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Neuroprotective Effect of Tangeretin against Potassium Dichromate-Induced Acute Brain Injury via Modulating AKT/Nrf2 Signaling Pathway in Rats

Authors : Ahmed A. Sedik, Doaa Mahmoud Shuaib

Abstract : Brain injury is a cause of disability and death worldwide. Potassium dichromate (PD) is an environmental contaminant widely recognized as teratogenic, carcinogenic, and mutagenic towards animals and humans. The aim of the present study was to investigate the possible neuroprotective effects of tangeretin (TNG) on PD-induced brain injury in rats. Forty male adult Wistar rats were randomly and blindly allocated into four groups (8 rats /group). The first group received saline intranasally (i.n.). The second group received a single dose of PD (2 mg/kg, i.n.). The third group received TNG (50 mg/kg; orally) for 14 days, followed by i.n. of PD on the last day of the experiment. Four groups received TNG (100 mg/kg; orally) for 14 days, followed by i.n. of PD on the last day of the experiment. 18- hours after the final treatment, behavioral parameters, neuro-biochemical indices, FTIR analysis, and histopathological studies were evaluated. Results of the present study revealed that rats intoxicated with PD promoted oxidative stress and inflammation via an increase in MDA and a decrease in Nrf2 signaling pathway and GSH levels with an increase in brain contents of TNF-α, IL-10, and NF-kβ and reduced AKT levels in brain homogenates. Treatment with TNG (100 mg/kg; orally) ameliorated behavioral, cholinergic activities and oxidative stress, decreased the elevated levels of pro-inflammatory mediators; TNF-α, IL-10, and NF-κβ elevated AKT pathway with corrected FTIR spectra with a decrease in brain content of chromium residues detected by atomic absorption spectrometry. Also, TNG administration restored the morphological changes as degenerated neurons and necrosis associated with PD intoxication. Additionally, TNG decreased Caspase-3 expression in the brain of PD rats. TNG plays a crucial role in AKT/Nrf2 pathway that is responsible for their antioxidant, anti-inflammatory effects, and apoptotic pathway against PD-induced brain injury in rats.

Keywords : tangeretin, potassium dichromate, brain injury, AKT/Nrf2 signaling pathway, FTIR, atomic absorption spectrometry
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