Cyclotron production of no-carrier-added palladium-103 by bombardment of rhodium-103 target

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Abstract

Electroplated rhodium foil was employed as the target for cyclotron production of palladium-103. An electrodissolution apparatus was found better than other dissolution methods in terms of personnel shielding and palladium-103 yield. The ion-exchange column chromatography method was simple and effective for the purification of palladium-103 and the final stripping agent of NH₄Cl + NH₃ (1:1) was more efficient than other agents. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Palladium-103; Cyclotron production; Rhodium target; Electrodissolution; Ion-exchange chromatography

1. Introduction

Interstitial implantation of radiation-emitting materials has been long recognized as effective method for tumor therapy. The advantage of interstitial implants is an opportunity to concentrate the radiation at the tumor site while minimizing radiation exposure to normal tissue. Commonly used implantable materials include radioactive gold-198 and radon-222. Use of these radioactive sources is not without shortcomings, however, since the highly penetrating radiation which is emitted not only subjects normal tissues to more destructive radiation, but can also make it difficult to adequately shield personnel. Another important radioisotope commonly used for permanent implantation is iodine-125. The general effectiveness of the isotope has been described in many publications (Fuks et al., 1991; Morton et al., 1988; Ragde et al., 1998). Palladium-103 has more favorable physical properties, including its low energy, rapid dose fall-off, short half-life, and total cumulative dose delivery at a higher dose rate than iodine-125 and is a promising radioisotope for localized tumor treatment.

Ling (1972) compared the effectiveness of iodine-125 based on a theoretical radiobiologic model using the linear quadratic model. The authors concluded that at the clinically prescribed doses, the predicted cell killing is better for palladium-103 in rapidly proliferating tumors, with an advantage for iodine-125 in slower-growing tumors. Animal studies by Nag et al. (1993, 1996) suggested that palladium-103 was more effective than iodine-125 in poorly differentiated tumor, while this superiority was less marked in well-differentiated cancer. Based partly on these assumptions, iodine-125 was commonly used in lower grade (Gleason Score 2–6) tumor and palladium-103 suggested to be used for higher grade (Gleason Score > 6) malignancy (Prestidge et al., 1998).

Production of palladium-103 can be accomplished by either cyclotron production or reactor production. For nuclear reactor production palladium-103 is produced by bombarding a target containing enriched palladium-102 with neutrons. In contrast to cyclotron production of palladium-103 where carrier-free palladium-103 can
be produced, nuclear reactor production is not carrier free, and the product always contains palladium-102. In addition, palladium-109, palladium-111, and other palladium contaminants can also be present. One drawback of reactor-produced palladium-103 is that the specific activity cannot be adjusted to provide for the production of a seed of predetermined therapeutic or apparent activity. A further possible disadvantage resides in the fact that large amounts of stable palladium-102 remain which may shield the low energy X-ray released when the palladium-103 nuclei disintegrate (John et al., 1995). Reactor-produced palladium-103 from enriched palladium-102 is also expensive because of the difficulty in enriching palladium-102 (only 1.02% natural abundance) from palladium metal. This paper discusses a method that can be used for commercial production of no-carrier-added palladium-103 with cyclotron.

2. Experiment

2.1. Targetry and irradiation

The radiation of the rhodium-coated target was performed with a model 30 cyclotron manufactured by IBA in Belgium at the Radiopharmaceutical Center of Shanghai Institute of Nuclear Research, Academia Sinica. The irradiation lasted for 10h at the 21 MeV energy of proton and a beam current intensity is 200 μA, measured by integrating the charge collected on the target. The target was prepared by periodic reverse plating a layer of rhodium, which was 10 cm long, 1 cm wide and 0.1 mm in depth, onto copper support. Rhodium (III) chloride hydrate (99.99% Merk product) is the main component of the electroplating solution. Electroplating temperature was 45°C. The negative electrode current density was 0.2 A/cm² and the positive one was 0.15 A/cm². Time ratio of the two electrodes (t₁/t₂) was 15(s): 5(s). The advantage of periodic reverse plating is that we can obtain even rhodium plating layer with uniform depth and few eyelets. Identification and assay of gamma-ray emitting radionuclides were carried out using a γ spectroscopy with high purity germanium (HPGe) detector (GEM-15190, EG&ORTEC, USA).

2.2. The dissolution of irradiated target

Due to the extremely low chemical reactivity of rhodium metal towards inorganic acid (i.e. H₂SO₄, HCl, HNO₃) and to other corrosive reagents (chloride, bromine, etc.), it is very difficult to dissolve the rhodium target. We evaluated the electrodissolution and oxidation dissolution method in this work. All the targets were dissolved 4 days after the end of bombardment (EOB).

