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Review

Lipidomics of human Meibomian gland secretions: Chemistry, biophysics, and physiological role of Meibomian lipids

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ABSTRACT

Human Meibomian gland secretions (MGS) are a complex mixture of diverse lipids that are produced by Meibomian glands that are located in the upper and the lower eyelids. During blinking, MGS are excreted onto the ocular surface, spread and mix with aqueous tears that are produced by lachrymal glands, and form an outermost part of an ocular structure called "the tear film" (TF). The main physiological role of TF is to protect delicate ocular structures (such as cornea and conjunctiva) from desiccating. Lipids that are produced by Meibomian glands are believed to "seal" the aqueous portion of TF by creating a hydrophobic barrier and, thus, retard evaporation of water from the ocular surface, which enhances the protective properties of TF. As lipids of MGS are interacting with underlying aqueous sublayer of TF, the chemical composition of MGS is critical for maintaining the overall stability of TF. There is a consensus that a small, but important part of Meibomian lipids, namely polar, or amphiphilic lipids, is of especial importance as it forms an intermediate layer between the aqueous layer of TF and its upper (and much thicker) lipid layer formed mostly of very nonpolar lipids, such as wax esters and cholesteryl esters. The purpose of this review is to summarize the current knowledge on the lipidomics of human MGS, including the discussions of the most effective modern analytical techniques, chemical composition of MGS, biophysical properties of Meibomian lipid films, and their relevance for the physiology of TF. Previously published results obtained in numerous laboratories, as well as novel data generated in the author's laboratory, are discussed. It is concluded that despite a substantial progress in the area of Meibomian glands lipidomics, there are large areas of uncertainty that need to be addressed in future experiments.

Contents

Abbreviations: APCI, atmospheric pressure chemical ionization; AT, aqueous tears; CB, chronic blepharitis (or eyelid inflammation); CE, cholesteryl esters; Cer, ceramides; Chl, cholesterol; Crb, cerebroside; C_s^{-1}, in-plane elasticity modulus; DAG, diacyl glycerols; DE, dry eye; DES, dry eye syndrome; ECL, equivalent chain length; EI, electron impact; ELC-FA, extremely long chain fatty acids (C_{28} or longer); ELS, evaporative light scattering; ESI, electrospray ionization; FA, fatty acids; FAl, fatty alcohol; FAm, fatty acid amides; FFA, free (non-esterified) fatty acids; FI, flame ionization; FID, flame ionization detector; FMW, full molecular weight; FS, fluorescence spectroscopy; GC, gas chromatography; GLC, gas-liquid chromatography; HC, hydrocarbons; HPLC, high performance liquid chromatography; IR, infrared spectroscopy; IT, ion trap; KCS, keratoconjunctivitis sicca; LT, Langmuir trough; MAG, monoacyl glycerols; MALDI, matrix assisted laser desorption; MG, Meibomian glands; MGS, Meibomian gland secretions; MS, mass spectrometry; MW, molecular weight; NMR, nuclear magnetic resonance spectroscopy; NP-HPLC, normal phase HPLC; OAHFA, (O-acyl)-omega-hydroxy fatty acids; OCC, open column chromatography; PC, phosphatidyl choline; PE, phosphatidylethanolamine; PL, phospholipids; PS, phosphatidylserine; Q-TOF MS, time-of-flight tandem mass spectroscopy; RP HPLC, reverse phase HPLC; RS, Raman spectroscopy; RT, retention time; SG, shotgun; SM, sphingomyelin; Sql, squalene; ST, sterols; TAG, triacyl glycerols; TBUT, tear film breakup time; TF, tear film; TFLL, tear film lipid layer; TLC, thin layer chromatography; UV, ultraviolet; VLC-FA, very long chain fatty acids (between C_{22} and C_{28}); WE, wax esters.

