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FREE RADICAL MECHANISMS OF IRON TOXICITY

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Recent studies demonstrate an importance of free radical-mediated iron toxicity. It is believed that its major mechanism is iron-catalyzed decomposition of hydrogen peroxide to form hydroxyl radical the Fenton reaction. Such a mechanism suggests that chelators. These have been earlier regarded only as the agents capable of accelerating iron excretion. May acquire additional anti –or prooxidant properties depending on the ability of iron-chelator complex to catalyze or suppress the Fenton reaction. Thus, chelators may suppress iron toxicity without accelerating iron excretion if they form the iron-chelator complexes inactive in the Fenton reaction.

In this work we have studied the effects of an oral chelator, 1-allyl-2-methy-3-hydoroxy-4-pyridinone (AMHP) , and two natural antioxidants possessing chelating properties, bioflavonoid rutin (vitamin P) and lipoic (LA, on *in vitro* and *in vivo* free radical-mediated damaging processes. We found that all the above compounds were able to chelate iron ions. While the structure of iron-rutin complex (? max 400-420 nm) remains uncertain, spectrophotometric and ESR studies proved the formation of Fe (Ⅲ) (AMHP) 2 (2max 453 nm g-factor 4.3) and Fe (Ⅱ) (DHLA) 2 (2max 590-620 nm. DHLA is dihydroxylipoic acid) complexes. The formation of iron-rutin complex was not accompanied by the generation of oxygen radicals, and this complex was inert in liposomal lipid peroxidation [1] . In contrast, the chelation of iron ions by AMHP or LADHLA resulted in the formation of superoxide ion depending on the iron valency. Thus, under anaerobic conditions AMHP formed a strong 2:1 iron complex (LgK 8.33 M2) with ferric ions, Under the same conditions. AMHP did not react with ferrous ions but oxidized them in the presence of molecular oxygen forming an identical ferric complex