2.2.1. Electrodissolution

The dissolution of the target was performed using the improved electrolysis apparatus (Lagunas-Solar et al., 1987). The rhodium metal target with thin layer of copper on the back, which was peeled off from the bulgy part of copper support by cutting machine, was placed onto the graphite plate (the positive electrode) and sealed by a rubber “O” ring and a current density of 0.5 A/cm² was then applied. The fragmentation rate, referring to proportion of the weight of rhodium powder produced by electrodissolution to the weight of target, was determined by measuring the content of rhodium in the electrolyte using UV-240 Visible Recording Spectrophotometer (Shimadzu), which was more accurate than weighting method. 2-(2-thiazolylazo)-5-diethylaminobenzoic acid was used as the selective developer for rhodium and absorbancy was determined at 674 nm. The improved electrodissolution cell is more suitable for routine, large-scale production; it is also more useful and considerably safer when handling a highly radioactive target in a remotely controlled processing system intended for this work.

2.2.2. Oxidization dissolution

The rhodium target, dissolving the thin layer of copper with HNO₃ on the back, was crushed down and put into 10 ml concentrate HCl with a stoichiometric level of KAuCl₄ and heated and stirred for 5h.

2.3. Radiochemical separation of palladium-103 from rhodium solution

Separation of palladium-103 was performed using anion-exchange chromatography. A 1.5 cm inner diameter glass column filled with Dowex 1 × 8 (Cl⁻) 100–200 mesh resin to a height of 10 cm was used. After preconditioning the resin with 6 M HCl, the rhodium solution was loaded on to the column. The eluants consisted of 0.03 M HCl, 6 M HCl and NH₃ + NH₄Cl (1:1). The separation efficiency for palladium and rhodium was monitored by measuring the activity of palladium-103 and rhodium-102 in the eluant fractions using γ spectroscopy.

3. Result and discussion

Metallic rhodium was selected as the target because of its favorable physical properties, such as high resistance to corrosion and high melting point (1966°C). However, a significant problem in using the rhodium target is that rhodium and many of its compounds are extremely difficult to dissolve. Some authors (Kenneth et al., 1997; Lagunas-Solar et al., 1984) used the soluble rhodium chloride trihydrate as target material instead of rhodium metal, but there are also some drawbacks of the
alternative. After irradiation with only 1 μA-beam current, the pressed RhCl₃·3H₂O target showed cavity and fragmentation (Ramli and Sharma, 1997). An insoluble black residue (12.67 ± 5.45% of total mass of the target) was also observed following the dissolution of the target. This residue has been identified as an extremely low chemical reactivity rhodium oxide (Lagunas-Solar et al., 1983). RhCl₃·3H₂O, which has a melting point of 100°C, decomposes to form rhodium oxide. When used as a target material, the energy dissipated is transferred very slowly, due to low thermal conductivity, to the cooled back plate and therefore causes a local melting of the target which leads to the formation of insoluble rhodium oxide, cavity and fragmentation. Furthermore, the presence of chlorine and oxygen in the target significantly decreases the reaction yield greatly. The use of metallic rhodium overcomes the above problems and has proved to be an excellent target material for irradiation in a cyclotron.

The yield of palladium-103 was about 1250 mCi at the EOB.

The electrodissolution results of different mass rhodium targets with rectangle shape are summarized in Table 1. Particular attention should be given to the fragmentation which affects the yield of palladium-103 because it is not possible to remove the trapped palladium-103. With the increase of current density the fragmentation increased dramatically, but the time for dissolution decreased greatly. The optimal selection of current density was between 0.4 and 0.6 A/cm² as the result of faster dissolution with less fragmentation. Under the radiation conditions the electrodissolution was judged as the most suitable method with regard to personnel safety and environmental protection.

We selected KAuCl₄ as the oxidant to dissolve rhodium target because it is simple and an easily manageable method for the dissolution of rhodium target. The chemical potential of the reaction is

\[ E = 0.572 + 0.0394 \lg([\text{Cl}^-]/[\text{Cl}]) + 0.0197 \lg([\text{AuCl}_4^-]/[\text{RhCl}_6^{3-}]) \]

At a given [Cl⁻], the last item—\( \lg([\text{AuCl}_4^-]/[\text{RhCl}_6^{3-}]) \)—gives little contribution to the potential, which can also be seen from the experimental results (Table 2). Temperature is the key factor affecting the reaction. Between room temperature and 60°C there was almost no dissolution of the target but at 100°C about 40% of the target dissolved. Using this approach with the residue under the same conditions did not dissolve the solid. Our inability to dissolve the residue in this way could result from formation of a layer of a compact insulation gold film on the surface of the target which inhibits further reaction. In addition, rhodium was passivated at high temperature.

Radioisotopes identified by half-life and γ-ray-energy measurements are listed in Table 3. Our experimental result conformed with Lagunas-solars’s (1987) under the low incident energy except that palladium-103 was not detected in his experiment.

