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**Hydration effects on skin microstructure as probed by high-resolution cryo-scanning electron microscopy and mechanistic implications to enhanced transcutaneous delivery of biomacromolecules.**

*Tan G, Xu P, Lawson LB, He J, Freytag LC, Clements JD, John VT.; J Pharm Sci. 2010 Feb;99(2):DOI: 10.1002/jps.21863.2010: 730-40.*

### **ABSTRACT**

Although hydration is long known to improve the permeability of skin, penetration of macromolecules such as proteins is limited and the understanding of enhanced transport is based on empirical observations. This study uses high-resolution cryo-scanning electron microscopy to visualize microstructural changes in the stratum corneum (SC) and enable a mechanistic interpretation of biomacromolecule penetration through highly hydrated porcine skin. Swollen corneocytes, separation of lipid bilayers in the SC intercellular space to form cisternae, and networks of spherical particulates are observed in porcine skin tissue hydrated for a period of 4-10 h. This is explained through compaction of skin lipids when hydrated, a reversal in the conformational transition from unilamellar liposomes in lamellar granules to lamellae between keratinocytes when the SC skin barrier is initially established. Confocal microscopy studies show distinct enhancement in penetration of fluorescein isothiocyanate-bovine serum albumin (FITC-BSA) through skin hydrated for 4-10 h, and limited penetration of FITC-BSA once skin is restored to its natively hydrated structure when exposed to the environment for 2-3 h. These results demonstrate the effectiveness of a 4-10 h hydration period to enhance transcutaneous penetration of large biomacromolecules without permanently damaging the skin.