An Evaluation of 99mTc-labeled Iminodiacetic Acid Derivatives of Phthaleins and Fluoresceins as Hepatobiliary Agents

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Previous studies on hepatobiliary scanning agent labeled with 99mTc have shown the importance of 99mTc chemical state in the labeling compounds; a low hydrolyzed state was necessary for a high and rapid excretion of the 99mTc radiopharmaceuticals.

Compounds structurally related to Rose Bengal (BG) and Sulfo bromophthalein (BSP) such as calcein, methyl xylol blue (MXB), phenolphthalein complexone (PPC), thymolphthalein complexone (TPC), and arizarin complexone (ALC), were labeled with 99mTc following the procedure to provide a low hydrolyzed Tc state. The labeling efficiencies were estimated as 100% in MXB, PPC, and PC, approximately 90% in TPC and calcein, and 78% in ALC by paper electrophoresis.

An increasing order of % dose recovered from the bile of rat during the 1st 1 hr was observed as follows; PC, TPC, MXB, PPC, ALC, and calcein.

So, 99mTc-PC is estimated as the most effective agent of the analyzed complexes with a hepatobiliary excretion of 61% in 1 hr. This figure is similar to that of 99mTc-HIDA and better than of 131I-RB and 99mTc-PG.

Distribution study in mice showed a rapid passage of the complex through the biliary tract into the intestine. Comparative result is observed in the scintigraphic studies in the rabbit. An excellent image of the gallbladder is obtained 40 min after the intravenous injection.

99mTc-(Sn)-Pyridoxylideneamines: New Hepatobiliary Radiopharmaceuticals of Low Toxicity

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A new method of labeling pyridoxylideneamines with 99mTc in an alkaline media (pH 8-9) has been established using divalent tin as the reductant (patent pending): a series of 99mTc-complexes including 99mTc-(Sn)-pyridoxylideneglycine, -alanine, -valine, -leucine, -isoleucine, -phenylalanine and -glutamate have been prepared, and various factors in preparation and biological properties of the complexes were evaluated. The labeling was achieved by a simple mixing procedure of the kit reagent with the 99mTcO4+ solution at room temperature with practically 100% efficiency.

A close relationship was observed between molecular hydrophobicity of 99mTc-(Sn)-pyridoxylideneamines and their biliary excretion properties as expected from the consideration on the presumed labeling mechanisms and the molecular structure: 99mTc-(Sn)-pyridoxylidene-valine, -leucine and -isoleucine are found to be promising hepatobiliary agents.

Quantitative distribution studies showed that more than 90% of the radioactivity that remained by the body, when injected as 99mTc-(Sn)-pyridoxylidene-valine or -isoleucine, was excreted into rat’s intestine through hepatobiliary system in 1 hr after intravenous administration along, with the urinary excretion of 10-15% activity of the total injected dose.

Scintigraphic studies of these two agents in rabbits showed a dynamic distribution of radioactivity similar to that obtained in rats, and the