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한국산 겨우살이의 Amyloid β Protein (25-35)에 의해 유도된 신경독성에 대한 보호효과

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Korean mistletoe protects Amyloid β Protein (25-35)-induced neurotoxicity

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Objectives

Semi-parasitic plants, mistletoes (Loanthaceae), have been traditionally used as sedative, analgesic, anti-spasmodic, cardiotonic and anticancer agents. However, there is no report about their effects on the central nervous system. Amyloid β protein (A β) (25-35) is believed to play a central role in the pathophysiology of Alzheimer's disease (AD). In the present study, the protective effect of methanol extract of Korean mistletoe (KM; Viscum album coloratum) against Aβ (25-35)-induced neurotoxicity in cultured neurons and memory impairment in mice were examined.

Materials and Methods

○ Materials

KM, primary cultured rat cortical neurons, Aβ (25-35)

○ Methods

Primary cortical neuronal culture were prepared from the forebrains of 15-day-old fetuses from pregnant SD rats. The 3-[4,5-dimethylthiazole-2-yl]-2,5-diphenyl-tetrazolium bromide (MTT) assay and Hoechst 33342 staining were performed for the measurement of neuronal cell death induced by Aβ (25-35). Aβ (25-35)-induced elevation of the cytosolic Ca^{2+} concentration ($[Ca^{2+}]_c$) was measured using fluo-4AM and generation of reactive oxygen species (ROS) was monitered by the fluorescent product of H_2DCF-DA. The protective effect of KM against Aβ (25-35)-induced memory impairment in mice was examined using passive avoidance test. Memory impairment model in mice was established via intracerebroventricular (i.c.v.) microinjection of Aβ (25-35) (8 nmol).

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Results

KM (10 to 50 μg/ml) prevented Aβ (25-35)-induced neuronal cell death. KM significantly inhibited Aβ (25-35)-induced elevation of the $[Ca^{2+}]_c$, glutamate release and generation of ROS. Aβ (25-35)-induced memory impairment was markedly improved by chronic administration of KM (25 and 50 mg/kg, PO, 8 days). In conclusion, KM significantly protected neurotoxicity induced by Aβ (25-35) in *in vitro* and *in vivo*. It may help to explain its inhibitory action on the progression of AD, and provide the pharmacological basis of its clinical usage in treatment of neurodegeneration in AD.

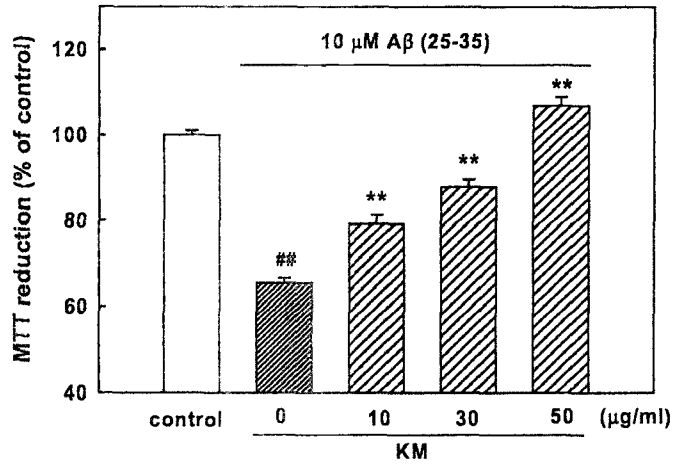

Fig. 1. Inhibitory effect of KM on Aβ (25-35)-induced cell death in cultured cortical neurons. Neuronal cell death was measured by the MTT assay.

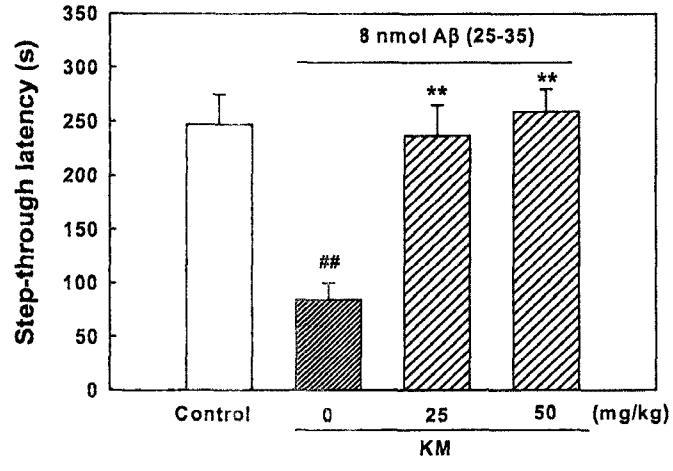

Fig. 2. Inhibitory Effect of KM on Aβ(25-35)-induced memory impairment as determined by passive avoidance test.