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SYNTHESIS AND EVALUATION OF Tc-99m AND Cu-62 LABELED FATTY ACID ANALOGS.

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Radiolabeled fatty acid analogs have been attracting great interest as myocardial imaging agents, and their labeling with generator eluated radionuclides, Tc-99m and Cu-62 are highly desirable. Based on our preliminary studies on Tc and Cu dithiosemicarbazone (DTS) complexes, two fatty acid analogs containing DTS molecule as the metal coordinating site were synthesized: a fatty acid analog containing DTS molecule at the ω-position (FA-DTS) and a phenyl fatty acid analog containing DTS molecule at the p-position (PFA-DTS).

These two fatty acid analogs were labeled with Tc-99m and Cu-64, and their biodistribution in mice were compared. As for Tc-99m labeled compounds, while myocardial radioactivity of Tc-99m-PFA-DTS remained, that of Tc-99m-FA-DTS cleared slowly. On the other hand, while myocardial accumulation of Cu-64 labeled PFA-DTS and FA-DTS were similar, FA-DTS showed faster blood clearance than PFA-DTS. As a result, heart/blood ratio of 1.3 at 30 min post-injection was obtained with Cu-64-FA-DTS.

The gathered results indicated good potentiality of PFA-DTS as for Tc-99m and FA-DTS as for Cu-62 labeled fatty acid analogs for myocardial imaging agents.

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TC-99m-DTPA-HSA AS A NEW BLOOD POOL SCANING AGENT.

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It has been known for several years that Tc-99m-HSA prepared with commercial kit has some problems due to its poor stability in vitro and in vivo. We have, therefore, developed a new HSA preparation coupled with DTPA providing a strong chelating site for Tc-99m.

Preliminary experiments evidenced that the labeling efficiency and in vitro stability of Tc-99m-DTPA-HSA were affected by DTPA/HSA coupling ratio(DTPA/HSA), pH, incubation time, and amount of reducing agent. The formulation of DTPA-HSA solution was optimized as follows in order to achieve the best blood retention in normal rats: [DTPA-HSA] = 10 mg/ml, DTPA/HSA = 5-6/1, pH 5-6. The blood level of the sample prepared as mentioned above gave 77.85 % at 1 hr after injection which was comparable to that of I-131-HSA (75.87 %) and 15-35 % better than those of conventional Tc-99m-HSA kits. At 24 hr after labeling the sample showed even better blood retention than I-131-HSA. Tc-99m-DTPA-HSA proved, thus, a desirable feature for the blood pool scanning agent.

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HIGH SPECIFIC ACTIVITY LABELING OF HSA AND MONOCLONAL ANTIBODIES. USE OF CLUSTERED COMPOUND : AMYLOSE - DEFEROXAMINE.

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Clustered compound, Amylose - Deferoxamine (AMY-DFO_{5-15}) was introduced to proteins in order to obtain high specific radioactivity. It was found that the biological activities of proteins have been kept enough as the one molecule of protein was conjugated with less than one clustered compound.

Blood retention of HSA-(AMY-DFO_{10})$_{0.9}$-Ga-67 was higher than that of HSA-I-131 [$T_{1/2}$(Ga-67)=30 hr, $T_{1/2}$(I-131)=5.7 hr].

Monoclonal antibodies, such as R11D10 and OC-125, showed high immunological reactivity after conjugation of clustered compounds. The immunological reactivity of 19-9, however, was lost after conjugation of AMY-DFO. It was suggested that this type of clustered compound can not be used with monoclonal antibody which recognizes the sugar structure of its antigen.

In conclusion, the clustered compound is useful to obtain the radiolabeled protein with high specific radioactivity as it can introduce a lot of DFO on one protein molecule.

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A RADIOPHARMACEUTICAL AS AMINO ACID METABOLISM MARKER (4). STEREOSPECIFIC BEHAVIOR OF MONOIODO-D-TYROSINE.

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Interesting enzymatic and in-vivo behavior of D-amino acid (AA) attracted our attention as potential marker of AA metabolic pathways, to be exploited as for future development of functional imaging radiopharmaceutical (RP). As labeling procedure, radioiodination has constituted the simplest methodology for stereoisomer, but hindered by deiodination. In this work, tyrosine, a natural and easy to label AA, was selected and the stereoisomeric effect of its I-125-monoiodinated L or D form (L-MIT, D-MIT) on deiodination was studied in various compartments. In in-vitro studies, L-MIT showed fast and temperature-dependent deiodination by mouse liver, kidney homogenate, while D-MIT was resistant to this enzymatic deiodination. In in-vivo mice biodistribution, D-MIT showed higher stability to deiodination than L-MIT. Also remarkable D-MIT biodistribution to pancreas, an indication of membrane transport associated feature (non-substrate in protein synthesis) was observed along with low liver uptake, fast blood clearance. Thus, high pancreas to other organ ratio (pancreas/liver = 4.48 pancreas/blood = 4.78, 10 min post i.v. inj.) was obtained. D-MIT has high potentiality for RP as membrane AA transport marker.