Experimental Report

Proposal: **9-12-351** **Council:** 4/2014

Title: Self-assembly of films from pharmaceutically acceptable components atthe air-water interface

This proposal is a new proposal

Researh Area: Soft condensed matter

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Samples: octylglucoside/DMPC in H2O/D2O
sodium dodecylsulphate/cetylpyridinium chloride/Eudragit (a methacrylic acid-ethyl acrylate copolymer)/H2O/D2O
SDS/lauric arginate/polyethylene oxide/H2O/D2O
SDS/lauric arginate/Aquoat (hydroxyl propyl methyl cellulose acetate succinate)/H2O/D2O

Instrument	Req. Days	All. Days	From	To
FIGARO	4	4	07/11/2014	11/11/2014

Abstract:

In this proposal we wish to further our studies of mesostructured films which form spontaneously at the air-solution interface on solutions of mixed surfactants. Here we wish to study two systems that will progress our understanding of film formation and our ability to prepare films from pharmaceutically acceptable components for drug delivery applications. We will first study the structure, and structure development in several new formulations consisting of pharmaceutical polymers, structured using orally acceptable surfactants, and second we will study the composition and structure of films formed on octylglucoside/DMPC mixtures where, on the basis of previous work, we have predicted the gradient in structure and composition at the interface. Selective deuteration and neutron reflectivity will provide unique insights into the structure and composition of these films, allowing future development of novel and sophisticated drug delivery systems.

Mesostructured thin films produced at the air-water interface offer new possibilities for controlled encapsulation at a critical length scale[1]. Driven by the simple but controllable flow of solution to an air interface where evaporation is occurring, dissolved and dispersed species continuously accumulate and form a structured film under ambient conditions. Here we focus on preparation of films from pharmaceutically acceptable components for drug delivery applications. We used neutron reflectivity to identify structures, and follow structure development, in two film-forming systems: first, novel film-forming solutions, using pharmaceutical polymers, structured using orally acceptable surfactants, and second, film formation in mixed surfactant-lipid systems to test predictions of film structure and formation resulting from transport of normally insoluble phospholipids to the air-solution interface via solubilisation in micelles.

Our research programme is focussed on identifying conditions where pharmaceutical-grade polymers and surfactants spontaneously form robust interfacial films within ~1hr, which continue to thicken, becoming several microns thick after 2-3 hours. Film formation is visible by eye even for dilute solutions (below 1wt% polymer, 0.01M surfactant) but thicker films are formed in more concentrated systems allowing removal of intact films from the interface. In this experiment we studied films formed from three pharmaceutical polymers including Eudragit (a methacrylic acid-ethyl acrylate copolymer), Aquoat (hydroxyl propyl methyl cellulose acetate succinate), and polyethylene oxide (PEO). Catanionic mixtures of surfactants have proved most effective in structuring these films so we used sodium dodecylsulphate (SDS) with cetylpyridinium chloride (CPC) in D_2O for most experiments. SDS is a very commonly used food and pharmaceutical additive, while the CPC is an anti-bacterial agent used in food and drug applications with an established safety profile for oral use (e.g.[2]). SDS was also used in a deuterated form, for experiments on air contrast matched water, giving an extra contrast in the reflectivity experiments.

We used the FIGARO temperature-controlled adsorption troughs at 28°C, (above the Krafft temperature for CPC), and monitored the %RH continuously during the experiments. We studied film formation for the three polymers at concentrations of 1.5wt% for Eudragit, and Aqoat or 1 wt% PEO since at higher concentrations PEO solutions became extremely viscous. The films were formed with either hydrogenated or deuterated SDS, and CPC at surfactant concentrations of 0.05M SDS:0.2M CPC, 0.1M SDS:0.2M CPC or 0.2M SDS:0.2M CPC. Films were also measured in the presences and absence of the hydrophobic drug Riboflavin at two concentrations (5mM and 15mM) to test the effect of hydrophobe encapsulation on film structures and growth. At these concentrations thick films which are easily recoverable from the solution surface grow within a few hours. Two or more film forming solutions were poured into troughs simultaneously and the reflectivity patterns were taken sequentially first at low, then high angle, and the evolution of the high angle patterns on the troughs was followed using alternate 5min data collections for several hours until the diffraction peaks observed at this angle stopped evolving. Figure 1 shows typical data sets for Eugradit, Aqoat and PEO films at 0.1M SDS:0.2M CPC, and a comparison of initial and final film structures for a PEO film in the presence of a low concentration of Riboflavin.

