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THE PRODUCTION AND CHARACTERIZATION OF SOME MEDICALLY USED RADIOISOTOPES

Laura Daraban, O. Cozar, T. Fiat, L. Daraban

Faculty of Physics, University Babes- Bolyai, Cluj- Napoca, Romania

Abstract
Radionuclides are often used in medicine diagnosis, clinical chemistry, molecular biology and other life sciences fields. The isotopic neutron sources of ^{241}Am-^{9}Be and ^{239}Pu-^{9}Be and the cyclotron are normally used for the production of some medical interest radioisotopes such as: ^{116m}In,^{56}Mn, ^{198}Au, ^{61,64}Cu. The radioisotope ^{64}Cu is both a positron and a beta emitter and is already used for labelling of PET imaging radiopharmaceuticals. In order to study the production of ^{64}Cu, the stacks consisting of ^{64}Zn foils, Ti monitor foils and Al catcher foils were irradiated at a Scanditronix MC40 cyclotron with a 19.5 MeV deuteron beam energy. The activities of the various product isotopes in the foils were analysed by γ-spectrometry with HPGe detectors. The average deuteron energies in the foils were calculated with the SRIM 2003 code. Theoretical excitation functions calculated with the Alice-91code were compared with the experimental ones and a reasonable agreement was found. This study provides the first experimental data regarding the deuteron induced ^{64}Zn(d,2p)^{64}Cu reaction on enriched ^{64}Zn.
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. A well-known PET radioisotope is ^{64}Cu, which is both a positron and a beta emitter, and is already used for labeling of radiopharmaceuticals for PET imaging (maximum range of β^+ in soft tissue ca. 2.7 mm and "average" range ca. 1 mm), as well as for systemic radiotherapy and radionuclide immunotherapy of tumours [5, 10]. The method of producing radioisotopes through a mechanism of irradiation with neutrons consists of bombarding some elements with different energy neutrons [1, 2]. Neutrons obtained from isotopic neutron sources of (α, n) type were used in this work. These neutron beams provided by these sources were obtained from nuclear reactions initiated by the radioisotopic constituents. The performance consists in a radionuclides production by using isotopic neutron sources having a fluence of about $10^3 - 10^6$ times lower than the nuclear reactor.

The cyclotron production methods of radioisotopes with medical applications have been studied by several groups [4, 5, 7, 10, 12, 13]. Among other possible methods for cyclotron production of ^{64}Cu, together with the short-lived positron emitter ^{61}Cu ($T_{1/2}$ = 3.4h), deuteron irradiation of zinc of natural isotopic composition via the (d,αxn) and (d,2pxn) 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 [5]. Table 2 shows the main nuclear reactions induced by deuterons in natural zinc including the calculated thick target yields of the corresponding radioisotope [4, 12]. As indicated in Table 1, deuteron irradiation of natural zinc leads to the simultaneous production of both Cu and Ga radioisotopes.

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

Radioisotope	**Nuclear reaction**	**Main γ-emission (keV) (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 $1.1\cdot10^{7}\,neutrons/s$ and $5.5\cdot10^{7}\,neutrons/s$.

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 source of ^{226}Ra with an activity of 3.33 kBq, which made possible an accurate determination of the radioisotopes peak energies.

In the case of the production of ^{64}Cu 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 at the JRC Ispra, for ca. 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 at the cyclotron were assessed by using high-resolution γ-spectrometry with HPGe detectors: CANBERRA and EG&G ORTEC USA, calibrated in energy at efficiency by using two certified standard ^{152}Eu sources (1μCi, 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: $^{197}Au(n,\gamma)^{198}Au$, $^{115}In(n,\gamma)^{116}In$, $^{55}Mn(n,\gamma)^{56}Mn$, $^{63}Cu(n,\gamma)^{64}Cu$, $^{65}Cu(n,\gamma)^{66}Cu$. The samples containing the target isotopes were irradiated by the neutron sources, the spectra of the product radioisotopes were then acquired and the disintegration curve was drawn. By analyzing each peak energy on the spectrum it can be determined the new produced radioisotope, but also it can be taken in account the disintegration curve, which provides the half-life of the formed radioisotopes, especially if they interfere on the same peak such as the annihilation peak at 511 keV for the copper isotopes.

^{64}Cu (with: $T_{1/2}$ = 12.70 h, β^- 578 keV EP, 38 %, β^+ , 653 keV EP, 18 %; γ at 1345.84 keV, 0.473 %) is a radioisotope suitable for labelling of a wide range of radiopharmaceuticals, for both PET imaging (maximum range of β^+ in soft tissue ≈ 2.7 mm and "average" range ≈ 1 mm), as well as immuno-radionuclide therapy of tumours.

