# Novel Promising Multifunctional Anti-Alzheimer's Dimers Derived from Traditional Chinese Medicines

Drug Discovery

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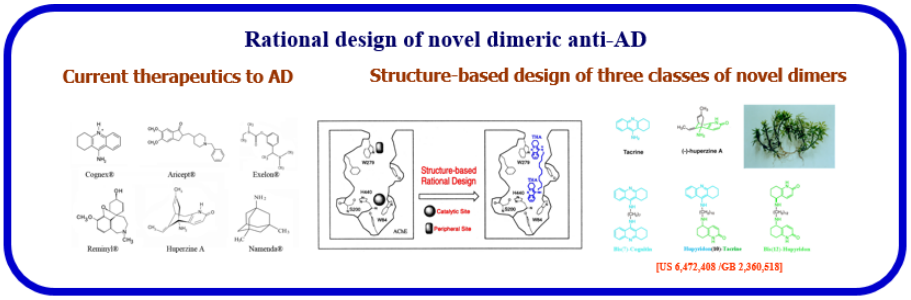
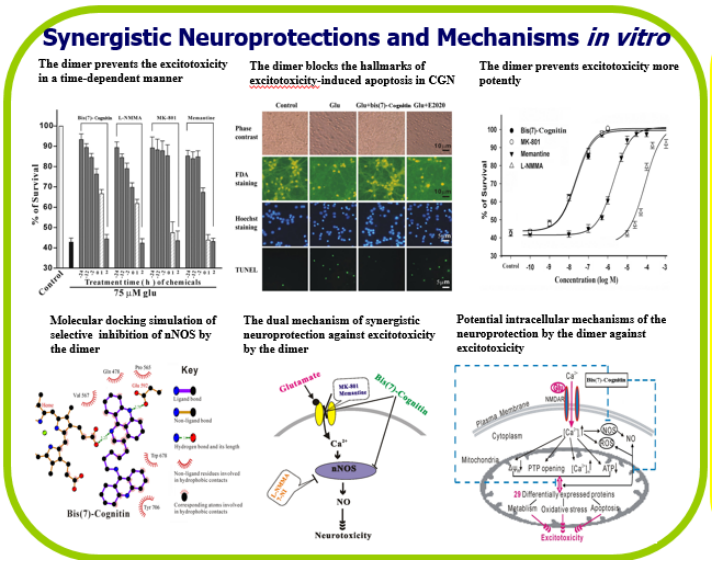
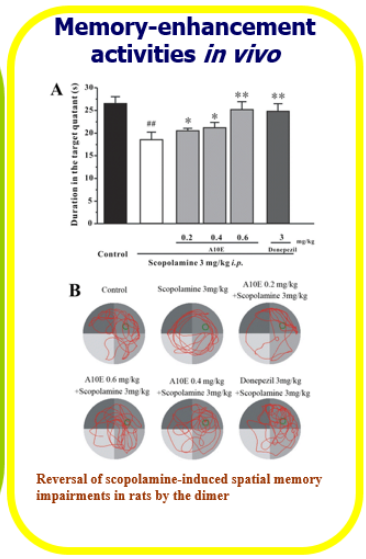
Alzheimer's Disease (AD) is a chronic neurodegenerative disease that attacks the brain and results in impaired memory, thinking and behavior in the elderly. No effective treatment is available now. Four acetylcholinesterase (AChE) inhibitors (Cognex®, Aricept®, Exelon® and Reminyl®) and N-Methyl-D-Aspartate receptor (NMDAR) antagonist (Namenda®) have been approved by the Food & Drug Administration USA for the treatment of AD. Huperzine A (HupA), a novel Lycopodium alkaloid was first discovered from Chinese medicinal herb Huperzia serrata.

Several new dimeric compounds derived from homo- or hetero dimers of tacrine and / or HupA have been developed in our laboratory. The cost to synthesize these new dimers is much lower than that to isolate HupA from the natural plant. The idea of dimerisation itself is a novel concept to modify the existing drugs on market. Comprehensive comparisons of these dimers and the existing agents with regard to their neuroprotections and memory enhancement were demonstrated in vitro and in vivo. The results suggest that these novel multifunctional dimers can be highly promising candidates for the development of new generation of disease-modifying therapeutics in AD.




## Representative Publications

1. Luo J, Li W, Zhao Y, Fu H, Ma DL, Tang J, Li C, Peoples RW, Li F, Wang Q, Huang P, Xia J, Pang Y, Han YF* (2010) Pathologically activated neuroprotection via uncompetitive blockade of N-methyl-D-aspartate receptors with fast off-rate by novel multifunctional dimer Bis(propyl)-cognitin. J Biol Chem. 285(26):19947-58.
2. Hu SQ, Wang R, Cui W, Zhang ZJ, Mak SH, Xu DP, Choi CL, Tsim Karl, Paul R. Carlier, Lee MY, Han YF* (2014) Inhibiting β-amyloid-associated Alzheimer's pathogenesis in vitro and in vivo by a multifunctional dimeric bis(12)-hupyridone derived from its natural analogue. J Mol Neurosci. 55(4):1014-21.
3. Chen HX, Xiang SY, Huang L, Lin JJ, Hu SQ, Mak SH, Wang C, Wang QW, Cui W, Han YF* (2018) Tacrine(10)-hupyridone, a dual-binding acetylcholinesterase inhibitor, potently attenuates scopolamine-induced impairments of cognition in mice. Metab Brain Dis. (In press)

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