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THE COPPER RADIOISOTOPES PRODUCTION OF MEDICAL INTEREST

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Abstract
The isotopic neutron sources of ^{241}Am-^{9}Be and ^{239}Pu-^{9}Be and the cyclotron were used for the production of some medical interest radioisotopes such as: ^{61,64}Cu. The ^{64}Cu radioisotope is both a beta and a positron emitter, being used for labelling of PET imaging radiopharmaceuticals. This radioisotope was also obtained by irradiation of ^{64}Zn target at a Scanditronix MC40 cyclotron with a 19.5 MeV deuteron beam energy. All produced radioisotopes were analysed by γ-spectrometry with Ge-Li detectors.
Keywords: radioisotopes, γ-spectrometry, neutron sources, cyclotron, PET, radiotherapy.

1. Introduction

Radionuclides are often used for imaging and as tracers to study processes in a wide variety of fields. In particular, they are commonly applied in diagnostic medicine, clinical chemistry, molecular biology, and research in the natural and life sciences [1]. A well-known PET radioisotope is ^{64}Cu, which is both a positron and a beta emitter, and is already used for labeling of some radiopharmaceuticals for PET imaging, as well as for systemic radiotherapy and radionuclide immunotherapy of tumours.

One of the most used method of producing radioisotopes is that of irradiation with neutrons obtained from isotopic neutron sources of (α, n) type [2, 3]. The performance in radionuclides production is about 10^3- 10^6 times lower than in the case of the nuclear reactor.

The cyclotron production methods of radioisotopes with medical applications have been studied by several groups [1, 4, 5, 6]. Among other possible methods for cyclotron production of ^{64}Cu, together with the short-lived positron emitter ^{61}Cu ($T_{1/2}$ = 3.4 h), deuteron irradiation of zinc of natural isotopic composition via the (d,αn) and (d,2pn) nuclear reactions has been studied. The experimental excitation functions for deuteron irradiation of natural zinc targets have been also measured in the energy range of 10 to 19 MeV [1]. Table 1 shows the main nuclear reactions induced by deuterons in natural zinc including the calculated thick target yields of the corresponding radioisotope [4, 5]. As indicated in Table 1, deuteron irradiation of natural zinc leads to the simultaneous production of both Cu and Ga radioisotopes.

Table 2. *Main nuclear reactions induced by deuterons in natural zinc target together with the γ-emissions energies and intensities of the produced radionuclides [1]*

Radioisotope	Nuclear reaction	Main γ-emission (keV) and Abundance (%)	Thick target yield (MBq/μA.h)
^{64}Cu T $_{1/2}$ = 12.70 h	^{64}Zn(d,2p) ^{66}Zn(d,α) ^{67}Zn(d,αn) ^{68}Zn(d,α2n)	1345.84 (0.473)	14.12 8.60 3.36 0.01 sum: 26.09
^{61}Cu T $_{1/2}$ = 3.33 h	^{64}Zn(d,αn)	656.01 (10.77)	179.20
^{67}Ga T $_{1/2}$ = 3.26 d	^{66}Zn(d,n) ^{67}Zn(d,2n) ^{68}Zn(d,3n)	184.58 (21.2) 300.22 (16.8) 393.53 (4.68)	15.28 3.78 0.21 sum: 19.27
^{66}Ga T $_{1/2}$ = 9.49 h	^{66}Zn(d,2n) ^{67}Zn(d,3n)	833.50 (5.896) 1039.35 (37.00)	109.12 0.29 sum: 109.41
^{69m}Zn T $_{1/2}$ = 13.76 h	^{68}Zn(d,p) ^{70}Zn(d,pn)	438.63 (94.77)	28.06
^{65}Zn T $_{1/2}$ = 244.26 d	^{64}Zn(d,p) ^{66}Zn(d,p2n) ^{64}Zn(d,n)+ decay	1115.55 (50.6)	0.29 ~ 0 ~ 0 sum: 0.29

2. Experimental

The irradiation block used for the neutron activation has two isotopic neutron sources of $^{241}Am-^{9}Be$ and $^{239}Pu-^{9}Be$ with a fluence of $1.1\cdot10^{7}$ n/s and $5.5\cdot10^{7}$ n/s respectively. These two sources are introduced in a closed-end tube, which is placed inside a paraffin block. The function of the pure paraffin block is to slow down the neutrons through multiple collisions with the hydrogen atoms. The so called “slowed down” neutrons end up in the lateral channels, where our samples are set. The gamma spectra of the obtained radioisotopes were acquired using a Ge(Li) detector KOVO type, coupled to a multichannel analyzer ICA-80 type. The calibration in efficiency was made using a ^{226}Ra source with an activity of 3.33 kBq. This made possible an accurate determination of the radioisotopes peak energies and therefore, the identification of their disintegration schemes.

