中国药理学与毒理学杂志 2013 27 (4): 731-738 ISSN: 1000-3002 CN: 11-1115/R

综述

可通过血脑屏障的乙酰胆碱酯酶重活化剂的研究进展

魏朝, 郑志兵, 李松

军事医学科学院毒物药物研究所药物化学研究室, 北京 100850

收稿日期 2013-2-27 修回日期 2013-5-17 网络版发布日期 2013-8-24 接受日期

摘要 神经性毒剂和有机磷农药是乙酰胆碱酯酶的不可逆抑制剂, 对人类生命安全构成重大威胁。目前可用于临床预防和治疗的药物大都为季铵型乙酰胆碱酯酶重活化剂, 对外周组织和血液中乙酰胆碱酯酶中毒具有较好的活化作用, 但季铵盐结构限制了血脑屏障通过率, 使这类重活化剂在中枢神经系统发挥作用有限。因此, 开发可通过血脑屏障的重活化剂是当前主要发展趋势。本文对可通过血脑屏障的重活化剂的研究进展进行了综述。

关键词 有机磷化合物 乙酰胆碱酯酶 血脑屏障 中枢神经系统

分类号 R971

Progress in acetylcholinesterase reactivators aiming to cross blood-brain barriers

WEI Zhao, ZHENG Zhi-bing, LI Song

Deparment of Medicinal Chemistry, Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences, Beijing 100850, China

Abstract

Organophosphate(OP)nerve agents and pesticides are irreversible inhibitors of acetylcholinesterase, posing a serious threat to human safety.Oximes,by reactivating acetylcholinesterase,are important adjunct therapeutics in OP poisoning.Oximes currently inuse for treatment of OP poisoning are functionalized pyridinium salts,while oximes are generally believed to reactivate phosphorylated acetylcholinesterase in the blood and peripheral tissues,access of these oximes to the central nervous system is severely restricted by blood-brain barriers due to their hydrophilic chemical structures.There fore,it's currently a major trend to develop blood-brain barrier-penetrable oximes to protect the central nervous system from toxicity of OP exposure.This paper reviewed the researches on acetylcholinesterase reactivators aiming to cross the blood-brain barrier.Biological activity evaluation and structure-activity relationship studies of these reactivators were also summarized.

Key words organophosphorus compounds acetylcholinesterase blood-brain barrier