

Role of Oxidative Stress and Nitric Oxide in the Protective Effects of Simvastatine against Isoniazid-Rifampicin-Induced Hepatotoxicity in Rats

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Abstract : Despite the great efficacy of isoniazid (INH) and rifampicine (RIF) combination in the treatment of tuberculosis, hepatotoxicity is the most common serious complication. The potential protective effect of simvastatin (sim) against combination-induced hepatotoxicity was investigated in the present study. The administration of INH-RIF combination (50mg/kg each for 14 days) resulted in a significant increased activities of serum alanine and aspartate aminotransferases, such effects were further supported by histopathological studies. INH-RIF combination produced a significant increase in liver lipid, decreased SOD and CAT, and a significant depletion of GSH level. Additionally, treatment with INH-RIF combination resulted in a significant increase in liver MPO activity. The lipid-lowering drug, Sim demonstrated in the current study an evident antioxidant action, such effect was mediated via decreasing the elevated MDA, MPO, and restoring liver CAT activity. Additionally, Sim restored liver NO level to near basal value Furthermore, one cannot rule out the lipid-lowering effect of Sim that would probably add to its beneficial hepatoprotective antioxidant activity, where Sim decreased the elevated cholesterol, TGs and LDL cholesterol level and increased the serum HDL cholesterol level.

Keywords : isoniazid, rifampicine, oxidative stress, nitric oxide

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