**Abstract**

Carbon tetrachloride (CCl4) is a strong hepatotoxic agent. The ability of the anti-inflammatory agent, lactoferrin (LF), to alleviate hepatic inflammation in a Wistar rat model administered with carbon tetrachloride (CCl4) was examined. Thirty male Wistar rats were segregated into 5 groups (6 rats per group): Control group, LF group (300 mg LF/kg b. wt daily for three weeks), CCl4 group (1 ml CCl4/kg b. wt once orally), LF-protected group (300 mg LF/kg b. wt daily for 3 weeks followed by 1 mL CCl4/kg b. wt once orally), and LF-treated group (1 mL CCl4/kg b.wt once orally followed by 300 mg LF/kg b. wt orally every day for three weeks). Erythrogram, leukogram, activity of oxidative stress markers (Superoxide dismutase [SOD], Glutathione peroxidase [GPx], and Malondialdehyde [MDA]), and expression of hepatic paraoxonase-1 (PON1), interleukin (IL)-1β, and IL-10 mRNA were determined. Histopathological examination of the hepatic tissue was carried out. CCl4 caused liver injury, loss of liver antioxidant activity of SOD and GPx, and a significant increase in the level of malondialdehyde in the serum. Moreover, CCl4 induced up-regulation of hepatic pro-inflammatory (IL-1β) factors, and down-regulation of anti-inflammatory (IL-10 and PON1) factors. Based on histopathological examination, the hepatic tissues had severe inflammation and were damaged. However, LF mitigated the liver damage, oxidative stress, and hepatotoxicity caused by CCl4. Overall, these results suggest that LF-mediated immunological mechanisms alleviate CCl4-induced hepatic toxicity and provide a novel perspective on the potential use of LF for prophylactic and therapeutic applications in treating liver diseases.

**KEYWORDS:**

Anti-oxidant enzymes; inflammation; liver; paraoxonase-1