UNIVERSITY OF LOUISVILLE

Department of Chemistry
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Research Seminar

Date: January 28, 2021
Time: 2.30 pm
Location: Microsoft TEAMS

Abstract

Spectroscopic Study of the Relationships between Tear Lipid Composition, Conformation, and Function

Meibomian gland and aqueous-deficient dry eye disease affect about 7 million people in the United States, causing symptoms that can lead to visual disturbance. Correlation between dry eye and an abnormal lipid layer of the tear-film has been found. The lipids give stability, lubrication, and confer anti-microbial properties to the tear film and the corneal surface. The lipids originate mostly from the Meibomian glands, and to a lesser extent, sebaceous glands of the eyelid. Cholesteryl ester (CE) and Wax ester (WE) lipids make up ~ 80% of human meibum and CE/WE ratio has been shown to decrease in patients with meibomian gland dysfunction. Model studies using synthetic CE and WE have provided some insight. However, the application to human meibum lipids is weak as human CE and WE contain variable amounts of hydrocarbon chain branching, saturation and chain length all of which could influence the structure and conformation and structure of the lipids. As almost all the WE and CE moieties found in human meibum cannot be purchased and have not been synthesized, it is almost impossible to model the diverse composition of human meibum lipids using synthetic WE and CE. Minor meibum lipids, such as phospholipids (PLs), are also of special interest due to their proposed interactions with other biomolecules such as Hyaluronic acid (HA), in the vitreous humor. Such interactions have also been proposed in synovial fluids to contribute to lubricating and protecting joint cavities. Moreover, HA-lipid binding could also be relevant to dry eye treatment, even as HA is used with other therapeutics in eye drops. Therefore, lipid-HA interactions and CE-WE relationships investigations using ^{1}H-NMR, and FTIR spectroscopy by our group, outlined below, will be discussed:

1.) Hyaluronic Acid – Lipid Binding: Quantification of interactions was done using binding profiles generated from ^{1}H-NMR between HA, and cholesterol, monoglyceride, palmitoyl palmitate, phosphatidic acid (PA), sphingomyelin (SM) and phosphatidylcholine (PC). *In-vitro* data suggests physiological levels of HA, PC and SM would result in only < 4% of the hydrophobic hydrogens of HA to be bound. This does not support the HA-lipid idea that HA-lipid interactions are relevant to vitreous liquefaction or joint lubrication but alludes to possible interactions in eye drop therapy.

2.) A Spectroscopic Study of the Composition and Conformation of Cholesteryl and Wax Esters Purified from Meibum: Meibum CE and WE from an older and younger donor was completely separated using adsorption column chromatography and separation was verified by ^{1}H-NMR. FTIR was used to measure the behavior of CEs and WEs from donors in a temperature-varied study of their phase transitions. Our results showed that CE changes the phase characteristics of meibum depending on whether it is more or less ordered than WE. Changes in the meibum CE/WE ratio could explain changes in meibum order with age and meibomian glad dysfunction (MGD) which may influence tear film stability. Langmuir trough surface rheology studies of meibum CE/WE mixtures are also underway to test our speculations. Infrared and ^{1}H-NMR spectroscopic studies of meibum from patients with auto-immune Sjogren's syndrome and dry eye symptoms are also on-going.