Table 2.1 Evolution in Understanding of the Stratum Corneum

1.	Disorganized, nonfunctional layer in various stages of shedding
2.	Homogeneous film—the "plastic wrap" model
3.	Lipid–protein compartmentalization—the "two-compartment" model
4.	Metabolically active tissue with ongoing modulations in structure and composition

earlier that organic solvent extraction destroyed the water-holding capacity of SC (12), Middleton showed that pulverization was as effective as solvent extraction, thereby providing evidence that SC lipids might be organized as osmotically active membranes within the SC. Shortly thereafter, the existence of separate lipophilic versus hydrophilic pathways of percutaneous absorption was suggested from physicochemical studies (13).

The destruction of stratum corneum during processing for routine histological and ultrastructural preparations obscured further advances until the early 1970s, when the cells of the SC were shown by frozen sectioning to comprise tightly arrayed, polyhedral structures in vertical, interlocking columns (2–4). The initial awareness of lipid–protein segregation to specific tissue compartments came with freeze-fracture replication, which showed, for the first time,

Table 2.2 Lines of Evidence for Lipid–Protein Compartmentalization in the Stratum Corneum

Pulverization destroys the water-holding capacity of SC (11).
Hydrophilic versus lipophilic substances cross separate SC pathways (13).
Freeze-fracture reveals lipid lamellae in SC interstices (5–7).
Frozen sections display neutral lipids in SC interstices (6).
SC can be dispersed into individual cells with organic solvents (14, 15).
Isolated SC membrane sandwiches account for most SC lipids (16).
X-ray diffraction shows ordered lipids in isolated SC membranes (17).
Catabolic enzymes colocalize with lipids in SC interstices (18–20).