Analysis of Meibum and Tear Lipids

Andrew D. Pucker, OD, MS,[1] and Jason J. Nichols, OD, MPH, PhD[2]

ABSTRACT The meibum is a lipid-rich secretion that is the primary component of the external layer of the tear film. The meibomian glands produce the meibum, and meibomian gland dysfunction can lead to degradation of the tear film. Such dysfunction can result in ocular irritation, inflammation, and clinical disease. Understanding this relationship is critical to preventing ocular disease; therefore, a search of peer-reviewed literature focusing on the collection, quantification, and analysis of normal and abnormal meibum and tear lipids was conducted. Numerous collection and quantification techniques are described, including their advantages and disadvantages. Studies indicate that the meibum and tear lipids consist of a large array of polar and nonpolar lipids; individual lipids or their classes can be correlated to pathology. Significant amounts of lipids are deposited on contact lenses, depending on the nature of their polymer chemistry. These findings taken together indicate that normal meibum and tear lipids are essential for normal ocular health. Additional studies are required to provide a better understanding of the meibum and tear film biomolecules so that more effective treatments for blepharitis, dry eye disease, and tear film-related contact lens complications can be devised.

KEY WORDS contact lenses, lipid analysis, lipid collection, lipid quantification, meibomian gland, meibomian gland dysfunction, meibum, silicone hydrogel contact lens, tear film

Accepted for publication July 2012.

From [1]The Ohio State University College of Optometry, Columbus, Ohio, and [2]The University of Houston College of Optometry, Houston, Texas, USA.

Grant Support: None

Neither author has any commercial or proprietary interest in any concept or product discussed in this article. Dr. Nichols has received research funding from Inspire, Alcon, CIBA Vision and Vistakon in the past year.

Single-copy reprint requests to Jason J. Nichols, OD, MPH, PhD (address below).

Corresponding author: Jason J. Nichols, OD, MPH, PhD, The University of Houston, 505 J. Davis Armistead Building, Houston, TX 77204-2020. Tel: 713-743-2471. E-mail address: jnichols@optometry.uh.edu

Published by Elsevier Inc. *The Ocular Surface* ISSN: 1542-0124. Pucker AD, Nichols JJ. Analysis of meibum and tear lipids. 2012;10(4):230-250.

I. INTRODUCTION

Although tear lipids have been studied for generations, the term *meibum* was not used to refer to the fatty layer of the human tear film until 1981.[1] Much has been learned since the mid-1900s, but much is still unknown about this critical lipid layer that is a vital aspect of tears. Some basic facts are apparent. The meibomian glands are large sebaceous holocrine glands with a simple, branched, acinar structure.[2] They contain acinar cells,[3] which produce a large number of lipids and proteins.[4-7] Once these cells mature, they lyse, and their cellular remains and contents are secreted.[3] The meibomian glands are located in the tarsal plates of the upper and lower eyelids, and each gland has a single duct whose orifice opens onto the eyelid margin.[2] The upper eyelid typically has 30-40 meibomian glands, and the lower eyelid typically has 20-30 meibomian glands.[8] The meibomian glands are significantly different from other holocrine glands found in the skin (eg, sebaceous glands),[9,10] and they are controlled by parasympathetic innervations and androgens.[11,12]

Polar lipids (glycerophospholipids, sphingophospholipids, and ω-hydroxy fatty acids) and nonpolar lipids (wax esters, cholesterol esters, diesters, free sterols, monoglycerides, diglycerides, triglycerides, free fatty acids, and hydrocarbons) are produced by the meibomian glands, and this secretion is termed meibum.[1,5,6,9,13-30] The meibum is excreted from the meibomian glands by the contraction of the orbicularis oculi.[31] Once expressed, the melting point of meibum is between 22.5°C and 45°C, and it is liquid or gel-like under normal conditions.[9,20,31,32] In health, the meibum is released from the glands onto the eyelid, and from there it enters the external lipid layer of the tear film.[33] The lipid layer has been reported to be as thin as 15 nm and as thick as 200 nm, with great variation in between these values.[34-38] Thinner lipid layers have been correlated to tear film instability and evaporation.[34,37]

The external lipid layer is made up of two segments: the outer nonpolar layer and the inner polar layer. The inner polar layer makes up one to three molecules of the layer's thickness; the polar layer creates tear film stability by allowing for an interphase between the aqueous tears and mucins and the nonpolar lipid layer.[38,39] The nonpolar lipids retard aqueous tear evaporation, which inhibits ocular inflammation induced by evaporation and increases tear osmolarity.[37,40,41]

OUTLINE

Abbreviations

GC	Gas chromatography
HPLC	High pressure liquid chromatography
IR	Infrared
LC	Liquid chromatography
m/z	Mass-to-charge ratio
MGD	Meibomian gland dysfunction
MS	Mass spectroscopy
NCA	Normal subjects with cholesterol esters absent
NCP	Normal subjects with cholesterol esters present
NMR	Nuclear magnetic resonance
PC	Phosphatidylcholine
PE	Phosphatidylethanolamine
TLC	Thin layer chromatography

Tiffany determined that there is "no typical" meibum composition, meaning that there is a great variation among normal subjects,[42] but many investigators have found significant differences between the meibum obtained from normal subjects and that obtained from subjects with blepharitis and/or dry eye disease.[16-18,20,26,39,43-52] These differences may disrupt the lipid layer of the tear film, leading to tear film evaporation. In 1961, Mishima and Maurice found that the meibomian glands produce the lipids that are responsible for maintaining tear film stability, while the other ocular glands do not have an effect on preventing tear film degradation (lacrimal, Harderian, goblet cells).[53] Craig and Tomlinson found that when the lipid layer is stable and intact, evaporation is retarded regardless of the lipid layer's thickness.[37] Iwata et al found that the evaporation rate of tears from the ocular surface increases fourfold with the removal of the tear film lipid layer.[41] King-Smith et al and Craig and Tomlinson also found that fast tear film thinning is correlated to thin lipid layer thickness, whereas thick lipid layers are correlated to slow tear film thinning.[37,38] These data alone make it clear that the lipid layer is vital for a stable tear film and prevention of dry eye disease.

In a literature review, Foulks suggested that dry eye disease symptoms significantly increase with a poor tear film lipid layer and that these symptoms are likely linked to an increase in tear film osmolarity, which occurs with tear film evaporation.[54] In a related study, King-Smith et al determined that tear evaporation is the likely cause of tear film breakup (likely rates between 3 and 7 micrometers/min), which could theoretically lead to tear osmolarities of 900 mOsm/L or more and could also significantly increase ocular inflammation.[40,55] This hypothesis is supported clinically by the findings of Shimazaki et al, who determined that sodium fluorescein staining is correlated with meibomian gland obstruction and/or dropout, which indicates that meibomian gland disease can cause changes to the ocular surface.[56]

The lipids produced by the meibomian glands have been analyzed for the better part of a century, and this pursuit