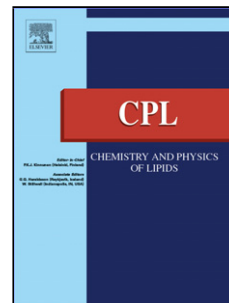


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The effect of non-deuterated and deuterated isopropyl myristate on the thermodynamical and structural behavior of a 2D *Stratum Corneum* model with Ceramide [AP]

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Highlights

- The effect of deuterated and non-deuterated isopropyl myristate on the SC lipid matrix is studied in Langmuir monolayers.
- The synthesis of deuterated IPM was successfully performed.
- The fluidizing effect of IPM is weak, even if certain miscibility with the SC lipids has been evidenced.
- Using the racemic CER[AP] or the natural D-form leads to different miscibility properties with IPM.
- The coupling between the alkyl chains changes if deuterated IPM is used.
- Deuteration of IPM improves its miscibility with the SC model.

Abstract:

Isopropyl myristate (IPM) is a widely used penetration enhancer in pharmaceutical formulations, however, its mechanism of action on a molecular scale is still not completely understood. Previous work using a quaternary *Stratum Corneum* (SC) lipid model in bulk suggested the incorporation of isopropyl myristate into the SC lipid matrix, phase separation, and perturbation of the multilamellar lipid assembly. Here, we used 2D Langmuir monolayers of a ternary SC lipid model, containing ceramide AP C18:18, stearic acid and cholesterol in a molar ratio of [1:1:0.7], respectively, to shed light on the mechanism of action of this important lipophilic penetration enhancer. To do so, the synthesis of chain deuterated isopropyl myristate was successfully performed in order to study the different coupling possibilities between the hydrogenated and deuterated IPM and the alkyl chains of the SC molecules. Our results indicate that only a small portion of IPM is able to mix with our SC model leading to a limited fluidizing effect (small increase of the wavenumber of CH₂ stretching vibration, increase of the SC layer flexibility), but will be squeezed out at higher lateral pressures. Furthermore, the deuteration of IPM enhances the miscibility with this SC model, probably due to a different coupling between the alkyl chains or the alkyl and deuterated chains. Additionally, using the pure D-form of CER[AP] in the SC model amplifies the obtained results.

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