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# Cholinesterase reactivators and bioscavengers for pre- and post-exposure treatments of organophosphorus poisoning

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## Abstract

© 2017 International Society for Neurochemistry.Organophosphorus agents (OPs) irreversibly inhibit acetylcholinesterase (AChE) causing a major cholinergic syndrome. The medical countermeasures of OP poisoning have not evolved for the last 30 years with carbamates for pretreatment, pyridinium oximes-based AChE reactivators, antimuscarinic drugs and neuroprotective benzodiazepines for post-exposure treatment. These drugs ensure protection of peripheral nervous system and mitigate acute effects of OP lethal doses. However, they have significant limitations. Pyridostigmine and oximes do not protect/reactivate central AChE. Oximes poorly reactivate AChE inhibited by phosphoramidates. In addition, current neuroprotectants do not protect the central nervous system shortly after the onset of seizures when brain damage becomes irreversible. New therapeutic approaches for pre- and post-exposure treatments involve detoxification of OP molecules before they reach their molecular targets by administrating catalytic bioscavengers, among them phosphotriesterases are the most promising. Novel generation of broad spectrum reactivators are designed for crossing the blood-brain barrier and reactivate central AChE. This is an article for the special issue XVth International Symposium on Cholinergic Mechanisms.

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## Keywords

Acetylcholinesterase, Bioscavenger, Nerve agent, Organophosphate poisoning, Oxime, Post-exposure treatment, Prophylaxis