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Neuroprotective Effect of Chrysin on Thioacetamide-Induced Hepatic Encephalopathy in Rats: Role of Oxidative Stress and TLR-4/NF-κB Pathway

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Abstract : This study aimed to investigate the possible neuroprotective effect of chrysin on thioacetamide (TAA)-induced hepatic encephalopathy in rats. Also, the effect of chrysin on motor impairment, cognitive deficits, oxidative stress, neuroinflammation, apoptosis and histopathological damage was assessed. Male Wistar rats were randomly allocated into five groups. The first group received the vehicle (distilled water) for 21 days and is considered as normal group. While the second one received intraperitoneal dose of TAA (200 mg/kg) at three alternative days during the third week of the experiment to induce HE and is considered as control group. The other three groups were orally administered chrysin for 21 days (25, 50, 100 mg/kg) and starting from day 17; rats received intraperitoneal dose of TAA (200 mg/kg) at three alternative days. Then behavioral, biochemical, histopathological and immunohistochemical analyses were assessed. Then behavioral, biochemical, histopathological and immunohistochemical analyses were assessed. Chrysin reversed TAA-induced motor coordination in rotarod test, cognitive deficits in object recognition test (ORT) and attenuated serum ammonia, hepatic liver enzymes, reduced malondialdehyde (MDA), elevated reduced glutathione (GSH), reduced nuclear factor kappa B (NF-κB), tumor necrosis factor-alpha (TNF-α) and Interleukin-6 (IL-6) brain contents. Chrysin administration also reduced Toll-4 receptor (TLR-4) gene expression, caspase-3 protein expression, hepatic necrosis and astrocyte swelling. This study depicts that chrysin exerted neuroprotective effect in TAA-induced HE rats, evidenced by improvement of cognitive deficits, motor incoordination and histopathological changes such as astrocyte swelling and vacuolization; hallmarks in HE, via reducing hyperammonemia, ameliorating hepatic function, in addition to its anti-oxidant, inactivation of TLR-4/NF-κB inflammatory pathway, and anti-apoptotic effects.

Keywords : chrysin, hepatic encephalopathy, oxidative stress, rats, thioacetamide, TLR4/NF-κB pathway
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