1 Molecular Structure and Function of the Skin Barrier

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1.1 INTRODUCTION

Terrestrial life was only made possible through the adaptive evolution of a waterproof barrier in the integument of organisms. This barrier is constituted by a uniquely organized lipid structure situated between the cells of the stratum corneum (Blank, 1952; Breathnach et al., 1973; Elias and Friend, 1975) (Figure 1.1).

The lipid structure's molecular organization has been determined in situ with the aid of a novel experimental approach: high-resolution cryo-electron microscopy of vitreous tissue section (CEMOVIS) defocus series combined with molecular dynamics (MD) simulation and electron microscopy (EM) simulation. It is arranged as stacked bilayers of fully extended ceramides with cholesterol largely associated with the ceramide sphingoid moiety (Iwai et al., 2012; Lundborg et al., 2018a) (Figure 1.2).

Recently, a thermodynamically equilibrated atomistic MD model of the skin's lipid structure has been constructed (Figure 1.2b) and validated against high-resolution CEMOVIS data from near-native skin using EM simulation (Lundborg et al., 2018a) (Figure 1.3). The atomistic MD model of the skin's lipid structure may be used for predicting, and potentially computer screening, percutaneous absorption of drugs and other chemical compounds (Lundborg et al., 2018b).

What follows is a brief account of the structure–function relationships of the human skin's lipid structure.

1.2 SKIN LIPID COMPOSITION AND PHASE STATE

The skin's lipid structure consists of a heterogeneous mixture of saturated, long-chain ceramides (of which about 15% are acyl-ceramides), free fatty acids, and cholesterol in a roughly 1:1:1 molar ratio (Wertz and Norlén, 2003). More than 300 different species have been identified in the ceramide fraction alone (Masukawa et al., 2009).