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Inonotus obliquus polysaccharides protect against Alzheimer's disease by regulating Nrf2 signaling and exerting antioxidative and antiapoptotic effects

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Abstract

Inonotus obliquus polysaccharide (IOPS) was initially separated and purified via precipitation from an aqueous extract with 80% alcohol, a DEAE-52 cellulose anion exchange column, and a Sephadex G-100 gel permeation chromatography system. IOPS was found to have a molecular weight of 111.9 kDa. In L-glutamic acid (L-Glu)-damaged HT22 cells, a 3-h pre-incubation with IOPS enhanced cell viability, inhibited apoptosis and caspase-3 activity, reduced the release of lactate dehydrogenase, restored the dissipated mitochondrial membrane potential, and suppressed the excess accumulation of intracellular reactive oxygen species. Compared with L-Glu-exposed cells, IOPS pre-treated cells exhibited reduced levels of Bcl-2 associated X protein (Bax) and Kelch-like ECH-associated protein 1 (Keap1) and enhanced levels of B-cell lymphoma-2 (Bcl-2), NF-E2p45-related factor 2 (Nrf2), heme oxygenase-1 (HO-1), superoxide dismutase-1 (SOD-1), and cysteine ligase catalytic subunit. In amyloid precursor protein/presenilin 1 (APP/PS1) transgenic mice, an 8-week course of IOPS improved the pathological behaviors related to memory and cognition, reduced the deposition of β-amyloid peptides and neuronal fiber tangles induced by enhanced phosphor-Tau in the brain, and modulated the levels of anti- and pro-oxidative stress enzymes. Additionally, IOPS enhanced the expression levels of Nrf2 and its downstream proteins, including HO-1 and SOD-1, in the brains of APP/PS1 mice. The present study successfully demonstrated the protective effect of IOPS against AD and revealed the possible mechanism underlying the ability of IOPS to modulate oxidative stress, especially Nrf2 signaling, and mediate mitochondrial apoptosis.

Keywords: Alzheimer's disease; Apoptosis; Inonotus obliquus polysaccharides; Nrf2; Oxidative stress.

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