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MECHANISM OF BONE ACCUMULATION OF Tc-99m-LABELLED PHOSPHATE COMPOUNDS. A.Ando, T.Hiraki, A.Ando, K.Hisada and T.Takeuchi. Schools of Paramedicine and Medicine, Kanazawa University. Kanazawa.

Mechanism of bone accumulation of Tc-99m-MDP, Tc-99m-EHDP and Tc-99m-pyrophosphate (PYP) has not been fully understood. The present study was undertaken to explain the mechanism of their bone accumulation.

We considered a hypothesis that uptake of these Tc-99m-phosphate compounds to the bone was based on the exchange reaction of its phosphoric acid radical with that of bone mineral. To prove this hypothesis, the following experiments were performed.

In this experiment, hydroxyapatite (HAP) crystal and bone powder were used as a model of bone. P-32-PYP was taken up into these bone models in 0.9% NaCl solution (pH 7.4). On the other hand, P-32-phosphoric acid radicals were released with PYP from P-32-labeled bone models.

From the results of these experiments, it became clear that bone accumulation of P-32-PYP was based on the exchange reaction of its phosphoric acid radical with that of bone mineral. Uptake of Tc-99m-PYP into bone models was very similar to the uptake of P-32-PYP into bone models.

From above-described facts, it was concluded that bone accumulation of Tc-99m-PYP was based on the exchange reaction of its phosphoric acid radical with that of bone mineral. And this mechanism would hold good in the case of Tc-99m-MDP and Tc-99m-EHDP.

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TECHNETIUM-99m LABELLED ETHYLENE DIAMINE-N,N-DIACETIC ACID (EDDA) DERIVATIVES FOR THE CHOLESCINTIGRAPHIC AGENTS. T.Maeda, Y.Karube, A.Kono, Y.Oya, Kyushu Cancer Center, Fukuoka

A variety of EDDA derivatives were synthesized and labelled with Tc-99m using stannous chloride at pH-7. Synthesized ligands were as follows; 1) N-(benzenesulfonyl)EDDA, 2) N-(p-chlorobenzenesulfonyl)EDDA, 3) N-(p-toluenesulfonyl)EDDA, 4) N-(p-ethylbenzenesulfonyl)EDDA, 5) N-(p-propylbenzenesulfonyl)EDDA, 6) N-(p-t-butylbenzoyl)EDDA. The stability and labelling efficiency of these compounds was investigated by the thin layer chromatography in several solvent systems. (solvent systems: saline, n-butanol: acetic acid: water; 4:1:1, ethanol: water: 7:3) Tissue distribution and imaging studies were performed with these compounds. Imaging studies in rabbits showed rapid blood clearance for all compounds with different organ localization. Tc-99m-(3), Tc-99m-(2) and Tc-99m-(1) were eliminated from the liver through the bile duct resulting in excellent visualization of the gallbladder and the intestine. The results of the distribution in rabbit of the Tc-99m labelled ligands as well as their chemical properties which show EDDA derivatives are promising new series of hepatobiliary radiopharmaceuticals.

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SYNTHESIS OF BIFUNCTIONAL CHELATING AGENT AS FOR THE 99m-Tc-RADIOPHARMACEUTICAL DESIGN. Y.Arano, A.Yokoyama, A.Misaki, T.Hosotani, A.Yamada, H.Tanaka, H.Saji, Y.Ishii, and K.Torizuka. Pharmaceutical Sciences and School of Medicine, Kyoto University, Kyoto.

To make the best use of the excellent property of 99m-Tc, development of bifunctional radiopharmaceuticals containing functional groups with biological activity and chelating property as well is attempted. Great potentiality of bis-thiosemicarbazone derivatives as bifunctional chelating agent is presented. Synthesis of glucose, glucuronic acid and long chain fatty acid derivatives of bis-thiosemicarbazone were achieved. In the synthesis of sugar derivatives, the aldehyde (C-1) and the carbonyl (C-2) groups resulted from a mild oxidation were reacted with two molecules of thiosemicarbazide. While in the fatty acid derivatives, the alkyl group was reacted with a freshly prepared bis-thiosemicarbazone.

Upon good control of labeling parameters, as already published (1), stable chelate of a 99m-Tc coordinated through the thiosemicarbazone was obtained.

In vivo distribution showed promising results as 99m-Tc labeled radiopharmaceuticals for cardiological investigations.

(1) A. Yokoyama, Y. Terauchi et al, J Nucl. Med. 17, 816-819, 1976.

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Tc-99m(Sn)PYRIDOXYLIDENETRYPTOPHAN AND Tc-99m(Sn)PYRIDOXYLIDENE-5-METHYLTRYPTOPHAN: POTENTIAL HEPATOBILIARY IMAGING AGENTS OF RAPID HEPATOBILIARY TRANSPORT AND LOW URINARY EXCRETION. M. Kato-Azuma and M. Hazue. Research & Development Section, Technical Department, NIHON MEDI-PHYSICS CO., LTD. Takarazuka, Hyogo Pref.

Tc-99m(Sn)Pyridoxylidenetryptophan [Tc-99m(Sn)P.Trp] and its 5-methyl derivative [Tc-99m(Sn)P.Me-Trp] have been prepared by our stannous reducing method in an alkaline medium, and the in vivo distribution of each complex was evaluated in rats and rabbits.

The following table shows the in vivo distribution of each complex in rats at 1 hr after the i.v. administration; each value represents % of total injected radioactivity in the organ of interest.

Tc-99m-Complex	1 ml Blood	Small Liver	Intestine	Kidneys	Urine
P.Trp	0.04	0.9	92.0	0.5	1.9
P.Me-Trp	0.05	1.4	91.3	0.5	1.7

Scintigraphic studies in rabbits indicated that the dynamic behavior of these Tc-complexes in rabbits is almost identical to that in rats; no visualization of the kidneys nor the urinary bladder was observed.

Above results suggest that both Tc-99m-(Sn)P.Trp and -P.Me-Trp are promising hepatobiliary imaging agents of rapid blood clearance, rapid hepatobiliary transport and extremely low urinary excretion.

Further studies, including the toxicity studies on these agents, are now in progress.