Abstract of the Dissertation

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This dissertation investigates the molecular interactions of various ophthalmic drugs and pharmacologically significant compounds with models of the tear film lipid layer (TFLL) using molecular dynamics (MD) simulations. The study focuses on benzalkonium chlorides (BAKs), latanoprost (LTP), surfactant protein G (SP-G), simulated in TFLL, and the H1 peptide derived from colicin U, simulated within model lipid bilayers. MD simulations provided detailed insights into the interactions of these compounds with lipid environments. LTP was observed to integrate into the TFLL. LTP demonstrated a significant tendency to migrate and incorporate into the lipid layer, influencing the structural dynamics of TFLL. This suggests that therapeutic efficacy could be enhanced through sustained release. The behavior of BAKs in TFLL highlighted their dual role, affecting both drug delivery and tear film (TF) integrity. Our simulations showed that BAK molecules at different concentrations could disrupt TFLL, leading to changes in lipid organization and potential TF destabilization. This necessitates careful consideration of the concentration used to balance preservative efficacy with maintaining TF stability. SP-G demonstrated a stabilizing effect on TFLL. By simulating SP-G in TFLL with varying concentrations of polar lipids, it was found that SP-G could adsorb to the water-lipid interface, integrate into the lipid layer, and thereby enhance its stability. This suggests a potential of amphiphilic nanoparticles similar to SP-G for therapeutic use in treating ocular surface disorders, particularly in stabilizing the TF in conditions like dry eye syndrome. The H1 peptide showed the ability to form pores in model lipid bilayers, indicating its potential as an antimicrobial agent. Simulations and experimental liposome tests confirmed that H1 peptides could disrupt bacterial membranes, forming stable water-filled pores. This indicates their potential use in treating bacterial infections on the ocular surface. However, observed interactions and non-selective structural disruptions indicate the need for further optimization, especially in the sensitive environment of the ocular surface. The publications included in this dissertation expand our understanding of drug interactions and potential therapeutics on the ocular surface, offering valuable insights for the development of safer and more effective ophthalmic drugs and compounds.