

Time course study of the influence of acute iron overload on kupffer cell functioning and hepatotoxicity assessed in the isolated perfused rat liver

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This study tested the hypothesis that acute iron overload (500 mg/kg) alters Kupffer cell functioning by promoting free radical reactions associated with the respiratory burst of liver macrophages, assessed in the isolated perfused rat liver under conditions of Kupffer cell stimulation by carbon infusion and inactivation by gadolinium chloride pretreatment. Total serum and hepatic iron levels were markedly enhanced compared with control values 2 to 24 hours after iron treatment. Total liver O₂ uptake progressively increased by iron overload reaching a maximum at 6 hours after treatment, an effect that was completely blocked by GdCl₃. Concomitantly, carbon-induced GdCl₃-sensitive liver O₂ uptake was either enhanced by 119% at 2 hours after iron overload, diminished compared with control values at 4 hours, or abolished at 6 hours. Iron-overloaded rats showed a marked increase in liver sinusoidal lactate dehydrogenase efflux at 4 and 6 hours after treatment, an effect that is exacerbated