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Drug penetration to ocular surface tissues

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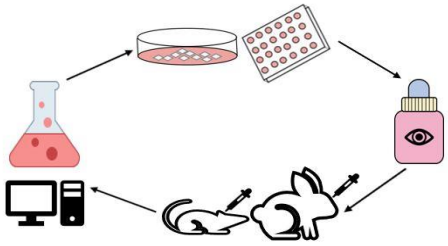
Summary

The current available therapies for dry eye disease(DED) are primarily focused on temporary symptomatic relief and thus require frequent application. Another major concern of most commonly used topical applications for DED is poor bioavailability of drugs due to low penetration and retention of drugs in ocular surface.

This project involves testing of drugs and drug delivery systems. The testing includes physical and chemical characterization and biological testing by *in vitro, ex vivo* and *in vivo* means . The project aims to generate data and tools in ocular surface tissue permeation and retention for topically applied drugs.



Characterization and *in vitro* testing of novel compounds, development and *in vivo* analysis of novel formulation

State-of-the-art

DED is a multifactorial disease of the tears and ocular surface which leads to various symptoms of visual disturbances, irritation, discomfort and possess potential risk of ocular surface damage. DED is a common disease with prevalence of between 5% and 34% around the world.

The topical administration is the most commonly used route of administration of drugs in eyes. However, the bioavailability of topically administered drugs is extremely poor. The major concerns of the topically administered drugs are the penetration and retention of drugs in the ocular surface. Thus, to develop a new treatment method for DED, a clear understanding of the retention and penetration of drugs in ocular surfaces is important. New drug delivery system including mucoadhesive materials and hydrogels could be of high value which can facilitate the permeation and extend drug residence time.

Techniques

- Chemical analytics - LC/MS, Liquid Scintillation
- Physical methods - Characterization of formulation (viscosity, pH, osmolarity)
- *In vitro* - Toxicity (MTT, LDH) and cellular uptake tests in corneal and conjunctival epithelial cells
- *Ex vivo* - Drug partition in cornea and conjunctiva
- *In vivo* - Fluorophotometry, optical coherence tomography (OCT)
- *In silico* - Pharmacokinetic modelling

Task description

- Evaluation of physiochemical properties defining ocular surface uptake and partition
- Testing of novel drug candidates for DED
- Testing and optimization of novel drug delivery systems for prolonged retention on ocular surface
- Investigate the corneal and conjunctival uptake and retention of the lead protease and kinase inhibitors
- Generate pharmacokinetic models to simulate and predict ocular drug permeation