Development of a New Cholescintigraphic Agent

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It is reported that lipophilic character of a chelate may be responsible for the rapid excretion through the bile. On this basis, a lipophilic ^{99m}Tc-penicillamine ethyl ester (^{99m}Tc-Pen ethyl ester) was chosen for this study.

The ^{99m}Tc-Pen ethyl ester was prepared using the $SnCl^2$ method and analyzed by thin layer chromatography and paper electrophoresis. Various complexes were detected, whenever a slight change of the labeling condition, such as pH, concentration of $SnCl_2$, reaction time, was carried out. Among these complexes, a high recovery of ^{99m}Tc in the bile of rats was observed in a complex prepared by addition of a freshly prepared solution of 2×10^{-5} M of $SnCl_2$ to a mixture of $^{99m}TcO_4^-$, 10^{-2} M of Pen ethyl ester and phosphate buffer (pH 7.7). This complex was more than 96% extractable into ethyl acetate and excreted through the bile more rapidly than the unesterified complex (^{99m}Tc-Pen Complex I). This result clearly indicates that the lipophilicity of a chelate closely relates with a rapid hepatobiliary clearance.

When this complex was intravenously administered in mice, the radioactivity retained in kidney, liver and blood were considerably higher than observed in ^{99m}Tc-Pen Complex I, though these two complexes were much the same in the concentration in gallbladder. This phenomenon can show the lower stability in vivo of ^{99m}Tc-Pen ethyl ester. In order to protect this complex from the decomposition in vivo by stabilizing it chemically, histidine was added to it. The addition of histidine showed a better organ distribution.

Evaluation of Resin-Sn^{2+} and Its Application on ^{99m}Tc-DOPA Labeling

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In our pursuit for technetium labeling mechanism, DOPA (3-(3,4-dihydroxyphenyl)-L-alanine), a clinically interesting biogenic amine, was considered as an interesting ligand to be studied, since in its presence, hydrolysis is predicted to compete with (monomer) complex reaction formation.

The labeling method itself is a very simple and rapid procedure because only a mixing of DOPA (10^{-2} M), buffer solution (Na acetate, pH 5.6) and $^{99m}TcO_4^-$ eluate (2 m*l*) in a syringe followed by the addition of Resin-Sn^{2+} (10^{-3}M, 2 mg) with an up-side-down movement is involved. The mixture is ready to be injected after a filtration through a Millipore filter.

Sephadex column chromatography (G-15) was used for the analysis and from the elution time the monomer and the polymer complexes were determined, which showed a great similarity to the data reported on penicillamine-^{99m}Tc complexes.

A very severe pH range, concentration of Resin-Sn^{2+} or DOPA was needed for the optimal condition of a monomer complex preparation, as compared with the labeling of penicillamine. The use of Sn^{2+} in solution even at very low concentration produced a rather high percentage of polymer complex. The use of Sn^{2+} adsorbed on cation exchange resin (Resin-Sn^{2+}), prevented the hydrolyzed complexes and increased the monomer ecomplex yield.

A selective mechanism is postulated. Once the

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