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An overview of copper radionuclides and production of ^{61}Cu by proton irradiation of ^{nat}Zn at a medical cyclotron

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Abstract

In this article, production methods and applications of copper radionuclides are overviewed with special attention toward ^{61}Cu, due to its interesting nuclear properties. Selection of production parameters for ^{61}Cu including: appropriate nuclear reaction, proton beam energy, target thickness and targetry method are discussed for NRCAM 30 MeV medical cyclotron. $^{64}Zn(p,\alpha)^{61}Cu$ was selected as the best reaction and ^{61}Cu was produced by 22 MeV proton bombardment of a 80 μm thick natural zinc target. After 180 μAh irradiation, the resultant activity of ^{61}Cu was 6.006 Ci (12.015 mCi/μAh). The chemical separation method was easy, quick and efficient (>95%) and yielded a no carrier added product with high chemical and radionuclidic purity (>99%). Detailed comparison with previous production methods confirms that our results are superior to other reports published to date.

Keywords: Copper-61; Production; Targetry; Radiochemical separation; Quality control

1. Introduction

Copper offers a relatively large number of radioisotopes that are potentially suitable for use in nuclear medicine (Anderson et al., 2003; Qaim, 2001; Bass et al., 1997; Cutler et al., 1999). There is a growing interest in the use of ^{64}Cu, ^{62}Cu, ^{61}Cu and ^{60}Cu for diagnostic purposes and ^{67}Cu and ^{64}Cu for targeted radiotherapy (Anderson et al., 2003).

Important nuclear characteristics of copper radioisotopes are given in Table 1.

1.1. Copper-67

Cu-67, the longest lived radioisotope of copper, is an attractive radionuclide for internal therapy with radiolabeled tumor associated monoclonal antibodies due to its suitable decay characteristics and favorable chemical behavior (Deshpande et al., 1988; Mausner et al., 1988; Wessels and Rogers, 1984; Mirzadeh et al., 1986; Hilgers et al., 2003; Anderson and Lewis, 2000; Green et al., 1988; Neirinckx, 1977a). Its half-life is comparable to the uptake and residence time of antibodies especially for solid tumors. This radioisotope has two important gamma ray transitions of 184.6 keV (49%) and 92 keV (23%). Therefore, it allows a diagnostic low dose experiment to determine biodistribution, prior to administration of a therapeutic dose of the same preparation (Dasgupta et al., 1991). Unfortunately, the production of this radioisotope is difficult. The simultaneously generated side products (Szelecsényi et al., 1994; Little and Lagunas-solar, 1983; Nortier et al., 1991) can significantly influence the separation procedure required (Schwarzbach et al., 1995). The most practical method of preparing ^{67}Cu is by the $^{67}Zn(n,p)^{67}Cu$ reaction in a nuclear reactor (O'Brien, 1969; Dasgupta et al., 1991; Schwarzbach et al., 1995; Brown and Callahan, 1972; Mushtaq et al., 1990). It is also produced using high-energy proton beams. The need for these high-energy physics facilities allows only limited availability of this radionuclide (McCarthy et al., 1999). Different nuclear

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Table 1
Nuclear characteristics of copper radioisotopes (Firestone et al., 1996)

Radionuclide	$T_{1/2}$	β^- MeV (%)	β^+ MeV (%)	EC (%)	γ keV(%)
Cu-67	61.83 h	0.576 (20%) 0.4827 (22%) 0.3914 (57%) 0.1825 (1%)	—	—	184.577 (48.7%) 93.311 (16.1%) 91.266 (7.0%)
Cu-64	12.7 h	0.5787 (39%)	0.65308 (17.4%)	43.6%	1345.77 (0.473%) 511 (34.79%)
Cu-62	9.74 min	—	2.927 (97.2%)	2.8%	511 (194.86%) 1173.02 (0.342%)
Cu-61	3.333 h	—	1.2164 (51%) 1.1489 (2.3%) 0.9334 (5.5%) 0.5604 (2.6%)	38.6%	656.008 (10.77%) 511 (120.87%) 373.05 (2.10%) 282.956 (12.2%) 67.412 (4.20%)
Cu-60	23.7 min	—	3.7719 (5%) 2.9456 (15%) 2.4784 (2.8%) 1.9805 (49%) 1.9105 (11.6%) 1.8352 (4.59%)	12.01%	3124.1 (4.8%) 2158.90 (3.34%) 1861.6 (4.8%) 1791.6 (45.4%) 1332.501 (88%) 1035.2 (3.7%) 826.4 (21.7%) 511 (185.19%) 467.3 (3.52%)

