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# Nootkatone elicits hepatoprotective and anti-fibrotic actions in a murine model of liver fibrosis by suppressing oxidative stress, inflammation, and apoptosis

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In this study, the hepatoprotective and anti-fibrotic actions of nootkatone (NTK) were investigated using carbon tetrachloride ($CCl_4$)-induced liver fibrosis in mice. $CCl_4$ administration elevated serum aspartate and alanine transaminases levels, respectively. In addition, $CCl_4$ produced hepatic oxidative and nitrative stress, characterized by diminished hemeoxygenase-1 expression, antioxidant defenses, and accumulation of 4-hydroxynonenal and 3-nitrotyrosine. Furthermore, $CCl_4$ administration evoked profound expression of pro-inflammatory cytokine expressions such as tumor necrosis factor-α (TNF-α), monocyte chemoattractant protein-1 (MCP-1), and interleukin-1β (IL-1β) in hepatic tissues, which corroborated with nuclear factor-κB (NF-κB) activation. Additionally, $CCl_4$-treated animals exhibited higher apoptosis, characterized by increased caspase 3 activity, DNA fragmentation, and poly (ADP-ribose) polymerase [PARP] activation. Moreover, histological and biochemical investigations revealed marked fibrosis in the livers of $CCl_4$-administered animals. However, NTK treatment mitigated $CCl_4$ -induced phenotypic changes. In conclusion, our findings suggest that NTK exerts hepatoprotective and anti-fibrotic actions by suppressing oxidative stress, inflammation, and apoptosis.

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