Title	Evaluation of ^{99}□Tc-labeled amino acids as radiopharmaceuticals. VI. N-pyridoxylidenehydrazine-N', N'-diacetic acid
Sub Title	
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Publisher	共立薬科大学
Publication year	1984
Jtitle	共立薬科大学研究年報 (The annual report of the Kyoritsu College of Pharmacy). No.29 (1984.) ,p.61- 62
JaLC DOI	
Abstract	
Notes	抄録
Genre	Technical Report
URL	https://koara.lib.keio.ac.jp/xoonips/modules/xoonips/detail.php?koara_id=AN00062898-00000029-0061

Evaluation of ^{99m}Tc-Labeled Amino Acids as Radiopharmaceuticals. VI. *N*-Pyridoxylidenehydrazine-*N'*, *N'*-diacetic acid*

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Several ^{99m}Tc complexes have been proposed as radiopharmaceuticals for hepatobiliary scintigraphy. Two series of ligands are currently used. One consists of iminodiacetic acid (IDA) derivatives, for example *N*-(2,6-diethylphenylcarbamoylmethyl)iminodiacetic acid (E-HIDA), which is one of the most widely used hepatobiliary radiopharmaceuticals. Recently, we reported that *N*-(*p*-toluenesulfonyl)ethylenediamine-*N'*,*N'*-diacetic acid and related compounds can be used for this purpose. The other series of ligands consists of *N*-pyridoxylideneamino acids, which are Schiff bases formed from pyridoxal (PL) and amino acids.

In the IDA derivatives, Tc should be chelated by the imino and carboxylate groups. In the pyridoxal Schiff bases, the Tc-chelating sites are supposed to be the azomethine N and phenolate O atoms in the pyridoxal moiety and the carboxylate group of the amino acid moiety, though no definite evidence is available.

The title compound, *N*-pyridoxylidenehydrazine-*N'*,*N'*-diacetic acid (PLHzDA), is a hydrazone of hydrazine-*N*,*N*-diacetic acid (HzDA) with PL. It has two sets of chelating groups, IDA and Schiff base, in the molecule. Therefore, the compound is a good model for the study of Tc chelation, and its ^{99m}Tc complex is expected to be a useful tracer for hepatobiliary imaging.

^{99m}Tc complexes of the compound and related hydrazones were evaluated as hepatobiliary imaging agents. Hydrazones used in the study were *N*-pyridoxylidenehydrazine-*N'*,*N'*-diacetic acid (PLHzDA), *N*-(3-hydroxy-4-pyridylmethylene)hydrazine-*N'*,-*N'*-diacetic acid (FHPHzDA), *N*-(4-pyridylmethylene)hydrazine-*N'*,*N'*-diacetic acid (INHzDA), and *N*-pyridoxylidene-*N'*,*N'*-dimethylhydrazine (PLDMHz). The hydrazones were complexed with ^{99m}Tc by the $SnCl_2$ method and the complexation was examined by thin-layer chromatography and high-performance liquid chromatography. ^{99m}Tc complexes of the hydrazones were administered to golden hamsters, and the distribution

* 本報告は *Chem. Pharm. Bull.*, **32**, 2262—2266 (1984) に発表
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indicated that clearance occurred through the hepatobiliary system.

Scintigraphic studies in rabbits indicated that ^{99m}Tc complexes of PLHzDA and FHPHzDA were good hepatobiliary tracers. However, as hepatobiliary radiopharmaceuticals, they are not as satisfactory as E-HIDA, since considerable radioactivity was present in the liver and kidneys. This may possibly be due to the presence of polymeric forms of ^{99m}Tc in the preparation. Attempts to improve ^{99m}Tc labeling and studies on metal chelation of these ligands are in progress.