An Evaluation of $^{99m}$Tc-labeled Iminodiacetic acid Derivatives of Phthaleins and Fluorescens as Hepatobiliary Agents


Kyoto University, Faculty of Pharmaceutical Sciences, and Kyoto University School of Medicine

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

Compounds structurally related to Rose Bengal (BG) and Sulfochromophthalein (BSP) such as calcein, methyl xylenol blue (MXB), phenolphthalein complexone (PPC), thymolphthalein complexone (TPC), and arizarin complexone (ALC), were labeled with $^{99m}$Tc 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, $^{99m}$Tc-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 $^{99m}$Tc-HIDA and better than of $^{131}$I-RB and $^{99m}$Tc-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.

$^{99m}$Tc-(Sn)-Pyridoxylideneaminates: New Hepatobiliary Radiopharmaceuticals of Low Toxicity

Makoto Kato, Nubuo Ueda and Masaaki Hazue

Technical Department, Nihon Medi-Physics Co., Ltd., Hyogo

A new method of labeling pyridoxylideneaminates with $^{99m}$Tc in an alkaline media (pH 8–9) has been established using divalent tin as the reductant (patent pending): a series of $^{99m}$Tc-complexes including $^{99m}$Tc-(Sn)-pyridoxylidene-glycine, -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 $^{99m}$TcO$_4^-$ solution at room temperature with practically 100% efficiency.

A close relationship was observed between molecular hydrophobicity of $^{99m}$Tc-(Sn)-pyridoxylideneaminates and their biliary excretion properties as expected from the consideration on the presumed labeling mechanisms and the molecular structure: $^{99m}$Tc-(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 retained by the body, when injected as $^{99m}$Tc-(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
gallbladder was clearly visualized within 5 min of injection.

The chemical and biological behavior of the $^{99m}$Tc-complexes showed no change for 60 days after the preparation of the kit reagent and for 48 hr. after technetium labeling.

Sn-pyridoxylidene-valine and -isoelucine kit reagents were found to be nontoxic in four animal species (mice, rats, guinea pigs, rabbits) even at the level of $500\times 10^3$ to $10^4$ times the proposed human dose.

The preliminary MIRD calculation was performed using animal distribution data to estimate the human internal exposure.

All results strongly indicated that $^{99m}$Tc-(Sn)-pyridoxylidene-valine and -isoelucine are promising low toxic agents for application in the diagnosis of human hepatobiliary disorders.

Studies on Variance of Labelling Yields of $^{99m}$Tc Compounds

M. TAKIZAWA*, K. MARUYAMA*, Y. OKUBO**, Y. SHIRASAWA** and G. SEKI**

*Department of Radiology, **Department of Pharmacy, Shinshu University Hospital, Matumoto

A term of validity of labelling yields and pH influence concerning $^{99m}$Tc Pyrophosphate (PP) and Phytate (PY) were examined by radiograph chromatography. Also $^{99m}$Tc labeling to Hippuran, o-Iodohippuran (OIH) and p-Aminohippuran (PAH) were examined.

Technetium labelled PP and PY were charged on a paper chromatography with 85% methanol, and measured by gamma counter with spectrometer. As a result of paper chromatography, labelled Tc-compounds were remained at the level of origin, but free TeO$_4^{-}$ had an Rf value with 0.67.

Hippuran, OIH and PAH were labelled by using TeO$_4^{-}$ with SnCl$_2$ method.

Some examination of labelled compound were practiced by male rats with the Wister species of 9 weeks. Rats were injected intravenously with 0.2 ml of Tc-compounds solution. After injection each one, three, six and ten minute later, rats were killed and were dissected for the uptake studies to each organs. Uptake of organs were compared with blood activity as a 100.0.

PY was labelled by $^{99m}$Tc after 25th, 39th, 53rd and 67th days and these dates were all after the term of validity. They had no change of labeling yield compared with the one in assay date.

Futhermore, after labelling in 6 and 12 hours, labelling yields was obtained no change.

Uptake of $^{99m}$Tc labelled compounds indicated that PAH was taken up by the kidney better than Hippuran and OIH.

$^{99m}$Tc-labeling of Red Blood Cells; in Vivo Method with Stannous Pyrophosphate

Masayasu KAN, Tatsuya MIYAMAE, and Morio SEKI

Department of Radiology, Saitama Medical School

The in vivo labeling of red blood cells with Tc-$^{99m}$ was studied in 36 cases. The labeling is easily performed with the pre-injection of cold stannous pyrophosphate (Sn-PYP) followed by $^{99m}$Tc-pertechnetate. This time we have intended to decide the optimum dose of Sn-PyP and the appropriate lag time between Sn-PYP injection and pertechnetate injection. The patients were injected with a various amount of Sn-PYP complex, which ranged from 0.10 mg/kg to 0.56 mg/kg (a vial of bone scanning kit containing 4mg of Tin and 20 mg of pyrophosphate). After an interval of 5 minutes (5 cases), 10 minutes (3 cases), 20 minutes (2 cases), 30 minutes (20 cases) and 60 minutes (6 cases), $^{99m}$Tc-pertechnetate of 10-15 mCi was injected, and the red cell labeling yield to each lag time was estimated.

The labeling yield of RBC increased with time.

Presented by Medical*Online