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Designed and Synthesis of Bi-functional Molecule as Anti-Alzheimer agent

Chen-Wei Huang (黃振瑋), Pei-Teh Chang (張佩德), Chao-Wu Yu (余兆武), Ravindra R. Deore and Ji-Wang Chern (陳基旺)

School of Pharmacy, College of Medicine, National Taiwan University, Taipei ,Taiwan

Alzheimer's disease (AD) was thought as age-related neurodegenerative disease. As the lifespan prolong, it will become one of the most costly disease in healthcare. Amyloid β plaques and neurofibillary tangles are observed in AD patients and become a promising target in drug development. Biometal like Zn^{2+} and Fe^{2+} homeostasis were considered important factors in Alzheimer. They could induce Aβ aggregation and produce reactive oxygen species (ROS) to enhance oxidarive stress contributing tau hyperphosphorylation and neurofibrillary tangle formation if the metal concentration was unregulated. We designed and synthesized a compound, J2326, containing neurotrophic activity and anti-amyloid aggregation ability. J2326 specifically induced neurite outgrowth in a concentration-dependent manner and had little mitogenic effect. These outgrew neurites were positive for mature neuronal markers; and were ERK-dependent but p38-indenpendent. Treatment with J2326 also enhanced neuronal survival under -amyloid (A) challenge. It inhibited the aggregation of A . *in vitro* in a concentration-dependent manner. The inhibition of A aggregation could be a consequence of directs targeting amyloid by J2326. Moreover, we found that J2326 restored the neurite outgrowths following A -induced neurodegeneration both *in vitro* and *in vivo*. These findings manifest the immense importance of this compound since it possesses both neurite outgrowth promotion and anti-amyloid aggregation activities. These biological novelties indicate J2326 may serve as a dual-function agent for Alzheimer's disease therapeutic strategy.