BETA RADIOPHARMACEUTICAL IDENTIFICATION BY QUENCH ANALYSIS

Rodney D. Ice
University Hospital, University of Michigan Medical Center, Ann Arbor, Michigan
and Mary Ann Dugan
Temple University School of Pharmacy, Philadelphia, Pennsylvania

With the increased use of beta-emitting radiopharmaceuticals in nuclear medicine, a greater potential for inadvertent errors in labeling and identification of radiopharmaceuticals exists. The use of shorter half-life radiopharmaceuticals has increased the need for adequate quality-control measures within radiopharmacy. Radionuclidic purity tests of gammaradiating radiopharmaceuticals have received considerable stature using gamma spectroscopy. However, there exists a need for a relatively simple radionuclidic purity test for beta-emitting radiopharmaceuticals (1).

Some widely used radiopharmaceuticals include the following beta-emitting radionuclides, tritium, carbon-14, phosphorus-32, sulfur-35, chlorine-36, calcium-45, nickel-64, and krypton-85. Existing methods for beta radionuclide determination require isolation of the radionuclide in question using chemical separation techniques to avoid interference with existing materials and to prevent mass or self absorption of the beta particle. The United States Pharmacopeia recommends the use of a series of absorbers placed between the beta-emitting source and a detector (2). By increasing the thickness of the absorbers, the range of the beta particle can be determined. The determined range of the emitted beta particle is directly related to the energy of the beta particle (E<sub>max</sub>) providing radionuclidic identification.

Liquid scintillation counting has been shown to be the present method of choice to quantitate beta-emitting radionuclides (3). The disadvantages of using liquid scintillation counting for qualitative analysis are the presence of quench and the large energy spectrum associated with the emitted beta particle. Quench, a shifting of the energy spectrum to an observed lower energy, is caused by the presence of interfering materials in the counting solution such as oxygen, chemicals associated with the formulation of the radiopharmaceutical, and/or any color associated with the product. Since quench decreases the observed counting rate, radionuclidic identification requires restoration of the observed spectrum by increasing the gain of the spectrometer or by making quench correction measurements.

In 1955 Harley and Hallden presented a means of identifying beta-emitters by applying the Feather analysis using aluminum absorbers (4,5). They compared the transmission of a standard beta emitter with an unknown beta emitter using various absorbing quantities of aluminum. The logarithms of the transmission of the two emitters with various absorbers were plotted against each other, producing a linear relationship. The E<sub>max</sub> was related to the slope of the line produced.

Based on the Harley-Hallden procedure, a technique has been developed for the identification of beta-emitting radiopharmaceuticals using a liquid scintillation counter. The procedure is easily incorporated into the quality-control program of a nuclear pharmacy.

METHODS AND MATERIALS

All radionuclides used for obtaining the standard calibration curve were purchased from New England Nuclear Corp. as inorganic salts in water or weak acid solution. Aquafuor, from Pilot Chemical, was the scintillator cocktail. A Packard Model 3375 Tricarb was used. The Tricarb was calibrated at the balance point operation (6). The final settings used were: gain, 10%; automatic background subtraction; PHA 50 to infinity.

Selection of standard radionuclides. There are several steps involved in establishing a maximum beta-energy curve to be used in the identification of unknown radiopharmaceuticals. For the development of the method, calcium-45 was selected as the basic standard.
because the maximum beta energy emitted from this nuclide is most centrally located for the radionuclides studied. The radionuclides selected in the establishment of the standard curve were \(^{38}\)S (0.167 MeV), \(^{63}\)Ni (0.067 MeV), \(^{36}\)Cl (0.714 MeV), \(^{3}H\) (0.018 MeV), \(^{14}\)C (0.156 MeV), \(^{48}\)Ca (0.250 MeV), and \(^{38}\)W (0.43 MeV). These radionuclides were selected because of the wide energy range represented (0.018–0.714 MeV).

