An Analysis of Proton Permeation in Liposomes Containing Novel Archaea-Inspired Lipids

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Drug delivery systems such as hydrogels and nanoparticles pose substantial limitations including premature leakage and toxicity risks regarding inhalation, respectively. Liposomes, which are vesicles composed of phospholipids, are an alternative system for biodegradable drug delivery. The specialized phospholipids of thermoacidophilic archaea are of particular interest because they allow archaea to survive in extreme conditions of pH as low as 0.7 and temperatures above 100°C. The hardiness of such phospholipids suggests that they may have applications in liposome-mediated drug delivery. This study examines the effects of four unique structural motifs of thermoacidophilic archaea on membrane proton permeability: methyl branching (1) and cycloalkanes (2) in hydrophobic tails, transmembrane tethering of hydrophobic tails (3), and ether linkages (4). These unique structural motifs of archaeal phospholipids may make such membranes less permeable to proton flux compared to membranes of most other organisms, thus allowing the thermoacidophilic archaea to withstand the high pH gradient of their environment. This hypothesis was tested using a modified fluorescence-based assay. The results of this experiment showed that the discrepancies between published and experimental permeability values were attributable to this study's use of a different concentration and solvent for valinomycin. Also, it was determined that the presence of ether linkages and cycloalkanes helps to reduce membrane proton permeability, while transmembrane tethering has no substantial effect. Furthermore, lipids with shorter tails exhibited lower proton permeability than lipids with longer tails, suggesting that longer tails may cause instability within the membrane.

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