

chain) and hydrophilic (headgroup) layers (Lundborg et al., 2018a). Likewise, it may be resistant to both hydration and dehydration because of its lack of exchangeable water between lipid leaflets. It may also be resistant to temperature and pressure changes because of its heterogeneous lipid composition and high cholesterol content, which stabilize gel-like chain packing (Iwai et al., 2012; Lundborg et al., 2018a) and thereby prevent both lateral domain formation and induction of “pores” or nonlamellar morphologies. Further, this bilayer arrangement may account for stratum corneum cell cohesion without advocating specialized intercellular adhesion structures such as desmosomes. The arrangement may hence allow for sliding of stratum corneum cells to accommodate skin bending. Finally, as the interaction between the individual layers of the lipid structure involves only hydrocarbons, the layers may be relatively free to slide with respect to one another, making the lipid structure pliable. The fully extended ceramide bilayer arrangement with high cholesterol content and heterogeneous saturated long-chain lipid composition may thus meet the barrier needs of skin by being simultaneously impermeable and robust.

1.9 CONCLUSION

Terrestrial life was only made possible through the adaptive evolution of a waterproof barrier in the integument of organisms. This barrier is constituted of a uniquely organized lipid structure situated between the cells of the horny layer of the skin. It was recently shown that this lipid structure is organized in an arrangement not previously described in a biological system—stacked bilayers of fully extended ceramides with cholesterol molecules largely associated with the ceramide sphingoid moiety.

The physical state of the skin’s lipid structure is that of a gel phase. Further, the lipid structure is likely formed via a phase transition from cubic-like to stacked lamellar morphology followed by a flip of the constituent lipid components from a folded (hairpin) to an extended (splayed chain) ceramide bilayer conformation.

The skin’s lipid structure is responsible for both the skin’s low permeability to water and other compounds and for the barrier’s robustness to environmental stress, such as hydration and dehydration, temperature and pressure changes, stretching, compression, bending, and shearing.

A validated atomistic MD model of the skin’s lipid structure that may be used for predicting, and potentially computer screening, percutaneous absorption of drugs was recently presented.

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