In the case of the ^{64}Cu production by deuteron irradiation at the Joint Research Centre Cyclotron in Ispra, Italy, a stack of 5 foils of ^{64}Zn of 14 ± 0.50 μm thickness together with the Ti monitor was prepared. In order to avoid any losses of activity by recoil processes, each of the foils was enveloped in a catcher foil of pure Al of 22.5 ± 1 μm thickness. The irradiation of the stack was carried out at the Scanditronix MC 40 cyclotron for about 3 h at a very low beam current in order to prevent any significant heating of the foils. The activities produced in the irradiated foils were assessed by using high-resolution γ-spectrometry with a HPGe detector, calibrated in energy at efficiency by using two certified standard ^{152}Eu sources (of 1μCi and 10μCi) at different geometries from the Ge crystals.

3. Results and discussion

Using neutron isotopic sources of Am-Be and Pu-Be, with a total fluence of $6.6 \cdot 10^7$ n/s, the following nuclear reactions were studied: $^{63}Cu(n,\gamma)^{64}Cu$, $^{65}Cu(n,\gamma)^{66}Cu$. The samples containing the target isotopes were irradiated by the neutron sources and the γ-spectra of the produced radioisotopes were then acquired. By analyzing each peak energy on the spectra, it can be determined the type of the new produced radioisotope.

It was also taken in account the disintegration curve, which provides the half-life of the formed radioisotopes, especially in the case of copper isotopes, when some interferences appear on the same peak such as the annihilation peak at 511 keV (Fig.1).

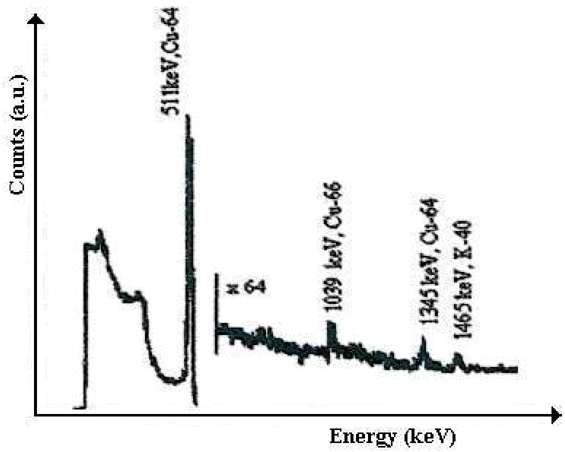

Fig.1 *Characteristic gamma spectrum of ^{64}Cu*

The appearance of the 511 keV annihilation peak on the γ-spectrum of the studied sample, clearly shows that it contains the ^{64}Cu radionuclide. The weak peak from 1345 keV corresponds also to ^{64}Cu from the reaction $^{63}Cu(n,\gamma)^{64}Cu$ with half-life of 12.7 h. Another weak peak on the spectrum from 1039 keV is due to ^{66}Cu from the reaction $^{65}Cu(n,\gamma)^{66}Cu$ with a short half-life of 5.15 min.

In order to produce ^{64}Cu used for PET experiments with high specific activity, deuteron irradiation on enriched zinc targets has been performed at a cyclotron. The experimental excitation functions for the $^{64}Zn(d,2p)^{64}Cu$ reaction up to 19.5 MeV deuteron energy by using the stack foil technique, were measured. The γ-spectrometry was used to measure qualitatively and quantitatively activities of the various produced radioisotopes (Fig.2). In all the acquired γ-ray spectra, the γ-peak of ^{64}Cu had a statistical counting uncertainty not greater than 5 %.

