Molecular dynamics and barrier property of stratum corneum in the presence of different molecules named as penetration enhancers

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Despite the enormous potential for pharmaceutical applications, the molecular details of the changes in the stratum corneum (SC) associated with high permeability are still not fully understood. There are many candidates of compounds that may facilitate transdermal drug delivery, called "penetration enhancers" including unsaturated hydrocarbons, lipids, monoterpenes, water or apolar solvents. These different molecules likely influence SC molecular components in very different ways. The aim of the present study is to characterize the molecular effect of different classes of molecules used as penetration enhancers on SC lipid and protein components.

At normal relative humidity and ambient temperature, the main fraction of SC lipid and protein components are solid and highly ordered, while there is a very minor co-existing fraction that is fluid/mobile. Changes in this minor fluid fraction is inherently difficult to detect in experimental studies, however, it is considered crucial to SC barrier and mechanical properties. Through recent developments, Polarization Transfer Solid-State NMR (PT ssNMR) method together with almost complete peak assignment of SC components permits the detection of small changes in the dynamics of the minor fluid lipid and protein components. Simultaneously it gives the information on the major fraction of solid components in the same intact SC sample. This method can provide molecular-level resolution to differentiate carbon segments of the lipid acyl chains, ceramide headgroup and cholesterol of the lipid fraction. Carbons of the amino acids in the terminals and the cores of keratin filaments can also be distinguished. In the present study, we use this NMR method to distinguish the effects of different classes of penetration enhancing molecules (monoterpenes, fatty acids, surfactant, Azone, and small polar compounds) on the fluidity in SC lipid and protein components. We study SC at different hydration levels corresponding to SC in ambient air and hydrated or occlusion conditions. The NMR studies are complemented with diffusion flow-through cell experiment that provides quantitative information on the barrier property. By correlating the effects on SC molecular components and SC barrier function, we aim at depended understanding of diffusional transport in SC and how this is related to the fluidity of the SC molecular components.

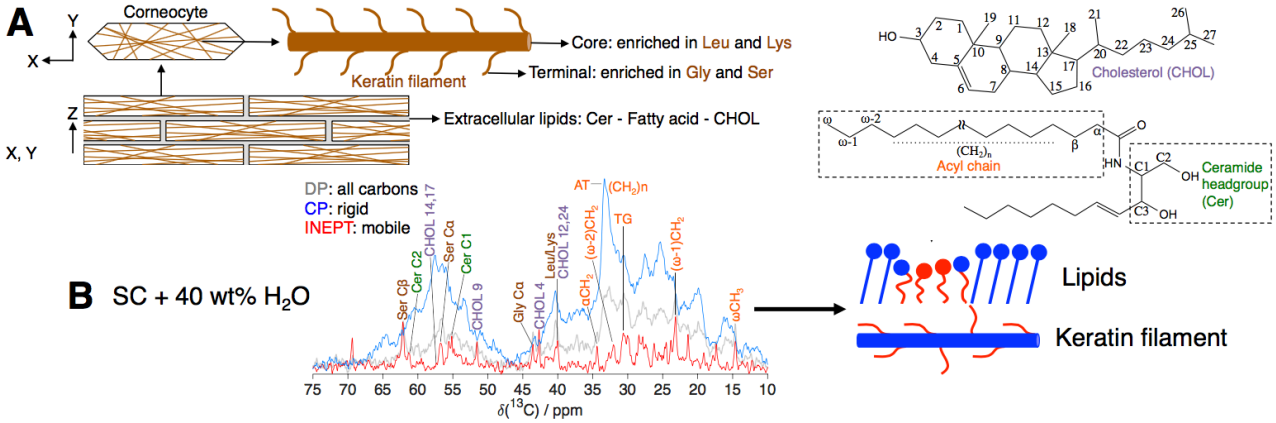

Figure 1 (A) The schematics illustrate the brick-and-mortar model of SC with corneocytes filled with keratin filaments, surrounded by a multilamellar lipid matrix. (B) ^{13}C MAS NMR spectra (DP: grey, CP: blue, INEPT: red) of the SC with 40 wt% water shown together with schematic interpretations of the molecular mobility of the SC protein and lipid components.

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