Interfacial Phenomena and the Ocular Surface

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ABSTRACT Ocular surface disorders, such as dry eye disease, ocular rosacea, and allergic conjunctivitis, are a heterogeneous group of diseases that require an interdisciplinary approach to establish underlying causes and develop effective therapeutic strategies. These diverse disorders share a common thread in that they involve direct changes in ocular surface chemistry as well as the rheological properties of the tear film and topographical attributes of the cellular elements of the ocular surface. Knowledge of these properties is crucial to understand the formation and stability of the preocular tear film. The study of interfacial phenomena of the ocular surface flourished during the 1970s and 1980s, but after a series of lively debates in the literature concerning distinctions between the epithelial and the glandular origin of ocular surface disorders during the 1990s, research into this important topic has declined. In the meantime, new tools and techniques for the characterization and functionalization of biological surfaces have been developed. This review summarizes the available literature regarding the physicochemical attributes of the ocular surface, analyzes the role of interfacial phenomena in the pathobiology of ocular surface disease, identifies critical knowledge gaps concerning interfacial phenomena of the ocular surface, and discusses the opportunities for the exploitation of these phenomena to develop improved therapeutics for the treatment of ocular surface disorders.

KEY WORDS dry eye disease, evaporation, glycocalyx, interfacial phenomena, mucins, microvilli, rheology, surface energy, tear film, tear film lipid layer

I. INTRODUCTION

Surfaces or interfaces are the thin boundary regions separating macroscopic phases. Knowledge of the phenomena occurring at these interfaces is essential, since the properties of materials near these regions differ profoundly from those in the bulk of the substance and the interactions of matter with its environment depend on these *interfacial* characteristics.[1] Most of the reactions and interactions in biology occur at interfaces, bringing attention to the importance of interfacial science for the advancement of knowledge and the development of technology in biology and medicine.[2]

For this review of the interfacial phenomena of the ocular surface, we define the "ocular surface" as comprising all cellular constituents that cover the exposed regions of the eye (corneal epithelium, limbus, conjunctiva), as well as the lid margin and the tear film, a complex fluid phase (Figure 1). As detailed below, our use of the term "ocular surface" thus encompasses a complex mixture of interfaces possessing varying degrees of distinct borders.

The earliest written record of tears dates from the fourteenth century BC, from the Ras Shambra clay tablets found in Syria containing a poem about the response of the virgin goddess Anat to the death of her brother Baal, when she "drinks her tears like wine."[3] Among the functions of the tear film are the delivery of nutrients and control of oxygenation of the cornea, the physical protection by the trapping and removal of particles, and the antimicrobial protection by some tear components.[4] The tear film components have a glandular origin (lacrimal and meibomian glands) and a cellular origin (goblet and epithelial cells), and its main constituents are water, proteins, electrolytes, mucins, and insoluble

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OUTLINE

lipids.[5-7] It is difficult to arrive at a consensus value for the thickness of the tear film for a given species and, surprisingly, no value could be located in the literature for a number of species used in ocular drug development.[8] This difficulty is in part due to the dynamic nature of its thickness profile associated with blinking and its obligatory thinning during the interblink interval. Furthermore, tear film thickness is affected by numerous other factors, including sex, age, and relative humidity.[9] Additionally, the definition of "thickness" of the tear film is complicated by a lack of consensus in the literature as to 1) the best method for determining tear film thickness (with differing approaches yielding differing values), and 2) exactly how cellular surface features such as microvilli and the glycocalyx with intrinsically associated mucin elements are accounted for in the measurement process.[9] Keeping these confounding variables in mind, for the human, there is general agreement that the tear film ranges in thickness between 3-10 μm,[9,10] while for rabbit the range is 7-11 μm.[11-13]

This review is focused on the human tear film with the inclusion of studies involving other species limited to a very small number of commonly employed laboratory and agricultural animals. In the investigation of interfacial properties of the ocular surface, these animals have largely served as specimen donors rather than being used for in vivo investigations. It should be noted that the tear film in general and the interfacial properties of the ocular surface in particular have been markedly understudied from a comparative perspective. There are likely numerous unique adaptations in tear film biology that are yet to be discovered, given the enormous variation in evolutionary history and environmental niches populated by the >50,000 species of vertebrates with whom humans share the planet. Also, studies involving laboratory/agricultural animals are not necessarily transposable to the human condition due to inherent differences in the biology of the ocular surface (tear chemical composition, blink rates,

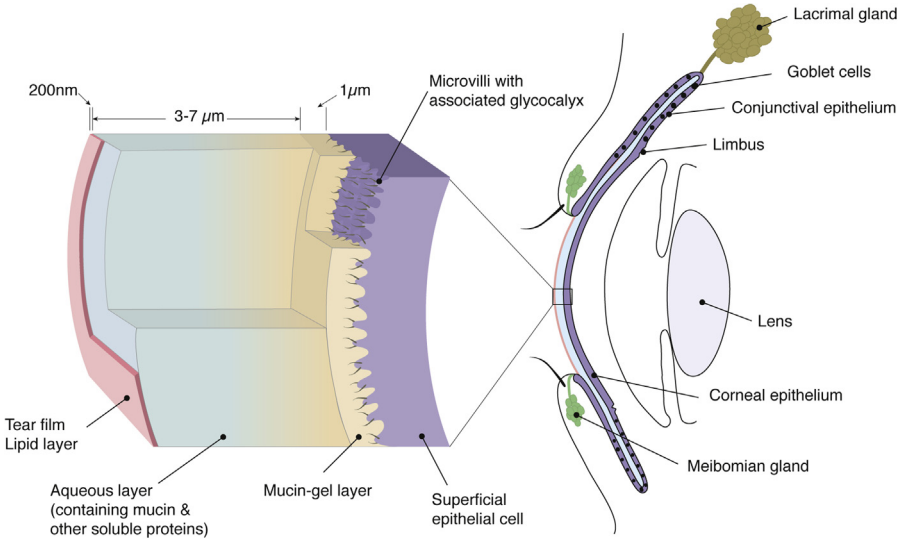

Figure 1. The ocular surface is a complex system that includes a series of interfaces. It is comprised of the superficial cells that line the exposed regions of the eye (corneal epithelium, limbus, and conjunctival epithelium), as well as the lid margin and the tear film. The tear film is a complex multilayered fluid phase. This figure represents the classical three-layered model, composed of a mucin-gel layer adjacent to the epithelial surface, an aqueous layer containing mucin, and other soluble proteins and a thin lipid film on the outermost surface.