reactions with charged particles are suggested for the production of ^{67}Cu such as ^{64}Ni(α,p)^{67}Cu (Sternlieb et al., 1961), ^{68}Zn(p,2p)^{67}Cu (Roberts et al., 1989; McGee et al., 1970; Dasgupta et al., 1991; Schwarzbach et al., 1995), ^{70}Zn(p,α)^{67}Cu (Qaim, 2001), and ^{nat}Zn(d,2pxn)^{67}Cu (Neirinckx, 1977a). It can also be produced by photonuclear reaction ^{68}Zn(γ,p)^{67}Cu from ZnO target (Yagi and Kondo, 1978; Polak et al., 1986; Marceau et al., 1970), RbBr(p,spall) (Grant et al., 1982) and As(p,spall) (Grütter, 1982) reactions. ^{67}Cu has failed to make significant impact in clinical nuclear medicine, mainly because it is available only in limited quantities (Jamriska et al., 1995).

1.2. *Copper-64*

Cu-64 has applications both for imaging and therapy (McCarthy et al., 1997; Anderson et al., 1992, 2003; Hilgers et al., 2003). The study of copper metabolism using radioactive copper tracers, i.e. ^{64}Cu, provides insight into potentially fatal inherited and nutritional disorders (Hetherington et al., 1986; Mushtaq et al., 1990; Dijkstra et al., 1997). Furthermore, ^{64}Cu radiopharmaceuticals are promising for investigation via PET, e.g. for cerebral and myocardial perfusion studies (Dearling et al., 1999; Packard et al., 2002; Green, 1987). ^{64}Cu labeled antibodies used in PET imaging of tumors can be utilized to determine individual radiation dosimetry prior to therapy with ^{67}Cu labeled antibodies (Anderson et al., 1992). Radioimmunoimaging of monoclonal antibodies labeled with ^{64}Cu can provide valuable information on the effectiveness of radioimmunotherapy with ^{67}Cu (Zweit et al., 1991). ^{64}Cu labeled Cu-PTSM can be used as a PET perfusion tracer for tumor blood flow (Mathias et al., 1991b) and ^{64}Cu labeled Cu-bleomycin can be used for tumor imaging (Neirinckx, 1977a). Different ^{64}Cu labeled complexes such as Cu-ASSM, Cu-ATSE and Cu-ATSM have recently been studied as hypoxia imaging agents (McQuade et al., 2005). ^{64}Cu-ATSM has also been studied for the treatment of hypoxic tumors (Obata et al., 2005). However, in many applications its usefulness is severely limited by its half-life (O'Brien, 1969; Marceau et al., 1970). A possible disadvantage of using ^{64}Cu in clinical applications is its β^- emission which could make a significant contribution to the radiation dose to the patient (Zweit et al., 1991).

As a radioisotopic tracer, ^{64}Cu is generally employed (Blower et al., 1996; Smith et al., 1999) because it is easily produced from stable ^{63}Cu by the (n,γ) reaction in a nuclear reactor or in the state of high isotopic purity by the ^{64}Zn(n,p)^{64}Cu reaction (O'Brien, 1969; Mushtaq et al., 1990; Zinn et al., 1994; Van Elteren et al., 1999; Roberts et al., 1989) but the yield is low and contamination from ^{67}Cu cannot be avoided (Szelecsényi et al., 1993). The more useful method is ^{64}Ni(p,n)^{64}Cu reaction on enriched ^{64}Ni, due to the high yield and purity of the product (Maziere et al., 1983; Szelecsényi et al., 1993; McCarthy et al., 1997; Hou et al., 2002; Bass et al., 1997; Blower et al., 1996; Tanaka et al., 1972). This method can be applied at small sized cyclotrons (McCarthy et al., 1997). The ^{64}Ni(d,2n)^{64}Cu reaction can also provide very high yields but it is not practical, due to the low energy and intensity of