Experimental Report

Proposal: **9-10-1309** **Council:** 10/2012

Title: Loading self-assembled fluorinatedphases with hydrophobic drugs

This proposal is a new proposal

Researh Area: Chemistry

Main proposer: **TABOR RICHARD**

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GARVEY Chris

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Samples: lamellar phase - sodium perfluorooctanoate, 1H,1H,2H,2H-perfluorooctanol, perfluorooctane
Ibuprofen

Instrument	Req. Days	All. Days	From	To
D11	0	1	12/06/2013	13/06/2013

Abstract:

The overall aim of this body of work is to design self-assembled soft matter phases for the administration of pharmaceuticals, with the current focus on understanding phases as they are loaded with drug molecules. This initial work will provide proof-of-principle with simple, model compounds. We have already selected promising phases that exhibit the desired structural, rheological and diffusion characteristics. However, we need to understand how the phase characteristics (internal structure such as lamellar spacings, microstructural phase separations) change when the phases are loaded with active molecules. These experiments will highlight structural and mechanistic features crucial to developing these materials further.

EXPERIMENTAL REPORT

“Loading self-assembled fluorinated phases with hydrophobic drugs”

Matthew Pottage, Chris Garvey, Isabelle Grillo and Rico Tabor

Proposal : 9-10-1309
Title : Loading self-assembled fluorinated phases with hydrophobic drugs
Instrument : D11
From :12/06/13 To : 13/06/13

The aim of this experiment was to explore the capacity of fluorinated amphiphiles to form stable mesophases that permitted the incorporation of hydrophobic drugs. In particular, we were curious to explore the structural evolution and evidence of any demixing effects when adding hydrophobic drugs to the fluorinated self-assembled phase.

The key results are:

1) the fluorinated liquid crystals studied here undergo a unique structural evolution from micelles to highly ordered lamellar phases
2) the lamellar phase is capable of sustaining low loadings of hydrophobic hydrocarbon drugs
3) the water spaces within the lamellar phase can incorporate high levels of hydrophilic drug and hydrotrope molecules or adjuvants.

Although low levels (<1 wt %) of the model hydrophobic drug molecule result in no detectable structural change to the liquid crystal characteristics (specifically the inter-layer spacing and membrane rigidity, as defined by the Caillé parameter), higher levels of drug loading result in a distinctive loss of order and relaxation of the membranes. However, the phase thus produced is still thermodynamically stable and has the characteristics of a poorly ordered lamellar system (Fig. 1).

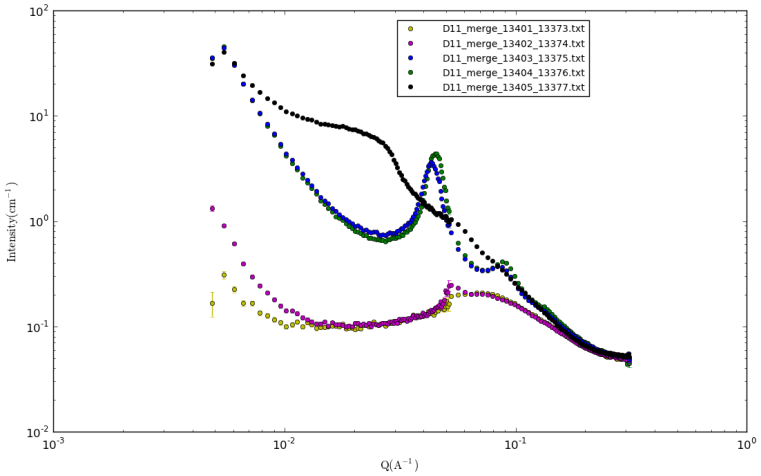

Fig 1: Evolution of a fluorinated lamellar phase upon addition of a partially fluorinated co-surfactant (bottom 4 traces) and high loading of a hydrophobic drug (uppermost trace, black symbols).

The incorporation of high levels of a hydrophilic drug into the water spaces of the system results in a moderate loss of order (Fig. 2), although again, the systems remain thermodynamically stable. This suggests that a system can be created wherein the hydrophobic drug is enclosed in the hydrophobic, fluorinated lamellar membranes, and a coadjuvant can be solubilised in the water spaces without a loss of function.

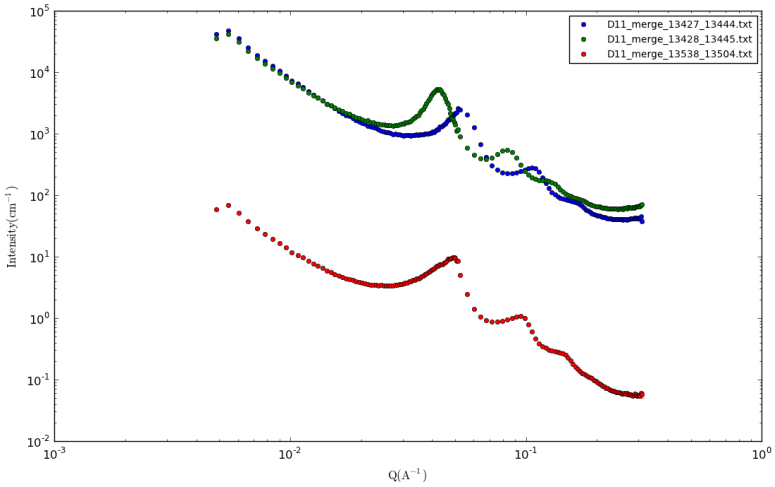

Fig 2: Evolution of a fluorinated lamellar phase upon addition of a partially fluorinated co-surfactant (bottom 4 traces) and high loading of a hydrophobic drug (uppermost trace, black symbols).

In conclusion, this experiment has demonstrated that fluorinated liquid crystals can provide stable vectors for the incorporation of both hydrophilic and hydrophobic drugs, and that SANS is a valuable technique for studying the structural evolution at the nanoscale that accompanies this process.

Part of this work is already published [1] with a further publication in progress [2].

References:

[1] M. J. Pottage, T. Kusuma, I. Grillo, C. J. Garvey, A. D. Stickland and R. F. Tabor, Fluorinated Lamellar Phases: Structural Characterisation and Use as Templates for Highly Ordered Silica Materials. *Soft Matter*, **10** (2014) 4902-4912.

[2] M. J. Pottage, T. Greaves, I. Grillo, C. J. Garvey, S. Mudie and R. F. Tabor, *in preparation.*