

SL104 Neurodegenerative Alzheimer's Disease and Its Therapy 알자이머 퇴행성 신경 질환과 이의 치료

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Alzheimer's disease is characterized by the presence of excessive amount of neuritic plaques containing amyloid β protein ($A\beta$) and impairment of cognitive function related with cholinergic dysfunction. Several lines of evidences indicate that $A\beta$ may play a important role in pathogenesis of AD and genetic mutation of ApoE, PS1 and PS2 genes is associated with early onset of the disease. In addition many reports have suggested that vascular dementia such as multi-infarct dementia and dementia of Alzheimer type could be induced by ischemia stroke. Although an enormous research effort have been directed towards discovering the cause of AD with the ultimate hope of developing safe and effective pharmacological treatments, the development of remarkable therapeutic drug for AD is not expected in the near future.

We have shown that a recombinant C-terminal fragments of APP has been closely linked with neurotoxicity in AD. This peptide is more toxic to neuron than $A\beta$ and induce strong inward current, blockage of LTP, disruption of Ca^{2+} homeostasis, behavioral disturbance and neuropathologic changes. These results provide an important clue for identification of altered metabolism of APP and etiological treatment by preventing the generation and deposition of toxic fragment of APP.

There are two critical therapeutic strategies aimed at preventing the symptoms of AD. First thing is to reduce the deposition of amyloid β protein or decrease the susceptibility of microtubules to tangle formation. Second thing is being targeted to improve the symptom of cognitive deficits by supplement of Acetylcholine (ACh) neurotransmission. However, because the cause of AD is not exactly known, many researcher have tried to reduce learning and memory impairment which is a primary symptom of AD.

We have first found that Dehydroevodiamine. HCl (DHED), a constituent of *Evodia Rutaecarpa*, has the strong anticholinesterase and antidementia activities as well as low toxicity and side effects in in vitro and in vivo test. Furthermore we identified that this compound has antiischemia effects. Therefore DHED might be used for the treatment of various dementia caused by ischemia stroke along with Alzheimers Disease.