

Nerve agents: Catalytic scavengers as an alternative approach for medical countermeasures

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Abstract

© 2016 The Royal Society of Chemistry. The use of scavengers is the most appealing alternative approach for pre- and post-exposure treatments of nerve agent (NA) poisoning. This can be achieved either by the use of biocatalysts or artificial enzymes. Administered scavengers act in the bloodstream by degrading toxic molecules before they reach physiological targets. The first generation scavengers were stoichiometric bioscavengers. Among them, human butyrylcholinesterase has proven to be safe and effective for protection against NA poisoning. However, stoichiometric neutralization of NAs requires administration of huge doses of costly biopharmaceuticals. On the other hand, catalytic scavengers are capable of detoxifying organophosphorus agents through a turnover mechanism. By virtue of turnover, much lower doses are needed for rapid neutralization of toxic molecules. Thus, introduction of catalytic scavengers will improve medical countermeasures in terms of efficacy and cost. Catalytic scavengers could also be used as active components in topical skin protectants, functionalized tissues, and decontaminating gels, foams and lotions. They could also be incorporated into chemical protective suits. Catalytic chemical scavengers are artificial enzymes such as functionalized cyclodextrins. Catalytic bioscavengers are enzymes. Evolved mutants of phosphotriesterases that degrade the most toxic NA enantiomers are the most promising scavengers. Other engineered enzymes of interest are cholinesterases, carboxylesterases and prolidases. Operational catalytic bioscavengers must be effective catalysts producible at low cost, not susceptible to induced immune response and iatrogenic effects, stable in the bloodstream and upon storage even under field conditions. Gene therapy and artificial enzymes are still in their infancy, but expectations for these approaches are high for the future of medical countermeasures.

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