Based on differences in the affinity of doubly charged PdCl₄²⁻ and triply charged RhCl₆³⁻, an ion-exchange

![Table 1](image)

<table>
<thead>
<tr>
<th>Area (cm²)</th>
<th>Current (A)</th>
<th>Current density (A/cm²)</th>
<th>Mass (g)</th>
<th>Fragmentation (%)</th>
<th>Time (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 x 10</td>
<td>10</td>
<td>1</td>
<td>1</td>
<td>78</td>
<td>0.2</td>
</tr>
<tr>
<td>1 x 3.5</td>
<td>2.8</td>
<td>0.8</td>
<td>0.364</td>
<td>50.3</td>
<td>0.50</td>
</tr>
<tr>
<td>1 x 3</td>
<td>1.8</td>
<td>0.6</td>
<td>0.2151</td>
<td>24.2</td>
<td>0.62</td>
</tr>
<tr>
<td>1 x 10</td>
<td>5</td>
<td>0.5</td>
<td>1</td>
<td>8</td>
<td>1.50</td>
</tr>
<tr>
<td>1 x 1.8</td>
<td>0.72</td>
<td>0.4</td>
<td>0.1801</td>
<td>5.1</td>
<td>0.64</td>
</tr>
<tr>
<td>1.0 x 0.25a</td>
<td>0.1</td>
<td>0.4</td>
<td>0.011</td>
<td>0</td>
<td>0.58</td>
</tr>
</tbody>
</table>

*aLagunas-Solar et al. (1987).*

![Table 2](image)

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Molar ratio of KAuCl₄ to rhodium</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>1:1</td>
<td>Very little</td>
</tr>
<tr>
<td>70</td>
<td>2:1</td>
<td>4.25%</td>
</tr>
<tr>
<td>80</td>
<td>1:1</td>
<td>15.26%</td>
</tr>
<tr>
<td>90</td>
<td>5:1</td>
<td>28.20%</td>
</tr>
<tr>
<td>100</td>
<td>5:1</td>
<td>40.00%</td>
</tr>
</tbody>
</table>

![Table 3](image)

<table>
<thead>
<tr>
<th>Radioisotopes</th>
<th>Half-life</th>
<th>γ-ray energies (keV) (probability per decay)</th>
</tr>
</thead>
<tbody>
<tr>
<td>¹⁰¹Rh</td>
<td>3.3a</td>
<td>127 (70%)</td>
</tr>
<tr>
<td>¹⁰²Rh</td>
<td>2.9a</td>
<td>698 (47%)</td>
</tr>
<tr>
<td>¹⁰¹mRh</td>
<td>4.26d</td>
<td>307 (87%)</td>
</tr>
<tr>
<td>¹⁰³Pd</td>
<td>16.9d</td>
<td>357 (0.061%)</td>
</tr>
<tr>
<td>¹⁰¹Pd</td>
<td>8.27d</td>
<td>296 (18%)</td>
</tr>
</tbody>
</table>
method was developed for the separation of palladium from rhodium. After eluting with 100 ml 0.03 M HCl, which is intend to remove Cu²⁺ and micro-base metal ion such as Zn²⁺, Fe³⁺, which adhere to the resin, the resin was eluted 10 ml fractions with 6 M HCl at a 4 ml/min flow rate. As shown in Fig. 1, 99.82% of rhodium was released by 120 ml of 6 M HCl solution and palladium-103 was not eluted off. The elution was continued for a total volume of 120 ml and 30 ml distilled water was then used to remove HCl remaining in the column. The mixed NH₃ + NH₄Cl (1 : 1) eluant (100 ml) was used to release palladium-103 from the resin. An amine complex is formed when ammonia solution is used as eluant. The amine complex of palladium behaves as a cation, so it is easily released from the anion resin, but the efficiency of elution was about 73% (Fig. 2). Only 33.28% of palladium-103 was eluted off in the initial 10 ml and there was a long tail
with low specific activity of palladium-103 after 100 ml ammonia elution. However, when ammonium chloride was added to the ammonia solution palladium was eluted more rapidly with high efficiency. About 70% of palladium was washed out in the first 10 ml and 95% of palladium was released from the resin with only 50 ml mixture (Fig. 3). It was observed with palladium that a mixture of ammonium chloride and ammonia solution gave more rapid elution than either eluant separately. Apparently, the $\text{PdCl}_4^{2-}$ was displaced from the resin by substitution of the chloride ion and by the formation of the ammine $\text{Pd(NH}_3)_4^{2+}$. The elution yield using the mixed eluant was 95%. The $\gamma$ spectrum of the palladium-103 elution solution is shown in Fig. 4 with a 99.8% nuclide purity. Dimethylglyoxime (DMG) is the best known extractant for palladium in analytical chemistry and was used by Tarapčík and Mikulaj (1981) to separate palladium-103 from the dissolved rhodium target solution. The separation efficiency using this method was low and Ramil and Sharma (1997) also drew the same conclusion. In the 0.1 M HCl medium, the total efficiency for sum of three extractions was only 69.81 ± 1.13%. From our experiment, ion-exchange column chromatography was a simple and effective way to separate palladium-103 from rhodium target solution. Since ammonia and ammonium chloride are components of electroplating solution for preparation of palladium-103 seeds, it was not necessary to remove any of them. The specific activity of palladium-103 has to be adjusted suitably for “molecular electroplating”.

5. Conclusion

The metal rhodium target system was suitable high beam current for large-scale production of palladium-103. The electrodissolution is a better way to dissolve the target and separation of palladium-103 from rhodium solution could be achieved by ion-exchange column with Dowex 1 × 8 resin and $\text{NH}_3 + \text{NH}_4\text{Cl}(1:1)$ as eluant.

**References**


