^{69m}Zn by the irradiation of metallic gallium of the natural isotopic composition with photons obtained by the bremsstrahlung electron beam with an energy of 55 MeV in the tungsten target. Radionuclide ^{69m}Zn was separated from the irradiated target using liquid extraction and ion-exchange chromatography. The obtained product contains a minor impurity of ^{65}Zn (less than 0.1% at the end of irradiation), which is undesirable for the subsequent biomedical use of ^{69m}Zn radionuclide. However, its content can be decreased if necessary when using enriched ^{71}Ga as a target.

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