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Nanoparticle-Delivered 2-PAM for Rat Brain Protection against Paraoxon Central Toxicity

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Abstract

© 2017 American Chemical Society. Solid lipid nanoparticles (SLNs) are among the most promising nanocarriers to target the blood-brain barrier (BBB) for drug delivery to the central nervous system (CNS). Encapsulation of the acetylcholinesterase reactivator, pralidoxime chloride (2-PAM), in SLNs appears to be a suitable strategy for protection against poisoning by organophosphorus agents (OPs) and postexposure treatment. 2-PAM-loaded SLNs were developed for brain targeting and delivery via intravenous (iv) administration. 2-PAM-SLNs displayed a high 2-PAM encapsulation efficiency (~90%) and loading capacity (maximum 30.8 ± 1%). Drug-loaded particles had a mean hydrodynamic diameter close to 100 nm and high negative zeta potential (-54 to -15 mV). These properties contribute to improve long-term stability of 2-PAM-SLNs when stored both at room temperature (22 °C) and at 4 °C, as well as to longer circulation time in the bloodstream compared to free 2-PAM. Paraoxon-poisoned rats (2 × LD 50) were treated with 2-PAM-loaded SLNs at a dose of 2-PAM of 5 mg/kg. 2-PAM-SLNs reactivated 15% of brain AChE activity. Our results confirm the potential use of SLNs loaded with positively charged oximes as a medical countermeasure both for protection against OPs poisoning and for postexposure treatment.

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Keywords

acetylcholinesterase, blood-brain barrier, drug delivery systems, organophosphorus agent, paraoxon, pralidoxime chloride, solid lipid nanoparticles

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