Indian Journal of Experimental Biology
Vol. 63, September 2025, pp. 715-725
DOI: 10.56042/ijeb.v63i09.19654

Ellagic acid improved neurodegeneration caused by ischemic stroke through the regulation of glutamatergic and synaptic signaling

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Received 13 May 2025; revised 13 June 2025

Ischemic stroke, caused by disrupted cerebral blood flow, leads to neurodegeneration through nutrient and oxygen deprivation. Despite ellagic acid's (EA) known antioxidant/anti-inflammatory roles in stroke, its direct modulation of synaptic NMDA/AMPA receptors remains unexplored. This study investigates EA's neuroprotection via glutamatergic signaling in ischemic stroke in a transient middle cerebral artery occlusion (MCAO) rat model. Wistar rats were divided into sham, MCAO, and EA-treated MCAO groups. Daily EA administration for 72 hours significantly improved neurobehavioral deficits and reduced cerebral edema in MCAO rats (P-value<0.001). EA increased anti-apoptotic Bcl-2 levels while decreasing pro-apoptotic CASP-3, protecting cortical neurons from ischemia-induced cell death. Furthermore, EA counteracted ischemia-induced declines in NR2a, NR2b, and GluR1 expression, while upregulated PSD95 expression (P-value<0.05). Oxidative stress (ROS) and neuroinflammatory cytokines (IL-6, IL-1β, TNF-α) were also reduced, though lipid peroxidation (MDA) remained unchanged. These findings demonstrate that EA mitigates ischemic neurodegeneration by enhancing synaptic survival signaling, suppressing apoptosis, and alleviating neuroinflammation and oxidative stress. The study highlights EA's potential as a therapeutic agent for ischemic stroke, warranting further clinical validation.

Keywords: Synaptic plasticity, Neuroinflammation, MCAO model, Neuroprotection, Receptor