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Hepatoprotective effect of glycyrrhizin and omega-3 fatty acids on nuclear factor-κb pathway in thioacetamide-induced fibrosis in rats

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Nuclear Factor Kappa B (NF-κB) is a key transcriptional regulator that plays important roles in the pathogenesis of hepatic inflammation and fibrosis in chronic liver diseases with subsequent development of hepatocellular carcinoma. NF-kB activation leads to production of pro-inflammatory and fibrogenic cytokines. Glycyrrhizin (GL) has been reported to suppress liver fibrosis and cirrhosis. Omega-3 fatty acids (ω-3) have anti-inflammatory effects and they have been reported to decrease hepatic injury and steatosis with subsequent fibrosis in Thioacetamide (TAA) fibrotic model.

Aim of the study: To investigate the effects of GL and ω-3 alone and in combination on liver inflammation and fibrosis in rats and to clarify the role of these natural compounds on NF-κB pathway.

Materials & Methods: 50 male Wistar rats randomized to 5 groups: Control group and 4 group received TAA 200 mg/kg i.p. twice weekly for 8 weeks. TAA group, (TAA + GL) group (received GL 25 mg/kg/day by oral tube dissolved in distilled water started with TAA), (TAA + ω-3) group (received ω-3 150 mg/kg/day by oral tube started with TAA), (TAA + GL + ω-3) group (received similar but combined doses of both natural compounds with TAA). All groups were investigated for the effects of GL and ω-3 by the assessment of ALT and AST activities, total bilirubin, albumin and total protein levels and liver MDA level by spectrophotometric analysis, liver NF-κB level by ELISA and immunohistochemistry as well as histopathological analysis of the extent of liver fibrosis and necroinflammatory activity.

Results: TAA caused liver injury indicated by significant increase in serum ALT and AST activities, total bilirubin level ($P<0.005$) with significant decrease in serum albumin and total proteins levels ($P<0.005$). These results were also confirmed histopathologically by the significant increase of the necroinflammatory scores ($P<0.005$) and extent of liver fibrosis. While GL, ω-3 and their combination protected the liver from TAA hepatotoxic effects as they significantly decrease serum AST activity and total bilirubin level, also they significantly increase serum albumin and total protein levels. The hepatoprotective effect of GL, ω-3 and their combination also confirmed by histopathological analysis as they significantly reduced the necroinflammatory scores and the extent of fibrosis. TAA caused significant increase in lipid peroxidation by increase liver MDA level ($P<0.005$). GL, ω-3 and their combination decrease significantly liver MDA level ($P<0.005$). We also found that TAA has been increased NF-κB level in liver tissue ($P<0.005$), while GL, ω-3 and their combination significantly decreased liver NF-ƙB level ($P<0.005$) and its tissue expression as detected by immunohistochemistry.

Conclusion: These results suggested that oxidative stress has an important role in the development of liver fibrosis mediated by the regulatory role of NF-κB. Furthermore, glycyrrhizin and omega-3 fatty acids, alone and in combination have potent anti-inflammatory, anti-oxidant and anti-fibrotic effects.

Biography

Laila A EISSA works for the Department of Biochemistry as faculty of Pharmacy in the University of Mansoura, Egypt. She has published nearly 30 articles in varied journals.

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