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A NEW TUMOR DIAGNOSIS RADIOPHARMACEUTICAL Tc-99m-DMS (II): PHARMACO-KINETICS IN HUMAN BODY.
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The pharmaco-kinetics of Tc-99m-(V)-Dimercaptosuccinic acid (DMS) in human body was studied using normal volunteers. There were no remarkable side effects by the i.v. administration of Tc-99m-DMS.

After i.v. injection of Tc-99m-DMS, most part of Tc-99m-DMS was excreted into the urine, 40% at 2 hours, 60% at 5 hours, 80% at 10 hours, respectively.

Disappearance time of Tc-99m-DMS from the blood was relatively quick and its half time was about 90 min.

The thin layer chromatography and column chromatography (Sephadex G-50) revealed that Tc-99m-DMS in the blood was combined to plasma protein, with no detectable Tc-99m-O_4^- and was excreted into the urine without any change.

The time course study indicated that Tumor/Tissue ratio was increased by reducing the back ground radioactivity and the scintigram was taken between 2and 3 hours after Tc-99m-DMS administration.

The exposure dose calculated by the MIRD method was as follows: total body 7.1 mrad/mCi liver 2.5mrad/mCi, intestine 6.5 mrad/mCi (based on biodistribution of five mice), bladder 0.23 rad/mCi (based on urine cumulative ratio of human).

The advantages of Tc-99m-DMS as a tumor seeking agent were (1) Scintigram could be obtained within 3 hours after i.v. administration. (2) There was no or very little excretion to intestine, and less accumulation to lacrimal and salivary glands than Ga-67-citrate. (3) Picture obtained was clear and suitable for emittion computed tomography.

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A NEW TUMOR DIAGNOSIS RADIO-PHARMACEUTICAL Tc-99m-DMS (III):CLINICAL STUDIES.
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In order to evaluate the usefulness of Tc-99m-Dimercaptosuccinic acid (DMS) as a tumor seeking agent, scintigraphic studies were performed in patients with various malignant tumors. Tc-99m-DMS, which was obtained at a labeling condition of a pH 8 and a very low concentration of $SnCl_2$, was injected intravenous and scintigraphy was taken at 2 or 3 hours after the administration using a conventional gamma camera. In some patients, the distribution was compared with Ga-67 citrate scintigraphy. [Results] Preliminary study showed the different characteristics of Tc-99m-DMS and Ga-67 citrate distribution in the tumor diagnosis. Tc-99m-DMS was superior in the head and neck tumor and soft tissue tumors. It is well known that previous radiation caused Ga-67 accumulation in the salivary glands. However, previous radiation did not affect Tc-99m-DMS distribution, indicating that Tc-99m-DMS would be useful for the follow the response to the treatment in the head & neck tumors.

The preliminary study showed that Tc-99m-DMS would be a promising tumor seeking agent and useful in the detection of malignant tumors, to assess their sites and to follow the response to the treatment.

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ALTERATION OF BIODISTRIBUTION OF Ga-67 CITRATE AND Tc-99m MDP IN RATS FOLLOWING TREATMENT WITH CHEMOTHERAPEUTIC AGENTS.
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Several examples of alterations of biodistributions of radiopharmaceuticals as the results of toxicities have been reported in the patients recieving chemotherapeutic agents. In the present study, alterations of biodistributions of Ga-67 citrate and Tc-99m MDP were investigated in rats following treatment with various chemotherapeutic agents. Antibiotics of mitomycin C, adriamycin, daunomycin, bleomycin and gentamycin, antimetabolite of methotrexate, and miscellaneous agents of vincristin and cisplastin were studied. All of these agents were administered into rats on the same method and basis of mg/m^2 of maximum tolerated dose as that in man. 5-10microCi of Ga-67 citrate was administered into the tail vein of rats 4-5days after treatment with chemotherapeutic agents, and 10microCi of Tc-99m MDP was also administered 18hours following Ga-67 administration. %dose/g tissue or organ of Ga-67 citrate 24hrs after injection and that of Tc-99m MDP 3hrs after injection were obtained. In these treated rats with cemotherapeutic agents, alterations of biodistributions were observed. Among them, alterations of kidney and liver uptakes were extremely remarkable.

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STUDIES ON F-18-LABELED PYRIMIDINES. TUMOR UPTAKES OF F-18-5-FLUOROURACIL, F-18-5-FLUOROURIDINE AND F-18-5-FLUORODEOXYURIDINE IN ANIMAL STUDY.
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Three F-18-labeled pyrimidines F-18-5FU, F-18-FUR and F-18-FdUR were examined regarding tissue distribution and tumor uptake in ascitic hepatoma AH109A-bearing rats. The tumor uptakes of F-18-5FU and F-18-FdUR were identical except for the period just after innoculation when F-18-FdUR uptake surpassed F-18-5FU uptake. The tumor-to-organ ratios obtained with F-18-FdUR were always 1.5 to 3 times higher than F-18-5FU and F-18-FUR. We concluded that F-18-FdUR was a proper radiopharmaceutical for tumor imaging.

Positron emission tomography of a rabbit tumor located on the chest with F-18-FdUR clearly showed the tumor within one hour.

Uptakes of F-18-FdUR in various tumor cell lines, such as MM48, and FM3A derived from mouse mammary carcinoma, were also examined.We found uptake in MM48 was higher than that in FM3A and AH109A.This suggested the different tumor uptake of F-18-FdUR may be related to tumor's viability.