SUPPRESSION BY ANTIOXIDATEIVE CHELATORS OF TOXIC EFFECTS OF IRON OVERLOAD IN RATS

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Iron overload (IOL) is a well-known origin of human and animal pathologies initiated or mediated by free radicals. To investigate the possibility of the inhibition of iron-initiated damaging processes by antioxidative chelators, we developed the animal models of IOL and studied the IOL effects on lipid peroxidation and oxygen radical production by neutrophils and macrophages. Iron overloading was achieved by feeding rats the diets supplemented with elemental iron for 42 days or infusing the animals interperitioneally with the $FeSO_4$ solution for 3 days IOL resulted in the sharply enhanced levels of TBA-reactive products in liver microsomes and the macrophage plasmalemma and oxygen radical over production by professional phagocytes (nonstimulated and PMA-stimulated peritoneal macrophages and blood leukocytes). To suppress iron-stimulated free radical processes, we administrated natural nontoxic substances possessing both chelating and antioxidant properties (bioflavonoid rutin, lipoic acid, and Bio-Normalizer, a natural Japanese food supplementation) to IOL rats, rutin and lipoic acid diminished free radical over production without diminishing iron levels in the blood probably due to the formation of iron-rutin or iron-lipoic acid complexes, which were unable to catalyzer free radical reactions. In contrast, Bio-Normalizer sharply decreased both the content of non-heme iron and lipid peroxidation in the plasmalemma of macrophages as well as the macrophage oxygen radical release. On these grounds we assumed that toxic effects of iron overload may be suppressed by antioxidative chelators via (1) scavenging of free radicals, (2) the enhanced excretion of iron, (3) the formation of inactive iron-chelator complexes incapable of catalyzing free radical reactions.

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