Acetaminophen-induced liver oxidative stress and hepatotoxicity: Influence of Kupffer cell activity assessed in the isolated perfused rat liver

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The influence of acetaminophen (APAP) treatment (400 mg/kg) on Kupffer cell function was studied in the isolated perfused liver by colloidal carbon infusion, concomitantly with parameters related to oxidative stress (thiobarbituric acid reactants (TEARS) formation and glutathione (GSH) content) and tissue injury (sinusoidal efflux of lactate dehydrogenase (LDH)). APAP led to increased rates of hepatic TEARS formation, GSH depletion, and higher sinusoidal LDH efflux compared to control values, without changes in the basal rate of O2, consumption. In addition, APAP significantly enhanced the rate of carbon uptake by perfused livers and the associated carbon-induced O2, consumption, with carbon-induced LDH effluxes being increased by 411% over control values or by 124% compared to basal LDH release in APAP-treated rats. APAP-induced changes in liver TEARS formation and GSH levels were attenuated by gadolinium chloride (GdCl3,) pretreatment, whereas those in carbon uptake, carbon-induced r