

PRELIMINARY STUDIES OF SEPARATION OF ^{67}Ga FROM ELECTROPLATED Zn TARGETS

Patrícia de A. Martins¹, Ideli M. de Oliveira¹, Neuza T. O. Fukumori¹, Margareth M.N. Matsuda¹ and João A. O. Jr¹

¹ Instituto de Pesquisas Energéticas e Nucleares, IPEN - CNEN/SP
Av. Professor Lineu Prestes 2242
05508-000 São Paulo, SP
patyosborne@yahoo.com

ABSTRACT

The ^{67}Ga -citrate complex scans are performed in a variety of malignant/benign tumours, inflammatory/infectious lesions and prognosis in Hodgkin's disease or non-Hodgkin's lymphoma. The ^{68}Zn ($p, 2n$) ^{67}Ga reaction is the most widely used for ^{67}Ga production. After irradiation ^{67}Ga is usually separated from Zn by ion exchange chromatography or by liquid extraction. Ion exchange uses strong acids that can damage the hot cells components and liquid extraction is a difficult method to automate. The aim of this study was to evaluate the separation of ^{67}Ga from Zn by thermal diffusion in concentrated acetic acid. The basis of this separation is the fact that ^{67}Ga diffuses at high temperature through Zn and can be removed by acetic acid. The preliminary experiments concerned the effect of heating temperature, heating time and time of diffusion in acetic acid on non irradiated electroplated natural Zn targets in Cu/Ni backings and also in Cu and Cu/Ni plates. The temperatures studied were room temperature, 100 °C and 200 °C for 30, 60 and 120 minutes. The plates were put inside a glass apparatus and stayed in contact with concentrated acetic acid for 30, 60 and 120 minutes. Samples of the acid were diluted 1:100 and then taken and the amounts of Zn, Cu and Ni were measured by the inductively coupled plasma optical emission spectroscopy technique. The results showed that the metal that was more dissolved by acetic acid was Cu, and the concentrations increased with increasing temperature and time.

1. INTRODUCTION

Most of the radiopharmaceuticals used in nuclear medicine may be classified into two groups: first, those prepared for the dynamic functional studies of certain organs in the body, and second, those designed to localize abnormalities in the body. Gallium-67 citrate (^{67}Ga -citrate) complex falls in the second radiopharmaceutical group [1].

The ^{67}Ga -citrate scans are performed in a variety of malignant/benign tumours, inflammatory/infectious lesions, to differentiate acute myocarditis from acute myocardial infarction, for the determination of treatment strategy and prognosis in Hodgkin's disease or non-Hodgkin's lymphoma [2-5].

^{67}Ga has a physical half-life of 78 hours and decays by electron capture with the emission of four main gamma rays of 0.093, 0.184, 0.296 and 0.388 MeV having relative abundance of 40, 24, 22 and 7 per cent, respectively. It can be produced by several nuclear reactions that occur in a cyclotron, such as ^{68}Zn ($p, 2n$) ^{67}Ga , ^{67}Zn (p, n) ^{67}Ga , $^{\text{nat}}\text{Ge}/^{\text{nat}}\text{Zn}$ ($p, 2n$) ^{67}Ga , ^{65}Cu

$(\alpha, 2n) {}^{67}\text{Ga}$, ${}^{64}\text{Zn} (\alpha, p) {}^{67}\text{Ga}$, ${}^{66}\text{Zn} (\alpha, p2n) {}^{67}\text{Ga}$, ${}^{66}\text{Zn} (d, n) {}^{67}\text{Ga}$ and ${}^{67}\text{Zn} (d, 2n) {}^{67}\text{Ga}$ [6-11].

${}^{67}\text{Ga}$ is usually cyclotron produced by proton bombardment of an enriched zinc-68 target in a $(p, 2n)$ reaction. There is a need to use enriched zinc targets in order to achieve higher production yields and also to produce less radioactive impurities.

After irradiation, the zinc target material is usually dissolved in 7,10 or 12 M HCl and ${}^{67}\text{Ga}$ separated from Zn by ion exchange chromatography or by liquid extraction. Ion exchange uses strong acids that can damage the hot cells components and liquid extraction is a difficult method to automate. ${}^{68}\text{Zn}$ target recovery is necessary because of the use of enriched target material [6 - 11].

