Nanoprecipitation for nanomedecine: formation and stability of the nanoparticles

F. Testard

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Abstract

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Laboratoire Interdisciplinaire sur l'Organisation Nanométrique et Supramoléculaire (LIONS), NIMBE, CEA, CNRS, Université Paris-Saclay, CEA-Saclay 91191 Gif-sur-Yvette Cedex (France))

Dispersed nanostructured liquid crystalline materials are promising candidates for drug delivery and other pharmaceutical applications[1]. They can be easily formed from nanoprecipitation or solvent shifting methods with amphiphiles, however the mechanism of their formation and their stability with time are still under debate.[2]

A particular case of such nanostructures was introduced in 2006 by Couvreur et al.[3] They take benefit of the amphiphilic properties of conjugates formed by the covalent link between a squalene moity and a drug (or a nucleosides) to form such dispersions. The high loading capacity of these nanoparticles and their specific structure induces a large improvement of their therapeutic efficacy in comparison to the single drug. To improve the use of these nanoparticles in drug delivery, a deeper understanding of the mechanism of formation could provide the keys for a better control over size distribution and stability. After a short summary on nanoprecipitation and solvent shifting methods, this presentation will focuses on the Squalenoyl based nanoparticles formation. Size and structural analysis by Small Angle Neutron Scattering revealed the paramount role of the solvent on the control of size[3] and the effect of the formulation parameters.[4]

References:

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2. C. Fong et al, "Lyotropic liquid crystal engineering–ordered nanostructured small molecule amphiphile self-assembly materials by design" **Chem. Soc. Rev.(2012)**, 41, 1297–1322
3. D. Demurtas, et al "Direct visualization of dispersed lipid bicontinuous cubic phases by cryo-electron tomography" **Nat Com (2015)** 6:8915 (DOI: 10.1038/ncomms9915)
4. Couvreur, P. et al. "Squalenoyl Nanomedicines as Potential Therapeutics" ***Nano Lett.*** **(2006)**, 6, 2544
5. . D. Saha et al ; *"The role of solvent swelling in the self assembly of squalene based nanomedicines"* **Soft Matter (2015)** 1 4173-4179.
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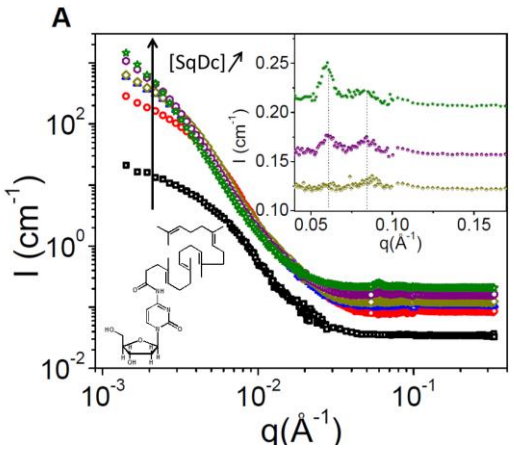

SANS patterns of the intermediate state of deoxycytidine squalene (SqDc) nanoparticles dispersion obtained with drop by drop nanoprecipitation (addition of SqDc/ ethanol–H solution into D_2O). top inset : zoom on the Bragg peaks, down inset : Molecular structure of deoxycytidine squalene.