IR Spectroscopy and Imaging in Skin Biophysics: Barrier Formation Kinetics and Lateral Diffusion across the Stratum Corneum

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(1) Barrier formation kinetics:

The primary barrier to permeability in human skin resides within the ~15 μm thick outermost layer, the stratum corneum (SC), formed from anucleated corneocytes embedded in a lamellar lipid matrix. Wide angle X-ray diffraction and IR spectroscopy studies of human SC reveal a substantial fraction of lipid orthorhombic chain packing. Fatty acids are important for formation of this phase. Thermotropic studies revealed the occurrence of an orthorhombic → hexagonal packing transition near the physiological temperature of skin. This transition is thermally followed by a hexagonal→disorder transition under non-physiological conditions. Substantially less well elaborated than the SC structure studies are investigations of the kinetics and mechanisms of the formation of lamellar structures, lipid packing motifs, and domain formation. Such information is of interest in a variety of fundamental areas in skin biophysics. Elucidation of the kinetic mechanism of lipid domain formation would help define potential pathways for permeation of hydrophobic species as well as to possibly provide clues as to why such a variety of ceramides and additional lipophilic species are present in skin. In addition, understanding the formation and dissipation kinetics of domains formed from particular ceramide and fatty acid species would aid in defining biological processes such as epidermal desquamation, which involves degradation of layered structures in the intercellular spaces. We will report on the results of IR kinetic studies in a standard three component model for the human SC consisting of equimolar NFA ceramide/stearic acid/cholesterol. Quenching experiments from a disordered state at 90C to physiological temperatures followed by time-dependent IR measurements provide the following sequence of events leading to the formation of lamellar structure: (a) Formation of ordered H-bonds in the ceramide polar regions (0-4hr), (b) ordering of bent structures (0-7 hr) and orthorhombic phase formation (0-3hr) in the ceramide chain regions, and (c) slower (4-8 hr) formation of hydrogen bonded dimers and extensive orthorhombic domains in the stearic acid component. The resultant stearic acid domains constitute the initial development of lamellar structure in these simple skin models.

(2) Lateral Diffusion across the Stratum Corneum

The majority of percutaneous penetration/permeation studies have focused on the ability of a substance to cross the stratum corneum (SC) barrier without considering competitive spreading and lateral diffusion processes that may take place simultaneously on the surface and within the SC, respectively. Along with these processes, the potential exists for the formation of a drug depot or reservoir in the SC which may have important consequences regarding dosing and controlled or timed-release. Lateral diffusion within the top layers of the SC and radial spreading mechanisms along surface furrows or glyphs are poorly defined although this information is of substantial pharmacological, toxicological, and cosmetic importance. In this experiment, we demonstrate the feasibility of mapping lateral spreading/diffusion in human SC with IR imaging. We tracked the spatial distribution and concentration of the common permeation enhancer, oleic acid (OA). In addition to providing temporal and spatial quantitative measures of OA concentration along networked furrows in the SC surface, similar images are generated for relatively glyph-free regions. Since the imaging results do not directly distinguish between OA spreading on the skin surface and that diffusing within the SC, we modeled the concentration profiles using two theoretical frameworks. A range of diffusion coefficients for lateral transport based on Fick's second law along with a paradigm of liquid spreading in V-shaped grooved networks based on Washburn's power law are compared with the imaging data. Although the unique capabilities of IR imaging permit us to monitor perturbations in endogenous component structure induced by permeants, alterations were not detected in the experiments with OA. In contrast, endogenous structural perturbations were demonstrated with similar IR imaging experiments of DMSO lateral diffusion.