The aim of this study was to evaluate the separation of ${}^{67}\text{Ga}$ from Zn by thermal diffusion in concentrated acetic acid. The basis of this separation is the fact that ${}^{67}\text{Ga}$ diffuses at high temperature through zinc and can be removed by acetic acid [12]. These preliminary experiments employed non-irradiated targets.

2. EXPERIMENTAL

2.1. Target Preparation

The preliminary experiments concerned the effect of heating temperature, heating time and time of diffusion in acetic acid on non-irradiated electroplated natural Zn targets in Cu/Ni backings and also in Cu and Cu/Ni plates.

The use of the thin nickel layer was required to prevent extensive intermetallic diffusion between the copper substrate and the zinc target material during irradiation at high proton beam current, and minimize chemical attack during target dissolution of copper surfaces that may have been bombarded by lost protons during irradiation [8].

Cu and Cu/Ni plates were prepared by a company and the electrodeposition of Zn was performed by using $0.45 \text{ mol.L}^{-1} \text{ ZnSO}_4 \cdot 7\text{H}_2\text{O}$ (Analytical Reagent Grade, Merck, Germany) solution, permanent current of 30 mA for 2:45 hours. A Zn/Cu/Ni target can be seen in Fig. 1.



Figure 1. Electroplated Zn Target in Cu/Ni plates

2.2. Diffusion Studies

The Zn/Cu/Ni, Cu/Ni and Cu targets plates were placed inside a proper dissolver device (Fig. 2). The plates were first maintained at room temperature and heated at 100 and 200°C (Oven FC 1.25, EDG, Brazil) for 30, 60 and 120 minutes. Then, they were put in contact with 20 mL Glacial Acetic Acid (Analytical Reagent Grade, Merck, Germany) for 30, 60 and 120 minutes.

All the plates were weighted in an analytical balance (AS 2000C, Marte, Brazil) before and after the diffusion period in acetic acid and samples of the acid were taken and the amounts of Zn, Cu and Ni were measured by the Vista-MPX simultaneous ICP-OES equipped with axially viewed plasma and concentric glass nebulizer.

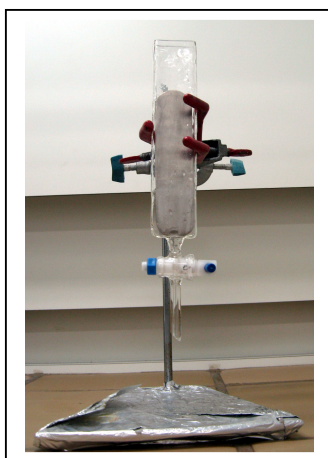


Figure 2. Dissolution apparatus

2.3. Chemicals Analyses

Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES, Varian Inc., Australia) has become one of the most efficient, modern and widely used analytical technique for direct inorganic determinations of low concentrations of the target trace elements with high sensitivity.

The system was equipped with 40 MHz free-running radiofrequency generator and simultaneous CCD solid-state detector, cooled at $-35\text{ }^{\circ}\text{C}$ by Peltier system. The optical system is thermally stabilized and contains no moving parts to ensure long-term stability. The echelle polychromator was thermostated at $34\text{ }^{\circ}\text{C}$, and provided spectral window spanning the range 167 to 785 nm. Argon was the plasma and auxiliary gas [13].

The plasma needed to be turned on 30 minutes prior to the analysis for stabilization. The optimum operating conditions are summarized in Table 1.

Table 1. ICP-OES Operation Parameters

Parameter	Setting
Power	1.4 kW
Plasma gas flow	15 L min ⁻¹
Auxiliary gas flow	1.5 L min ⁻¹
Spraychamber type	Glass cyclonic
Torch	Standard axial torch
Nebulizer type	Seaspray
Nebulizer gas flow	0.75 L min ⁻¹
Pump rate	10 rpm
Sample uptake delay	10 s
Replicate read time	5 s
Stabilization time	10 s
Rinse time	10 s
Number of replicates	3

Purified water used to prepare the standard solutions was obtained from the Milli-RX-45 water system (Millipore, USA). The calibration and blank solutions were stabilized in 3% v/v concentrated HNO₃ (Analytical Reagent Grade, Merck, Germany).