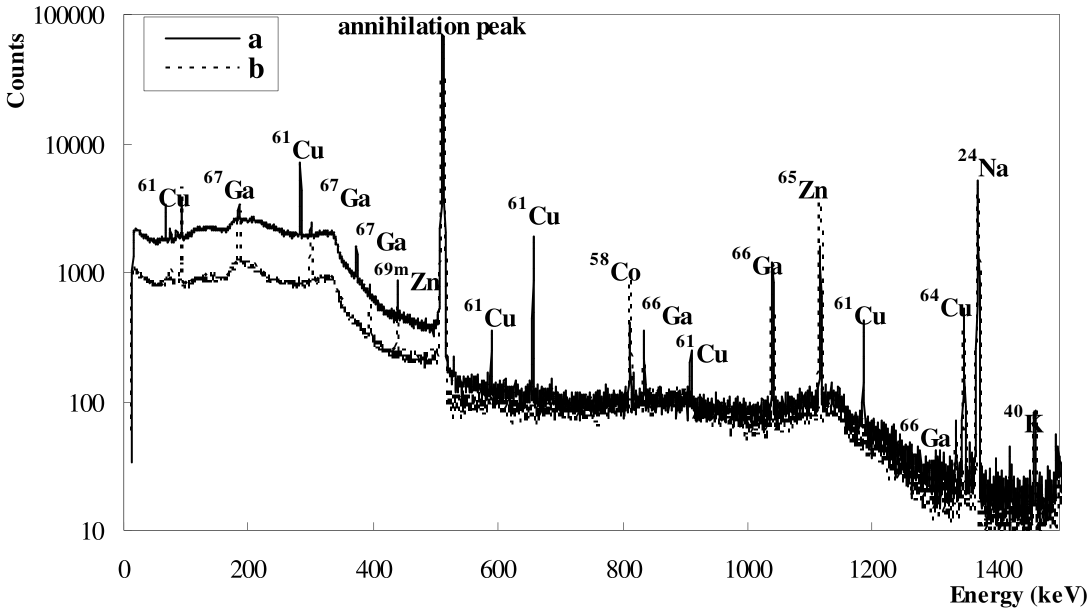

Fig.2 *Two γ-ray spectra of an activated ^{64}Zn foil acquired twice after one day (a) and after two days (b) respectively from the end of irradiation*

Two typical γ-ray spectra of an activated ^{64}Zn foil together with the enveloping Al foils acquired twice after one day (spectrum a) and after two days (spectrum b) respectively from the end of the deuteron irradiation (Fig.2). The γ–peak of ^{64}Cu (1345.84 keV) together with those of ^{61}Cu (282.96, 656.01, 1185.23 keV) are well resolved.

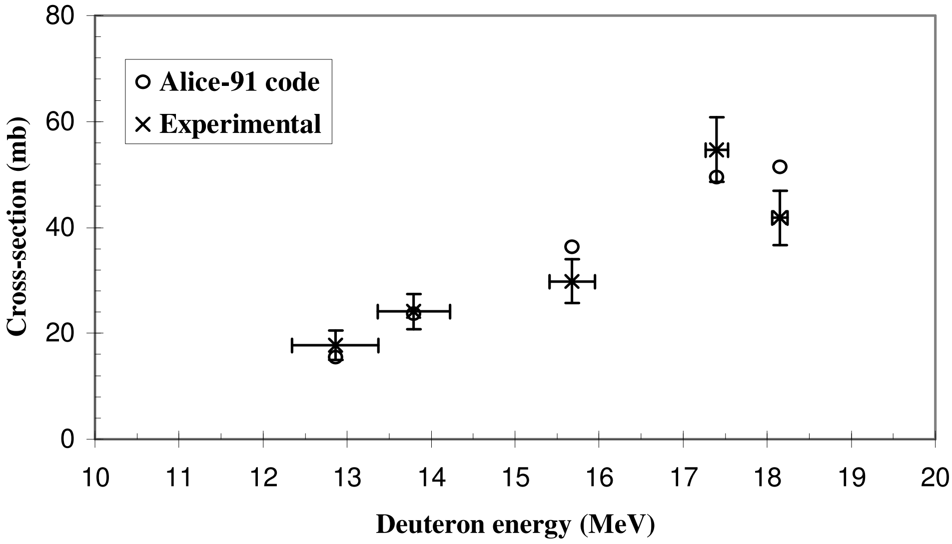

Fig.3 *Measured excitation function of the* $^{64}Zn(d,2p)^{64}Cu$ *reaction*

The excitation function of the reaction ^{64}Zn(d,2p)^{64}Cu in the deuteron energy range below 19.5 MeV is shown in Fig.3 The cross-section uncertainties were determined by considering uncertainties of ^{64}Cu measured activities and deuteron integrated beam current. The different deuteron energy uncertainties have been calculated using SRIM 2003 code [7] by taking into account thickness uncertainties of the different foils of the stack. The theoretical function calculated with the Alice-91 code is also shown for comparison. The theoretical and experimental functions are in good agreement. As predicted by theory, the thick target yields of ^{64}Cu in the cases of deuteron irradiation of natural Zn or of enriched ^{64}Zn samples are only slightly different and are in good agreement with values reported in the literature [1, 5] for deuteron irradiation of natural Zn. The advantage of using enriched ^{64}Zn as target material is that simultaneous Ga radioisotope production (Fig.2) is practically avoided [4].

4. Conclusions

It is shown that by using the isotopic neutron sources some radioisotopes with great importance in nuclear medicine such as: ^{116m}In, ^{198}Au, ^{56}Mn, ^{64}Cu, could be produced in local physical and clinical laboratories. This is a great advantage taking into account their short half-life and the transport difficulties.

The production of ^{64}Cu and its experimental excitation functions via the $^{64}Zn(d,2p)^{64}Cu$ reaction, determined by the stack foil technique on enriched ^{64}Zn material are in good agreement with theoretical curves and with previously reported results on deuteron irradiation of natural Zn.

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