

Phosphodiesterase inhibitors for the treatment of Alzheimer's disease

Published date: Sept. 27, 2017

Technology description

Summary

This technology is a synthesized class of quinolone-containing compounds that function as potent phosphodiesterase inhibitors for the treatment of Alzheimer's disease.

Unmet Need: Inhibition of amyloid beta plaque accumulation for treatment and prevention of Alzheimer's disease

Alzheimer's disease (AD) is a devastating neurodegenerative disorder marked by memory loss and synaptic dysfunction. There are currently no effective treatments for reversing the brain's deterioration to restore memory. Post-mortem analyses of brains of patients with AD have established accumulated amyloid beta (A-beta) plaque accumulation as playing a significant role in disease progression. A-beta accumulation is partially due to an overactive secretase enzyme, which produces A-beta following the cleavage of amyloid precursor protein. This suggests that inhibition of secretase enzymes could be a potential therapeutic for AD. PDE5 phosphodiesterase inhibitors have been shown to modulate secretase activity, but have yet to be studied in a model of AD.

The Technology: Phosphodiesterase inhibitors capable of targeting accumulated amyloid beta deposits for the treatment of Alzheimer's disease

This technology describes a class of quinoline-containing compounds with PDE5 inhibitory function capable of reducing amyloid beta plaques to treat AD. PDE5 inhibitors increase cyclic guanosine monophosphate (cGMP) levels by inhibiting the degradative action of PDE5 on cGMP. cGMPs are important nucleotide secondary messengers that regulate many cellular processes, including blood flow, cell differentiation, neural transmission, glandular secretion, and gene expression. While related PDE5 inhibitors are already approved drugs for the treatment of erectile dysfunction and pulmonary hypertension, they have not been tested for the treatment of AD. In addition, compounds identified in this technology were shown to improve cognitive function in mice as measured by tests of spatial memory, contextual fear conditioning, and long-term potentiation. Furthermore, this technology exhibits hallmarks of an efficient therapeutic with high potency, selectivity, and blood-brain-barrier (BBB) permeability. This technology also includes computational and structural information for finding and screening for additional PDE5 inhibitors.

Publications

Puzzo D, Sapienza S, Arancio O, Palmeri A. "Role of phosphodiesterase 5 in synaptic plasticity and memory" Neuropsychiatr Dis Treat. 2008 Apr; 4(2): 371-387.

Application area

Small molecule therapeutics for the treatment of AD

Treatment of other diseases characterized by elevated amyloid beta plaques

Screening platform for PDE5 inhibitors

Screening platform for compounds that reduce secretase activity

Research tool for studying the role of amyloid beta plaques in Alzheimer' s disease

Advantages

Compounds exhibit high PDE5 inhibitory potency

Demonstrated BBB permeability

High selectivity reduces harmful side effects

Reduces cognitive impairment in a mouse model of AD

PDE5 inhibitors are already approved for the treatment of erectile dysfunction and pulmonary hypertension

Institution

[Columbia University](#)

Inventors

[Donald W. Landry](#)

联系我们



叶先生

电话：021-65679356

手机：13414935137

邮箱：yeyingsheng@zf-ym.com