ANALYTICAL PITFALLS WITH 99mTc-LABELED COMPOUNDS

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The rapid growth of the number of 99mTc-labeled compounds in nuclear medicine requires analytical techniques that can accurately identify various components in these products. In our opinion, the recent literature contains much misleading analytical data concerning the identification and purity of various technetium compounds. Generally in these papers only a single chromatographic system was used whereas bioassay was relied on heavily. We feel that perhaps this situation should be reversed and that analytical techniques should be emphasized. Multi-component products are much more easily identified using chemical techniques instead of bioassay. Variation of the parameters to obtain a high yield is easier when the chemical components are known rather than the organ distribution. Finally, species differences do not overshadow the results in analytical techniques as they often do in bioassay.

Since the different chemical forms of technetium show different biological behavior, failure to identify and quantify these forms has resulted in misuse of the compound, claims of in vivo instability which are not accurate, incorrect internal radiation dose calculations, and general confusion and often abandonment of compounds which are extremely valuable if obtained in their pure form.

This study compares various analytical methods now in use to point out the advantages and disadvantages of each method in the hope that this will inspire the introduction of further analytical analysis in nuclear medicine.

METHODS AND MATERIALS

Commonly used 99mTc-labeled compounds were analyzed by anion exchange chromatography at pH 2–3, by paper chromatography with both nitrogen-purged 85% methanol and nitrogen-purged saline as solvents, and by gel chromatography. The first three are commonly used chromatographic methods and need no further explanation. The fourth, gel chromatography, was performed on a 0.9 × 35-cm column of Sephadex G25 eluted with nitrogen-purged saline (1). A standard apparatus is shown in Fig. 1. Table 1 contains the quantitative data for each sys-

Received Aug. 23, 1971; revision accepted Oct. 28, 1971.

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FIG. 1. Gel chromatography apparatus.

<table>
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<tr>
<th>TABLE 1. QUANTITATIVE CHROMATOGRAPHIC DATA</th>
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<tr>
<td>Tc(IV) Hydroyzed Reduced Tc TcO2(VII)</td>
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<tr>
<td>Anion exchange HSA eluate eluate adsorbed</td>
</tr>
<tr>
<td>Whatman paper in 85% methanol (RI)* origin origin 0.5–0.6</td>
</tr>
<tr>
<td>Whatman paper in saline (RI) 0.85–0.95 0.85–0.95 origin 0.65–0.80</td>
</tr>
<tr>
<td>Gel chromatography (Sephadex G25) void void† 12–20 ml adsorbed 38–46 ml</td>
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* RI is defined as the migration distance of the sample component divided by the migration distance of the solvent front.  
† The void volume is the elution volume for a substance that is completely excluded from the gel.

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systems show three components, $\text{TcO}_4^-$, Tc-DTPA, and hydrolyzed Tc whereas the methanol and anion systems show only two, $\text{TcO}_4^-$ and presumably Tc-DTPA. These data are to be compared with the data for another preparation of Tc-DTPA which is commercially available under the trade name Renotec. As can be seen in Fig. 3, analysis by either methanol or the anion system would indicate that both preparations are similar, i.e., both contain mostly Tc-DTPA. The gel and saline systems, however, show that the two products differ greatly in that the hydrolyzed technetium peak is greatly enhanced in the case of Renotec. This difference is corroborated by the biological distributions for the two preparations which are shown in Fig. 4. As can be seen, the urinary excretion is much less for Reno-tee than for Tc-DTPA. However, using either the methanol or anion exchange system, one would suspect the compounds to be identical.

The second set of examples involves the preparation of Tc-HSA using a low pH preparation and a high pH preparation according to procedures pub-
We feel that as nuclear medicine continues to grow so will the confusion concerning the biological distribution one would expect with a certain compound unless a multiple analytical approach is incorporated. We therefore strongly encourage the increased use of analytical procedures in nuclear medicine.

**ACKNOWLEDGMENT**

This work was performed under the auspices of the United States Atomic Energy Commission and was presented in part at the 18th Annual Meeting of the Society of Nuclear Medicine, June 28–July 2, 1971, Los Angeles, California.

**REFERENCES**


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**FIG. 5.** Analysis of ⁹⁹ᵐTc-HSA (low pH method).

Both compounds were prepared by adding TeO₄⁻ to a solution of stannous chloride and HSA at the appropriate pH. Figure 5 shows the analytical data for the preparation using the low pH procedure. Again the gel and saline systems show three components; TeO₄⁻, Te-HSA, and hydrolyzed technetium, whereas the methanol and anion systems show only two: TeO₄⁻ and presumably pure Te-HSA. Figure 6 shows the analytical data for the preparation in which the TeO₄⁻ is added at pH 6. Here again the methanol and anion systems show the preparation to be comparable to the low pH procedure. However, the gel and the saline systems show three components, TeO₄⁻, Te-HSA, and hydrolyzed technetium. Reviewing the gel and saline data from the two preparations we see that these two preparations are quite different in the quantity of Te-HSA and hydrolyzed technetium. These analytical data are consistent with the biological data obtained by us. The Te-HSA prepared at high pH has considerable liver uptake whereas the Te-HSA prepared at low pH has a normal blood pool distribution, reaffirming the purity of the product as obtained in the analytical analysis.