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Isoorientin attenuates lipopolysaccharide-induced pro-inflammatory responses through down-regulation of ROS-related MAPK/NF-κB signaling pathway in BV-2 microglia

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Abstract Isoorientin (ISO) is a flavonoid compound in the human diet, and has been known to possess various bioactivities. However, the effects of ISO on microglia inflammation have not been investigated. The current study investigates the neuroprotective effect of ISO in LPS-activated mouse microglial (BV-2) cells. ISO significantly increased the BV-2 cells viability, blocked the protein expression of inducible nitric oxide synthase and cyclooxygenase-2, and decreased the production of nitric oxide, pro-inflammatory cytokines including tumor necrosis factor-α and interleukin-1β. The activation of mitogen-activated protein kinases (MAPKs) was blocked by ISO, and NF-κB nuclear translocation was decreased by ISO both alone and together with NF-κB inhibitor (PDTC) and MAPKs inhibitors (U0126, SP 600125, and SB 203580). Furthermore, ISO strongly quenched intracellular reactive oxygen species (ROS) generation. ROS inhibitor (*N*-acetyl cysteine, NAC) significantly inhibited pro-inflammatory cytokines release and NF-κB and MAPKs activation, indicating that ISO attenuated neuroinflammation by inhibiting the ROS-related MAPK/NF-κB signaling pathway.

Keywords Isoorientin · Neuroinflammatory · Microglia · MAPK kinases · NF-κB · ROS

Abbreviations

BV-2 cell	Mouse microglial cell line
ISO	Isoorientin
LPS	Lipopolysaccharide
ROS	Reactive oxygen species
NO	Nitric oxide
MAPKs	Mitogen-activated protein kinases
NF-κB	Nuclear factor κB
TNF-α	Tumor necrosis factor
IL	Interleukin
iNOS	Inducible nitric oxide synthase
COX	Cyclooxygenase

Introduction

Microglial are the resident innate immune cells in the central nervous system, and plays a pivotal role in the innate immune response [1]. Microglial activation plays an important role in neurodegenerative diseases through producing several pro-inflammatory enzymes and cytokines. Activated microglial cells are able to scavenge dead cells from the central nervous system and secrete different neurotrophic factors for neuronal survival [2, 3]. While over-activation of microglial cells cause various autoimmune responses and lead to neurodegenerative diseases, such as Alzheimer's disease, Huntington's disease, Parkinson's disease, and multiple sclerosis and stroke [4–6]. Meanwhile, over-activated microglial cells can induce significant and highly detrimental neuronal damage and neurodegenerative processes through excess production of various pro-inflammatory mediators and neurotoxic compounds, such as tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6), reactive oxygen

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