The Cu²⁺, Ni²⁺ and Zn²⁺ standard solutions for the working calibration curves were prepared by diluting the single element ICP grade standard solution (100 µg mL⁻¹, Merck, Germany). The range of the calibration curve was from 0.0 to 10.0 µg mL⁻¹.

The samples were diluted to 1:100 with purified water and analyzed by introducing them directly into the hot plasma where Cu²⁺, Ni²⁺ and Zn²⁺ were atomized and determined at 327.395, 230.299 and 213.857 nm, respectively. The selected wavelengths were the most sensitive, where there was less spectral interferences.

3. RESULTS AND DISCUSSION

3.1. Diffusion Studies

The plates were weighted before the heating procedure and after the diffusion period in acetic acid. Figures 3, 4 and 5 show the mass difference of the 3 plates studied in this work, after heating and contact with concentrated acetic acid.

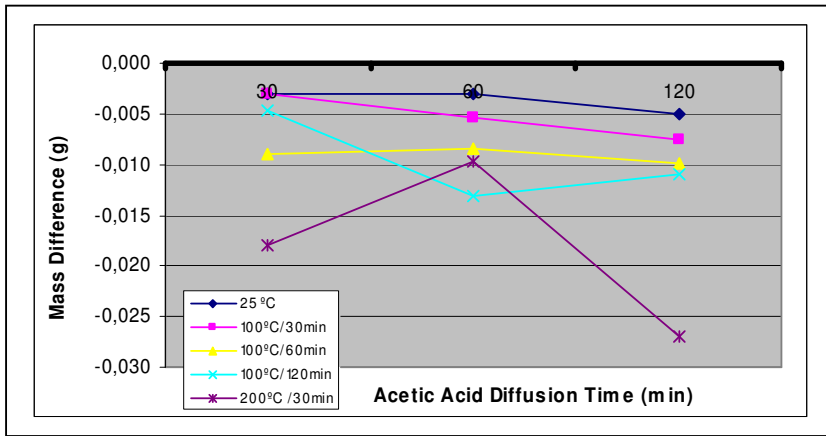


Figure 3. Mass Variation of Cu Targets after Acetic Acid Diffusion at 25 °C, 100 °C and 200 °C

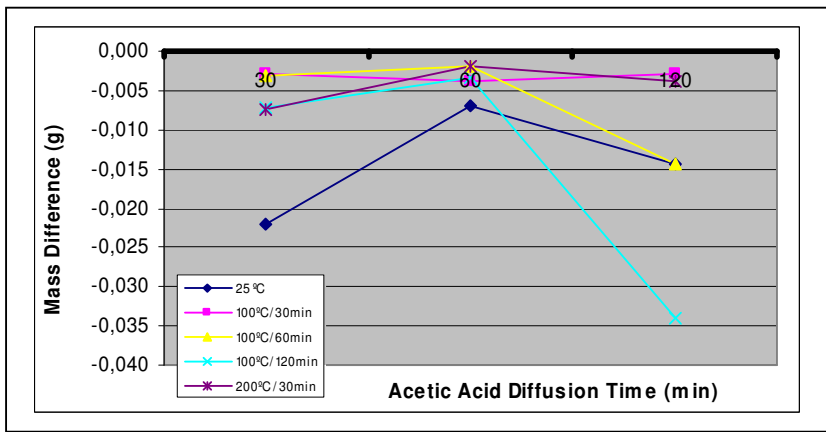


Figure 4. Mass Variation of Ni Targets after Acetic Acid Diffusion at 25 °C, 100 °C and 200 °C

