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[Lab. of Pharmaceutics]

**Heparin-induced release of extracellular-superoxide dismutase form (V) to plasma.**

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EC-SOD in serum is heterogeneous with regard to heparin-affinity and can be divided into five fractions (I) to (V), whereas fibroblast-secreted EC-SOD consists mainly of form (V). An intravenous injection of 50 i.u. of heparin/kg body weight into two healthy volunteers led to an immediate rise of serum EC-SOD level by 2.4-2.8-fold. The half-life of serum EC-SOD after the prompt rise was about 90 min. The *in vivo* experiment using rats and an *in vitro* experiment strongly suggested the EC-SOD released into the plasma reconstituted the interaction with glycocalyx on the vascular endothelial cell surface in accordance with the elimination of heparin from the vascular system.

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**The heparin-binding site of human xanthine oxidase.**

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The enzyme xanthine oxidase (XOD) has an affinity for heparin and can bind to cultured porcine aortic endothelial cells. The heparin-binding sites in human XOD (h-XOD) are studied. From a chymotryptic digest of cyanogen bromide fragmented h-XOD, two peptides with an affinity for heparin-HPLC, A-1 and A-2, were isolated. Amino acid sequence analysis showed that both peptides had lysine and/or arginine residues. The A-1 region may direct its charged side chains toward the solvent while burying its hydrophobic side chains against the hydrophobic inside, because the A-1 peptide forms a highly amphipathic structure. Peptide A-2 contains triple lysine residues and constitutes a hydrophilic region.

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**Molecular analysis of extracellular-superoxide dismutase gene associated with high level in serum.**

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By molecular analysis of the EC-SOD coding region from the group II individuals in Sweden, a single nucleotide substitution of G to C generating an amino acid change of arginine-213 to glycine has been identified in the region associated with the heparin affinity of the enzyme. The same mutation was detected in the Japanese as a homozygote in both alleles of 2 hemodialysis patients and as a heterozygote in one allele of all the healthy group II individuals and 17 hemodialysis patients. The amino acid substitution may result in the decrease of the heparin affinity which is favorable for the existence of EC-SOD in the serum.