MEDICAL PROPHYLAXIS TO MITIGATE CHEMICAL THREATS

Optimization Of Asoxime Formulations For Enhanced Solubility And Reactivation Efficacy: Implications For Nerve Agent Poisoning Treatment And Design Of Novel Autoinjector

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Nerve agents exert their toxic effects by irreversibly inhibiting the enzyme acetylcholinesterase (AChE; EC 3.1.1.7). Current treatment protocols typically involve the administration of atropine in conjunction with an AChE reactivator (oxime). Numerous AChE reactivators have been investigated as potential broad-spectrum antidotes, with asoxime (also known as HI-6) emerging as a leading candidate due to its potent reactivation activity and widespread recommendation by military organizations.

In pursuit of optimizing the pharmacological properties of asoxime, we synthesized twelve different salts of the compound, including sulfate, chloride, acetate, bromide, phosphate, mesylate, tartarate, iodide, malonate, salicylate, maleinate, and tosylate. The solubility of these salts was evaluated under various temperature conditions in aqueous media, saline, and atropine-saline solution. Notably, the mesylate salt exhibited the highest solubility among all tested anions.

Furthermore, our study investigated the influence of counterions on the reactivation efficacy of asoxime in vitro. Results revealed that the choice of counteranion did not significantly impact the reactivation process, highlighting the robustness of asoxime as a reactivator regardless of salt formulation.

Lastly, leveraging our findings, we contributed to the design of a novel autoinjector for the treatment of nerve agent poisonings, featuring HI-6 and atropine as active components. This advancement holds promise for enhancing the effectiveness and accessibility of antidote delivery in emergency scenarios.

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