Study of transdermal permeation of large molecules by coarse-grained molecular dynamics simulation

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Abstract

Skin permeation of large hydrophilic molecules remains a challenge. The barrier function of mammalian skin is mainly attributed to the stratum corneum (SC), the outer protective layer, consisted by flat dead cells filled with keratin and surrounded by lipid bilayers. Within the SC, the lipid bilayers are the major responsible for the skin impermeability to relatively large compounds (molecular weight over 500 Da).

The stratum corneum and the skin permeation phenomena can be study by molecular dynamics simulation (MD). Lipid bilayers are studied by MD for a long time, but the most studied ones are cell membranes. There are a few studies on membranes resembling the SC lipids, and even fewer focused on skin permeation. We have developed a membrane model to be identical to the SC lipid bilayers. The composition of the membrane was based in previously reported values for young-normal skin samples and in accordance with previously reported simulations: ceramide-2, lignoceric acid, cholesterol and cholesterol sulphate. This model was used to study skin permeation of large molecular aggregates. The simulations were in accordance with experimental results, and were a valuable tool to understand the mechanism responsible for the transdermal permeation of such large aggregates.