Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Neuroprotective Effects of Metalloporphyrins Against Chemical Threat Agents

Category

Biodefence Therapeutics

Problem

There is a need for treatments that decrease seizures and oxidative stress after exposure to chemical warfare agents

Technology Overview

Metalloporphyrins can prevent oxidative stress and neuronal cell loss that occurs after chemical threat agent exposure

IP Status

- Patents issued- US, Australia, New Zealand, Russia
- Patents pending- Japan and Canada
- Available for Exclusive or Non-Exclusive Licensing

Advantages

- Inhibits oxidative stress and neuronal cell loss
- Efficacious against multiple chemical threat agents
- Favorable pharmacokinetic properties

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Problem: Chemical warfare agents are an immense threat to both military personnel and civilians. The central nervous system is a sensitive target for chemicals toxicants that interact with receptors and signaling mechanisms. Exposure to nerve agents, metabolic poisons, or high levels of sulfur mustard can trigger seizure and loss of consciousness. Currently, there are limited treatments available that prevent seizures induced by chemical threat agents. Studies have established that controlling seizure activity and downstream consequences is critical for survival after nerve agent exposure and that oxidative stress plays a central role in seizure-induced brain injury. Thus, there is a need to develop efficacious neuroprotective treatments that attenuate oxidative stress after chemical threat agent exposure.

Solution: Researchers from the University of Colorado have found that metalloporphyrins, such as AEOL10150, can be used to counteract the negative effects chemical threat agents such as nerve agents and their surrogates on the central nervous system. AEOL10150 is a catalytic antioxidant with broad spectrum activity against superoxide radicals, hydrogen peroxide and lipid peroxyl radicals. The inventors have shown that AEOL10150 is able to cross the blood-brain barrier in rats, and that it is neuroprotective against pilocarpine, diisopropyl fluorophosphate and soman neurotoxicity. Specifically, they found that it was able to attenuate oxidative stress and prevent hippocampal cell loss induced by these treatments. The ability of AEOL10150 to inhibit neuronal damage induced by soman treatment is shown in **Figure 1.**

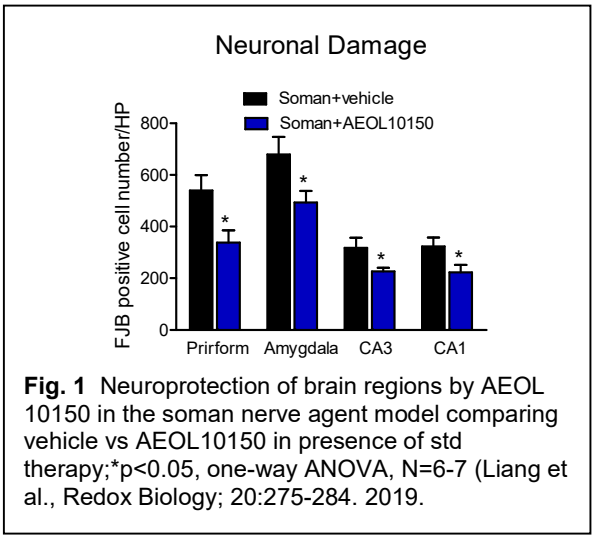

Fig. 1 Neuroprotection of brain regions by AEOL 10150 in the soman nerve agent model comparing vehicle vs AEOL10150 in presence of std therapy;*p<0.05, one-way ANOVA, N=6-7 (Liang et al., Redox Biology; 20:275-284. 2019.

Advantages and Value Propositions:

In 2015, the global biodefense market was valued at 9.68 billion, and it is expected to grow to 18 billion by 2024, registering a CAGR of 6.43%. Metalloporphyrins such as AEOL10150 have great potential to be used as treatments that counteract the effects of chemical threat agents. AEOL10150 inhibits oxidative stress and cell loss, suggesting it could prevent brain injury caused by seizures. It is efficacious against several threats including radiation, chlorine and mustard gas and is effective when administered post-exposure. It has favorable pharmacokinetic properties after subcutaneous injection, which is ideal for its use as a medical countermeasure. Phase 1 human clinical trials have also been completed using AEOL10150 with a low incidence of adverse effects.

Additional Documents and Sources: "Neuroprotective Effects of Metalloporphyrins Against Chemical Threat Agents." U.S. Patent No. 9,295,674.

Pearson JN, Rowley S, Liang L-P, White AM, Day BJ, & Patel, M. Reactive oxygen species mediate cognitive deficits in experimental temporal lobe epilepsy. *Neurobiology Of Disease.* 2015;82:289-297. doi:10.1016/j.nbd.2015.07.005

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