Experimental report

19/08/2024

Proposal: 9-10-1798 **Council:** 4/2023

Title: Micelles-in-liposomes: a novel system for transdermal drug delivery

Research area: Soft condensed matter

This proposal is a resubmission of 9-12-686

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Samples: DiMil
CBD

Instrument	Requested days	Allocated days	From	To
D22	2	1	26/09/2023	27/09/2023

Abstract:

Several strategies have been developed to breach the skin barrier for transdermal administration of active compounds and one of the most studied is the use of deformable liposomes. The aim of the proposal is the structural characterization of a new liposome-based carrier, designed to improve the stability of the system to obtain a sustained drug release. The hypothesized micelles-in-liposomes structure will be investigated as a function of composition, micelles/liposome ratio, and method of preparation. Structural results will help in the selection of the most promising formulation and preparation method, suitable to be implementable on large scale.

Report

SANS experiments have been performed on different nano-sized systems for drug delivery, micelles, liposomes and core-shell NPs.

In particular, we report the interaction of proteins with iron oxide NPs. The iron oxide is scarcely visible by SANS, because its contrast in D_2O is almost zero for neutrons, being the SLDs very similar ($6.34 \cdot 10^{10}$ cm^{-2} for D2O and $6.68 \cdot 10^{10}$ cm^{-2} for maghemite).

To verify the interaction of proteins with nanoparticles NPs have been incubated with BSA at 1:4 nanoparticles/protein weight ratio. The scattered intensity of the mixed samples has been measured by SAXS and SANS techniques, and the corresponding data are reported in Figure. The SAXS intensity profile of NPs with BSA is superimposable to the one of NPs in all the investigated q range, the interaction with BSA, if any, being undetectable. This result is not surprising because the intensity scattered by nanoparticles is orders of magnitude higher than the one scattered by BSA, as visible in Figure 4 B, where the intensity profile of BSA in solution, at the same concentration as in the mixed sample (0.5 mg/ml), is reported for comparison.

Parallel SANS experiments help decipher any interaction between the RCL NPs and BSA. Figure 4 d reports the data measured for BSA at c = 2.5 mg/ml and for the mixed sample. The fingerprint of the BSA profile is visible in the mixed profile, revealing a large contribution of unbounded, free, BSA, as expected at this high protein content. In the low q region, the intensity is higher than that of the naked NPs, suggesting an interaction of BSA with the nanoparticles. Structural analysis of the form factor of the complex has been performed after the subtraction of the contribution to the intensity spectrum of free BSA, about 90%. The complex has been modeled by the form factor of a core-shell flat ellipsoid, characterized by a central core (SLD $6.7 \cdot 10^{10}$ cm^{-2}) with a thickness of 3 nm and a diameter of 70 nm surrounded by a shell about 3 nm thick. Notably, the core size corresponds to the smaller nanoparticles observed by SAXS. Moreover, the parameters of the shell are compatible with the presence of a BSA corona around NPs, being the thickness well-matched with the shorter axis of BSA.

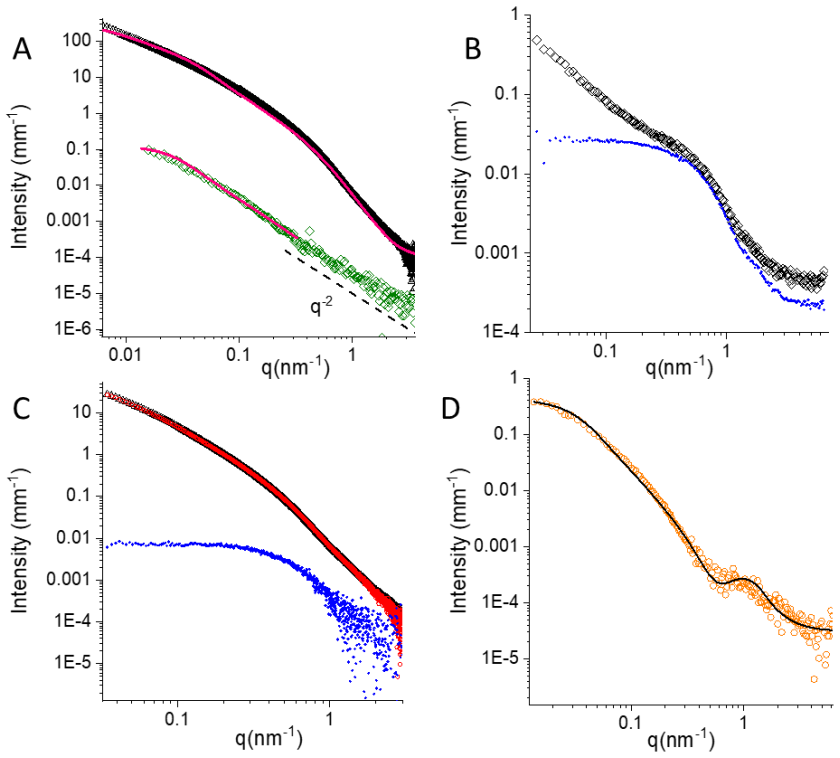

Figure: a) SANS (green diamonds) and SAXS (black triangles) intensity profiles of NPs; fitting curves (pink lines) obtained with a disk-like form factor. b) SAXS: BSA at 0.5 mg/mL (blue dots) and NPs (2 mg/mL) without (black triangles) and with (red dots) BSA (0.5 mg/mL). The spectra of NPs without and with BSA are superimposable in all the q range. c) SANS: BSA at 2.5 mg/mL (blue dots) and NPs (10 mg/mL) (black diamonds) with BSA (2.5 mg/mL). d) SANS intensity profiles of NPs (10 mg/mL) with BSA (2.5 mg/mL) after subtraction of the BSA intensity contribution (orange dots); fitting curve (black line) obtained with a core-shell disk-like form factor.