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Research Article

Diosmin Protects Against Cyclophosphamide-induced Liver Injury Through Attenuation of Oxidative Stress, Inflammation and Apoptosis

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Abstract

Objective: The present study aimed to investigate the possible protective mechanisms of diosmin against cyclophosphamide (CP)-induced liver injury in rats, focusing on oxidative stress, inflammation and apoptosis. **Materials and Methods:** Rats were administered diosmin at doses 50 and 100 mg kg^{-1} weeks prior to CP injection. Two days after CP administration, rats were sacrificed and samples were collected. **Results:** The CP administration induced liver injury evidenced by the histopathological changes and significant increase in liver marker enzymes, lipid peroxidation and nitric oxide levels. Liver reduced glutathione (GSH) and antioxidant enzymes were significantly declined. Gene expression and protein levels of the pro-inflammatory cytokines, tumor necrosis factor alpha and interleukin 1 beta were significantly increased in liver of CP-administered rats. Pre-treatment with diosmin counteracted CP-induced oxidative stress and inflammation. In addition, diosmin protected against CP-induced apoptosis as assessed by down-regulation of BAX and up-regulation of Bcl2 at both gene and protein levels. **Conclusion:** The present study provides evidence that diosmin exerts protective effect against CP through induction of antioxidant defenses and suppression of inflammation and apoptosis. These findings represent a novel protective mechanism of diosmin against CP-induced hepatotoxicity.

Key words: Diosmin, flavonoids, chemotherapy, hepatotoxicity, inflammation, apoptosis, cyclophosphamide, BAX, oxidative stress

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Competing Interest: The author has declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.