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Generation of Free Radicals by Interaction of Iron with Thiols in Human Plasma

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Oxidative stress has been associated with a number of diseases in humans. Among the sources that can generate oxidative stress, it has been reported that iron can generate reactive oxygen species (ROS) with thiol. In iron overload state, increased thiol levels in plasma appeared to be associated with human mortality. In this study we examined whether iron could interact with thiols in plasma, generating ROS. In human plasma, unlike with Fe(Ⅲ), Fe(Ⅱ) increased lucigenin-enhanced chemiluminescence in a concentration-dependent manner, and this was inhibited by SOD. Boiling of plasma did not affect chemiluminescence induced by Fe(Ⅱ). However, thiol depletion in plasma by pretreatment with N-ethylmaleimide (NEM) decreased Fe(Ⅱ)-induced chemiluminescence significantly, suggesting that Fe(Ⅱ) generated superoxide anion by the nonenzymatic reaction with plasma thiol. Consistent with this findings, albumin, the major thiol contributor in plasma, also generated ROS with Fe(Ⅱ) and this generation was inhibited by pretreatment with NEM. Treatment with Fe(Ⅱ) to plasma resulted in significant reduction of oxygen radical absorbance capacity (ORAC) value, suggesting that total antioxidant capacity could diminished in iron overload state. In conclusion, in iron overload state, plasma may be affected by oxidative stress mediated by nonenzymatic reaction of Fe(Ⅱ) with plasma thiol.