

用於認知障礙症治療的新型多功能病情調節二聚體

Novel Multifunctional and Disease-modifying Dimers for Treating Alzheimer's Disease

通過用藥物保護神經元達到預防和治療的效果

Preventing and treating Alzheimer's disease via neuronal protection with drugs

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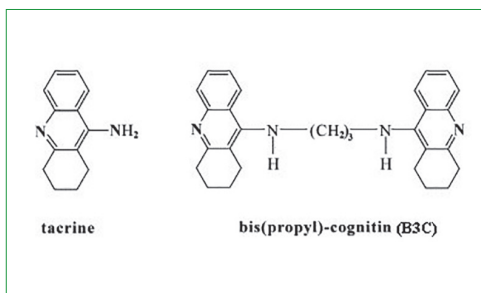
特色與優點

- 具多功能神經保護協同作用，能保護神經元
- 可修復記憶障礙
- 能改變認知障礙症的病程發展

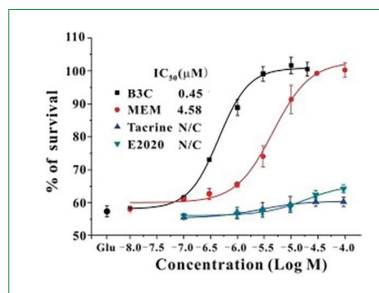
應用

- 預防及標本兼治認知障礙症
- 改善記憶

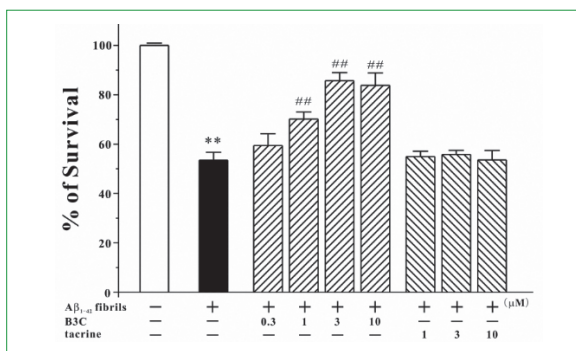
認知障礙症主要發生於老年人身上。患者會出現記憶、思維和行為等方面認知功能障礙。目前治療認知障礙症的藥物只能改善症狀，成效非常有限。因此，進一步研發抗神經系統退行性疾病的新藥，以預防及標本兼治認知障礙症，將具有重要的科學意義和經濟價值。理大以現有治療認知障礙症的藥物他克林(Tacrine)為基礎，發展出一系列二聚體。這些二聚體能同時針對多個認知障礙症治療的標靶點，包括抑制乙酰膽碱酯酶及對抗神經毒性等。團隊進行的細胞及動物實驗研究結果顯示，新型二聚體比現有藥物更能有效地對抗認知障礙症。



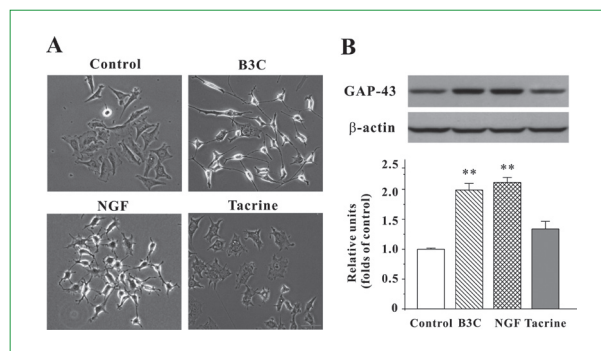
他克林及他克林二聚體的化學結構
Chemical structure of tacrine and tacrine dimer



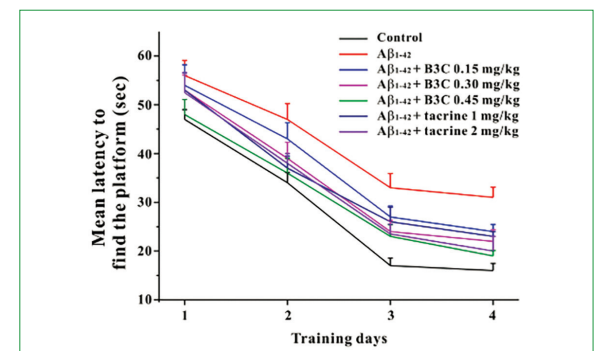
實驗研究結果顯示，二聚體(B3C)比現有藥物美金剛(Memantine, MEM)、他克林(Tacrine)或多奈哌齊(Donepezil, E2020)具有更強的神經保護作用。Compared with existing drugs Memantine (MEM), Tacrine and Donepezil (E2020), the dimer (B3C) has more potent effect in preventing excitotoxicity-induced neuronal loss *in vitro*.



二聚體(B3C)可對抗由澱粉樣蛋白引起的神經毒性，比現有藥物他克林(Tacrine)更能有效地保護神經元。The dimer (B3C) protects against Ab1-42 Fibrils-induced Neurotoxicity in PC12 Cells, and has a stronger neuronal protection effect than existing drug (Tacrine).



二聚體(B3C)具有誘導PC12細胞分化的效用。The dimer (B3C) induced neuronal differentiation in PC12 cells toward a neuronal phenotype.



水迷宮實驗顯示，二聚體(B3C)能使有認知障礙老鼠的記憶及學習能力回復正常水平。According to water maze tests, the dimer (B3C) has reversed the memory and learning deficits induced by beta-amyloid (Aβ) in mice.

Mainly affecting the ageing population, Alzheimer's disease (AD) is a chronic neurodegenerative disease characterized by the impairment of cognitive functions such as memory, thinking and behaviors. Currently, the single targeted anti-AD drugs have low efficacy and can only improve the symptoms. Therefore, further research and development of more efficacious and disease-modifying agents for the prevention, treatment and restoration of neurodegenerative disorders will have tremendous scientific and economic values.

PolyU has developed a series of dimers derived from tacrine, a drug currently used for treating Alzheimer's disease. These dimers are multi-targeting drugs which can inhibit acetylcholinesterase and anti-neurotoxicity. When compared with the existing drugs, these novel multifunctional dimers have shown more promising anti-AD effects on models with AD *in vitro* and *in vivo*.

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Special Features and Advantages

- Multi-functional synergistic effect to prevent neuronal loss
- Repair memory deficits
- Promote disease-modifying process

Applications

- To prevent and treat AD, addressing both the symptoms and root cause
- To enhance memory



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