Thymoquinone alleviates the experimentally induced Alzheimer's disease inflammation by modulation of TLRs signaling

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Abstract

Alzheimer's disease (AD) is characterized by a robust inflammatory response elicited by the accumulation and deposition of amyloid-β (Aβ) within the brain. Aβ induces detrimental inflammatory responses through toll-like receptors (TLRs) signaling pathway. Thymoquinone (TQ), the main active constituent of Nigella sativa oil, has been reported by several previous studies for its potent anti-inflammatory effect. The aim of this study is to elucidate the effect of TQ in improving learning and memory, using a rat model of AD induced by a combination of aluminum chloride (AlCl3) and d-galactose (d-Gal). TQ was administered orally at doses of 10, 20, and 40 mg/kg/day for 14 days after AD induction. Memory functions were assessed using the step through passive avoidance test. Amyloid plaques were shown to be present using hematoxylin and eosin staining. Tumor necrosis factor-alpha (TNF-α) and Interleukin-1beta (IL-1β) levels in brain were assessed via ELISA and profiling TLR-2, TLR-4, myeloid differential factor 88, toll–interleukin-1 receptor domain-containing adapter-inducing interferon-β, interferon regulatory factor 3 (IRF-3), and nuclear factor-κB (NF-κB) expressions via real-time polymerase chain reaction. TQ improved AD rat cognitive decline, decreased Aβ formation and accumulation, significantly decreased TNF-α and IL-1β at all levels of doses and significantly downregulated the expression of TLRs pathway components as well as their downstream effectors NF-κB and IRF-3 mRNAs at all levels of doses ($p < 0.05$). We concluded that TQ reduced the inflammation induced by d-Gal/AlCl3 combination. It is therefore reasonable to assign the anti-inflammatory responses to the modulation of TLRs pathway

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