Development of an Injectable Formulation for a Novel Lipid A Analog (LPA) by Cryoprotective Effects of Various Saccharides in the Freeze-Drying

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Summary
A sonicated dispersion of the novel lipid A analog (LPA) was freeze-dried in the presence of various additives such as saccharides and polyalcohols and their cryoprotective effects during were investigated. Fusion of the vesicles was measured by determining fluorescence energy transfer and size distribution. The ability of the additives as cryoprotectants was varied. The addition of polyalcohols led to considerable fusion. Although monosaccharides, similar to disaccharides, completely prevented the fusion of the vesicles during lyophilization, they showed far less ability to retain the entrapped calcein of the vesicles compared to disaccharides. Differential scanning calorimetry heating profiles of vesicles that had been lyophilized with various additives were obtained. Disaccharides and monosaccharides again markedly differed in the thermal properties. This variety in cryoprotective ability can be attributed to differences in the extent of their interaction with the LPA head group.