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FUNDAMENTAL STUDIES ON THE TUMOR UPTAKE OF Tc-99m-(V)-DMS.

I.Yomoda, K.Horiuchi, H.Masuda, A.Yokoyama, *H.Ohta,*K.Endo and *K.Torizuka. Faculty of Pharmaceutical Sciences and *School of Medicine, Kyoto University, Kyoto.

As reported Tc-99m-(V)-DMS has offered good characterization as for tumor imaging namely in patients with medullary thyroid carcinoma. The design of this radiopharmaceutical has been based on the formation of pentavalent oxoanion, TcO_4^{3-}, derived from the Tc-complex dissociation equilibria in dynamic living systems.
As a first approach to test this postulate, in in-vitro studies, the effect of degree of dilution on the Tc-complex dissociation was followed by thin layer chromatography(solvent=n-ButOH:AcOH:Water=3:2:3) and by the Ehrlich ascites tumor cell uptake.
Under dilution process, Tc-99m-(V)-DMS complex dissociation was detected to be occuring as a new peak at Rf:0.65(original sample peak Rf:0.45) increased along with the degree of dilution and decreased with the addition of ligand. This phenomenon was paralleled with the uptake by the Ehrlich tumor cells. An increased in the dilution factor induced as high tumor cells uptake as 10 to 20 times.
Thus, data gathered represents good basis of the postulate, as for the participation of metal technetium complex dissociation toward some functionally active species, TcO_4^{3-}, relevant to the metabolically active tumor cells. Further studies are under progress.

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EFFECTS OF CITRATE ON THE IN VIVO BEHAVIOR OF GA-67. H.Kohno, T.Suzuki, Y.Ohkubo and A.Kubodera*. Tohoku College of Pharmacy, Sendai.*Science University of Tokyo, Tokyo.

It has been reported that citrate ion influenced the physico-chemical behavior of Ga-67. Recently, we also observed that the binding capacity of Ga-67 to Ehrlich tumor cells or rat liver cells was significantly lowered by sodium citrate. The aim of this experiment is to study the influences of citrate on the in vivo behavior of Ga-67. Male Wistar rats weighing 180-250g were anesthetized with urethane and a catheter for blood sampling was inserted into the right external jugular vein. Ga-67-citrate or -chloride containing various doses of sodium citrate was injected through the catheter, and a 20ul volume of the blood was repeatedly drawn 11 times up to 8 hours After the last sampling, each rat was sacrificed and various tissues were taken for the distribution study. Some pharmacokinetic parameters were calculated using a personal computer. The blood disappearance pattern of Ga-67 was changed depending on the doses of sodium citrate. Especially, the disappearance rate of Ga-67 at very early phase was dramatically increased by extremely low doses of sodium citrate. A little changes in the tissue distribution of Ga-67 was appeared depending on the doses of sodium citrate.

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EFFECT OF RING SISE ON TUMOR SPECIFICITY OF ALICYCLIC α-AMINOACIDS. K.Shiba,H.Mori,and K.Hisada. Kanazawa University. Kanazawa.

The selective affinity of Synthetic non-metabolized aminoacids such as 1-Aminocyclopentanecarboxylic acid and α-Aminoisobutyric acid for tumor tissue had let us to study the tumor-localizing characteristics of a series of alicyclic α-aminoacid analogs.
We synthesized five C-14 labeled alicyclic α-aminoacids without α-hydrogen(8-through 4-membered ring systems)by our modified Bücherer synthesis and carried out tissue distribution and whole-body autoradiographic studies on these aminoacids.
Five C-14 labeled alicyclic α-aminoacids were intravenously injected through tail vein into separate groups of the mice with Ehrlich tumor.
At 10,30,60,120min after injection,tumor and other tissues were excised.
These tissues were oxidized with a sample oxidizer and counted in a liquid scintillation spectrometer.
These studies showed that every these amino acids had high tumor specificity,namely high tumor uptake and tumor to tissue ratios increased with time,although there was a trend to increase with decreasing ring size in homologous series(8-through 4-membered ring systems)in terms of both tumor uptake and tumor to tissue ratios.

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Tc-99m LABELING OF MONOCLONAL ANTIBODY USING BIFUNCTIONAL CHELATING AGENT.

Y.Arano, T.Furukawa, A.Yokoyama, H.Sakahara, T.Nakashima, H.Saji, K.Endo and K.Torizuka. Faculty of Pharmaceutical Sciences, School of Medicine, Kyoto University, Kyoto.

The use of p-carboxyethylphenylglyoxal bis(N-methylthiosemicarbazone) (CE-DTS) as the bifunctional chelating agent for the Tc-99m labeling of monoclonal antibody (MAb) was estimated. A MAb against human thyroglobulin was chosen for this preliminary study on applicability of CE-DTS, based on 1) immunoreactivity of the new conjugate, 2) in vivo stability of Tc-99m labeled conjugate. The effects of CE-DTS conjugation to MAb and subsequent Tc-99m labeling on the immunoreactivity of MAb were evaluated by RIA, and the stability of Tc-99m labeled MAb was traced by HPLC. When CE-DTS was conjugated to MAb at the molar ratio of 1:1, and Tc-99m labeling was performed at pH 6.2 in the presence of stannous chloride, a stable Tc-99m labeled MAb with its original immunoreactivity was obtained. In vivo study in mice showed the percent of injected dose of radioactivity and the blood clearance alike those of I-131 labeled MAb. Then the stability of the labeled MAb in vivo as well as in vitro was demonstrated.
From the present study, applicability of the bifunctional chelating agent, CE-DTS, for the labeling of MAb with Tc-99m became evident. These results provided good basis for future studies in radioimmunodetection using more useful MAb for diagnostic studies.