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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 ^{99m}Tc (^{99m}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 ^3H -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 ^{57}Co EDDA were in dialyzable forms, whereas tumor-nonlocalizing compounds such as ^{99m}Tc AcEDDA (*N*-acetyl-EDDA), $^{57}\text{CoCl}_2$, and ^{57}Co AcEDDA were in undialyzable or protein-bound forms. ^{99m}Tc EDDA and ^{57}Co 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 ^{99m}Tc EDDA or μ -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 ^{99m}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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