J Develop Drugs 2018, Volume: 7
DOI: 10.4172/2329-6631-C2-030

AS-6 suppresses lipopolysaccharide–induced neuroinflammation in BV2 microglial cells via inhibition of NF-κB and MAPK pathway

Jun Young Park, Sun-Hyung Ha, Fukushi Abekura, Hak Seong Lim and **Cheorl-Ho Kim**
SungKyunKwan University, South Korea

4-O-carboxymethylascochlorin (AS-6, MW 462.96) isolated from Ascochyta viciae has been known to promote cell cycle arrest and inhibit invasion of tumor cells. We have previously studied structurally similar compounds ascochlorin (ASC; MW 404.93) and ascofuranone (AF; MW 420.93) with regard to its anti-inflammatory activity. In this study, we have found that the production of nitric oxide (NO), a main regulator of inflammation, is suppressed by AS-6 on BV2 microglial cells, when induced by LPS. In addition, AS-6 attenuated the increase in cyclooxyenase-2 (COX-2) protein and mRNA levels in lipopolysaccharide (LPS)-activated BV2 microglial cells in a dose-dependent manner. Moreover, AS-6 inhibited the expression and release of pro-inflammatory cytokines of tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β) in BV2 microglial cells. At the intracellular level, AS-6 inhibited LPS-induced nuclear translocation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) in BV2 microglial cells. Therefore, we investigated whether AS-6 affects mitogen-activated protein kinase (MAPK) phosphorylation, a process known as the upstream signaling regulator. AS-6 dramatically reduced the expression level of the phosphorylated forms of ERK, JNK, and p38 in LPS-activated BV2 microglial cells. These results indicate that AS-6 is a promising suppressor of the vascular inflammatory responses and AS-6 suppresses the LPS-induced inflammatory response in BV2 microglial cells by suppression of NF-κB and MAPKs signaling. Accordingly, AS-6 is suggested as a beneficial agent for the treatment of diseases that are associated with inflammation.

wnsdud2057@naver.com