PE11) Nrf2-mediated Neuroprotection against Oxygen-Glucose Deprivation/Reperfusion Injury by Novel Compound from *Polygonum multiflorum*

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1. Introduction

Neuroinflammatory response-induced neuronal cell death may be involved in various neurodegenerative disorders such as Parkinson's Disease (PD) and Alzheimer's Disease (AD), and is caused at least, in part, by microglial activation. Microglia, which are resident immune cells in the brain, are both active sensors and variable effectors in normal and pathological brains. Even though natural compounds have been used for treating several neurodegenerative diseases, few studies have focused on their traditional use and mechanisms of action. The novel compounds have been isolated from *Schisandra chinensis*, which has been used for centuries in Southeast Asia as a food and for its anti-inflammatory, anti-viral, and neuroprotective effects. In this study, we examined the effect of novel compounds from *Schisandra chinensis* on TLR2/4 agonist-induced neuroinflammation in microglia.

2. Materials and Method

Human neuronal SH-SY5Y cells were investigated by analyzing cell viability, lactate dehydrogenase levels, expression of molecules related to apoptotic cell death, and using biochemical techniques, flow cytometry, and western blot assays.

3. Results and Discussion

Emodin reduced OGD/R lead to neurotoxicity in SH-SY5Y cells. OGD/R significantly increased levels of cleaved PARP, cleaved caspase-3, cleaved caspase-9, p53, p21, and Bax protein. However, emodin treatment effectively inhibited these OGD/R-induced changes. Emodin treatment also increased HO-1 and NQO1 expression in a dose- and time-dependent manner, and caused ARE transcription activity and nuclear Nrf2 accumulation. Emodin phosphorylated AMPK and GSK3b, and pretreatment of cells with an AMPK inhibitor suppressed emodin-induced nuclear Nrf2 accumulation and HO-1 and NQO1 expression. AMPK inhibitor treatment decreased GSK3b phosphorylation, suggesting that AMPK is upstream of GSK3b, Nrf2, HO-1, and NQO1. Emodin's neuroprotective effect was completely blocked by HO-1, NQO1, and Nrf2 knockdown and an AMPK inhibitor, indicating the action of AMPK/GSK3b/Nrf2/ARE in the neuroprotective effect of emodin subjected to OGD/R.

4. References

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