ESRF	**Experiment title:** Structural Characterization of the Stabilizer Layer of Diluted Organic Nanodispersions Produced by Antisolvent Precipitation	**Experiment number**: SC 4493
Beamline: ID02	**Date of experiment**: from: 17.05.17 to: 19.05.17	**Date of report**: 14.08.17
Shifts: 6	**Local contact(s)**: Dr. Peter Boesecke	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

Schuldes Isabel*[(1)], Noll Dennis*[(1)], Götz Klaus*[(1)], Unruh Tobias[(1)]

[(1)]Chair of Crystallography and Structural Physics, University of Erlangen-Nuremberg, Erlangen, Germany

Report:

Introduction and motivation

The production of organic nanoparticles through antisolvent precipitation (AS) is a less invasive and low-cost alternative to widely used top-down methods like high-pressure homogenization (HPH) [1]. The stabilization mechanism of particles produced by AS is not well understood despite of being of great importance for the production of organic nanosuspensions for pharmaceutical applications [2-3]. The aim of the experiment is to use the combination of small angle X-ray and neutron scattering (SAXS and SANS) studies to examine the structure of organic nanoparticles prepared by AS with special focus on the stabilizer layer. The results will help to understand the different stabilities in contrast to previous results of nanoparticles produced by HPH, and the role of the residual organic solvent in the dispersion medium, which is used in the AS method. The complementary SANS data are collected at the MLZ (Garching, Germany).

Samples and experiment

For the experiment, different organic nanoparticles were produced beforehand with AS: the hydrophobic target material (Coenzyme Q10, trimyristin or tripalmitin) is dissolved in an organic solvent (acetone) and injected into water which contains stabilizer, anionic sodium dodecyl sulfate (SDS), nonionic pentaethylene glycol monododecyl ether ($C_{12}E_5$) or no stabilizer. Different scattering length density (SLD) contrasts of the components (target material, stabilizer, acetone and water) were chosen to allow the determination of the size, the orientation and the constitution of the stabilizing layer, in combination with the SANS data. The samples were measured in its original concentration of 0.01 wt% and in its concentrated form, 0.1 wt%. Further, some nanodispersions were produced without stabilizer and stabilized afterwards with SDS in order to examine the difference in the stabilization.

For the SAXS data collection at the ID02 beamline, the samples (84 in total) were filled individually into a Peltier controlled flow-through quartz-capillary in air. Each sample was measured for 10-30 x 0.1-0.3 s at two different sample-detector distances (1.2 m and 6 m). The beamline was operated at 12.519 keV, corresponding to a wavelength of 0.99 Å. The trimyristin and tripalmitin samples were measured at a low temperature (5°C and 7°C) below their

crystallization temperature and at a high temperature (52°C and 65°C, respectively) above their melting temperature to access the emulsion and the suspension state of the sample. For the suspensions, wide-angle X-ray scattering (WAXS) was recorded simultaneously.

Preliminary results

Fig. 1 shows SAXS curves of the diluted 0.01 wt% and concentrated 0.1 wt% version of a SDS-stabilized tripalmitin nanodispersion, whereby the 0.1 wt% one was measured in the suspension state at 5°C and in the emulsion state at 65°C.

The simultaneous WAXS measurements of the suspensions reveal that the choice of the stabilizer influences the internal structure of triglyceride nanoparticles as the WAXS pattern of triglyceride nanosuspensions stabilized with SDS and $C_{12}E_5$ exhibit different Bragg reflections. Especially the structure of the nanosuspension stabilized with SDS seems to differ from known structural polymorphs of triglycerides. Fig. 2 shows the WAXS pattern of a 0.1 wt% trimyristin nanosuspension stabilized with $C_{12}E_5$.

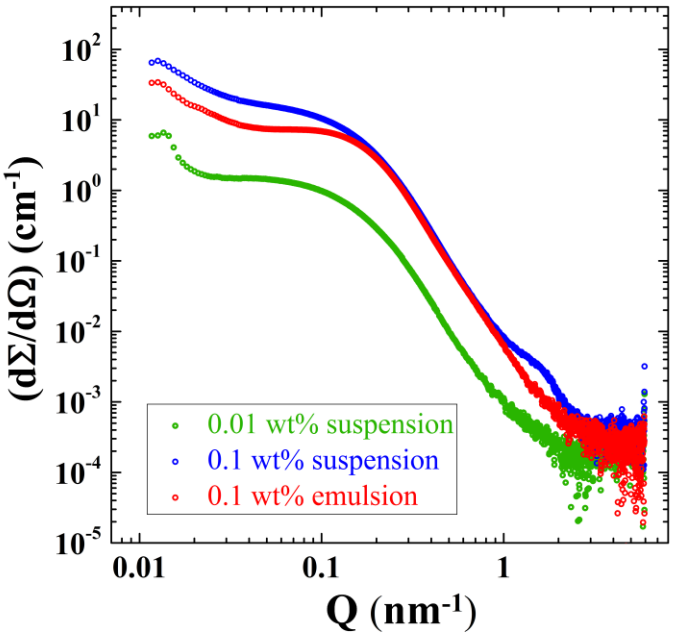

***Figure 1**: SAXS curves of different forms of a SDS-stabilized tripalmitin sample: 0.01 wt% (green) and 0.1 wt% (blue) suspension at 5°C and 0.1 wt% emulsion at 65°C (red).*

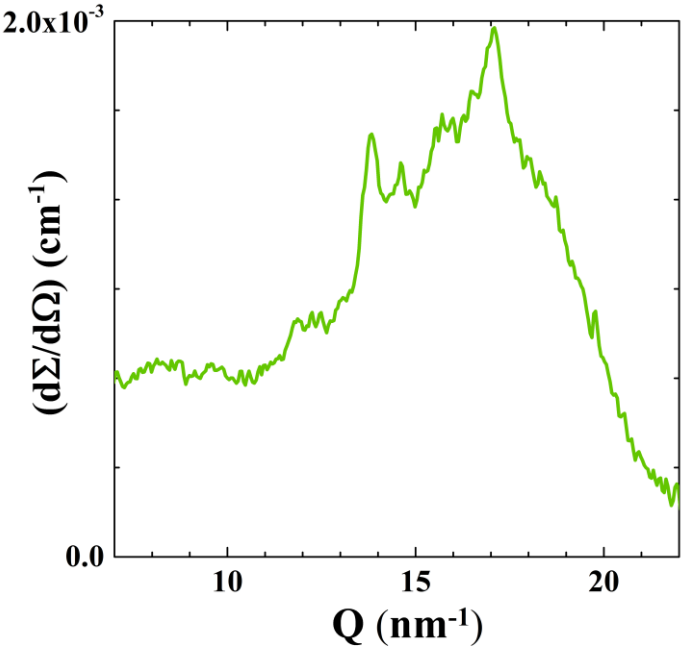

***Figure 2:** WAXS pattern of a 0.1 wt% trimyristin nanosuspensions stabilized with $C_{12}E_5$.*

The SAXS data of the experiment in combination with the additional SANS data will reveal the molecular structure and the composition of the stabilizer layer of organic nanoparticles produced by AS and the interaction with the residual organic solvent. The different internal structures of triglyceride nanosuspensions stabilized with SDS and $C_{12}E_5$ will be determined by evaluating WAXS data and corresponding differential scanning calorimetry (DSC) measurements.

References

[1] Oliveira, D., INTECH Open Access Publisher, 2011
[2] Thorat, A. A., Chem. Eng. J., 181 (2012) 1
[3] Lepeltier, E., Advanced drug delivery reviews, 71 (2014) 86