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Radioactive Metal Complexes with Affinity for Tumors. II. Biodistribution of Radioactivity in Cellular and Subcellular Fractions of Tumor Tissues.*

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We reported previously that radioactivity was concentrated in tumor tissues of experimental animals a few hours after the administration of the complexes of ethylenediamine-N,N-diacetic acid (EDDA) with $^{99\text{m}}$ Tc ($^{99\text{m}}$ Tc EDDA) and 57 Co (57 Co EDDA). The tumor tissues were clearly visualized in scintigrams. Higher affinity for tumor was observed with μ -oxo 57 Co EDDA, a complex prepared by treatment of 57 Co EDDA with hydrogen peroxide. The 51 Cr, 59 Fe, 64 Cu and 67 Ga complexes of EDDA as well as 3 H-labeled EDDA were not concentrated in the tumor.

To elucidate the mechanism, the EDDA complexes with tumor localizing activity and related radioactive compounds were administered to experimental animals bearing tumors or abscess and the biodistribution of the radioactivity was determined. The blood and tissues were separated, fractionated and analyzed. In blood, ^{99m}Tc EDDA and ⁵⁷Co EDDA were in dialyzable forms, whereas tumor-nonlocalizing compounds such as ^{99m}Tc AcEDDA (*N*-acetyl-EDDA), ⁵⁷CoCl₂, and ⁵⁷Co AcEDDA were in undialyzable or protein-bound forms. ^{99m}Tc EDDA and ⁵⁷Co EDDA showed the large tumor/blood and tumor/muscle ratios of the radioactivity which indicated the high affinity for tumor tissues.

Ehrlich solid tumor removed from mice administered intravenously with $^{99\text{m}}\text{Tc}$ EDDA or $\mu\text{-}\text{oxo}$ ^{57}Co EDDA were homogenized and separated into the nuclear, mitochondrial, microsomal, and cytosol fractions and the radioactivity of each fraction was measured. The results showed that $^{99\text{m}}\text{Tc}$ radioactivity became concentrated in the nuclear fraction 3 h after the administration and a considerable part of the ^{57}Co was present in the nuclear and mitochondrial fractions immediately after the administration.

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