Experimental report

13/09/2022

Proposal: 9-13-1035 **Council:** 4/2021

Title: Configurations of Zwitterionic, Cationic and Nonionic Surfactants in Model Stratum Corneum Membrane Studied by Neutron Diffraction

Research area: Soft condensed matter

This proposal is a resubmission of 9-13-974

Main proposer: Yao CHEN

Experimental team: Zongyi LI
Yao CHEN
Mingrui LIAO
ZEYUAN ZHUANG

Local contacts: Bruno DEME

Samples: Cholesterol
C24 Acid
C14LPC
CER NS C24
dC8EO4
hC8dEO4
dC14hLPC

Instrument	Requested days	Allocated days	From	To
D16	5	5	17/09/2021	22/09/2021

Abstract:

Surfactant is widely used as drug carrier and penetration enhancer due to the amphiphilic property and self-assembly ability. The hydrophobic interaction between the surfactant tail and lipid layers has been accepted to perturb the hydration layer and lipid packing in SC, which enhances the skin permeability. However, how the surfactant interacts with model lipid membrane, especially with its SPP layers, is still not clear yet. In this proposal, the interaction of cationic surfactant, nonionic surfactant and zwitterionic surfactant with model SC membranes is investigated by neutron diffraction to reveal the difference between surfactant types.

Configurations of Zwitterionic, Cationic and Nonionic Surfactants in Model Stratum Corneum Membrane Studied by Neutron Diffraction

RB number: 9-13-1035
PI: Dr. Yao Chen
Beamline: D16
Local contact: Bruno Deme
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Related publications: One paper in preparation and one published: *Journal of Colloid and Interface Science 608* ***(2022)*** *405–415* 406.

Introduction

Skin is a barrier to protect our body from hazardous external environment. Meanwhile, it is also a target for drug delivery because the transdermal routes are non-invasive, easy to self-administrate, easy to improve patient compliance and flexible to provide different release dynamics. One of the greatest challenges for transdermal delivery lies in the limited number of drugs that are amenable to administration by these routes.

To gain a comprehensive understanding of the molecular arrangements for different types of surfactant in the model SC bilayer with neutron diffraction, we propose to investigate the interactions of cationic surfactant C16HAB, nonionic surfactant (C8E4) and zwitterionic surfactant (C14LPC) with model SC membranes. Molecular dynamic (MD) simulation is an important tool for model SC membrane study. Comparing with our previous results of cationic surfactant, our primary simulation results illustrate that, zwitterionic surfactant C14LPC cannot completely become inserted into the SC lipid bilayer, which is proved by the density profiles of the C14LPC molecules. The RDFs show that the cationic quaternary ammonium and the anionic phosphate polar center form two hydration layers outside of the SC bilayer, which is quite different from the one hydration layer of cationic surfactant. Moreover, as for nonionic surfactant, it shows that the whole polar EO chain of C8E4 inserts into the SC bilayer, which even makes the bilayer more condensed and no obvious hydration layer can be observed. These observations are different from the surfactant arrangements in the phospholipid bilayers.

Neutron diffraction experiments

Membrane preparation: Model membrane preparation method is kept the same as in the literature. Equimolar mixture of CHOL, CER and FFA was dissolved in chloroform/methanol (2:1 v/v) solution at a concentration of 10 mg/mL. N-lignoceroylsphingosine (CER NS (C24)) is used as CER, and lignoceric acid (C24) is used as FFA in our experiment.C16HAB, C14LPC and C8E4 at 10.0 mol % of the total lipids are added to the investigating the influence of surfactant on the lipid membrane. The lipids were sprayed on a silicon substrate in an area of 1.2×4.0 cm2 using a sample applicator. The temperature was controlled at ~ 25 ^{o}C and spraying rate was set to 20 µL/min. The solvent was evaporated by a gentle flow of nitrogen during spraying followed by vacuum to completely remove the solvent. 10 mg of lipids in total was sprayed on the substrate. The sample was equilibrated close to the melting temperature at ~70 ^{o}C for ~30 min and gradually cooled down to room temperature. The samples were then hydrated with three different D2O/H2O mixtures, i.e., 8:92, 50:50, and 100:0 (v/v) at 90% relative humidity (RH).

