From Monolayers to Liposomes: Physicochemical Insights into Lipid-Surfactant Interactions in Viral Envelope Models

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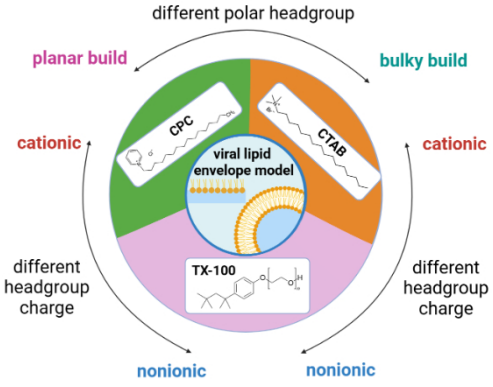
The high genetic variability of viruses is a major challenge in the effective treatment of viral infections, as it hinders the development of efficient long-term antiviral therapies [1,2] . In this context, surfactants capable of altering the physicochemical properties of viral envelopes that are independent of genomic mutations, represent a promising alternative strategy [3,4] .
The aim of this study was to compare the ability of surfactants of different structures and charges, used at concentrations below their critical micelle concentration (CMC), to affect model lipid envelopes of selected viruses under various environmental conditions. Models of the SARS-CoV-2 lipid envelope (DOPC:DMPS:PI, 50:35:15 molar ratio) and the Influenza virus lipid envelope (DOPE:DMPS:SM, 50:35:15 molar ratio) were prepared as Langmuir monolayers (2D structures) and liposomes (3D structures). First, we compared the effect of two cationic surfactants - cetylpyridinium chloride (CPC) build of a planar polar headgroup and cetyltrimethylammonium bromide (CTAB) with a bulky polar headgroup, on SARS-CoV-2 lipid envelope model. The combination of Langmuir technique and surface potential measurements for planar systems along with dynamic light scattering (DLS) and fluorescence microscopy for spherical bilayer structures revealed a stronger impact of CPC on examined models due to its enhanced ability to penetrate lipid layers. Also, we examined how ionic strength affects this process, showing that higher ionic strength enhances the effectiveness of the surfactants. To gain deeper insight into lipid-surfactant interactions of CPC and CTAB, we applied Langmuir technique and DLS supplemented with spectrofluorimetry in mixed lipid-surfactant systems (i.a. DOPC:DMPS:SM:CPC) with varying molar ratios using SARS-CoV-2 and Influenza viral lipid envelope models. Obtained results allowed us to choose the optimal lipid-surfactant ratio to obtain stable structures. Additionally we compared the efficiency of cationic surfactants (CPC, LAE) and nonionic surfactants (Triton X-100, $C_{10}EO_8$) on a model Influenza virus envelope and a simplified model of a human cell membrane (DMPC:Chol 7:3) in PBS buffer. The results indicate distinct mechanisms of action between cationic and nonionic surfactants, with nonionic surfactants exhibiting a stronger disruptive effect on lipid layers. The obtained results show the importance of the environment, surfactant charge, polar headgroup structure, and concentration in interactions between surfactant and phospholipid membrane models.

Keywords:
viral lipid envelopes, surfactants, Langmuir, liposomes



Structures of the surfactants used to investigate the physicochemical alterations in the model viral lipid envelopes

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