The role of L-carnitine and *Solanum nigrum* as food supplement and antioxidant against thiamethoxam-induced hepatotoxicity in male rats

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Abstract
This research was carried out to investigate the role of L-carnitine and *Solanum nigrum* seeds as food supplement and antioxidant against thiamethoxam induced hepatotoxicity in male rats. The present results showed insignificant decrease in the activity of ALT, AST, ALP, GGT, LDH enzymes and significant decrease in the concentration of total bilirubin in LC and SNS-treated group compared to control. Also, the present results showed significant increase in the values of ALT, AST, ALP, GGT, LDH and total bilirubin after administration of TMX compared to the control group. While, the combination groups treated with LC + TMX or SNS + TMX revealed significant decrease in the values of ALT, AST, ALP, GGT, LDH and bilirubin as compared to TMX-treated group. Administration of LC or SNS alone showed insignificant increase in serum total protein, albumin, globulin and albumin /globulin ratio compared to control group. On the other hand, TMX-treatment caused significant decrease in the levels of total protein, albumin, globulin and albumin /globulin ratio compared to the control group. In comparison with TMX-treated group, administration of LC+TMX and SNS+TMX showed significant (P<0.05) decrease in the levels of total protein, albumin, globulin and albumin /globulin ratio. The values of cholesterol, triglycerides, LDL-C, VLDL-C and HDL-C were showed insignificant changes in LC-treated group and SNS-treated group compared to control group. The results of cholesterol, triglycerides, LDL-C, VLDL-C and HDL-C were significantly increased while, serum HDL-C was significantly decreased after administration of TMX compared to the control group. On the other hand, the combination of LC+TMX and SNS+TMX-treated groups showed significant decrease in the levels of cholesterol, triglyceride, LDL-C, VLDL-C while, the level of HDL-C was significantly increased compared to TMX-treated group. Oral administration of LC and SNS showed insignificant changes in TBARS, SOD, GPX and GR and significant increase in GSH levels as compared to the control group. The treatment of adult male rats with TMX alone showed significant increase in the levels of TBARS and significant decrease in the levels of GSH and the activities of SOD, GPX and GR as compared to the control rats. While, the combination of LC+TMX and SNS+TMX showed significant decrease in TBARS level and a significant increase in the level of GSH, SOD, GPX and GR as compared to TMX-treated group. The level of caspase-3 significantly decreased in the TMX-treated group as compared with control group. While, treatment with LC and SNS plus TMX significantly increased the level of caspase-3 as compared to the TMX-treated group. Administration of LC or SNS revealed insignificant changes in P53 and TNF-α gene expression as well as, insignificant changes in AFP and Bcl2 compared to control group. While in TMX-treated group P53 and TNF-α gene expressions significantly downregulated, as well as AFP and Bcl-2 significantly upregulated compared to control group. Treatment with LC + TMX and SNS+ TMX significantly upregulated P53 and TNF-α expressions as well as significantly downregulated AFP and Bcl-2 as compared to the TMX-treated group. The present results showed insignificant (P>0.05) decrease in the activity of ALT, AST, ALP, GGT, LDH enzymes and significant (P<0.05) decrease in the concentration of total bilirubin in LC and SNS-treated group compared to control. Also, the present results showed significant increase (P<0.05) in the values of ALT, AST, ALP, GGT, LDH and bilirubin after administration of TMX compared to the control group. While, the combination groups treated with LC + TMX or SNS + TMX revealed significant (P< 0.05) decrease in the values of ALT, AST, ALP, GGT, LDH and bilirubin as compared to TMX-treated group. Administration of LC or SNS alone showed insignificant (P>0.05) increase in serum total protein, albumin, globulin and albumin /globulin ratio compared to control group. On the other hand, TMX-treatment caused significant (P<0.05) decrease in the levels of total protein, albumin, globulin and albumin /globulin ratio compared to the control group. In comparison with TMX-treated group, administration of LC+TMX and SNS+TMX showed significant (P<0.05) increase in the levels of total protein, albumin, globulin and albumin /globulin ratio compared to the control group. The values of cholesterol, triglycerides, LDL-C, VLDL-C and HDL-C were showed insignificant changes in LC-treated group and SNS-treated group compared to control group. The results of cholesterol, triglycerides, LDL-C, VLDL-C and HDL-C were significantly increased while, serum HDL-C was significantly decreased after administration of TMX compared to the control group. On the other hand, the combination of LC+TMX and SNS+TMX-treated groups showed significant decrease in the levels of cholesterol, triglyceride, LDL-C, VLDL-C while, the level of HDL-C was significantly increased compared to TMX-treated group. Oral administration of LC and SNS showed insignificant changes in TBARS, SOD, GPX and GR and significant increase in GSH levels as compared to the control group. The treatment of adult male rats with TMX alone showed significant increase in the levels of TBARS and significant decrease in the levels of GSH and the activities of SOD, GPX and GR as compared to the control rats. While, the combination of LC+TMX and SNS+TMX showed significant decrease in TBARS level and a significant increase in the level of GSH, SOD, GPX and GR as compared to TMX-treated group. The level of caspase-3 significantly decreased in the TMX-treated group as compared with control group. While, treatment with LC and SNS plus TMX significantly increased the level of caspase-3 as compared to the TMX-treated group. Administration of LC or SNS revealed insignificant changes (P>0.05)
in P53 and TNF-α gene expressions as well as, insignificant changes (P> 0.05) in AFP and Bcl2 compared to control group. While in TMX-treated group P53 and TNF-α gene expressions significantly (P< 0.05) downregulated, as well as AFP and Bcl-2 significantly (P< 0.05) upregulated compared to control group. Treatment with LC + TMX and SNS+ TMX significantly (P< 0.05) upregulated P53 and TNF-α expressions as well as significantly (P< 0.05) downregulated AFP and Bcl-2 as compared to the TMX-treated group.