Ⅱ-42

Protective effect of *Ilex latifolia* (IL) against amyloid ß protein (25-35)-induced neurotoxicity

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Beta amyloid protein에 의해 유도된 독성에 대한 *Ilex latifolia* 의 뇌신경 보호효과

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Objectives

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive loss of cognitive ability and by neuropathological features including senile plaque, neurofibrillary tangles and neuronal loss in selective brain regions. Amyloid ß protein (Aß) or Aß peptide fragments have been suggested to play important roles in the pathogenesis of AD. Aß-induced neurotoxicity is accompanied by increase of intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$) and generation of reactive oxygen species (ROS). The leaves of *Ilex latifolia* (IL), which is one original species of ku-ding-cha, is generally consumed in southern china as a tea-like beverage. It has been demonstrated to possess coronary vasodilative action and is used in the treatment of coronary heart disease and myocardial infarction. In the present study, we investigated the protective effects of IL against Aβ (25-35)-induced neurotoxicity in cultured neurons and memory impairment in mice.

Materials and Methods

○ Materials

IL (: ethanol extract of *Ilex latifolia*), Aβ (25-35), Passive avoidance apparatus

○ Methods

Neuronal cells, cultured from 16-day-old fetuses of SD rats, were treated by Aβ (25-35) for 36 h. Viability of cultured cells was measured by 3-[4,5- dimethylthiazole -2-yl]-2,5-diphenyl-tetrazolium bromide (MTT) assay and Hoechst 33342 staining. A β-induced elevation of the $[Ca^{2+}]_i$ and generation of ROS were measured by

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fluorescence dyes using laser scanning confocal microscopy. Aß (25-35)-induced memory impairment was established by intracerebroventricular microinjection of 15 nmol Aß (25-35) in mice and was examined using passive avoidance test.

Results

IL (10-100 μg/ml) inhibited Aß (25-35)-induced neuronal cell death.(Fig. 1) Aß (25-35)- induced elevation of $[Ca^{2+}]_i$ and generation of ROS were inhibited by IL. These results suggest that IL may ameliorate Aß (25-35)-induced neuronal cell death by interfering $[Ca^{2+}]_i$ increase and inhibiting ROS generation. Chronic administration of IL (25-100 mg/kg, 8 days) markedly improved memory impairment induced by Aß (25-35) in mice without affecting general motor function.(Fig. 2) In conclusion, the present study provides the pharmacological basis of IL as a promising agent for the treatment of neurodegeneration in AD.

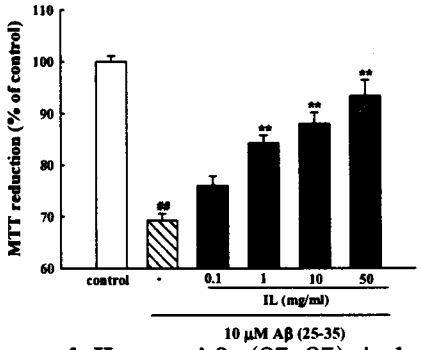

Fig 1. Inhibitory effect of IL on Aß (25-35)-induced neuronal cell death in cultured cortical neurons.

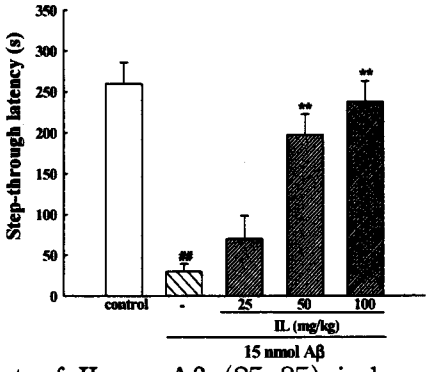

Fig 2. Inhibitory effect of IL on Aß (25-35)-induced memory impairment.