Inhibition of neuroinflammation by novel derivatives of Biochanin A

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Hyperactivation of microglia is known to spark the release of inflammatory mediators, which have been shown to contribute to neurodegenerative disease progression and severity. Hence, targeting of these immune mechanisms could lead to future therapeutic or preventive strategies for dementia diseases[1]. Estrogens have been shown to improve the symptoms of neurodegenerative diseases by binding to estrogen receptors (ERs) and producing an anti-inflammatory effect. Isoflavones are phytoestrogens that have been known to display anti-inflammatory effects. Biochanin A (BCA) is a ERβ-selective isoflavone phytoestrogen found in red clover[2]. In this study, we have synthesized two BCA derivatives 1 and 2, and evaluated them for anti-inflammatory effect on lipopolysaccharide (LPS) activated BV-2 cells. Cultured BV-2 microglia were treated with compound 1 (5, 10, 15 and 20 µM) and compound 2 (5, 10, 15 and 20 µM) 30 min before stimulation with LPS (100 ng/ml) for a further 24 h. Supernatants were collected and levels of nitric oxide (NO), tumor necrosis factor alpha (TNFα), cytokine IL-6 and prostaglandine E2 (PGE2) were measured using ELISA. Compounds 1 and 2 produced a significant and concentration-dependent reduction in the production of NO. However, Compound 1 blocked the production of TNFα, while Compound 2 showed no effects. Both compounds did not produce significant reduction in IL-6 and PGE₂ production. Our results suggest that compound 1 exhibited inhibition of neuroinflammation in LPS-activated BV2 microglia. There is a need for further investigation of the mechanism(s) of action of these compounds in the light of the observed effects on pro-inflammatory mediators.