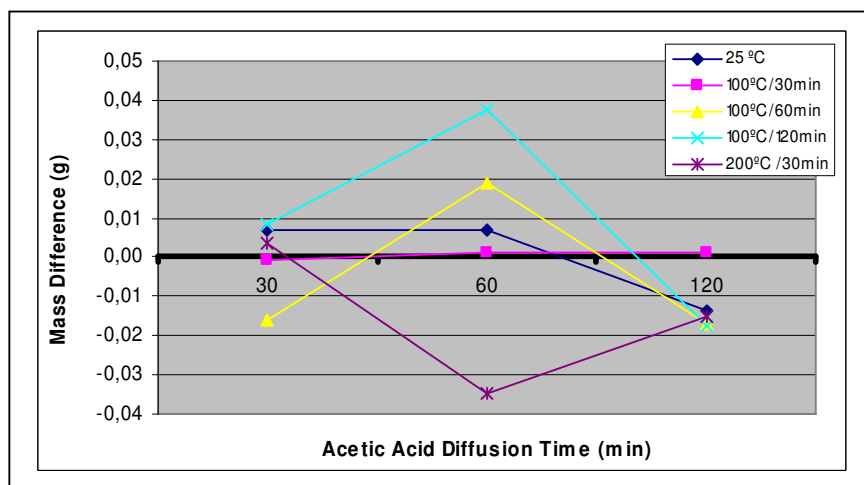


Figure 5. Mass Variation of Zn Targets after Acetic Acid Diffusion at 25 °C, 100 °C and 200 °C

Fig. 3 showed that copper targets presented the largest dissolution in all experiments, compared with all plates, increasing with temperature and diffusion time.

The experiments with the Ni/Cu plates (Fig. 4) showed that the loss of mass is the same when the heating time is 30 minutes. For the other conditions the loss of mass increases with diffusion time and heating time. Sometimes it was observed a higher loss of mass due to defects on the Ni plating.

The results in Fig. 5 shows that the worst condition of loss of mass is when the target was heated at 200 °C. In some cases there was an increase in the mass due to the absorption of liquid by the Zn target.

The mass of Zn electroplated in Cu/Ni plates was 0.8 ± 0.1 g.

3.2. Chemical Analysis

The results of the analysis of the samples taken from the diffusion in acetic acid are shown in Fig. 6, 7, 8 and 9.

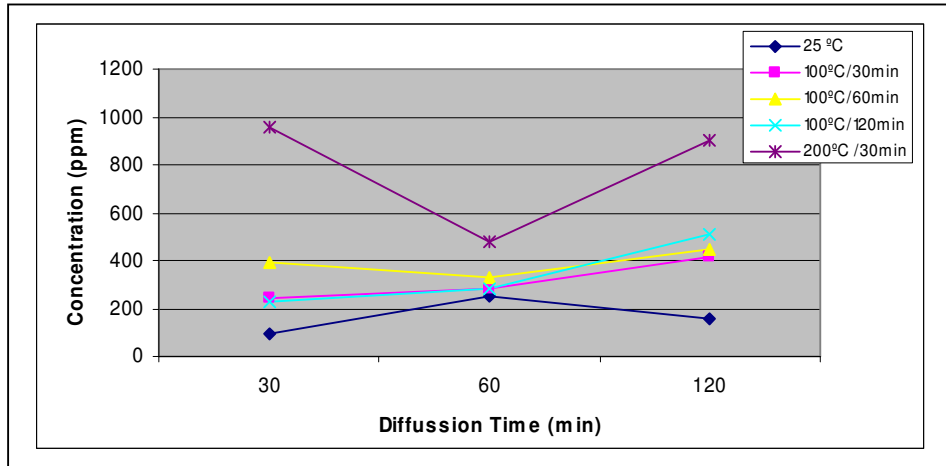


Figure 6. Cu Concentration after Acetic Acid Diffusion at 25, 100, 200 °C (Cu plates)

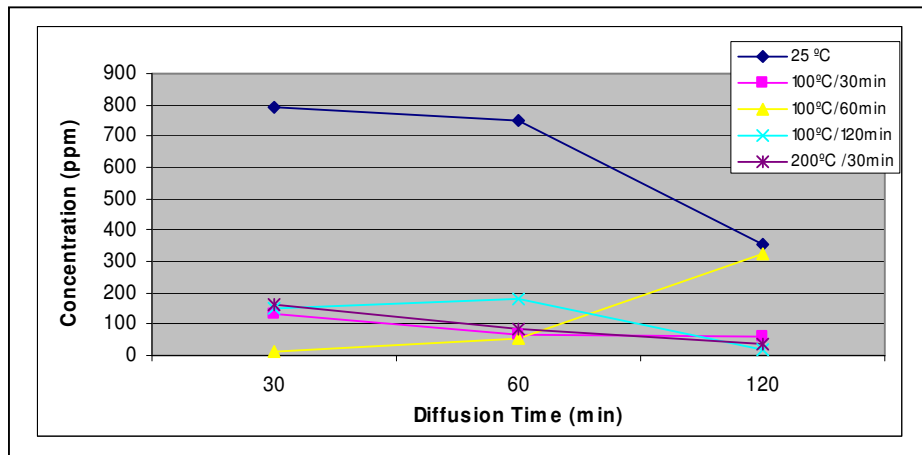


Figure 7. Ni Concentration after Acetic Acid Diffusion at 25, 100, 200 °C (Ni/Cu plates)

