Neuroprotective Effects of Metalloporphyrins Against Chemical Threat Agents

**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 fluorophospho 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.

**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.