## Regression of Fibrosis by Apigenin in Thioacetamide-Induced Liver Fibrosis Rat Model through Suppression of HIF-1/FAK Pathway

Authors : Hany M. Fayed, Rehab F. Abdel-Rahman, Alyaa F. Hessin, Hanan A. Ogaly, Gihan F. Asaad, Abeer A. A. Salama, Sahar Abdelrahman, Mahmoud S. Arbid, Marwan Abd Elbaset Mohamed

Abstract : Liver fibrosis is a serious global health problem that occurs as a result of a variety of chronic liver disorders. Apigenin, a flavonoid found in many plants, has several pharmacological properties. The aim of this study was to evaluate the antifibrotic efficacy of apigenin (APG) against experimentally induced hepatic fibrosis in rats via using thioacetamide (TAA) and to explore the possible underlying mechanisms. TAA (100 mg/kg, i.p.) was given three times each week for two weeks to induce liver fibrosis. After TAA injections, APG was given orally (5 and 10 mg/kg) daily for two weeks. Biochemical, molecular, histological and immunohistochemical analyses were performed on blood and liver tissue samples. The functioning of the liver, oxidative stress, inflammation, and liver fibrosis indicators were all evaluated. The findings showed that TAA markedly increased the activities of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), as well as the levels of malondialdehyde (MDA), focal adhesion kinase (FAK), hypoxia-inducible factor-1 (HIF-1), nuclear factor-κB (NF-κB), transforming growth factor-beta (TGF- $\beta$ ), tumor necrosis factor-alpha (TNF- $\alpha$ ) and interleukin-1 $\beta$  (IL-1 $\beta$ ) with a reduction in albumin, total protein, A/G ratio, GSH content and interleukin-10 (IL-10). Moreover, TAA elevated the content of collagen Ι, α smooth muscle actin ( $\alpha$ -SMA), and hydroxyproline in the liver. The treatment with APG in a dose-dependent manner has obviously prevented these alterations and amended the harmful effects induced by TAA. The histopathological and immunohistochemical observations supported this biochemical evidence. The higher dose of APG produced the most significant antifibrotic effect. As a result of these data, APG appears to be a promising antifibrotic drug and could be used as a new herbal medication or dietary supplement in the future for the treatment of liver fibrosis. This effect might be related to the inhibition of the HIF-1/FAK signaling pathway.

Keywords : apigenin, FAK, HIF-1, liver fibrosis, rat, thioacetamide

Conference Title : ICEP 2022 : International Conference on Ethnopharmacology and Pharmacognosy

Conference Location : Amsterdam, Netherlands

Conference Dates : September 15-16, 2022

1