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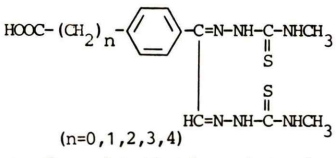
Tc-99m LABELED PROTEINS USING BIFUNCTIONAL CHELATING AGENT(V):Tc-99m LABELED HSA.

Y.Arano, Y.Magata, A.Yokoyama, K.Yamamoto, H.Saji, Y.Ishii, and K.Torizuka. Faculty of Pharmaceutical Science and School of Medicine,Kyoto University,Kyoto.

In labeling proteins with Tc-99m using bifunctional chelating agent(BCA),a selective binding of Tc-99m with the chelating moiety is estimated. However,owing to the great number of amino acid residue present on the protein surface,limitations have been detected.



Thus,in our research for better BCA,the distance between the chelating and protein moietry(spacer length)was considered. Various BCAs(n=0~4)were synthesized,and their coupling to HSA and Tc-99m labeling were carried out.Each agent was coupled to HSA by mixed anhydride method or azido method,and purified through DEAE-Sepharose Cl-6B column chromatography.Then,labeled with Tc-99m in the presence of a minute amount of stannous ion.In Vitro stability was very high,and no free Tc-99m was detected in every case.In Vivo studies showed higher blood retention in the case of n=2, and this result was attributed to the spacer length structure.Further derivatives and labeling conditions are now under progress.

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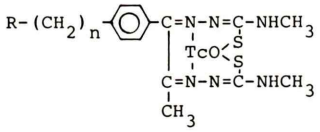
DEVELOPMENT OF Tc-99m-PHENYLALKYLAMINE BIFUNCTIONAL RADIOPHARMACEUTICALS FOR MYOCARDIAL IMAGING.

A. Yokoyama, T. Hosotani, Y. Arano, K. Horiuchi, K. Yamamoto, N. Tamaki and K. Torizuka. Faculty of Pharm. Sciences and School of Medicine. Kyoto Univ. Kyoto.

Development of myocardial imaging agent based on Tc-99m have attracted great attention, in spite of the spread use of Tl-201. We designed several bifunctional chelating agents, containing lipophilic benzene ring with tertiary or quaternary amine derivatives of bis-thiosemicarbazone (BTS). In this work, labeling of dimethylamino-BTS(p-DPA-BTS) with Tc-99m was carried out using the Sn-Resin method. Paper electrophoresis indicated the presence of cationic Tc-complex. Scintiphotos from white long-ear rabbit injected with Tc-p-DPA-BTS through the ear vein, revealed the doughnut like shape of the myocardium.Section images made available with the HEADTOME II (Shimazu) also showed promissing evidence. Further labeling studies and animal test with quaternary amine derivatives is now under progress.



R= $(CH_3)_3N$, $(CH_3)_2N$, $(C_2H_5)_2N$

* p-DPA-BTS: R=$(CH_3)_2N$, n=2

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EFFECT OF ALUMINUM ON BIODISTRIBUTION OF Tc-99m-DMSA.

H. Matsushima, T. Sanada, N. Ueda and M. Hazue. Research & Development, Technical Department, NIHON MEDI-PHYSICS CO., LTD., Takarazuka.

The effect of aluminum on the biodistribution of some Tc-99m radiopharmaceuticals is well known.

In this study, the effect of varying aluminum concentration, ranging from 0 to 3.0 μg/ml aluminum in Tc-99m pertechnetate, on the biodistribution of Tc-99m-DMSA in rats was investigated experimentally. Tc-99m pertechnetate containing aluminum was prepared by adding pH=5.5 aluminum solution. Also,Tc-99m pertechnetate containing aluminum from commercial generator was tested in this experiment.

The results indicated that more than 0.2 μg/ml aluminum concentration in Tc-99m pertechnetate caused the abnormal liver uptake of Tc-99m-DMSA preparations. This liver uptake increased drastically with increasing aluminum concentration.

Tc-99m-Al-Colloid of about 0.3μm in diameter was detected in the Tc-99m-DMSA using Nucleopore Filtration Method.

When pH=4.5 aluminum solution was used as the aluminum source, above mentioned liver uptake was not observed. So, we suppose that aluminum ions in Tc-99m pertechnetate exist in the form of high valence polymer at 5 to 6 pH range and cause Tc-99m-Al-Colloid.

The chromatographic system consisting of Whatman No. 3MM and ammonium chloride(1M)-Urea(5M) mixture is useful for detecting the Tc-99m-Al-Colloid.

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HPLC ANALYSIS OF Tc-99m(Sn)PYRIDOXYLIDENEAMINATES AND Tc-99m(Sn)-N-PYRIDOXYLAMINATES: ITS CHEMICAL AND BIOLOGICAL IMPLICATIONS.

M. Kato-Azuma and M. Hazue. Research & Development, Technical Department, NIHON MEDI-PHYSICS CO., LTD., Takarazuka.

The titled Tc-99m complexes with twenty-two different amino acid moieties were analyzed by high performance liquid chromatography (HPLC). Each preparation showed three radioactivity peaks on its HPLC profile, and the different retention times as well as the different ratios of the peaks were given for these agents. The results obtained by peak-isolation/re-injection experiments and dilution with buffers of various pH indicated that the three components in each preparation were not inter-convertible with each other. The three components of Tc-99m(Sn)-N-pyridoxyl-5-methyltryptophan [Tc-99m-PMT] were found to equally undergo rapid hepatobiliary excretion. The mixed ligand experiments revealed that each of the three peaks consists of a bis-type Tc-99m complex, i.e. two molecules of the ligand coordinate to one technetium atom. Furthermore, the electrical neutrality of the complexes was shown by electrophoresis.

All the above results allowed us to propose the possible structures; the three complexes would be the three geometrical isomers of *bis*(pyridoxylideneaminato)technetium(IV) or *bis*(N-pyridoxylaminato)technetium(IV), and the complex I with the shortest retention time could be assigned to the *u-fac*-isomer, complex II to the *mer*-isomer, and complex III with the longest retention time to the *s-fac*-isomer.