Studies on the labeling reaction revealed that a high biliary excretion of $^{99m}$Tc was obtained only when a chemically well characterized $^{99m}$Tc-PG complex was applied; a low hydrolyzed Tc state, either as Tc (IV) or Tc (V) is regarded as coordinated with a ligand at a molar ratio of two pyridoxal to one glutamic acid. The low hydrolyzed Tc state is considered to be kept stable through the coordination of four group, namely two phenol OH of pyridoxal, $-\text{C}=\text{N}-$ and COOH groups. A similar Tc state has been estimated in $^{99m}$Tc-HIDA and $^{99m}$Tc-PC as the effective chemical state for an efficient biliary excretion.

A kit method for the preparation of $^{99m}$Tc-PG with Tc in a low hydrolyzed state is formulated.

The ligand is previously prepared and then the labeling reaction with $^{99m}$TcO$_4^-$ is performed under such controlled condition of pH and Sn$^{2+}$ ion concentration to provide the low hydrolyzed Tc state. A 0.2 M solution of ligand is prepared by heating (120°C, 30 min) an equimolar mixture of pyridoxal hydrochloride and mono-sodium glutamate dissolved in saline solution (0.15 M) at pH 8.5. To one ml of ligand, $^{99m}$TcO$_4^-$ (3 ml), 6–8 mg of Sn-adsorbed resin (300–550 μg of SnCl$_2$) are added and mixed for 2 min, and then heated on water bath for another 2–3 min. Both ligand and Sn-adsorbed resin formulations are stable for more than 3 months when stored in amber ampoule.

An Evaluation of $^{99m}$Tc-HIDA Complex as a Cholescintigraphic Agent

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In the labeling reaction of N–(2,6-dimethylphenylcarbamoylmethyl)–iminodiacetic acid (HDA) with $^{99m}$Tc, several complexes with different chemical characteristics were observed depending upon slight changes in the labeling conditions. Following intravenous injection, the complex detected in the bile of rats was limited to a single one named as Complex II, hereafter. The labeling condition chosen for Complex II and the exchange reaction between this complex and the penicillamine indicated that in this complex, $^{99m}$Tc was probably coordinated with HIDA in a low hydrolyzed state.

This complex is excreted rapidly through the bile and, within 1 hr., about 65% of the total activity injected is recovered from the bile of rats. The organ distribution of this complex was studied by radioassay in mice and by scintillation camera in rabbits. In both cases, an effective accumulation of radioactivity was observed in the gallbladder.

These results suggest that $^{99m}$Tc chemical state, namely the low hydrolyzed state, is closely related to bile excretion behavior, therefore, this complex can be estimated as a potentially useful cholescintigraphic agent.

The metabolism of HIDA must, however, be further studied before a clinical trial. In vivo formation of nitrilotriacetic acid, a potential carcinogen, might possibly be involved.