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^{64}Cu separation from ^{67}Ga waste product: co-production of ^{64}Cu and ^{67}Ga

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1. Introduction

^{64}Cu is one of the most useful and versatile radio-copper radionuclide in the nuclear medicine owing to its multiple decay scheme, which involve electron capture (41%), β^- (40%) and β^+ (19%) decays, and has an intermediate half-life for radiopharmaceutical synthesis of many compounds[1]. These properties make its radiopharmaceuticals useful for PET imaging of tumors and targeted radiotherapy labeled on small compounds and monoclonal antibody[2][3].

Several production methods have been investigated for the ^{64}Cu radioisotope production, proton beam irradiation of an enriched ^{64}Ni target material using ^{64}Ni(p,n)^{64}Cu nuclear reaction and an enriched ^{68}Zn using ^{68}Zn(p,αn)^{64}Cu, or deuteron irradiation of an ^{64}Ni using ^{64}Ni(d,2n)^{64}Cu[3]. However, each production method has some advantage and disadvantage, respectively. Among them, the highest production yields are obtained with the proton or deuteron beam irradiation on ^{64}Ni target. But, the reliable and effective recovery process for the recycling of enriched ^{64}Ni is absolutely necessary to establish because of the highly expensive cost of target material. Although the production yields of ^{68}Zn(p,αn)^{64}Cu nuclear reaction, side-reaction during the proton beam irradiation on ^{68}Zn target for ^{67}Ga production, is lower than those of ^{64}Ni target, the former method is the most economical production procedure because of no extra irradiation and no ^{64}Ni recovery process necessary[4].

In this paper, we describe the effective separation of ^{64}Cu, produced by side nuclear reaction during proton irradiation of ^{68}Zn, from ^{67}Ga waste with dithizone extractant in CCl_4[5] and ion chromatography.

2. Methods and Results

2.1. Materials

All reagents used for production were of analytical grade. Enriched ^{68}Zn (isotopic purity > 98%) was obtained from Isoflex Russia. Diisopropyl ether, hydrochloric acid, carbon tetrachloride, dithizone and hydrogen peroxide were purchased from Aldrich.

Anion exchange resin AG1-x8 (100~200 mesh) was supplied by BioRad.

2.2. Preparation of extractant and anion exchange resin column

The extractant of ^{64}Cu from ^{67}Ga waste product was prepared as a 0.01% dithizone in CCl_4.

The anion exchange column (ϕ 1 x 7 cm) used for purification and concentration of ^{64}Cu solution obtained by dithizone extraction followed by back extraction with 7.2 N HCl was prepared by washing and pre-equilibrating with DM water and 7.2 M HCl.

2.3. Proton irradiation of ^{68}Zn target and recovery of ^{67}Ga waste

The ^{67}Ga was produced via the ^{68}Zn(p,2n)^{67}Ga reaction using a 200 μA beam of 30 MeV proton for 7.5 hours. After irradiation, the ^{67}Ga was separated from the ^{68}Zn target using diisopropyl ether-7 M HCl solvent extraction system. ^{68}Zn and ^{64}Cu including ^{57}Ni, ^{55}Co impurities were collected in 7 M HCl aqueous phase of solvent extraction. For recovery of ^{68}Zn from aqueous phase with anion exchange resin, the normality of aqueous phase was adjusted to 2N with addition of DM water and then the solution was loaded on anion exchange column. The eluant from the column was collected for ^{64}Cu separation and ^{68}Zn eluated with DM water was kept for ^{68}Zn recycling.

2.4. Radionuclide analysis of ^{67}Ga waste and ^{64}Cu separation

The gamma-ray and radioactivity of radioisotopes in ^{67}Ga product waste were measured with HPGe(High Purity Germanium) detector coupled with MCA(ORTEC EG&G) (Fig.1. and Table 1.). The gamma-ray detection efficiencies of HPGe detector were determined by measuring the gamma-rays from 80keV up to 2MeV from NIST standard source. The gamma-rays of ^{64}Cu, ^{67}Cu, ^{57}Co, ^{57}Ni, ^{67}Ga and ^{66}Ga were confirmed in the ^{67}Ga product waste and the activities of ^{64}Cu and ^{67}Cu at EOB (End of bombardment) were 1,208mCi and 6.05mCi, respectively.

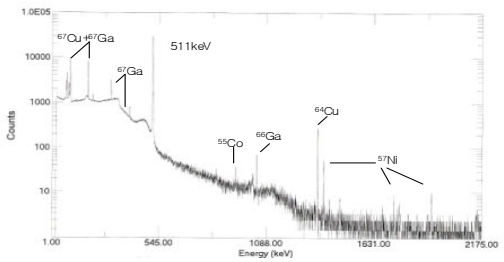

Fig.1. Gamma-ray spectrum of ^{67}Ga product waste. The spectrum was obtained by using HPGe detector coupled with MCA.

Table 1. Physical properties* and radioactivities of radioisotopes found in ^{67}Ga product waste.