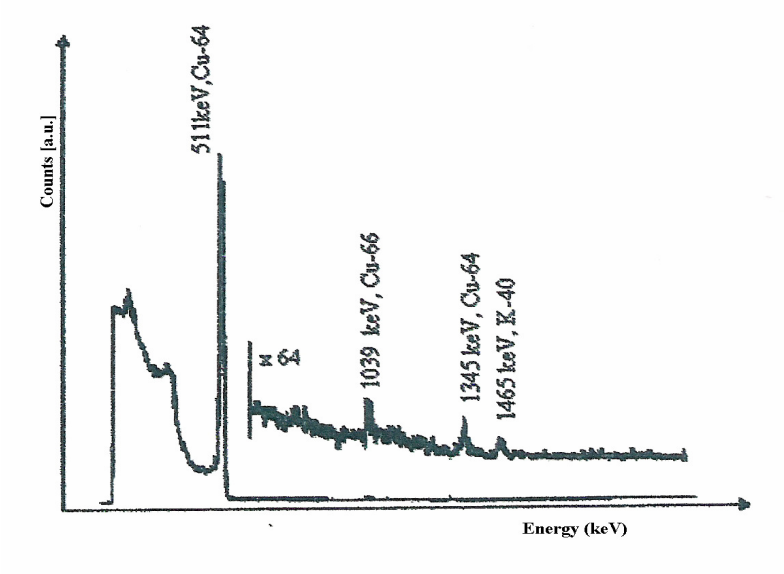

Fig.1 *Characteristic gamma spectrum of* ^{64}Cu

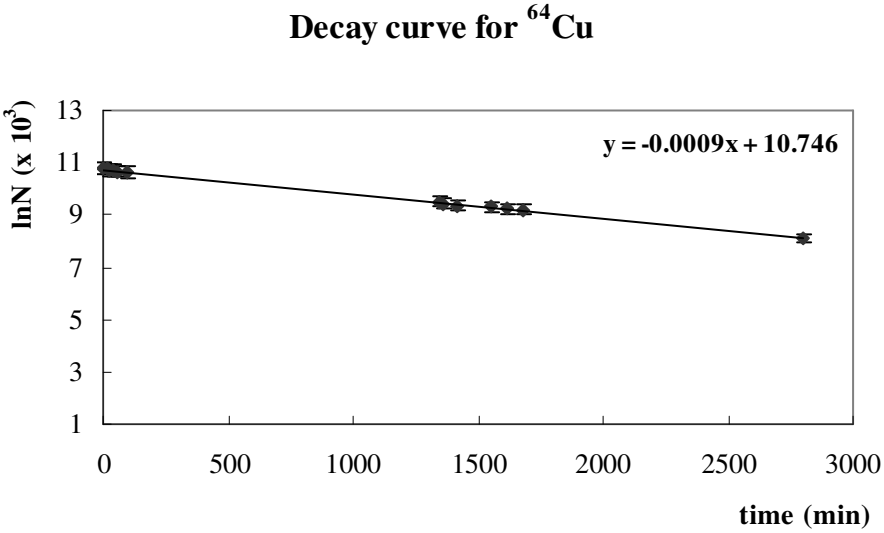

Fig.2 *Decay time calculation for* ^{64}Cu

It can be noticed the appearance of the 511 keV annihilation peak, which shows that the sample contains the ^{64}Cu radionuclide. Also, the peak at 1349 keV is well defined, which corresponds to ^{64}Cu from the reaction $^{63}Cu(n,\gamma)^{64}Cu$ with half-life of 12.7 h, but there is another low peak at 1039 keV of ^{66}Cu with short half-life of 5.15 min from the reaction $^{65}Cu(n,\gamma)^{66}Cu$. By processing our data, we obtained a half-life of 12.83 h for ^{64}Cu compared with the theoretical half-life of 12.7 h (Fig. 2).

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. In all the acquired γ-ray spectra, the γ-peak of ^{64}Cu had a statistical counting uncertainty not greater than 5 %.

