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Involvement of Nrf2 in Kolaviron-Mediated Attenuation of Behavioural Incompetence and Neurodegeneration in a Murine Model of Parkinson's Disease

Authors : Yusuf E. Mustapha, Inioluwa A Akindoyeni, Oluwatoyin G. Ezekiel, Ifeoluwa O. Awogbindin, Ebenezer O. Farombi

Abstract : Background: Parkinson's disease (PD) is the most prevalent motor disorder. Available therapies are palliative with no effect on disease progression. Kolaviron (KV), a natural anti-inflammatory and antioxidant agent, has been reported to possess neuroprotective effects in Parkinsonian flies and rats. Objective: The present study investigates the neuroprotective effect of KV, focusing on the DJ1/Nrf2 signaling pathway. Methodology: All-trans retinoic acid (ATRA, 10 mg/kg, i.p.) was used to inhibit Nrf2. Murine model of PD was established with four doses of MPTP (20 mg/kg i.p.) at 2 hours interval. MPTP mice were pre-treated with either KV (200 mg/kg/day p.o), ATRA, or both conditions for seven days before PD induction. Motor behaviour was evaluated, and markers of oxidative stress/damage and its regulators were assessed with immunofluorescence and ELISA techniques. Results: MPTP-treated mice covered less distance with reduced numbers of anticlockwise rotations, heightened freezing, and prolonged immobility when compared to control. However, KV significantly attenuated these deficits. Pretreatment of MPTP mice with KV upregulated Nrf2 expression beyond MPTP level with a remarkable reduction in Keap1 expression and marked elevation of DJ-1 level, whereas co-administration with ATRA abrogated these effects. KV treatment restored MPTP-mediated depletion of endogenous antioxidant, striatal oxidative stress, oxidative damage, and inhibition of acetylcholinesterase activity. However, ATRA treatment potentiated acetylcholinesterase inhibition and attenuated the protective effect of KV on the level of nitric oxide and activities of catalase and superoxide dismutase. Conclusion: Kolaviron protects Parkinsonian mice by stabilizing and activating the Nrf2 signaling pathway. Thus, kolaviron can be explored as a pharmacological lead in PD management.

Keywords : Garcinia kola, Kolaviron, Parkinson Disease, Nrf2, behavioral incompetence, neurodegeneration
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