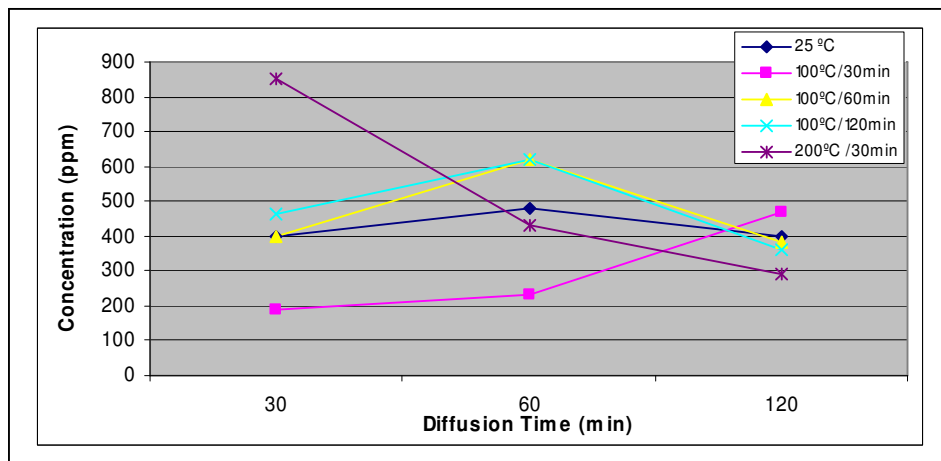


Figure 8. Zn Concentration after Acetic Acid Diffusion at 25, 100, 200 °C (Zn/Ni/Cu plates)

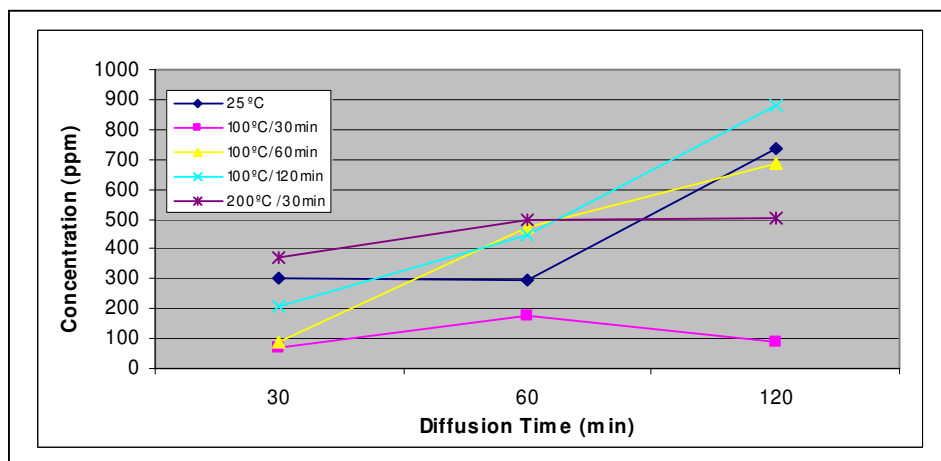


Figure 9. Ni Concentration after Acetic Acid Diffusion at 25, 100, 200 °C (Zn/Ni/Cu plates)

Cu concentration was high when the experiments were performed with the Cu plates (Fig. 6). The concentration of Cu was lower than detection limits when the experiments were performed with Ni/Cu and Zn/Ni/Cu/ plates. This confirms that nickel is effectively protecting Cu from dissolution.

The concentration of Ni was high in both plates, especially in higher temperature and time. The same behavior was observed for the Zn analysis.

For determinations of metals in the ICP-OES analytical technique is very efficient since the samples are liquid, do not need pretreatment and a 1:100 dilution factor showed to be adequate for ^{67}Ga production and purification.