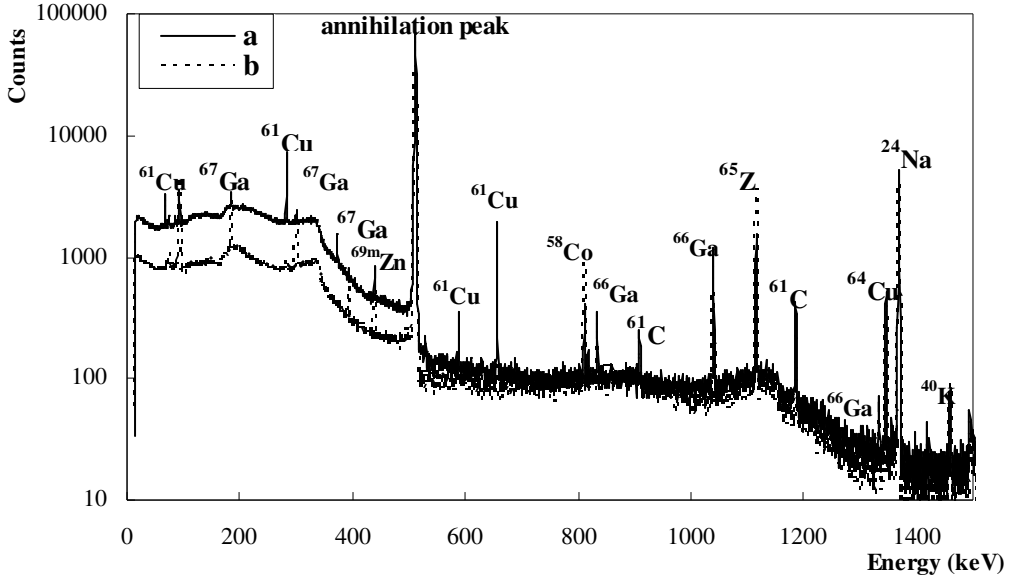

Fig.3 *Two γ-ray spectra of an activated ^{64}Zn foil acquired twice after one day (spectrum a) and two days (spectrum b) respectively from end of irradiation*

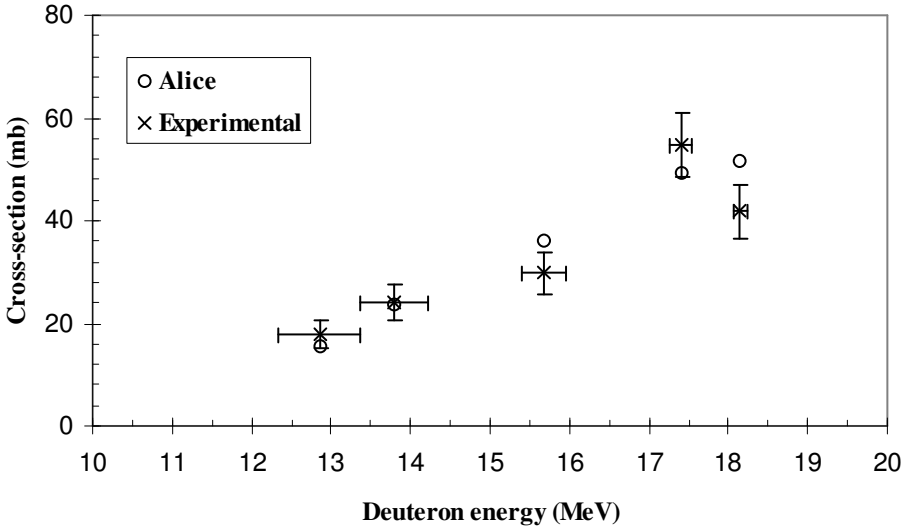

Fig.4 *Measured excitation function of the ^{64}Zn(d,2p)^{64}Cu reaction*

Figure 3 shows 2 typical γ-ray spectra of an activated ^{64}Zn foil together with the enveloping Al foils acquired twice after one day (spectrum a) and two days (spectrum b) respectively from end of the beam. In the spectrum b, the decay of ^{61}Cu is visible. 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.

Figure 4 shows the excitation function of the reaction ^{64}Zn(d,2p)^{64}Cu in the deuteron energy range below 19.5 MeV. 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 by taking into account thickness uncertainties of the different foils of the stack. The theoretical function calculated with the Alice-91 code is also reported 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 are only slightly different and are in good agreement with values reported in the literature [5, 12] for deuteron irradiation of natural Zn. The advantage of using enriched ^{64}Zn as target material is that simultaneous Ga radioisotope production is practically avoided [4].

4. Conclusions

It can be noticed that by using the isotopic neutron sources some radioisotopes with great importance in nuclear medicine, could be produced at the place of application in clinical laboratories such as: ^{116m}In, ^{198}Au, ^{56}Mn, ^{64}Cu. As predicted in literature [3] for these radioisotopes, some small differences in the energetic levels values are reported and their study is worth to be continued.

Also, the production of ^{64}Cu and its experimental excitation functions via the ^{64}Zn(d,2p)^{64}Cu reaction, were determined by the stack foil technique on enriched ^{64}Zn material in the deuteron energy range below 19.5 MeV and are reported for the first time and show a relatively good agreement with theoretical curves and with previously reported results on deuteron irradiation of natural Zn. Our work shows that the use of such enriched material could be interesting as an alternative to other methods for regular production of the ^{64}Cu radioisotope, which is generating considerable interest for applications in Nuclear Medicine.

5. References

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