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Andrographolide activates Keap1/Nrf2/ARE/HO-1 pathway in HT22 cells and suppresses microglial activation by A β 42 through Nrf2-related inflammatory response

Won Keun Oh and Ji Yeon Seo
Seoul National University, South Korea

Therapeutic approach of Alzheimer's disease (AD) has been gradually diversified. We examined the therapeutic and preventive potential of andrographolide, which is a lactone diterpenoid from *Andrographis paniculata*, and focused on the Kelch-like ECH-associated protein (Keap1)/nuclear factor (erythroid-derived), (Nrf2)-mediated heme oxygenase (HO)-1-inducing effects and the inhibitory activity of amyloid beta (A β)₄₂-induced microglial activation related to Nrf2 and nuclear factor κ B (NF- κ B)-mediated inflammatory responses. Andrographolide induced the expression and translocation of Nrf2 from the cytoplasm to the nucleus, thereby activating antioxidant response element (ARE) gene transcription and HO-1 expression in murine hippocampal HT22 cells. Andrographolide eliminated intracellular A β ₄₂ in BV-2 cells and decreased the production of interleukin (IL)-6, IL-1 β , prostaglandin (PG)E₂ and nitric oxide (NO) because of artificial phagocytic A β ₄₂. It decreased pNF- κ B accumulation in the nucleus and the expression of inducible nitric oxide synthase (i-NOS) and cyclooxygenase (COX)-II in the microglial BV-2 cell line. In summary, andrographolide activates Nrf2-mediated HO-1 expression and inhibits A β ₄₂-overexpressed microglial BV-2 cell activation. These results suggested that andrographolide might have the potential for further examination of the therapeutics of AD.

Biography

Won Keun Oh has acquired his PhD degree in studies about natural product's chemistry from Korea Advanced Institute of Science and Technology (KAIST). He has worked as a Visiting Scholar in Baylor College of Medicine, USA (2002-2004). He also worked in Korea Research Institute of Bioscience and Biotechnology (KRIBB) as a Principle Researcher (2005-2007) and moved to College of Pharmacy in Chosun University as Assistant Professor (2007-2013). He has worked at College of Pharmacy in Seoul National University as Associate Professor of Pharmacognosy since 2013. He has undertaken more than ten projects of the Korean Government including Individual Basic Science and Engineering Research Program (2012-2015), the Procurement and Development of Foreign Biological Resources (2010-2016) and the Korea Bioactive Natural Material Bank (KBNMB, 2012-2017), et al.

wkoh1@snu.ac.kr

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