

SCAVENGING LIPOSOMES: PROMISING UNIVERSAL ANTIDOTE TO TREAT DRUG-INDUCED TOXICITY

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Calcium channel blocker (CCB) overdose is potentially lethal. Verapamil and diltiazem are particularly prone to acute toxicity due to their dual effect on cardiac and vascular tissues. Unfortunately, conventional decontamination measures are ineffective in accelerating blood clearance and, to date, few efforts have been made to develop antidotes. The only recent innovation in this field is the off-label use of parenteral lipid emulsions which, by scavenging the drug *in situ*, can restrict its distribution in tissues and hinder its pharmacological effect. Alas, these emulsions exhibit a relatively low capture capacity. To address the issue, long-circulating liposomes bearing a transmembrane pH gradient are proposed as novel and more efficient detoxifying agents of CCB poisoning. In this research, we verified the efficacy these nanocarriers in reversing the cardiovascular effects of verapamil in rats implanted with telemetric pressure/biopotential transmitters. In animals orally intoxicated to verapamil, an intravenous injection of the liposomal antidote attenuated the reduction in blood pressure much more efficiently than the commercially available lipid emulsions. Areas under diastolic, systolic, and mean pressures curves were significantly reduced by up to 60% and the time to hemodynamic recovery was shortened from 19 to only 11 h. This work confirmed the protective effect of pH-gradient liposomes against cardiovascular failure after CBB intoxication. The proposed detoxifiers greatly outperformed the lipid emulsions and stand as a promising versatile antidote with minor adverse effect-to-benefit ratio.