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Pinocembrin inhibits lipopolysaccharide-induced inflammatory mediators production in BV2 microglial cells through suppression of PI3K/Akt/NF-κB pathway

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Abstract
Pinocembrin, one of the primary flavonoids from Pinus heartwood and Eucalyptus, has been reported to have anti-inflammatory and antioxidant activity. This study was designed to evaluate the inhibitory effects of pinocembrin on inflammatory mediators production in LPS-stimulated BV2 microglial cells. The results showed that pinocembrin dose-dependently inhibited LPS-induced inflammatory mediators TNF-α, IL-1β, NO and PGE_2 production. Pinocembrin also inhibited LPS-induced iNOS and COX-2 expression. Moreover, pinocembrin inhibited LPS-induced PI3K, Akt phosphorylation, and NF-κB activation, which were required for inflammatory mediators production. Furthermore, treatment of pinocembrin induced nuclear translocation of Nrf2 and expression of HO-1. In conclusion, our data indicated that pinocembrin inhibited LPS-induced inflammatory mediators production by suppressing PI3K/Akt/NF-κB signaling pathway.
Keywords: Pinocembrin; LPS; NF-κB; PI3K; microglia

1. Introduction

Microglia, the main immune defense cells in the brain, has been reported to play critical roles in immune surveillance under normal conditions (Kim et al., 2000). Microglia activation has been reported to play an important role in the pathogenesis of several neurodegenerative disorders (Liu and Hong, 2003a). In neuroinflammatory pathology, LPS stimulated microglia could induce NF-κB activation and inflammatory mediators such as TNF-α, PGE_2 and NO production (Jin et al., 2006). Excessive production of these inflammatory mediators could cause neuronal damage and death (Bazan et al., 1995). Accumulated evidences suggested that inhibition of microglial activation and inflammatory mediators production had the ability to attenuate the severity of neurodegenerative diseases (Dheen et al., 2007; Rock and Peterson, 2006). Therefore, we tried to find compounds from natural products that had the ability to inhibit inflammatory mediators production.

Pinocembrin (Fig. 1A), one of the primary flavonoids from Pinus heartwood and Eucalyptus, has been reported to have a variety of pharmacological activities such as anti-inflammatory and antioxidant activities (Saad et al., 2015). Previous studies showed that pinocembrin inhibited LPS-induced TNF-α, IL-1β and IL-6 production in RAW264.7 cells in vitro (Soromou et al., 2012). Pinocembrin also attenuated 6-OHDA-induced neuronal cell death in SH-SY5Y cells (Jin et al., 2014). In vivo, pinocembrin was found to inhibit LPS-induced acute lung injury in mice and inhibit LPS-induced endotoxic shock in mice (Soromou et al., 2014). However, the effect of