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PREPARATION AND BIODISTRIBUTION OF Ga-67 LABELED FIBRINOGEN CONJUGATED WITH WATER SOLUBLE POLYMER CONTAINING DEFEROXAMINE: A POTENTIAL THROMBUS IMAGING AGENT.

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In order to introduce a large number of deferoxamine(DFO) on fibrinogen(Fib), the cluster method using dialdehyde starch(DAS) has been investigated as a new protein labeling technique. The rat distribution pattern of Ga-67 Fib-(DAS-DFO) conjugate obtained with this technique was compared with that of Ga-67 Fib-DFO conjugate.

The blood clearance of Ga-67 Fib-(DAS-DFO) was slightly faster than Ga-67 Fib-DFO, and the liver radioactivities of both conjugates showed a similar behavior, approaching 35% of the total injected dose at 24 hr after the administration.

The Ga-67 Fib-(DAS-DFO) was also administered into rabbits having the fresh thrombus. The cardiac blood pool was seen until 24 hr after the administration. The thrombus was clearly visualized as a hot spot at 6 hr after the administration.

These results suggest that Ga-67 Fib-(DAS-DFO) is a promising clinical diagnostic agent for detection of thrombi.

This work has been supported in part by the New Drug Development Committee under the Ministry of Health and Welfare of Japan.

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DEVELOPMENT OF RADIOPHARMACEUTICALS USING A NEW REACTIVE POLYMER AS A CARRIER (I): PREPARATION OF Ga-67-DFO-POLYSUCCINIMIDE-FIBRINOGEN CONJUGATE.

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It has been reported that biologically active proteins are labeled directly by radioisotopes for in vivo diagnosis and a new labeling approach using a poly saccharide containing deferoxamine(DFO), a bifunctional chelate,as a carrier is undergoing.[1] We newly synthesized a reactive polymer of polysuccinimide introducing DFO,which was conjugated with fibrinogen by disulfide bond using a coupling agent of DTBP.

This Ga-67-DFO-polysuccinimide-fibrinogen conjugate had a specific activity of 0.4mCi/mg protein and fully retained the clottability of native fibrinogen in vitro.Its biodistribution in rats revealed a rapid disappearance of the radioactivity from circulating blood.

In vivo studies in rabbits with induced thrombi in the femoral artery showed a high thrombus-to-blood in radioactivity ratio of 8.46 in 24 hr after injection.

These results suggest that this Ga-67-DFO-polysuccinimide-fibrinogen conjugate is promising for a thrombus imaging agent.

1) K.Takahashi,et al.:Japanese J. Nucl.Med.:20(7) 1229(1983)

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I-123 LABELLING OF NEOGALACTO-HSA USING IODOGEN.

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A synthetic glycoprotein, neogalacto-HSA (Gal-HSA) has been regarded as a possible agent for the functional imaging of hepatic parenchymal cells. In this presentation, the optimal condition for I-123-Gal-HSA preparation and its biodistribution in rats were reported.

Gal-HSA was labelled with I-123 using Iodogen(1,3,4,6-tetrachloro-3α,6α-diphenylglycouril). I-123 source used was produced by a Te-124(p,2n)I-123 reaction and purified with ion-exchange resins. It was found that the following condition for iodine labelling gave no detectable protein aggregate with gel-filtration chromatography: volume of reaction mixture; 1.0 ml, protein; >4 mg, Iodogen; 5×10^{-8}—2×10^{-7}mol, NaI-123; <2 mCi at calibration, pH; neutral(0.2M borate buffer) 5°C, 30 min. Upon labelling with 2×10^{-7}mol of Iodogen under the condition given above, the labelling yield reached to ca. 95 %. The biodistribution of I-123-Gal_{29}-HSA(galactose /HSA = 29/1; molar coupling ratio) was studied with normal female S.D. rats. At 10 min after the i.v. injection of 200 μg I-123-Gal-HSA, 95±0.5 % of the total activity was found in liver. The liver activity diminished almost within 1 hr($T_{\frac{1}{2}}$ = ca. 25 min), and redistributed in digestive organs and thyroid, then ca. 70 % of the activity was excreted into urine 24 hr after the injection.

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DEVELOPMENT OF TC-99M-NEOGALACTO-HSA AS A POSSIBLE AGENT FOR HEPATIC FUNCTIONAL IMAGING.

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A specific receptor which recognizes the exposed galactose terminal of circulating blood glycoproteins exsists on the plasma membrane of hepatic parenchymal cells. Since it is known that the concentration of receptors depends on the stage of liver diseases, the uptake of radiolabelled glycoprotein by receptors could be applied to the scintigraphic assessment of liver disfunction.

Neogalacto-HSA(Gal-HSA) was synthesized by coupling the galactose derivative to HSA by amidination and Gal-HSA monomer was isolated by gel-filtration chromatography. Gal-HSA was labelled with Tc-99m using $SnCl_2$ as a reducing agent. Under the optimal condition for labelling in aqueous solution, the labelling yield reached to ca. 95 % and was stable for 24 hr. The biodistribution of Tc-99m-Gal_{29}-HSA(galactose/HSA = 29/1; molar coupling ratio) was studied with normal female S.D. rats of ca. 190 g body weight. At 15 min after i.v. injection of 200 μg Tc-99m -Gal-HSA, 91±0.6 % of the total activity was located in liver and no specific distribution was observed in other than liver. The liver activity was mainly excreted through biliary duct into feces with a half-life time of ca. 90 min. 10 % of the activity was excreted into urine within 3 hr.