Interactions of detergents with lipid bilayers and monolayers studied by Isothermal Titration Calorimetry and Infrared Reflection Absorption Spectroscopy

Annette Meister, Andreas Kerth, Katja Beyer, Alfred Blume

Martin Luther University Halle-Wittenberg, Institute of Physical Chemistry, Mühlpforte 1, D-06108 Halle, Germany

The use of colloidal vehicle systems based on physiological relevant substances offers a valuable starting-point for the optimisation of drug delivery systems e.g. liposomes. Their stability against detergents depend on a number of factors like the chemical nature and concentration of the used detergent, the chemical structure of the lipids, buffer and pH conditions, and surface charges [1]. Furthermore, mixed lipid/detergent systems play an important role for the investigation of membrane properties and functions as well as the reconstitution and stabilization of membrane proteins [2]. The partitioning of surfactants into lipid bilayer membranes can be followed by isothermal titration calorimetry. This method offers the unique possibility to determine the full set of thermodynamic parameters including partition coefficients from one and the same experiment [1,3].

Lipid monolayers (Langmuir monolayers) often serve as model systems for biological membranes because they essentially represent half of a lipid bilayer membrane. Their interaction with surfactants can be followed by infrared reflection absorption spectroscopy (IRRAS). This is a technique of growing interest providing molecular-level information for various classes of substances (e.g. fatty acids, lipids, surfactants, peptides, and proteins) in Gibbs and in Langmuir monolayers. It monitors the phase transitions occurring in monolayer films at the air-water interface and allows to investigate Gibbs adsorption isotherms of water-soluble amphiphilic substances, such as surfactants.

We studied the interaction of the surfactant sodium dodecyl sulfate (SDS) and the anesthetic dibucain with lipid monolayers of 1,2-dimyristoyl-*sn*-glycero-3-phosphocholine (DMPC) and 1-palmitoyl-2-oleoyl-*sn*-glycero-3-phosphocholine (POPC) at the air-water interface. In order to obtain separate information about the structural changes of both, the lipid and the surfactant component during the interaction, isotopically labelled DMPC-d_{54} was used to follow the incorporation of SDS into the lipid monolayer [4]. The methylene stretching bands of the SDS alkyl chain can easily be distinguished from those of the deuterated lipid, which appear in a different spectral region. For the interaction of dibucaine with DMPC and POPC the amide III band was used to follow the incorporation process. From the intensity of the characteristic IR band of the surfactant and the lipid we could directly calculate the surface partition coefficients describing the amount of incorporated surfactant in the lipid monolayer. The partition coefficients were determined at different surfactant concentrations and surface pressures and were compared to partition coefficients of the bilayer system, obtained under similar conditions by isothermal titration calorimetry. The best agreement between monolayer and bilayer data was obtained for monolayers held at a pressure of 29.5 to 33.2 mN/m, which can be considered as the bilayer-monolayer equivalence pressure.

References

1 Hildebrand, A.; Neubert, R.; Garidel, P. and Blume, A. (2002) Langmuir **18**, 2836-2847.

2 Lichtenberg, D. (1996) In *Handbook of nonmedical application of liposomes*, Lasic, D.; Barenholz, Y.; Eds.; CRC Press: Boca Raton, FL, Vol. 2, Chapter 13, p. 199.

3 Heerklotz, H.; Seelig, J. (2000) Biochim. Biophys. Acta **1508**, 69-85.

4 Meister, A.; Kerth, A.; Blume, A. (2004) J. Phys. Chem. B **108**, 8371-8378.