Improved Yields of Iodine-124 from the Enriched Tellurium-124 Dioxide/Aluminum Oxide Target


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Abstract. The escalating clinical application of Positron Emission Tomography results from the novel radiotracers which are available to monitor specific biochemical or physiologic processes. Future developments of the technique will require an increasing availability of additional unique radioligands and radionuclides. Iodine-124, a radionuclide whose potential for both diagnostic and therapeutic applications is widely recognized, has been prepared at Memorial Sloan-Kettering Cancer Center on a weekly basis for several years (1). With its characteristic 4.18 day half life and complex decay scheme (2) which includes positron emission (22.0 ± 0.5%) and electron capture (78 ± 0.5%), this radionuclide has been shown to be appropriate for radiotracers describing slow physiologic processes with the clearance of non-specific radioactivity. The refinements and modifications being engineered into the cyclotron target system to increase the absolute yield of recoverable radioactivity from each irradiation and its chemical processing of the reusable solid target matrix are described.

INTRODUCTION

Treatment decisions in oncology are increasingly guided by information on the biologic characteristics of the tumor, including size, location and extent of tumor. In addition specific tumor biologic property information such as measurement of cellular proliferation and the expression of particular tumor proteins, will further influence the treatment decisions. Nuclear Medicine, a specialty of medical imaging which uses a variety of radionuclides incorporated into specifically designed radiopharmaceutical tracers to achieve a time-dependent molecular image, is ideally suited for the measurement of regional biology.

The emergence of clinical Positron Emission Tomography (PET) has allowed a routine and essentially non-invasive assessment of cancer, neurological disorders, and coronary artery disease in humans. Essential to the acceptance and clinical utilization of this technology has been the availability of specifically F-18 labeled fludeoxyglucose for injection. Continued development of novel drugs designed and engineered to complement the pharmacokinetics of the clinical molecular target will be forthcoming due to the joint efforts between academia, industry and regulatory agencies. At Memorial Sloan-Kettering Cancer Center, the recognition of the potential impact for PET has resulted in the Center’s procurement and current installation of a replacement cyclotron. During the time of decommissioning of The Cyclotron Corporation, model CS-15 cyclotron and the installation of the replacement cyclotron (EBCO Technologies, Inc., model TR 19/9 cyclotron), evaluation of methods for overcoming accelerator and chemical constraints imposed upon the iodine-124 radioactivity recoverable from the solid target system are being investigated. The preliminary results of this investigation are presented.

METHODS AND MATERIALS

General

Chemicals and solvents of the highest available quality were purchased from Sigma Chemical, J.T, Baker, and Fisher Scientific. All HPLC solvents were filtered (0.45 mm, nylon or PTFE, Alltech) prior to use. Water (ultra-pure, ion free quality) was obtained from a Millipore Alpha-Q Ultra-pure water system.
Enriched tellurium dioxide/aluminum oxide solid targets were irradiated on the CS-15 cyclotron at Memorial Sloan Kettering Cancer Center. The enriched granular elemental tellurium-124 was purchased from NF Chemical, Port Chester, NY and had an initial isotopic composition of 99.7% with Te-125 accounting for <0.28%. The tellurium dioxide was synthesized from the metal as described previously (1).

Multichannel analyses were performed using an end window HPGe detector (83.5 cm³, FWHM 1.8 keV @ 1.33 MeV) and Canberra model 35 plus Analyzer. A BioScan model 200 imaging scanner and autochanger 1000 was used to analyze thin layer radiochromatograms.

X-ray Analysis

The X-ray crystallography/spectroscopy data produced from the powder method of diffraction on various samples of unirradiated tellurium oxide/aluminum oxide melts was provided by Dr. L. Tadaro and colleagues at Hunter College (Chemistry Department, New York, NY). Using this technique, the “crystal” is a fine powder and subjected to a beam of monochromatic x-rays. The mass of powder is equivalent to a single crystal rotated about all possible axes and one or more particles of the sample will be so oriented that their planes make the correct Bragg angle for reflection. The awareness of the Bragg angle derived from the diffraction pattern, and known x-ray wavelength employed in the analysis, allows the determination of the spacing of the reflecting lattice planes. For this study the radiation monochromatic wavelength sought was Kα at 1.54056 Å but the average of the Kα and Kβ x-ray was 1.5418 Å from the copper source.

