Mechanisms underlying iron and copper ions toxicity in biological systems: Pro-oxidant activity and protein-binding effects

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Iron and copper ions, in their unbound form, may lead to the generation of reactive oxygen species via Haber-Weiss and/or Fenton reactions. In addition, it has been shown that copper ions can irreversibly and non-specifically bind to thiol groups in proteins. This non-specific binding property has not been fully addressed for iron ions. Thus, the present study compares both the pro-oxidant and the non-specific binding properties of Fe3+ and Cu2+, using rat liver cytosol and microsomes as biological systems. Our data show that, in the absence of proteins, Cu2+/ascorbate elicited more oxygen consumption than Fe3+/ascorbate under identical conditions. Presence of cytosolic and microsomal protein, however, differentially altered oxygen consumption patterns. In addition, Cu2+/ascorbate increased microsomal lipid peroxidation and decreased cytosolic and microsomal content of thiol groups more efficiently than Fe3+/ascorbate. Finally, Fe3+/ascorbate and Cu2+/ascorbate inhibited in different w