Neutron diffraction results

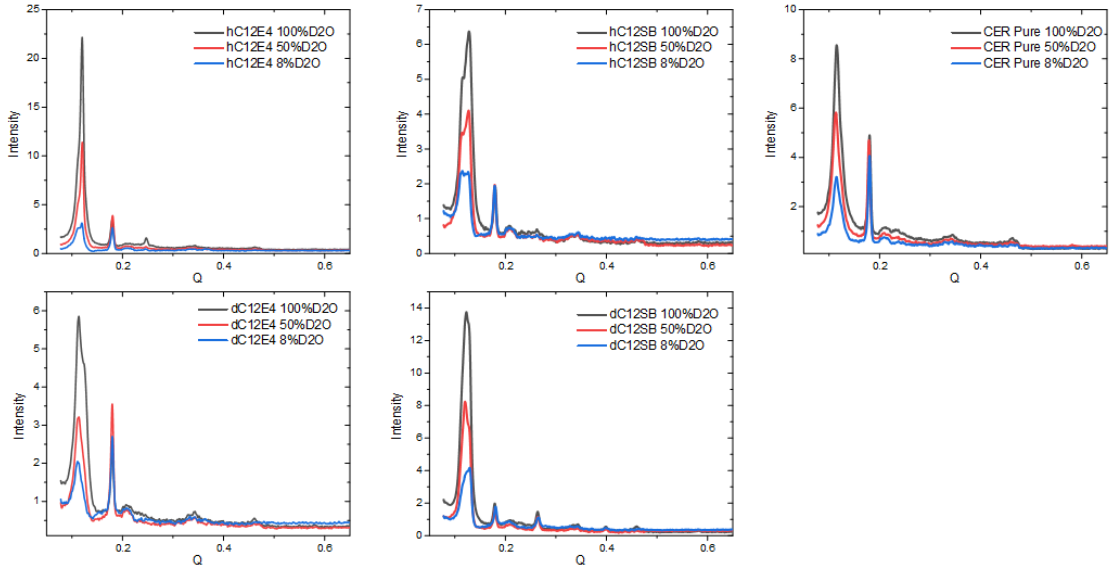

Figure 1. Neutron diffraction one dimensional plot of intensity vs q for the CER/CHOL/FFA membrane and the C/CER/CHOL/FFA mixed membranes hydrated and measured at 100% D_2O, 50% D_2O and 8% D_2O, with each surfactant being controlled at 10 mol%.

