Experimental report

12/02/2017

Proposal: 9-10-1465 **Council:** 4/2016

Title: Effect of surfactant head group onthe location of steroidal drugs into monolayers of surfactant

Research area: Chemistry

This proposal is a continuation of 9-10-1348

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Samples: SDS
testosterone heptanoate
4-cholesterone
adrenosterone

Instrument	Requested days	Allocated days	From	To
FIGARO	5	4	08/07/2016	13/07/2016

Abstract:

Many drug molecules are very water insoluble which limits their commercialization and use by patients. Solubilisation in surfactant micelles is an attractive means of increasing the apparent aqueous solubility of a drug and thereby ensuring its successful delivery and ultimate use by patients. Surprisingly, however, very little is known about the relationship between surfactant and drug structure and the micelle's ability to solubilise drugs. As a drug's incorporation into surfactant monolayers mirrors its distribution in surfactant micelles, here focus on the study of drug distribution into surfactant monolayers. The present study aims to determine the level of incorporation and the extent of penetration of 3 hydrophobic steroidal drugs, 4-cholesten-3-one, testosterone enanthate and adrenosterone, into monolayers formed by the surfactant dodecyltrimethylammonium bromide using neutron reflecticity in combination with contrast variation. The results will be correlated with SANS and MD studies determining the location of the drugs in the micelles and thereby aid a better understanding of the relationship between surfactant and drug structure and micelle solubilisation capacity.

Experiment 9-10-1465 examined the amount and site of solubilisation of 2 steroidal, drug-like molecules (i.e. 4-cholesten-3-one (4-chol) and adrenosterone (ADRENO) in the monolayers formed by a range of surfactants, namely the anionic surfactant, sodium dodecyl sulphate (SDS), the cationic surfactant, (dodecyltrimethylammonium bromide (DTAB)) and the zwitterionic surfactants (dodecylphosphorylcholine (DPC) and dodecyldimethylammoniopropylsulphate (DDAPS). All the surfactants were available both their protiated and deuterated forms, the latter courtesy of a custom synthesis from the Oxford Deuteration Facility. During these studies, the detailed structure of the various surfactant monolayers in the absence and presence of drug was determined. All experiments are performed at only one surfactant concentration, namely 2 times the cmc as our previous studies have shown that surfactant concentrations above the cmc are the most relevant for understanding drug solubilisation in micelles. 4 contrasts were used, namely d-SDS in acmw and in D_2O, and h-SDS in acmw and in D_2O). The results of the analysis of the neutron reflectivity for the surfactant monolayers in the absence of drug as two layers consisting of the surfactant tails (L1) and surfactant heads (L2) are given in

surfactant (2xcmc)					
	DDAO	DDAPS	DPC	DTAB	SDS
chain L1 =	**11.2**	**8.4**	**7.2**	**8.0**	**8.5**
Vf=	0.53	0.92	0.66	0.77	0.41
SP=	64.0	34.0	34.5	44.0	58.6
head L2 =	4.07	4.58	5.33	4	3.5
SE (Γ) SAA	5.22	3.93	3.37	3.76	3.97
α	31.82	42.31	49.36	44.20	41.81

Table 1. SP is the penetration of solvent into the head group region while Vf is the volume fraction of chains, SE SAA is the surface excess of surfactant and a is the area per surfactant molecule.

The neutron reflectivity days in the presence of drug were analysed assuming that a variety of possible locations of the drug, specifically it was present as an additional layer below the surfactant monolayer (Model 1), it was present in the head group region of the surfactant monolayer (Model 2), or it was present in the tail region of the monolayer (Model 3). The neutron reflectivity data best fit the model whereby 4-CHOL and ADRENO both resided in surfactant table region. Table 2 (4-CHOL) and Table 3 (ADRENO) shows the results of the analysis obtained using Model 3. The analysis of the data is on-going.

surfactant and 4-CHOL(2xcmc)					
SAA	DDAO	DDAPS	DPC	DTAB	SDS
chain L1	10.52	9.30	9.22	9.10	13.86
head L2	4.07	4.58	5.33	6.00	4.00
SLD-1 tail	6.20	6.01	3.87	5.91	3.92
Vf SAA tail	0.89	0.86	0.53	0.84	0.54
Vf drug tail	0.11	0.14	0.47	0.16	0.46
SP head	0.48	0.35	0.37	0.49	0.70
SE SAA	4.36	3.73	2.30	3.58	3.50
SE drug	0.32	0.36	1.17	0.39	1.73
Stoichiometry	13.45	10.38	1.97	9.22	2.03
α	38.11	44.55	72.18	46.35	47.40
roughness	3.5	3.7	3.8	3.6	4.5

surfactant and adreno (2xcmc)					
SAA	DDAO	DDAPS	DPC	DTAB	SDS
d1 tail	11.00	8.74	7.43	8.71	9.20
d2 head	4.07	4.58	5.33	6.00	4.00
SLD-1 tail	6.10	6.26	5.47	5.98	5.80
Vf SAA tail	0.85	0.88	0.74	0.83	0.80
Vf drug tail	0.15	0.12	0.26	0.17	0.20
SP head	0.64	0.28	0.63	0.55	0.63
SE SAA	4.37	3.59	2.57	3.38	3.43
SE drug	0.64	0.42	0.76	0.58	0.73
Stoichiometry	6.80	8.58	3.40	5.84	4.71
α	37.99	46.32	64.71	49.19	48.44
Roughness	4.06	3.5	3.5	3.6	3.5