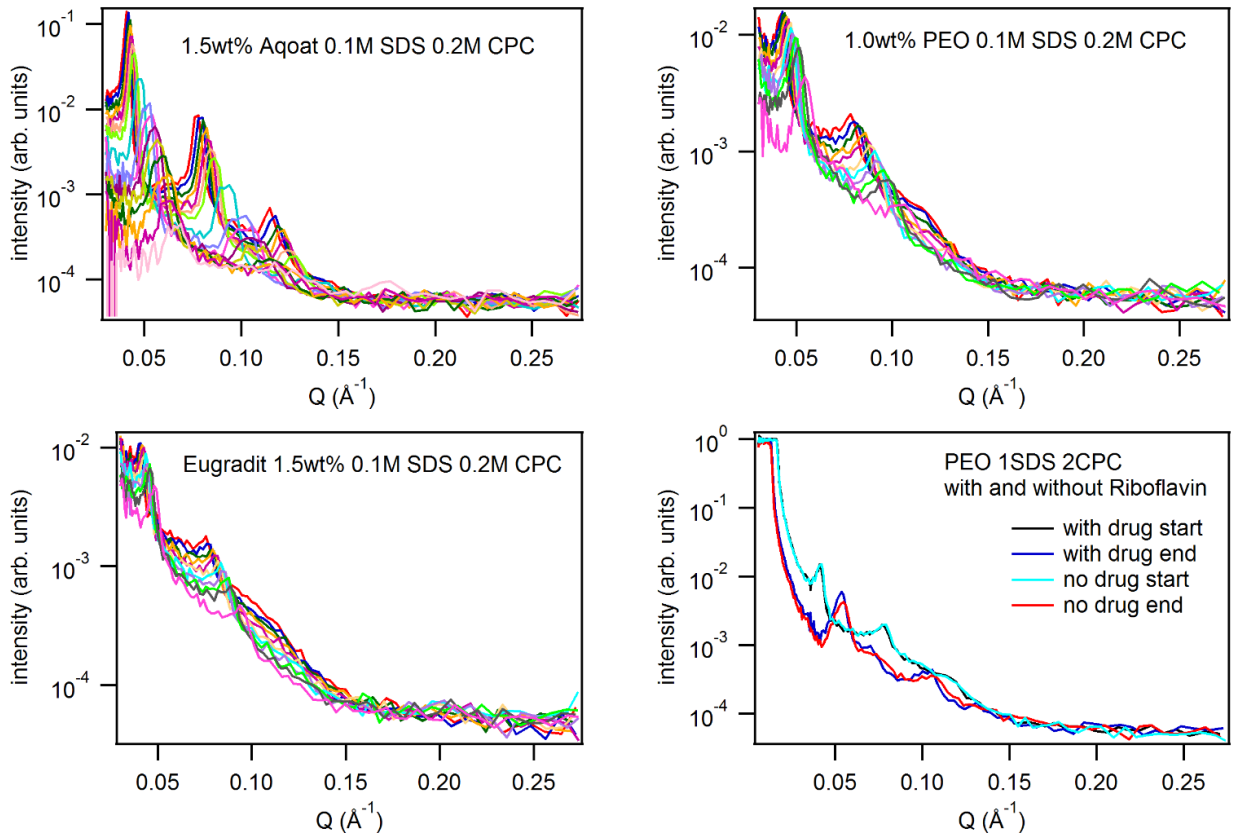

Figure 1: Neutron reflectivity patterns for films growing on 0.1M SDS, 0.2M CPC solutions on D_2O for the three polymers studied, plus a comparison for a film grown in the presence and absence of 5mM Riboflavin.

The reflectivity patterns from the films usually begin by showing 2 peaks which can be indexed either to a lamellar phase or a 2D hexagonal phase aligned parallel to the solution surface. With time the peaks move to higher Q, indicating a shrinkage of the repeat distances in the films, probably due to surface dehydration. Aqoat films gave the most well defined structures with the sharpest peaks, while Eugradit films had the least well -ordered mesophases. Under some conditions other peaks appear, most frequently resulting in final structures which can be indexed as a 2D hexagonal phase of close-packed cylindrical micelles. At both concentrations of Riboflavin studied, the addition of drug had no apparent effect on the initial film structure but some small effects did appear in d-spacings (but not changes in structure) at the end of film growth. Films did however take slightly longer to reach the same shift in peak position in the presence of high concentrations of the drug. Further analysis of these reflectivity patterns are continuing, to quantify the rates of film evolution for each type of polymer and to understand the changes in peak intensity and position which occur during film development.

We also attempted to study film formation, which was predicted to occur, on solutions of octyl glucoside (OG) with POPC or the phospholipid DPPC alone, based on previous studies.[3] The %RH was controlled via air-diffusers mounted on the lids of the Figaro adsorption troughs and flow of dry N_2 gas through the cells during the measurements, which allowed some control of the %RH. However unfortunately under the experimental conditions trialled we did

not observe any interfacial layering, possibly due to convection effects disrupting formation of surface layers for these smaller molecular species.

Further work is continuing on the films prepared using pharmaceutically acceptable polymers, to test further edible surfactant combinations and to develop other polymer surfactant mixtures suitable for tablet coatings. We aim to publish this work to support applications for funding to continue work in this area.

References

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