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Neuroprotective insights of isorhamnetin against amyloid $\beta(25-35)$ -induced oxidative insult and neuronal degeneration in rodent model: Perspectives on future therapeutics for Alzheimer's disease

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The amyloid- β (A β) is the major protein component of brain senile plaques in Alzheimer's disease (AD) and is known to be directly responsible for the production of free radicals toxic to brain tissue. The present study was designed to elucidate the neuroprotective effect of Isorhamnetin (IRN), a flavone aglycones against the pathogenesis of AD. Experimental AD in rats was produced by intracerebroventricular administration of A $\beta_{(25-35)}$ peptide. Employing the following strategies of neurobehavioral, biochemical, immunohistochemistry, docking and molecular approach, we explored the attenuating effects of IRN against A $\beta_{(25-35)}$ peptide induced hippocampal neuronal loss and memory impairment. The present study has proven that IRN also reduced the expression of BACE-1 via inactivation of GSK3 β and NF κ B inhibition thereby inhibiting the accumulation of A β . Furthermore, IRN up regulated the phosphorylated GSK-3 β and down regulated the expression of phosphorylated P-38 thereby inhibiting the Nrf-2 ubiquitination and improved the nuclear translocation of Nrf-2 which subsequently alleviated the expression of inflammatory cytokines which further reduced the ROS and RNS generation. Considering all the results, it can be suggested that IRN not only acts via antioxidant and anti-inflammatory activity but also by modulating the expression and function of AD related proteins. Hence, an amalgamation of *in vivo, in vitro* and *in silico* evidence might be supportive to delineate the neuroprotective potentials of IRN in the therapy of AD.

Biography

Thangarajan Sumathi completed her PhD in 2002 at University of Madras. Currently, she is working as an Assistant Professor in Department of Medical Biochemistry, University of Madras. She is guiding eight PhD students and four research scholars have been awarded PhD degree. She has 20 years of teaching and research experience. Her area of specialization is Neurodegenerative Diseases (Alzheimer's disease, Parkinson's disease and Huntington's disease). She has more than 40 publications in reputed journals and sponsored research projects. She is a life member of ISAR, IAES, IABS, NJLS, ZSI, etc. She is a Reviewer of many international journals like *Neurochemistry International, Experimental Biology and Medicine*, etc. She is an Editorial Board Member of *Current Updates in Gerontology* and *International Journal of Brain Disorder Therapy*.

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