

Novel Compounds and Methods for Treating Alzheimer's and Related Diseases

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Technology description

Summary

The brain cholinergic system is thought to play an important role in learning and memory. The loss of cholinergic neurons early in the course of Alzheimer's Disease may thus be an etiological factor in the cognitive decline that is the hallmark of that disease. Therefore, potentiating cholinergic transmission has been the main pharmacological approach for the treatment of AD patients. Inhibition of acetylcholinesterase (AChE) or butyrylcholinesterase (BChE) enhances cholinergic transmission by reducing enzymatic degradation of acetylcholine.

AChE inhibitors are now used clinically to help restore cognitive function in AD patients. However the therapeutic index for inhibition of AChE is quite low. Drugs with this mechanism of action have to have the proper pharmacodynamic properties to achieve even a marginally useful clinical effect without unacceptable side effects. The presence of BChE in brain tissue makes this enzyme another possible target for increasing the activity of the cholinergic system.

The present invention provides a series of novel and potent tricyclic compounds that have a range of selectivity for inhibiting AchE, as compared to BchE, and possess neuroprotective activity in cell culture models. Also provided are methods of using these compounds to treat a number of different medical conditions such as Alzheimer's Disease, mild cognitive impairment, and other dementia-related disorders.

Institution

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