**Abstract**

**Background:** In the current study, we have investigated the effect of each of curcumin (CUR) and sulfamethoxazole (SMX) either separate or mixed together (CUR + SMX) on biochemical, hematological and histological alternations associated with carbon tetrachloride (CCl4)-induced liver fibrosis in mice.

**Results:** CCl4, caused changes of several biomarkers, proving its hepatotoxic effects, such as an increase in aminotransferases liver enzymes alanine and aspartate transaminases (ALT, AST), malondialdehyde (MDA), and nitric oxide (NO) formation, with a decrease in superoxide dismutase (SOD), glutathione reductase (GSSG),total antioxidant capacity (TAO), glutathione (GSH), total protein, and albumin, compared to a negative control mice group. Compared to the CCl4 group of mice, the CUR and SMX separate and/or together (CUR + SMX) treatments showed significance in (p < 0.001), ameliorated liver injury (characterized by an elevation of (ALT, AST) and a decrease (p < 0.001) in serum albumin and total protein), antioxidant (characterized by a decrease in (p < 0.001) MDA, NO; an increase (p < 0.001) SOD, GSSG, TAO; and reducing GSH), hematological changes (characterized by a decrease (p < 0.001) in white blood cells count and an increase (p < 0.001) in platelets count, hematocrit levels, hemoglobin concentration, and (p < 0.05) red blood cells count), SDS-PAGE electrophoresis with a decrease in protein synthesis and changes in histological examinations.

**Conclusions**: CUR and SMX either separate or together (SUR + SMX) may be considered promising candidates in the prevention and treatment of liver fibrosis.

**Keywords:** Fibrosis, Carbon tetrachloride, Curcumin, Sulfamethoxazole, Oxidative stress, Histopathology