**Absorption ratio determination.** Approximately 10,000 dpm/10 µl were counted for each radionuclide in 15 ml of scintillation cocktail. Increasing quantities of chloroform (quenching agent) were added, ranging from 0.2 ml to 1.0 ml. The observed radioactivity was determined after each addition of quenching material. Assuming the first count as unity, successive counts decreased in relative activity due to increased quench (increased light absorption by the chloroform). Each successive count was compared to the initial count to give an absorption ratio \((A_0/A)\). Each radionuclide was analyzed in the same manner (Table 1). The \(A_0/A\) ratios for each radionuclide were plotted on log-log paper against the \(A_0/A\) ratios for \(^{48}\)Ca at each specific quantity of added chloroform (Fig. 1).

**Absorption ratio slope determination.** The slope of the curve for each nuclide was calculated by the formula

\[
\frac{\log (Y_2/Y_1)}{\log (X_2/X_1)} = \text{Slope}
\]

where X and Y are intercepts for an individual curve. Thus in Fig. 1 the slope for \(^{38}\)S is 0.583. See Table 2 for the absorbed ratio slopes.

\[
\frac{\log (Y_2/Y_1)}{\log (X_2/X_1)} = \frac{\log (1.45/1.25)}{\log (2.00/1.55)} = \frac{0.116}{0.111} = 0.58.
\]

**TABLE 2. ABSORPTION RATIO SLOPE DETERMINED FROM PLOTTED LOGS \(A_0/A\) OF VARIOUS RADIONUCLIDES AGAINST LOGS \(A_0/A\) OF \(^{48}\)Ca**

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Energy (MeV)</th>
<th>Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^{3}H)</td>
<td>0.018</td>
<td>0.30 ± &lt;0.01</td>
</tr>
<tr>
<td>(^{3}He)</td>
<td>0.067</td>
<td>0.28 ± &lt;0.01</td>
</tr>
<tr>
<td>(^{14})C</td>
<td>0.156</td>
<td>0.64 ± 0.04</td>
</tr>
<tr>
<td>(^{36})S</td>
<td>0.167</td>
<td>0.60 ± 0.07</td>
</tr>
<tr>
<td>(^{48})Ca</td>
<td>0.250</td>
<td>1.00</td>
</tr>
<tr>
<td>(^{18})W</td>
<td>0.430</td>
<td>2.90 ± 0.29</td>
</tr>
<tr>
<td>(^{36})Cl</td>
<td>0.714</td>
<td>10.08 ± 1.80</td>
</tr>
</tbody>
</table>

**FIG. 1. Absorption ratio slope determination.**

**FIG. 2. Standard beta identification curve.**
After establishing the standard curve (Fig. 2), unknown beta-emitting radiopharmaceuticals were identified by counting each sample with successive increase of chloroform, determining an $A_0/A$ ratio per amount of quench, and calculating the slope from the plot of $A_0/A$ ratio of unknown versus $A_0/A$ ratio of $^{46}$Ca. This slope was compared to the standard curve and $E_{\text{max}}$ of the unknown radiopharmaceutical established. Unknown radiopharmaceuticals shipped by the manufacturer were assayed and identified.

**DISCUSSION**

The identification of an unknown beta-emitting radiopharmaceutical requires the counting of the sample with added amounts of chloroform, establishing the degree of quench associated with the chloroform, calculating the slope when plotted against a $^{46}$Ca standard, and locating the slope on the calibration curve. The radiopharmaceutical is identified by the maximum beta energy associated with the slope.

Radiopharmaceuticals such as $^{14}$C and $^{35}$S, with very similar maximum beta energies, 0.158 and 0.167 MeV, respectively, cannot be separately identified by this technique. The standard deviation for the two similar beta energies overlap.

This technique can be expanded to higher energy emitters by using a different quenching agent and a different reference standard. Use of other reference standards would require a different standard beta identification curve.

A method has been established for the identification of beta-emitting radiopharmaceuticals without chemical separation or use of absorbers. Use of the method outlined and the standard curve presented allows radionuclidic identification as well as simultaneous assay of a beta-emitting radiopharmaceutical.

**REFERENCES**

2. The Pharmacopeia of the United States of America, 18th rev, Easton, Mack Publishing Co, 1970