

Ashwagandha attenuates organ oxidative stress and inflammation in tramadol treated and withdrawal rats

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This study investigated the ameliorative effects of Ashwagandha (*Withania somnifera*, ASH) on liver and kidney function, brain oxidative stress, and proinflammatory cytokines in rats subjected to tramadol (TRE) treatment and withdrawal regime. Two main rat groups: Group A (Treatment) were orally treated for 6 weeks, Control (0.5%CMC), ASH (200 mg/kg), TRE (40 mg/kg), and TRE+ASH groups. Group B (Withdrawal), were orally treated for ten weeks, Control, ASH (CMC six weeks followed by ASH four weeks), TRE (increasing doses, 40, 80 then 120 mg/kg/day for six weeks followed by CMC four weeks), and TRE+ASH (TRE increasing doses six weeks followed by ASH four weeks). The TRE+ASH groups showed a significant improvement compared to TRE treated and withdrawal groups. That includes reduction in AST, ALT, urea, and creatinine values indicating improved liver and kidney functions. Also, the brain cortex and brainstem tissues revealed enhanced antioxidant defence (CAT, GST, GPX, GSH and TAC) and reduced oxidative stress markers (NO and MDA). In addition, the proinflammatory cytokines (TNF- α and IL-1 β) in cortex were significantly ($P \leq 0.05$) reduced by ASH supplementation. These results suggest ASH supplementation ameliorates the liver and kidney functions, oxidative brain damage and neuroinflammation during both treatment and withdrawal of TRE.

Keywords: Tramadol induced liver dysfunction, Tramadol induced kidney dysfunction, *Withania somnifera* supplementation, Oxidative stress markers, Brain cortex, Brainstem, Proinflammatory cytokines expression