Four Characteristics and a Model of an Effective Tear Film Lipid Layer (TFLL)

P. Ewen King-Smith, PhD,[1] Melissa D. Bailey, OD, PhD,[1] and Richard J. Braun, PhD[2]

ABSTRACT It is proposed that a normal, effective tear film lipid layer (TFLL) should have the following four characteristics: 1) high evaporation resistance to prevent water loss and consequent hyperosmolarity; 2) respreadability, so it will return to its original state after the compression-expansion cycle of the blink; 3) fluidity sufficient to avoid blocking secretion from meibomian glands; 4) gel-like and incompressible structure that can resist forces that may tend to disrupt it. These characteristics tend to be incompatible; for example, lipids that form good evaporation barriers tend to be disrupted by compression-expansion cycles. It is noted that clues about the function and organization of the TFLL can be obtained by comparison with other biological lipid layers, such as lung surfactant and the lipid evaporation barrier of the skin. In an attempt to satisfy the conflicting characteristics, a "multilamellar sandwich model" of the TFLL is proposed, having features in common with the skin evaporation barrier.

KEY WORDS blinks, evaporation resistance, evaporative dry eye, lipid layer structure, lipid monolayers, meibomian gland dysfunction, skin lipid barrier, X-ray analysis

I. COMPARISON OF BIOLOGICAL LIPID LAYERS

Deficiency of the tear film lipid layer (**TFLL**) is the basis of evaporative dry eye,[1] and therefore an understanding of this layer is fundamental to the diagnosis, management, and treatment of dry eye disorders. Here, it is proposed that a normal, effective TFLL should have the following four characteristics:

1. It should have a high evaporation resistance to prevent water loss and consequent hyperosmolarity.
2. It should have good respreadability, so that the lipid layer returns to its original state after the compression-expansion cycle of the blink.
3. It should be sufficiently fluid that it does not block secretion from meibomian glands.
4. It should be gel-like and incompressible so that it can resist forces that may tend to disrupt it.

Some of these characteristics tend to be incompatible. The gel-like, incompressible property (characteristic 4) would evidently tend to be at odds with fluidity (characteristic 3). Additionally, monolayers having high evaporation resistance (characteristic 1), such as saturated fatty acids and their esters,[2] tend to show poor respreadability (characteristic 2).[3,4] Thus, lipid layer composition and structure must involve compromise and trade-off between apparently conflicting characteristics.

Rantamaki et al discussed how a comparison of two biological lipid layers, namely, the TFLL and lung surfactant, can lead to insights into the relation of their function and composition.[5] Both layers are "respreadable" in that they withstand compression-expansion cycles, either from breathing or from blinking. However, evaporation resistance is important for the TFLL, but not for the lung lipid layer; given the small size of the alveoli, the enclosed air would rapidly become saturated, even if the evaporation resistance were comparable to that of the tear film lipid layer. Here, we extend this approach to the comparison of biological lipid layers involved in the prevention of evaporation, as summarized in Table 1.

A. Function.

Table 1 compares function and composition for six different biological lipid layers. Although the TFLL and lung surfactant are respreadable and withstand compression-expansion cycles, the other four layers are not subjected to such cycles. However, they, like the TFLL, are all thought to be barriers to evaporation,[6-10] as indicated in Column 3 of Table 1.

Accepted for publication May 2013.

From the [1]College of Optometry, Ohio State University, Columbus, Ohio, and [2]Department of Mathematical Sciences, University of Delaware, Newark, Delaware, USA.

Financial support: R01 EY017951 (King-Smith), NSF 0616483 and 1022706 (Braun).

The authors have no proprietary or commercial interest in any product or concept described in this article.

Single-copy reprint requests to P. Ewen King-Smith, PhD (address below).

