ABSTRAKT

Understanding the topical drug delivery at basic physico-chemical and biophysical levels is still challenging. One of the main reasons is the specificity of the processes involved, depending on the delivery target.

The tear film lipid layer plays a vital role in ocular health and serves as a target for topical ophthalmic drug delivery. This doctoral thesis investigates two topics related to topical eye delivery, including a case study of drug delivery systems and their major components in the tear film lipid layer, and the effect of a lipid modification on a lipid-associate peptide as a potential drug.

This research is conducted by using molecular dynamics simulations, which are comple- mented by various experimental techniques.

The research about the drug delivery systems is threefold: the first objective is to study the impact of commonly used preservatives on the tear film lipid layer; the second one is to explore the influence of the latanoprost drug on the tear lipids; the third one is to investigate different drug delivery systems containing latanoprost drug and their interaction with the lipid layer in the tears. These studies are conducted by combining molecular dynamics simulations and the experiments involving the Langmuir-type lipids film. The key findings of this research have practical implications for the ocular drug delivery. Namely, the investigation revealed that preservatives, despite their potential advantages in drug formulation, alter the function of the tear lipids. Furthermore, the study reveals that the tear film lipid layer can accumulate a high concentration of latanoprost, and we hypothesized that this behaviour can be used for a long time-scale release. Moreover, we identified unique mechanisms of incorporation of different drug carriers within the tear film lipid layer for various commercial drug formulations.

The second area of the research explores innovative strategies for utilizing the drug-lipids interactions to develop or enhance ophthalmic drugs. Specifically, it investigated the influence of palmitoylation on lipid-peptide interactions, employing the PAG peptide as a model for general peptide drugs. The main objective was to explore how this lipid modification impacts the properties of PAG in various lipid environments. The study was carried out using all- atom simulations. The findings of this study suggest that palmitoylation can be employed as a method to modulate the interactions between peptides and lipids, thereby opening up possibilities for the development of novel ophthalmic drugs.

This combined research contributes to gain a deeper knowledge of the physico-chemical processes involved in the topical drug delivery systems using the tear film lipid layer as an example. In particular, we revealed how individual components of the latanoprost delivery systems are involved in the drug accumulation and release within the tear lipids. Furthermore, the insights gained into the influence of peptide palmitoylation can lead to the development of innovative therapeutic drugs for ocular diseases.