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1. Introduction

Our vision is an invaluable gift that allows us to navigate the world that surrounds us. Through vision we learn and recognize each other. More than 80% of information that we receive from the outside world, is obtained through vision. Thus, maintaining a good vision is critical for our survival in the ever-changing world, while its deterioration causes many problems ranging from a minor nuisance to an insurmountable obstacle. The health of ocular surface is critical for acute vision and, therefore, needs to be monitored, maintained, or restored in case of an ocular disease or a developing pathological condition. One such condition is *dry eye* (DE) [1] There is no doubt that DE is a potentially debilitating condition (or disease) whose symptoms range from minor to severe, in which case the patients are facing constant difficulties in everyday living. The onset of DE is invariably linked to a quick deterioration of an ocular surface structure called *tear film* (TF). Normally, TF is a continuous, complex, multilayered structure (Fig. 1) composed of water, inorganic salts, carbohydrates, lipids, and proteins that covers the entire exposed ocular surface and fulfils the protective, lubricatory, nutritional, and antimicrobial roles [2,3]. One of the main functions of TF is to keep the delicate corneal, conjunctival, and epithelial cells moist. Being a very thin structure, TF of an open eye is relatively unstable, and within several seconds breaks up thus exposing the underlaying ocular structures such as cornea and conjunctiva (Fig. 2). In healthy individuals with no ocular surface pathologies, TF is stable for 10 s or more, while in DE patients its intactness lasts for less than 6 s [4,5]. This parameter is routinely called TF break-up type (TBUT or, sometimes, TFBUT) and is a common diagnostic tool regularly used in ophthalmic practice to diagnose DE. Short TBUT leave the ocular surface exposed to the air, which irritates the cornea and causes excessive blinking and tearing. In severe cases the ocular surface desiccates and an irreversible damage to the cornea may occur [6].

TF originates primarily from two different sources – lacrimal (or lachrymal) glands that produce *aqueous tears* (AT) and Meibomian glands (MG) which are also known as the palpebral glands, tarsal glands, or tarsoconjunctival glands. MG are a variety of sebaceous

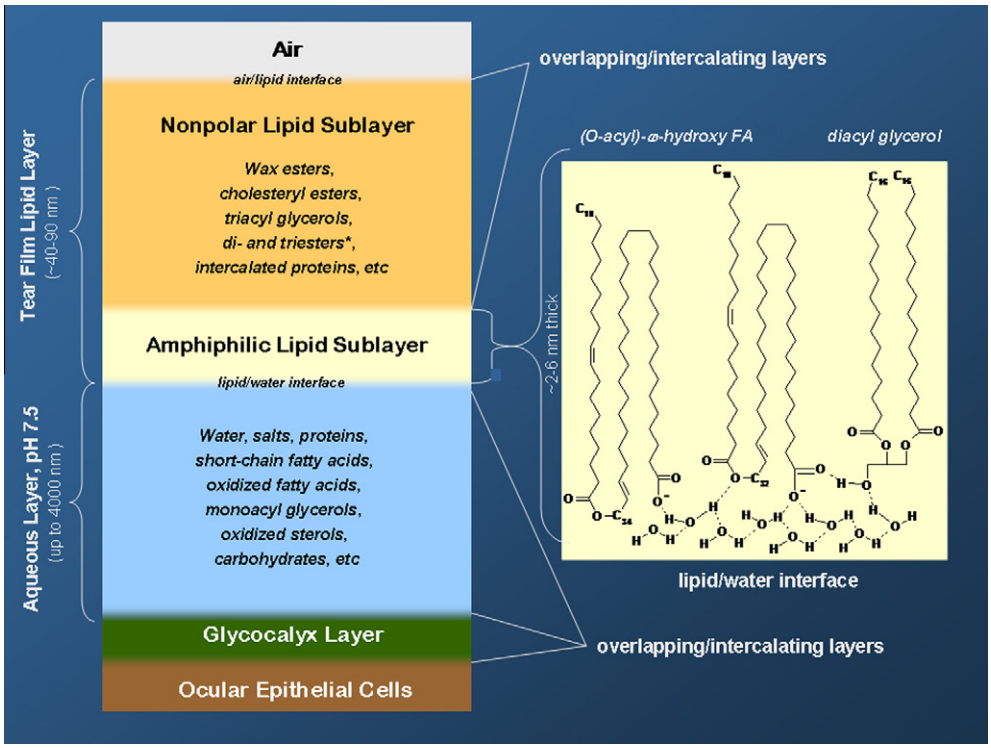

Fig. 1. Tear film and tear film lipid layer. (reprinted from [43] with permission)