Corresponding author: P. Ewen King-Smith, PhD, College of Optometry, Ohio State University, 338 West 10th Ave., Columbus, Ohio 43210, USA. Tel: 614-292-3939. E-mail address: king-smith.1@osu.edu

 The Ocular Surface ISSN: 1542-0124. King-Smith PE, Bailey MD, Braun RJ. Four characteristics and a model of an effective tear film lipid layer (TFLL). 2013;11(4):236-245.

OUTLINE

I. Comparison of Biological Lipid Layers
   A. Function.
   B. Composition.
II. Role of Long, Saturated Hydrocarbon Chains in Evaporation Resistance of Meibum
   A. In a normal eye, the lipid layer has a high evaporation resistance compared to lipid monolayers.
   B. Evaporation resistance increases exponentially with saturated chain length.
   C. Meibum contains long, saturated hydrocarbon chains.
III. Spreadability of Lipid Layer after Blink
   A. Some lipids collapse irreversibly on compression and do not return to their original state after expansion.
   B. Other lipids return close to their original states after a compression/expansion cycle.
IV. Viscosity of Meibum
   A. Unsaturation and branching of hydrocarbon chains affect melting temperature of lipids.
   B. Meibum contains unsaturated and branched hydrocarbon chains.
V. "Dewetting" of the Lipid Layer with Excessive Fluidity of Meibum
   A. The normal lipid layer resists "leveling" (smoothing) by surface tension, indicating a gel-like structure.
   B. Dewetting of the lipid layer can occur when the lipid layer is unusually fluid.
VI. Conclusions — Implications for Lipid Layer Structure: A Multilamellar Sandwich Model
VII. Appendix: Evaporation Resistance of the Tear Film Lipid Layer

B. Composition.

The TFLL and lung surfactant layer have some similarity of composition in that they both contain polar lipids (such as phospholipids)[11-15] and surfactant proteins, particularly the hydrophobic proteins SP-B and SP-C.[13,15-16] These surfactant proteins are thought to have a role in the respreading of lung surfactant during the breathing cycle,[13,15] and while their function in the tear film is unknown, they may play a corresponding role in the blink cycle.

Whereas the main components of lung surfactant are polar phospholipids,[13,15] the other five layers, which are all thought to be evaporation barriers, are composed mainly of nonpolar lipids.[6-10] There is considerable variation in the type of nonpolar lipids in different types of layer (Table 1). Whereas wax and cholesteryl esters are the main nonpolar lipids in the TFLL, other types of nonpolar lipids are common in the other four evaporation barrier layers. However, all five evaporation barriers have one striking feature in common; they all contain many, very long (≥19 carbons) saturated hydrocarbon chains.[6-10] The saturated chains in lung surfactant, which does not function as an evaporation barrier, have generally fewer than 19 carbons. The corresponding entries in Table 1, Column 5 match those in Column 3, to emphasize the correlation between saturated chain length and evaporation barrier function.

II. ROLE OF LONG, SATURATED HYDROCARBON CHAINS IN EVAPORATION RESISTANCE OF MEIBUM

A. In a normal eye, the lipid layer has a high evaporation resistance compared to lipid monolayers.

"Evaporation resistance" is a measure of the ability of a surface layer to retard evaporation of water. It is described

Table 1. Comparison of different biological lipid layers by function and major components

Biological lipid layer	Respreadable?	Evaporative barrier?	Major components	Saturated hydrocarbon chain length ≥ 19?	References
Tear film lipid layer (TFLL)	Yes	Yes	Wax esters, Cholesteryl esters, Polar lipids, Surfactant proteins	Yes	11,12,22
Lung surfactant	Yes	No	Phospholipids Surfactant proteins	No	13,15
Human skin lipid	No	Yes	Ceramides Cholesterol Fatty acids	Yes	8,9
Skin lipid secretions (tree frog)	No	Yes	Wax esters, Triglycerides	Yes	10
Plant lipid layer (cuticle)	No	Yes	Hydrocarbons Ketones Alcohols	Yes	7
Arthropod lipid layer	No	Yes	Hydrocarbons	Yes	6