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PROCEEDINGS ABSTRACT

Protective effects of a *Capparis spinosa* extract, alone and in combination with silymarin, on the hepatic injury and critical liver function markers of rats exposed to acetaminophen

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Acetaminophen (APAP) overdose is a major cause of acute drug-induced liver injury worldwide, largely mediated by oxidative stress, lipid peroxidation, and hepatocellular necrosis. Although silymarin is widely used as a hepatoprotective agent, its efficacy may be insufficient in severe intoxication, highlighting the need for effective adjunct therapies. *Capparis spinosa*, a flavonoid-rich medicinal plant with established antioxidant and anti-inflammatory properties, represents a promising candidate for complementary hepatoprotection. In this study, 42 male Wistar rats were randomly assigned to seven groups (n=6 each): a vehicle control group, an APAP-only treatment group (2 g/kg orally, on day 8), an APAP- plus silymarin-treated (100 mg/kg) group, three groups receiving APAP plus a *C. spinosa* ethanolic extract at 100, 200, or 400 mg/kg, and a group receiving APAP as well as a combined treatment with silymarin and the *C. spinosa* extract (200 mg/kg) group. These treatments were administered orally for 10 consecutive days, and animals were sacrificed on day 11. Hepatic injury was assessed through the measurement of the serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, albumin, and total protein levels, in addition to histopathological evaluation using the modified Suzuki score (0–4 scale) for centrilobular necrosis, sinusoidal congestion, and inflammatory infiltration. The undertaken APAP administration induced severe hepatic injury that was characterized by centrilobular necrosis, inflammatory infiltration, and disruption of hepatic architecture, resulting in significantly elevated modified Suzuki scores ($p<0.001$ *versus* control). Serum ALT, AST, ALP, and total bilirubin levels were found elevated by more than 100% above those of the control group, whereas albumin and total protein were found decreased by approximately 52% and 46%, respectively, as a result of the APAP administration ($p<0.001$ *versus* control in all cases). Silymarin treatment markedly attenuated these alterations, by reducing the necrosis score to 0.93 (± 0.10) and by decreasing the serum ALT, AST, ALP, and total bilirubin levels by approximately 71%, 81%, 64%, and 65%, respectively, while increasing those of albumin and total protein by 69% and 46% when compared to those of the APAP-only receiving rats ($p<0.001$ *versus* APAP-only treatment in all cases). The herein employed treatment with the *C. spinosa* ethanolic extract exhibited a dose-dependent hepatoprotective effect. The 100 mg/kg dose reduced the serum

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ALT, AST, ALP, and total bilirubin levels by 48%, 64%, 43%, and 40%, respectively (p<0.001 *versus* APAP-only treatment in all aforementioned cases), whereas the 200 mg/kg dose provided greater biochemical and histological improvement, with reductions of 62%, 77%, 62%, and 58%, respectively in the levels of the aforementioned biochemical parameters (p<0.001 *versus* APAP-only treatment in all cases). Notably, the 400 mg/kg dose of the *C. spinosa* extract restored hepatic architecture and normalized all measured parameters to levels comparable with those achieved by silymarin (p>0.05 *versus* APAP plus silymarin treatment). The combination of silymarin with the *C. spinosa* extract (200 mg/kg) produced the strongest hepatoprotective effect against the APAP-induced hepatotoxicity, yielding the lowest modified Suzuki scores and reducing the serum levels of ALT, AST, ALP, and total bilirubin by 77%, 84%, 69%, and 81%, respectively, relatively to those of the APAP-only treatment group; on the other hand, the albumin and total protein levels were increased by 96% and 64% (p<0.001 *versus* APAP-only treatment in all cases; p<0.05 *versus* APAP plus silymarin treatment in the cases of AST, ALP, and total protein). These findings indicate that the administration of a *C. spinosa* ethanolic extract can exert a significant and dose-dependent hepatoprotection against an APAP-induced liver injury, with the 400 mg/kg dose demonstrating an efficacy that is comparable to that of silymarin.

Keywords

acetaminophen; caper; drug-induced liver injury; hepatotoxicity; silymarin

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Conflicts of interest statement

None to declare.

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