POSTER ABSTRACT PRESENTATIONS

SESSION TITLE: ADVANCES IN EM TECHNOLOGY AND PROCESSING

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Abstract P-2: Multiscale Molecular Dynamics Simulations of the Skin Membranes as a Tool for the Interpretation of the Transmission Electron Microscopy Images

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Background: Human skin can inhibit chemical penetration which limits the clinical applications of transdermal drug delivery. The stratum corneum (SC) is the primary barrier and organized in lamellar membranes containing the lipids of ceramides (CER), free fatty acids (FFA), and cholesterol (CHOL). One of the most widely used ways to overcome the SC is the addition of chemical penetration enhancers (CPEs) to active ingredients. There are various methods, which have been employed to explore the mechanisms by which CPEs with drugs can change the morphology of SC including transmission electron microscopy. Here, we propose to use multiscale coarse-grained (CG) molecular dynamics (MD) simulations for the interpretation of the images of the SC from the electron microscopy experiments.

Methods: We utilized the MARTINI force field for the CG simulations. We employed the mixed-lipid bilayer model of SC consisting of CER, CHOL, and FFA in a 1:1:1 molar ratio assembled with CHARMM-GUI web-service. The systems of the SC model membrane and various enhancers were simulated in the NPT ensemble with the polarizable water model and the reaction field approach for the long-range electrostatics with the usage of Gromacs 2019.4 software.

Results: The membrane model was validated with standard characteristics: thickness, diffusion of the lipids, order parameters, and density profiles. After, we have added CPEs and active ingredients to the systems: menthol and osthole as control simulations, ethanol with linoleic acid and lidocaine as test simulations. We have observed the membrane desegregation in the case of menthol and osthole formulations similar to the published results while the permeation of lidocaine with ethanol and linoleic acid did not cause the disruption of the membranes but increased its fluidity and permeability properties.

Conclusion: The method of multiscale coarse-grained molecular dynamics simulations can be utilized for the prediction and interpretation of morphology change of SC in addition to various substances.

Key Words: chemical penetration enhancers • stratum corneum • multiscale molecular dynamics simulations • TEM imaging

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