4. CONCLUSION

The results showed that Cu is readily attached by acetic acid so the Zn target must be prepared with a thin nickel layer to prevent the dissolution. The heating time must be kept lower than 200 °C to decrease the loss of mass during the diffusion. The future experiments aim the use of irradiated Zn targets.

The simultaneous, multi-element nature of the ICP-OES technique allows the determination of a larger number of elements in a very brief time period. This method is designed to reduce analysis time, to minimize or eliminate the sample treatment step. Automatic continuous flow screening techniques may result in cost reductions; enhance versatility, increase speed and minimization of operator errors [14].

5. REFERENCES

1. M. L. Thakur. Gallium-67 and Indium-111 Radiopharmaceuticals. *Int. J. Appl. Radiat. Isotopes.* **28**, pp.183-201 (1977).
2. M. F. Tsan. Mechanism of Gallium-67 Accumulation in Inflammatory Lesions. *J. Nucl. Med.*, **26**, pp. 88-92 (1985).
3. M. F. Tsan, Scheffel U. Mechanism of Gallium-67 Accumulation in Tumors. *J. Nucl. Med.* **27**, pp. 1215-1219 (1986).
4. R. A. Ferrari, P. Frata, C. Pizzocaro, C. Crippa, A. Tucci, F. Facchetti, L. Grazioli, S. M. Magrini, G. Rossi. Late computed tomography scan response improvement and gallium scintigraphy evaluation as on treatment prognostic parameters to tailor treatment intensity in patients with Hodgkin's lymphoma. A prospective phase II study. *Ann. Onc.*, **19**, pp. 951-957 (2008).
5. M. Y. Hung, M. J. Hung, C. W. Cheng. Use of Gallium-67 Scintigraphy to Differentiate Acute Myocarditis from Acute Myocardial Infarction. *Tex Heart Int J.*, **34**, pp. 305-309 (2007).
6. H. B. Hupf, J. E. Beaver. Cyclotron Production of Carrier-Free Gallium-67. *Int. J. Appl. Radiat. Isotopes.*, **21**, pp. 75-79(1970).
7. L. C. Brown. Chemical Processing of Cyclotron Produced ^{67}Ga . *Int. J. Appl. Radiat. Isotopes.*, **22**, pp. 710-713 (1971).

8. L. C. Brown, A. P. Callahan, M. R. Skidmore, T. B. Wilson. High-Yield Zinc-68 Cyclotron Targets for Carrier-Free Gallium-67 Production. *Int. J. Appl. Radiat. Isotopes*, **24**, pp. 651-655 (1997).
9. C. Naidoo, T. N. Van der Walt. Cyclotron Production of ^{67}Ga (III) with a tandem $^{\text{nat}}\text{Ge} - ^{\text{nat}}\text{Zn}$ target. *Appl. Radiat. Isotopes*, **54**, pp. 915-919 (2001).
10. Y. Nagame, M. Unno, H. Nakahara, Y. Murakami. Production of ^{67}Ga by Alpha Bombardement of Natural Zinc. *Int. J. Appl. Radiat. Isotopes*, **29**, pp. 615-619(1978).
11. J. R. Dahl, R. S. Tilbury. The Use of a Compact, Multi-Particle Cyclotron for the Production of ^{52}Fe , ^{67}Ga , ^{111}In and ^{123}I for Medical Purposes. *Int. J. Appl. Radiat. Isotopes*, **23**, pp. 431-437 (1972).
12. H. Lundoqvist, V. Tolmachev, A. Bruskin, L. Einarsson, P. Malmberg. Rapid Separation of ^{110}In from Enriched Cd Targets by Thermal Diffusion. *Appl. Radiat. Isotopes*, **46**, pp. 859-863 (1995).
13. V. Calderon, Analysis of environmental samples with the Varian 710-ES following US EPA guidelines, *ICP-OES Application Note Number 39*, Varian Inc., Australia.
14. L. C. Trevizan, F. V. Silva, A. R. A. Nogueira, J. A. Nobrega, Evaluation of a rapid semi-quantitative analysis approach using inductively coupled plasma optical emission spectrometry with axial viewing, *Microchemical Journal*, **86**, pp. 60-64 (2007).