

## Anti-Neuroinflammatory and Anti-Apoptotic Efficacy of Equol, against Lipopolysaccharide Activated Microglia and Its Neurotoxicity

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**Abstract :** Neuroinflammation may mediate the relationship between low levels of estrogens and neurodegenerative disease. Estrogens are neuroprotective and anti-inflammatory in neurodegenerative disease models. Due to the long term side effects of estrogens, researches have been focused on finding an effective phytoestrogens for biological activities. Daidzein present in soybeans and its active metabolite equol (7-hydroxy-3-(4'-hydroxyphenyl)-chroman) bears strong antioxidant and anticancer showed more potent anti-inflammatory and neuroprotective role in neuroinflammatory model confirmed its in vitro activity with molecular mechanism through NF- $\kappa$ B pathway. Three major CNS cells Microglia (BV-2), Astrocyte (C6), Neuron (N2a) were used to find the effect of equol in inducible nitric oxide synthase (iNOS), cyclooxygenase (COX-2), MAPKs signaling proteins, apoptosis related proteins by western blot analysis. Nitric oxide (NO) and prostaglandin E2 (PGE2) was measured by the Gries method and ELISA, respectively. Cytokines like tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and IL-6 were also measured in the conditioned medium of LPS activated cells with or without equol. Equol inhibited the NO production, PGE-2 production and expression of COX-2 and iNOS in LPS-stimulated microglial cells at a dose dependent without any cellular toxicity. At the same time Equol also showed promising effect in modulation of MAPK's and nuclear factor kappa B (NF- $\kappa$ B) expression with significant inhibition of the production of proinflammatory cytokine like interleukin -6 (IL-6), and tumor necrosis factor - $\alpha$  (TNF- $\alpha$ ). Additionally, it inhibited the LPS activated microglia-induced neuronal cell death by downregulating the apoptotic phenomenon in neuronal cells. Furthermore, equol increases the production of neurotrophins like NGF and increase the neurite outgrowth as well. In conclusion the natural daidzein metabolite equol are more active than daidzein, which showed a promising effectiveness as an anti-neuroinflammatory and neuroprotective agent via downregulating the LPS stimulated microglial activation and neuronal apoptosis. This work was supported by Brain Korea 21 Plus project and High Value-added Food Technology Development Program 114006-4, Ministry of Agriculture, Food and Rural Affairs.

**Keywords :** apoptosis, equol, neuroinflammation, phytoestrogen

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