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GENERATION OF OXYGEN RADICALS IN LONG-EVANS
CINNAMON RATS WITH HEREDITARY HEPATITIS AND
HEPATOCELLULAR CARCINOMAS

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LEC rats are inbred strain rats that spontaneously develop acute hepatitis about 3–5 months after birth and survivors from hepatitis (about 50%) finally develop hepatocellular carcinoma. The hepatic disorder in LEC rats is associated with their abnormal copper metabolism. Metal catalyzed reactions often give rise to oxygen radicals. Therefore, some cellular activities related to superoxide generation and antioxidant defense mechanism were examined.

An enhanced concentration of GSSG (oxidized glutathione) and activities of glutathione reductase indicated the existence of oxidative stress in the LEC rat liver. In fact, LEC rats exhibited higher glutathione oxidation abilities catalyzed by copper than Wistar rats. Auto-oxidation of GSH is catalyzed by Cu(II) ions and the superoxide anion($O_2^{\cdot-}$) is formed by the oxidation of GSH and of GS-Cu complex.

The activity of Mn-superoxide dismutase was increased. Activity of Cu, Zn-superoxide dismutase was also increased compared to the normal stage (at 9 wks of age). These results suggest that H_2O_2 generation is increased in the liver of the LEC rat. On the other hand activities of catalase and glutathione peroxidase, which are reduction enzymes of H_2O_2 , were decreased from the normal stage. These results suggest that cellular accumulation of H_2O_2 and $\cdot OH$, which could be produced from H_2O_2 in the presence of Cu(I), causes cellular damage leading to hepatitis and cancer.