INTERACTION OF ALKYLPHOSPHOLIPIDS WITH TETHERED BILAYER LIPID MEMBRANES

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Synthetic alkylphospholipids (APLs) are stable analogs of lysophosphatidylcholine, which are being investigated as potential antitumor agents. APLs exert their activities by acting on cell membranes [1], however understanding of their interaction with lipid bilayers is still lacking. In this work we investigated three APLs differing in hydrocarbon chain length and headgroup composition – miltefosine (hexadecylphosphocholine), edelfosine (1-O-octadecyl-2-O-methyl-sn-glycero-phosphocholine) and perifosine (Octadecyl-(1,1-dimethyl-4-piperidylio) phosphate). We used tethered bilayer lipid membranes (tBLMs) formed on self-assembled monolayer modified gold surface as an artificial membrane model [2] and measured its interaction with APLs. We employed electrochemical impedance spectroscopy (EIS) to assess defect formation and fluorescence lifetime imaging microscopy (FLIM) to observe membrane structural changes through microviscosity measurements. Incubation of APLs with tBLMs composed of dopc and cholesterol induced dielectric membrane damage in a time and concentration-dependent manner, with miltefosine being less damaging compared to edelfosine and perifosine at the same concentrations. APLs' induced damage was also demonstrated to be partially reversable at moderate concentrations, reaching a point in EIS spectra after which it shifts back towards lower defect densities. FLIM measurements showed that besides defect formation APLs also induce changes in membrane organization and form mobile micron-scale cholesterol-rich domains.

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[2] T.Penkauskas, G.Preta, BiologicalApplicationsOfTetheredBilayerLipidMembranes (Biochimie, 2019)