Utilizing PcTx1 Loaded Lipid Nanoparticles as a Novel Anticoagulant in the Development of a Low-Cost Microneedle Device for Rapid Ischemic Stroke Treatment

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Strokes are a leading cause of global mortality and disability, with ischemic strokes accounting for the majority of cases. Even worse, the current treatment for ischemic stroke, tissue plasminogen activator (tPA), is slow, expensive (~$11,000 uninsured), and inaccessible to millions of people worldwide. This project aimed to develop a low-cost combination therapeutic for rapid ischemic stroke treatment, functioning similarly to an EpiPen for anaphylaxis. By utilizing recombinant PcTx1, a peptide with clot-targeting properties, and Hirudin, a naturally occurring thrombin inhibitor, both encapsulated in pegylated glutathione-conjugated lipid nanoparticles, the study sought to create an accessible, effective emergency intervention. Three assays validated the nanoparticle formulation and drug efficacy. First, a peptide quantification assay identified pegylated glutathione-conjugated lipid nanoparticles as optimal, achieving 91% encapsulation efficiency and rapid release kinetics, with over 95% release within 8 minutes. Second, a neurotoxicity assay using Caenorhabditis elegans confirmed the formulation's safety at therapeutic dosages. Lastly, an in vitro fibrin-lysis assay demonstrated superior anticoagulant efficacy of Hirudin-PcTx1 loaded nanoparticles compared to both free Hirudin and tPA, achieving a fibrinolytic area of 0.36 cm^2 at 12 hours. Overall, the assays showed incredibly promising results, most notably demonstrating a level of fibrinolytic capability that surpasses previously observed treatments. The resulting loaded nanoparticle offers a portable, low-cost, and efficient solution for rapid fibrinolysis, addressing a critical need in underserved communities who might not have access to tPA.

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