E. Radiopharmaceuticals, Radionuclide

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TUMOR UPTAKE OF RADIOACTIVE METAL CHELATES ENCAPSULATED IN LIPOSOMES. I. Ogihara and S. Kojima Department of Pharmaceuticals, Teikyo University, Kanagawa

Co-60, Cr-51, Fe-59 and Ga-67 chelated to nitrilotriacetic acid(NTA) and ethylenediaminetetraacetic acid(EDTA) were encapsulated in liposomes and their tissue distributions in S-180 sarcoma-bearing mice after i.v. injection were studied. Free (not encapsulated) Co-60 and Cr-51, chelated to either NTA or EDTA, were almost excreted by 24 h after the i.v. injection. Fe-59-EDTA and Ga-67-EDTA were also excreted. Fe-59-NTA was distributed to all tissues, presumably because Fe-59 parted from NTA and followed the iron metabolism. Ga-67-NTA was distributed mainly in the tumor and liver. When these metal chelates were encapsulated in liposomes, their distributions were much different from those of free forms. They stayed longer in the body and were delivered to the tumor efficiently, whichever metal chelate was encapsulated. Especially, Ga-67-NTA encapsulated in liposomes showed much larger accumulation of radioactivity in the tumor than that of other metal chelates. The value was also larger than that of free Ga-67-NTA. The distribution of C-14-labelled liposomes indicated that liposomes themselves accumulated predominantly to the tumor. It is suggested that Ga-67-NTA encapsulated in liposomes was delivered to the tumor by liposomes and then stayed there due to the Ga-67 affinity for the tumor.

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Tc(V)-DMS TUMOR ACCUMULATION MECHANISM : STUDIES ON CELLULAR DISTRIBUTION. I.Yomoda, K.Horiuchi, and A.Yokoyama. Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto.

Clinical usefulness of the newly developed tumor imaging agent, Tc-99m(V)-DMS have been reported. Previous basic studies have shown the involvement in the tumor cell accumulation of a pentavalent Tc oxoanion, TcO_4^{3-} dissociated from the Tc-complex. In our search for the tumor cell accumulation mechanism, studies on the localization of the dissociated technetium species at cellular level was estimated of interest. In this study, the Tc(V)-DMS in-vitro Ehrlich tumor cell uptake followed by the cell fractionation using the method of Brunette-Till were carried out and the radioactivity distribution in various cellular fractions were investigated. More than 50 % of whole cell radioactivity was detected in the intracellular fractions. The radioactivity level found in membranes was about 15 % with only slight changes upon cell washings or incubation time, but extended changes were detected in the intracellular fraction. Comparative studies with the diffusible anion, TcO_4^-, Tc-colloid with high membrane adsorption, and Tc-DMSA, a kidney imaging agent, are carried out and the intracellular radioactivity localization transported through in anionic form ,TcO_4^{3-} is discussed.

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COMPARISON OF Ga-67 NITRATE, Ga-67 CITRATE, Ga-67 MALATE AND Ga-67 EDTA. A.Ando,I.Ando, T.Hiraki and K.Hisada. Schools of Allied Medical Professions and Medicine, Kanazawa University, Kanazawa.

This study was undertaken to investigate the relation among the chemical form of Ga-67 compounds, tumor accumulation rate and adsorption rate to ion-exchange resin. Each preparation of carrier-free Ga-67 compounds (Ga-67 citrate, Ga-67 nitrate, Ga-67 malate, Ga-67 EDTA) was injected i.v. into the rats s.c. transplanted with Yoshida sarcoma. Tumor and various organs were excised 3, 24 and 48 hours after administration of these compounds, and Ga-67 was measured. Concerning Ga-67 citrate containing various amounts of stable gallium, the accumulation rates for tumor and organs were assayed. On the other hand, the adsorption rate of Ga-67 citrate, Ga-67 nitrate and Ga-67 EDTA to the ion-exchange resin in rabbit serum were measured.

In the case of Ga-67 nitrate, Ga-67 citrate and Ga-67 malate, the accumulation rate of Ga-67 in tumor and organs were very similar one another, although that of Ga-67 EDTA in these tissues was very small. In the case of Ga-67 nitrate and Ga-67 citrate, adsorption rates of Ga-67 to the cation exchange resin were 55-70 % after an hour incubation, but those for Ga-67 EDTA were very small. Concerning Ga-67 citrate containing stable gallium, accumulation rates for tumor and organs(except for bone) decreased with amount of stable gallium.

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ON THE RADIOACTIVE INDIUM BINDING ACID MUCOPOLYSACCHARIDE IN TUMOR, LIVER AND INFLAMMATORY LESION. A.Ando,I.Ando,M.Katayama,S. Sanada,T.Hiraki,N.Tonami and K.Hisada. Schools of Allied Medical Professions and Medicine, Kanazawa University, Kanazawa.

This study was undertaken to determine the structure of In-114m binding acid mucopolysaccharide in tumor, liver and inflammatory lesion. In-114m chloride was injected into the mice s.c. implanted with Ehrlich tumor and the rats in which inflammatory lesion was induced by the method of s.c. injection of turpentine oil. Tumor, liver and inflammatory lesion were excised and homogenized. After digestion of each homogenate with protease, In-114m binding acid mucopolysaccharide of molecular weight about 10,000 was separated with the method previously described. To determine the species of the In-114m binding acid mucopolysaccharide, this acid mucopolysaccharide was treated with chondroitinase ABC, heparinase, heparitinase and keratanase, separately. On the other hand, neutral saccharide in the structure of In-114m binding acid mucopolysaccharide was assayed.

In-114m binding acid mucopolysaccharide was not digested with the above mucopolysaccharase, and the acid mucopolysaccharide contained neutral saccharide in large quantities. Based on the present results, it was deduced that the In-114m binding acid mucopolysaccharide in the above tissues was keratan polysulfate.