Experimental Report

Proposal: **9-10-1348** **Council:** 4/2014

Title: Location of various steroidal molecules in monolayers of surfactant

This proposal is a new proposal

Researh Area: Chemistry

Main proposer: **LAWRENCE Jayne**

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Local Contact: CAMPBELL Richard

Samples: C17H37NSO3
C26H40O3
C22H32O3
C19H28O2
NaC12H25SO4

Instrument	Req. Days	All. Days	From	To
FIGARO Adsorption troug	3	3	10/10/2014	13/10/2014

Abstract:

Many drug molecules are both water-insoluble and lipophilic/slightly amphiphilic which limits their commercialisation and use by the patient. Solubilisation of water insoluble drug in surfactant micelles is an attractive means of increasing their apparent aqueous solubility thereby ensuring their delivery and ultimate use by patients. Surprisingly little is known about the relationship between surfactant and drug structure and the micelle's ability to solubilise drug. As a drug's incorporation into surfactant monolayers mirrors its distribution in surfactant micelles, the study of drug distribution into surfactant monolayers should provide useful information about drug solubilisation. This study aims to determine the level of incorporation and the extent of penetration of three lipophilic drugs, testosterone and two of its ethyl esters, into monolayers formed by sodium dodecyl-sulphate and N,N-dimethyldodecylammoniopropanesulfonate. The results study will be correlated with SANS studies determining the location of the drugs in the surfactant micelles and thereby aid a better understanding of the relationship between surfactant and drug structure and micelle solubilisation capacity.

Location of various steroidal molecules in monolayers of surfactant

(9-10-1348: FIGARO: 10/10/2014-13/10/2014)

Experimental team Yussif Saaka, Richard Campbell and Jayne Lawrence

Background

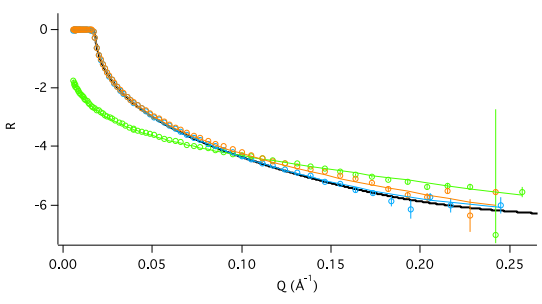
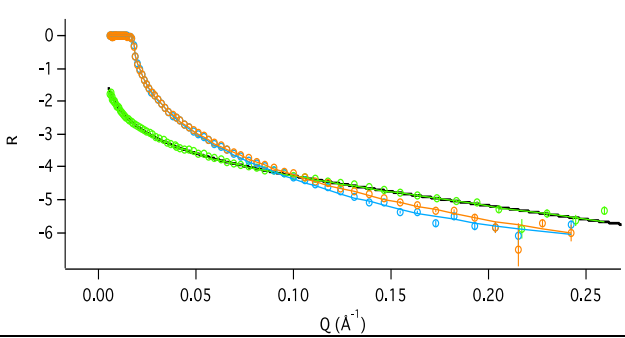
Many drug molecules are both water-insoluble and lipophilic/slightly amphiphilic which limits their commercialisation and use by the patient. Solubilisation of water insoluble drug in surfactant micelles is an attractive means of increasing their apparent aqueous solubility thereby ensuring their delivery and ultimate use by patients. Surprisingly little is known about the relationship between surfactant and drug structure and the micelle's ability to solubilise drug. As a drug's incorporation into surfactant monolayers mirrors its distribution in surfactant micelles, the study of drug distribution into surfactant monolayers should provide useful information about drug solubilisation.

Aim

The aim of the study was to determine the level of incorporation and the extent of penetration of the lipophilic drug, testosterone heptanoate (TH) into monolayers formed by sodium dodecyl-sulphate (SDS).

Results and Discussion

For each SDS concentration studied, 4 contrasts namely *h*-SDS/H_2O, *h*-SDS/D_2O, *d*-SDS/H_2O, *d*-SDS/D_2O were measured at 3 concentrations below the cmc, namely 0.1, 0.2 and 0.5 times the experimentally determined cmc of SDS and 3 concentrations above the cmc, namely 1, 1.5 and 2 times the cmc. For each system the aqueous phase was saturated with TH before adding the SDS and measuring its behaviour at the air-water interface using neutron reflectivity. After which 10 times the amount of TH required to saturate the monolayer was added to its surface by the careful addition of an aliquot of 5 mg/mL TH in hexane and the behaviour of the surface characterised using neutron reflectivity. Above SDS concentrations above the cmc, we measured the neutron reflectivity profile in the presence and of a saturated amount of TH (taking into account here micelle formation). Thereafter, we added sufficient of a 5 mg/mL TH in hexane solution to the interface in order to saturate the monolayer with Th. The neutron reflectivity data was simultaneously fitting using MOTOFIT. The figure below shows a fit obtained to the data above and below the cmc.

0.5 x the cmc of SDS in the presence of TH	1.5 x the cmc of SDS in the presence of TH
	

The Table summarises the data obtained from the fits.

	Concentration of SDS as a function of its critical micelle concentration					
	0.1	0.2	0.5	1	1.5	2
Chain thickness (Å)	5.65	7.07	8.08	8.03	8.47	7.61
Surface excess of the SDS	2.6	3.3	3.8	3.8	4.0	3.6
Volume fraction of heads	0.27	0.34	0.39	0.39	0.41	0.37
Volume fraction of drug	0.27	0.36	0.40	0.41	0.41	0.43
Surface excess of drug	0.25	0.33	0.36	0.37	0.37	0.39
Stoichiometry of surfactant:drug	10.7	10.2	10.4	10.1	10.7	9.1

A fixed head group thickness of 3.5 Å was used to analyse the data

In brief, the preliminary results show that the TH nestles under the surfactant head groups (there is no evidence of TH sitting in the surfactant monolayer) and that the stoichiometry of drug molecules to surfactant molecules at the air-water interface is consistent over a broad range of concentrations (i.e. below and above the critical micelle concentration of SDS) and thus adsorption appears to be synergistic, rather than competitive, in nature.

Further studies are required to explore why the stoichiometry of the of the drug to the surfactant at the air-water interface is different to that observed in the micelles, i.e. 10:1 at the air-water interface as opposed to 2:1 in the surface micelles.