Liposomal Encapsulation to Reduce Propofol Adsorption in Extracorporeal Membrane Oxygenation (ECMO) Systems

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Extracorporeal Membrane Oxygenation (ECMO) is a life-saving cardiopulmonary support system for patients with severe cardiac and/or respiratory failure. Its use has increased substantially since the COVID-19 pandemic, with over 200,000 ECMO-supported hospitalizations reported by 2022. Patients on ECMO require multiple medications; however, reliable dosing guidelines remain limited due to drug sequestration within ECMO circuits. Propofol, a widely used sedative, is particularly susceptible to circuit adsorption because of its high lipophilicity (log P = 3.8), with up to 70% of the drug lost within the first 30 minutes of administration. This increases the risk of inadequate sedation and potential toxicity from dose escalation. To address this challenge, it was hypothesized that liposomal encapsulation of propofol could reduce circuit adsorption while maintaining sedative efficacy. A dipalmitoylphosphatidylcholine (DPPC) liposomal formulation was synthesized and evaluated. Ex vivo ECMO studies showed significantly reduced drug adsorption for up to 60 minutes compared to Diprivan® and only ~34% drug loss after 30 minutes. To further reduce adsorption, a more rigid hydrogenated soy phosphatidylcholine (HSPC) liposomal formulation was developed. However, HSPC exhibited reduced adsorption for only 15 minutes and ~57% drug loss after 30 minutes, likely due to burst drug release under ECMO shear stress. These findings suggest an optimal membrane rigidity that balances structural stability with resistance to shear-induced rupture. Overall, the results support further investigation of DPPC-based liposomes, including cholesterol-mediated membrane rigidity optimization, in vivo validation, and physiologically based pharmacokinetic modeling to inform dosing in ECMO populations.

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