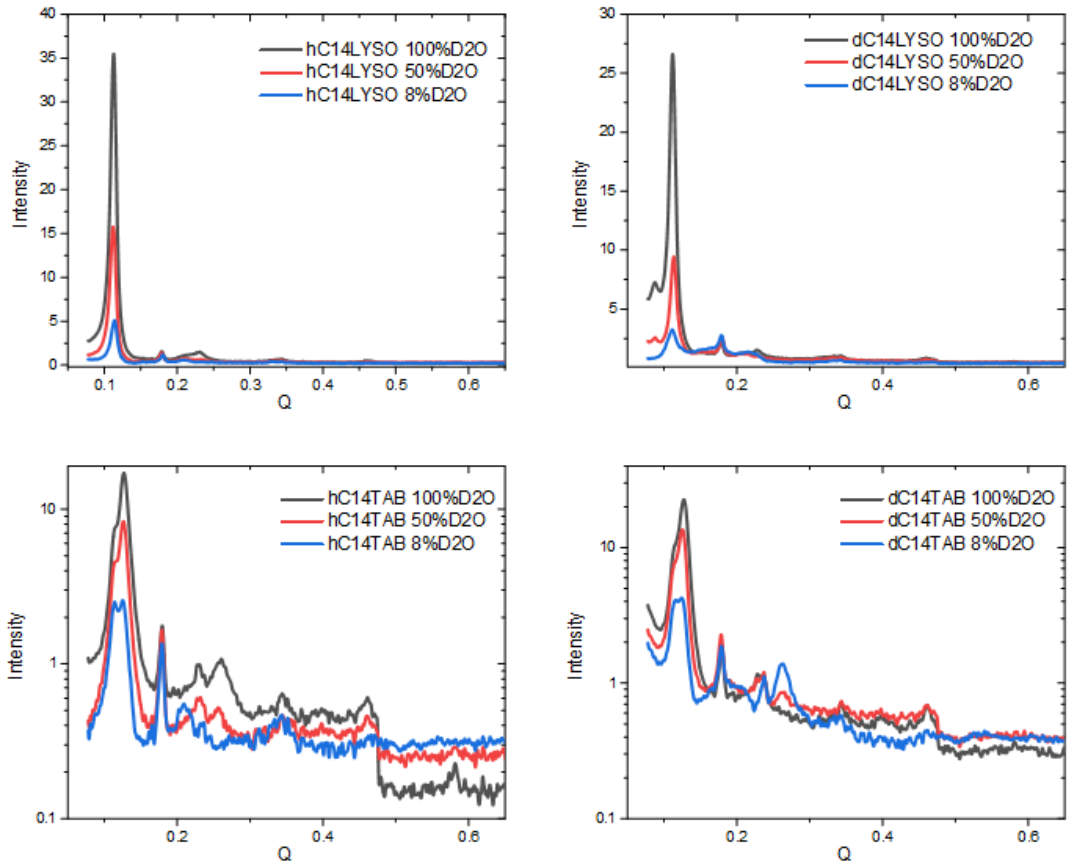

Figure 2. Neutron diffraction one dimensional plot of intensity vs q for t the C14TAB/CER/CHOL/FFA , and C14LYSO/CER/CHOL/FFA mixed membranes hydrated and measured at 100% D_2O, 50% D_2O and 8% D_2O, with each surfactant being controlled at 10 mol%.

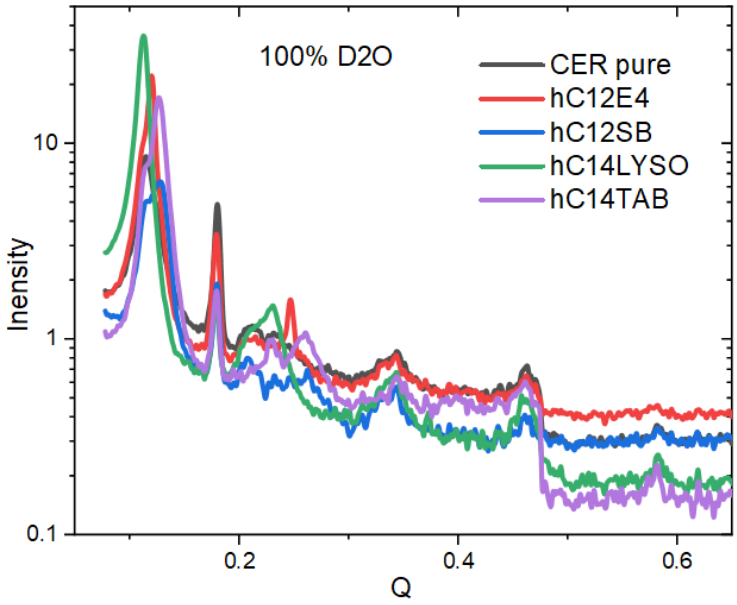

Figure 3. Comparison of the diffraction patterns with the presence of different h-surfactants at 100% D2O.

Summary

We clearly observed the impact of surfactant types on the hydration and repeating distance of the surfactant mixed CER/FFA/CHOL membranes. Nonionic C12EO4 has very little impact on repeating distance, but it spuriously increases the hydration enormously. Zwitterionic surfactant and lipids has huge impact on the repeating distance and largely increase the membrane hydration.