INDUSTRIAL PILOT PROJECT

Contrast matching of selectively deuterated glycerides for neutron scattering studies of lipid nanoparticles

THE INDUSTRIAL CHALLENGE

Larodan is a highly specialized producer of research grade lipids and deuterated lipid analogues. Commercial availability of these molecules is limited worldwide and therefore optimizing production and validating the structure of the deuterated analogues is valuable. Since the use of lipid nanoparticles for mRNA delivery in the COVID-19 vaccines, there is extensive research into how different lipid components and their location within the lipid nanoparticle contribute to function. Using deuterated lipid analogues in combination with neutron scattering is one of the few methods to perform these studies.

WHY USING A LARGE SCALE FACILITY

Small angle scattering by X rays (SAXS) or neutrons (SANS) is a unique tool to validate and compare hydrogenous (H) and deuterated (D) lipid analogues, both as single components and within structured lipid nanoparticles. Neutrons are particularly sensitive to different ratios of H and D atoms. Selective deuteration, i.e. tuning the number of H and D atoms changes the neutron scattering. By varying the number of H and D atoms in a molecule (lipid) and in solution (solvent), we are able to engineer a system where the lipid and solvent scattering are equal. This enables us to use neutron scattering to highlight specific components or cargo. A benchtop SAXS kit at an ordinary lab can, in turn, be used to compare the lipid phase behavior in hydrogenous (H) and deuterated (D) analogues. However, contrast matching, when the lipid scattering matches the solvent scattering, is only possible at a neutron facility.

HOW THE WORK WAS DONE

Benchtop SAXS was performed in excess water at 25, 37 and 45 °C using bulk lipid samples. The SANS experiment was performed using lipid nanoparticles containing deuterated lipid analogues and performed on the ZOOM beamline at ISIS Neutron and Muon Source, England, in collaboration with Dr. James Doutch.

THE RESULTS AND EXPECTED IMPACT

Our SAXS experiments showed that the lipid deuteration performed by Larodan did not significantly impact the lipid structures. The SANS data showed we could accurately predict the contrast match point (i.e. the H_2O : D_2O ratio required for the solvent scattering to match the lipid scattering for deuterated lipid analogues inside lipid nanoparticles). By combining the SAXS and SANS data we now have the data needed to validate the use Larodan's deuterated lipid analogues to study the precise location of specific lipid components within lipid nanoparticles.

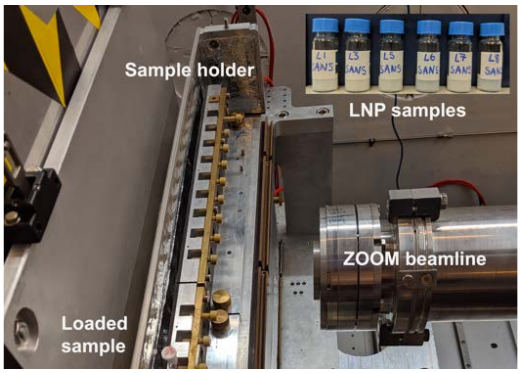

Figure 1. Inside the ZOOM beamline sample environment (inset, samples prior to loading).

"With these exciting techniques and the excellent collaboration with KI, Larodan has been able to launch a whole new product line for the international market"
/Carl Johan Arevång, Larodan

Karolinska Institutet

Larodan Research Grade Lipids

UKRI Science and Technology Facilities Council
ISIS Neutron and Muon Source

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