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Gallic acid and ferulic acid protect the liver from thioacetamide-induced fibrosis in rats via differential expression of miR-21, miR-30 and miR-200 and impact on TGF-β1/Smad3 signaling

ABSTRACT This study evaluates the possible protective effects of gallic acid (GaA) and ferulic acid (FeA) against an experimentally induced liver fibrosis by thioacetamide (TAA) in rats. Animals were divided into: Control group, GaA group (20 mg/kg/day, p.o), FeA (20 mg/kg/day, p.o), TAA group (receiving 250 mg/kg twice/week, I.P), TAA + GaA group, TAA + FeA group (received the same previous doses) and TAA+silymarin group (received silymarin at 100 mg/kg/day+TAA as mentioned above). After 6 consecutive weeks, animals were sacrificed and the assessment of liver functions, oxidative stress biomarkers and histopathological examination of the liver tissues were performed. In addition, the effect on TGF-β1/Smad3 signaling and the expression of miR-21, miR-30 and miR-200 were evaluated. The results showed that administration of GaA or FeA with TAA induced a significant reduction in serum ALT, AST and ALP activities and protected the integrity of liver tissues. Furthermore, they increased the activities of the hepatic antioxidant enzymes; superoxide dismutase and catalase while decreased malondialdehyde content to a normal level. The hepatic expression of TGF-β1, phosphorylated and total Smad3 proteins were significantly decreased. In addition, miR-21 expression was downregulated while miR-30 and miR-200 expressions were upregulated by administration of gallic acid or ferulic acid. In conclusion, gallic and ferulic acids exhibit hepatoprotective and antioxidant effects against TAA-induced liver fibrosis in rats. These effects are mediated through inhibition of TGF-β1/Smad3 signaling and differentially regulating the hepatic expression level of miR-21, miR-30 and miR-200.

Keywords: Liver fibrosis Antioxidant Micro RNA TGF Smad3 qRT-PCR