RESULTS AND DISCUSSION

Nuclear medicine scans, particularly Positron Emission Tomography (PET), directly exploit the dissimilarity of tumor cell characteristics in comparison to normal cells. Malignant transformations apparently alter the enzymology of cells as evidenced by an increased rate of glycolysis, protein synthesis rate and DNA syntheses (3). Examples of compounds labeled with iodine-124 at various stages of clinical investigation for specific studies within our program of improvement in cancer detection and treatment have been previously reported (4). Concurrent with the technical improvements being made with the intrinsic resolution and reconstruction of images, are the increased need for a variety of short-lived, radiolabeled substrates possessing the unique potential to serve as indicators of “in-vivo” alteration of biochemical processes. Despite the complex decay scheme for iodine-124, the spatial resolution of images of this radionuclide are excellent. As a result of the radiopharmaceutical chemistry advances and the installation of the replacement cyclotron, the clinical requests for increased availability of the iodine-124 have occurred. Considering such non-classical PET radionuclides and the introduction of the new generation of cyclotrons, the maximum rate at which radionuclides can be produced on solid targets will not be restricted solely to the cyclotron parameters and now the thermal performance of the target materials becomes a significant factor (5).

Several publications have appeared in the recent literature on the influence of target conditions and impurity ions within the target material on the yield of radioactive iodine achievable from the dry distillation recovery process (6-8). Despite these studies no definitive confirmation of the influence of the impurity cations has been provided; only that the regeneration of the tellurium dioxide has improved total radioiodine production following irradiation. All procedures described for regeneration and/or recovery of enriched tellurium result in a percentage loss of stable enriched material (2,8). The financial cost and limited availability of highly enriched tellurium-124 make this aspect of the target processing a critical component. The improved absolute recovery from the “reusable” target for the production of iodine-124 by modification of the target chemical structure was felt to be a simple but effective means to achieve the task. Our initial study on the effects of both temperature and time for distillation indicated only marginal increase to the iodine-124 yield. Subjecting the irradiated target to a second dry distillation processing without further irradiation resulted in a minimal recovery of residual iodine-124. Our results for several typical irradiations of the tellurium dioxide/aluminum oxide solid solution target system are shown in Table I.

<table>
<thead>
<tr>
<th>Target Composition</th>
<th>Irradiation Conditions (µampere-hours)</th>
<th>Material Loss/Irradiation</th>
<th>“Recoverable” Yield (% Calculated to EOB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TeO₂/Al₂O₃</td>
<td>&lt; 50</td>
<td>Not detectable</td>
<td>51% (+ 10)</td>
</tr>
<tr>
<td>TeO₂/Al₂O₃</td>
<td>≤ 100</td>
<td>Not detectable</td>
<td>61% (+ 10)</td>
</tr>
<tr>
<td>TeO₂/Al₂O₃</td>
<td>&gt; 100</td>
<td>Not detectable</td>
<td>59% (+ 10)</td>
</tr>
</tbody>
</table>
The cyclotron target material was initially described (1) as a solid solution target based upon the lack of reflection for this admixture to polarized light under microscopic examination. However, powdered x-ray diffraction has subsequently indicated that the target material is crystalline with a tetragonal unit cell. These results appear in figure 1 with unit cell dimensions calculated at $a \& b = 4.8083 \, \text{Å}$, $c = 7.6106 \, \text{Å}$. All angles are exactly 90 degrees.

**FIGURE I.** X-ray diffraction of powdered Te$_2$O$_3$/Al$_2$O$_3$ target material.

Diffraction directions are determined by the shape and size of the unit cell but the intensity of the diffracted beams are determined by the positions of the atoms within the unit cell. For a tetragonal crystal, the corresponding general equations (9) involving the unit cell dimensions are:

$$\lambda = 2 \, d \, \sin \theta \quad \text{Bragg Equation}$$

and

$$1/d^2 = ((h^2 + k^2)/a^2 + l^2/c^2)$$

where $d$ is the interplanar spacing resulting in:

$$\sin^2 \theta = \lambda^2/4((h^2 + k^2)/a^2 + l^2/c^2)$$

Since a crystal contains planes of atoms and these planes influence the properties and behavior of the material, we conclude that the recoverable iodine-124 yield could potentially be enhanced as a result of subtle changes to the interplanar spacing and atomic packing factor. Our intention is to evaluate the target recovery characteristics of the solid solution achieved upon substitution of an “inert” cationic species. Initially silicon in the form of silicon dioxide is to be substituted for the aluminum oxide. Other effects of the substitution upon the target material science considerations will be evaluated as the Memorial Sloan Kettering Cyclotron being sited within the Citigroup Biomedical Imaging Center as a consortium radiochemistry facility initiates operation.

**CONCLUSION**

The reproducible and consistent delivery of iodine-124 over the past several years attests to the longevity of the tellurium dioxide/aluminum oxide cyclotron target system. The documentation of the retention of a tetragonal unit cell of the enriched tellurium-124 dioxide indicates the potential for enhancing lattice imperfections involving the aluminum oxide component of the target mixture as a means for increased recovery of radioactivity. It is surmised that both radiation chemical effects upon the crystal structure and substitution of “inert” cationic impurities could result in the increased recoverable yield of iodine-124.

**REFERENCES**


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