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Kynurenic Acid (KYNA) Attenuates Oxidative Stress and Mitochondrial damage in 6-OHDA-induced Dopaminergic Neuronal Cell Death

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Objectives

Kynurenic acid (KYNA), tryptophan metabolite is known to have cell protective effect against various insults in the brain. But so far, the protective mechanism is largely unknown. In this study, we investigated how the KYNA exerts protective effect against 6-OHDA, a causative molecule of Parkinsonian syndrome, using SH-SY5Y cells.

Materials and Methods

Materials : cell line : human neuroblastoma, SH-SY5Y cells

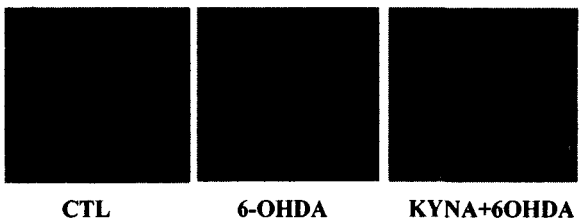
reagent : 6-hydroxydopamine, kynurenic acid, tetramethyl rhodamine ethyl ester

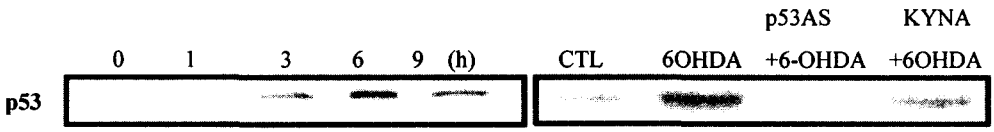
DCF-DA, anti-p53 antibody, Ac-LEHD-AMC, Ac-DEVD-AMC

Methods : Alarmablue assay, Western blotting, Caspase substrate cleavage assay

Fluorescent microscope, Phase-contrast microscope

Results and Discussion





Incubation of SH-SY5Y cells with 6-OHDA induced reactive oxygen species (ROS), increased expression of p53, followed by mitochondrial dysfunction such as mitochondrial membrane potenial (MMP). Moreover, caspase-9 and caspase3 were significantly activated and triggered apoptosis.

Interestingly, pretreatment of KYNA reduced significantly the ROS, expression level of p53 and damage

of mitochondria, eventually inhibited the cell death. Our result suggested the ROS and p53 mediated 6-OHDA induced cell death and KYNA down-regulated ROS and expression of p53, leading to inhibiting the cell death.

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