RI	Half-life	Activity (mCi at EOB)	γ-ray(abundance %)
^{64}Cu	12.7h	1,208	511(34.8), 1345.8(0.47)
^{67}Cu	61.8h	6	91.3(7),93.3(16),184.5(48)
^{67}Ga	78.2h		93.3(39),184.5(21),300.0(16.6)
^{57}Ni	35.6h	12	127.2(17),511(87), 377.6(81.7)
^{55}Co	17.5h	180	477.2(20),931.1(75),408.5(17)
^{57}Co	271d	< 0.1	122.1(85.6), 136.5(10.7)

* Data were taken from *National Nuclear Data Center, Chart of Nuclides*, http://www.nndc.bnl.gov.

The developed ^{64}Cu separation procedure from ^{67}Ga waste is summarized in a flow chart (Fig. 2.). The ^{67}Ga waste(vol.: about 350mL) obtained from ^{68}Zn recovery anion exchange column, installed in the ^{67}Ga processing hot-cell, was transferred into a 2L beaker and pH adjustment to 3 was performed with c-NaOH addition. In order to make the total volume to 1.4 L, DM water was added. For solvent extraction, a 140mL volume of 0.01% dithizone solution in CCl_4 was added to solution and thoroughly mixed for about 5 min. The mixture was transferred to separatory funnel and the organic phase containing ^{64}Cu and ^{67}Cu was collected in the beaker. The extraction efficiency of ^{64}Cu was quantitatively almost 100%. A few drops of 30% H_2O_2 solution were added to organic phase until color change from green to orange-red. ^{64}Cu was back-extracted with same volume of organic phase of 7.2N HCl. The back-extraction yield was about 90%, measured with the comparison of counts of ^{64}Cu gamma-ray of aqueous and organic phase. In order to reduce the volume of ^{64}Cu solution, anion exchange resin was applied. The aqueous phase obtained with back-extraction was loaded onto anion column (ϕ 1 x 7 cm) and DM water was eluted to recover ^{64}Cu from column.

The total processing time and the separation yield of ^{64}Cu from ^{67}Ga product waste were about 2 hrs and more than 90%, respectively. The pure radio-copper ^{64}Cu/^{67}Cu solution was effectively separated and its radionuclidic purity was checked with HPGe-MCA system(Fig. 3.).

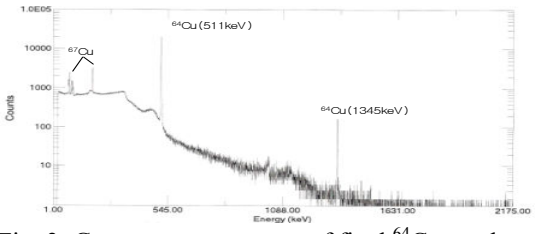

Fig. 3. Gamma-ray spectrum of final ^{64}Cu product.

3. Conclusion

The efficient chemical separation method using solvent extraction (0.01% dithizone in CCl_4 – HCl) followed by ion exchange chromatography was developed for ^{64}Cu separation from ^{67}Ga product waste.

The procedure was tested with one-fifth volume of ^{67}Ga product waste and the processing system for the large scale production is been constructing.

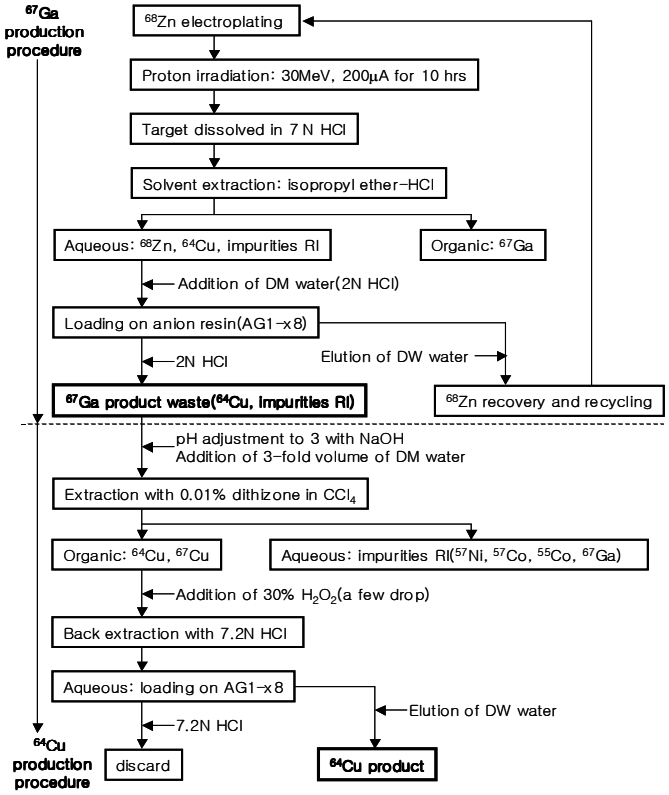

Fig.2. Flow chart of ^{67}Ga production and ^{64}Cu separation from ^{67}Ga waste.

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