ELSEVIER

Current Opinion in Colloid & Interface Science 12 (2007) 60–67

Current Opinion in COLLOID and INTERFACE SCIENCE

www.elsevier.com/locate/cocis

Biomimetic amphiphiles: Biosurfactants

J.R. Lu *, X.B. Zhao, M. Yaseen

Biological Physics Group, School of Physics and Astronomy, University of Manchester, Manchester M60 1QD, UK

Available online 21 May 2007

Abstract

Several types of natural and biomimetic surfactants have recently been reported. These biosurfactants bear the same common structural features as conventional surfactants, but the presence of bioactive functionalities incorporates new features such as structural complementarity and biological specificity into the common character of self-assembly driven by amphiphilicity. This review provides an outline of trend in recent biosurfactant research. Whilst these biosurfactants are attractive to many potential applications, further characterisation of their physiochemical properties will benefit the design and fabrication of functional biomaterials and accelerate our advances in nanobiotechnology.

Keywords: Biosurfactants; Self-assembly; Peptides; Amphiphiles; DNA surfactants; Lipid surfactants; Liposurfactants; Neutron reflection

1. Introduction

Biosurfactants refer to small amphiphiles with low molecular weight and with at least one of the moieties bearing a clear biological functionality. These amphiphilic molecules are usually water-soluble, but their critical micellar concentrations (CMC) are low, typically on the order of 10^{-5} M, and are reluctant to vary with salt type and concentration. Although they bear the structural features similar to conventional surfactants, biosurfactants may appear in very different chemical forms. Several types of new biosurfactants have recently been reported, including single alkyl chain phosphocholine (C_nPC), DNA surfactant (C_nDNA), lipopeptide surfactant (C_nAm) and full peptide surfactant (A_nA_m). The hydrophobic moiety in each of these biosurfactant molecules is either an alkyl chain (C_n) or a hydrophobic amino acid sequence (A_n) and the hydrophilic moiety is a lipid head, or a sequence of sugar ring, short peptide and DNA strand. Thus the main difference in chemical character lies in the hydrophilic head; this allows for a wide range of variation in their physical and biological properties.

Selection of the type and size of each moiety enables a delicate balance between surface activity and biological function and this represents the most effective approach of harnessing the power of molecular self-assembly. Biosurfactant design has focused on exploiting the combined benefit of surface activity with biomimetic performance over the past few years. Examples include the design of full peptide surfactants that exploits structural specificity of peptides to promote the formation of hydrogels as 3D tissue scaffolds [1,2•] and the construction of DNA surfactants that utilises the alkyl tail to promote surface and interfacial assembly, with the DNA strand exposed on the outer surface to undertake Watson–Crick base pairing with its complementary strand [3••]. Similar strategies have been applied to tuning peptide structures to improve their effectiveness and selectivity in antimicrobial and antiviral activities [4,5].

This article aims to provide an overview of the recent advances in biosurfactant research and highlight the main issues that need to be addressed. Because of the structural simplicity, biosurfactants are ideal model systems for both experimental and theoretical approaches aimed at establishing the structure–function relationship. A substantial amount of early work has already been done to characterise natural dichain phospholipids grafted with sugar, amino acid and nucleic acid groups. This area of research has been well reviewed by Lang [6•] and Berti [7•]. This review will cover a group of simple biosurfactants with good aqueous solubility under physiological conditions and with distinct biological characteristics.

2. Single alkyl chain PC surfactant (C_nP_mC)

Natural dichain phospholipids play many important roles in biological systems and have been extensively studied [8].

* Corresponding author. Tel.: +44 161 3063926.
E-mail address: j.lu@manchester.ac.uk (J.R. Lu).

1359-0294/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.cocis.2007.05.004

Among many other effects, lipids bearing phosphocholine (PC or P_2C, where $m=2$)) confer protein reducing potential and provide cell surface with biocompatibility [9]. Unlike natural lipids, single alkyl chain PC surfactants are mostly water-soluble and are attractive for a range of technological applications including drug delivery (Fig. 1). Because they bear zwitterionic head groups, they are ideal models for understanding the effect of zwitterionic heads on their surface and interfacial properties. The results from the soluble PC surfactants have allowed a direct comparison with our previous work on nonionic [10–12] and ionic [13–15] surfactants. The interesting findings for C12PC from surface adsorption studied by surface tension and neutron reflection included the intermediate CMC of ca 1 mM, the area per molecule at the CMC (A_{cmc}) of ca 50 Å^2, the high hydration capacity of the PC head groups and the ability to resist dehydration against temperature increase and salt addition [16,17•]. A further intriguing observation from neutron reflection in combination with partial deuterium labelling was the low fraction of the alkyl chain in water for all the PC surfactants studied (C_nP_mC, where $n=10,12,14$ and 16, $m=2$), suggesting that the PC head groups controlled not only water association but also the fraction of alkyl chain immersed. These structural characteristics together with their lack of responses to temperature, salt addition and pH are distinctly different from ionic surfactants such as sodium dodecyl sulphate (SDS) and dodecyl trimethyl ammonium bromide (C_{12}TAB) and nonionic surfactants such as pentaethylene glycol monododecyl ether ($C_{12}E_5$) and may be associated with their unique feature of surface biocompatibility.

Further structural analysis from neutron reflection [18••] has revealed that the thickness of the PC head group regions and that of the entire PC surfactant layers showed little responses to surface coverage and changes in alkyl chain length. Although these observations imply that the alkyl chains would tilt in a manner similar to dichain phospholipids such as dipalmitoyl glycerol phosphocholine (DPPC) [19•–21] the hydrophilic PC head groups were found to stand vertically over the entire concentration range studied. This is in contrast to the varying PC head group conformations in DPPC layers where transition from parallel to vertical PC head orientations was associated with the phase change from liquid expanded to liquid condensed state. Whilst many of the structural conformations from the C_nPC surfactant layers are similar to *n*-dodecyl-*N*,*N*-dimethylamino acetate, another zwitterionic surfactant studied by Hines et al. [22], the marked increase in surface excess for the betaine surfactant arising from dehydration was not observed from the PC surfactants.

Yaseen et al. [17•] have extended the C_nPC study to examine the effect of the spacer length between the two charged units in the zwitterionic head on the layer structure using

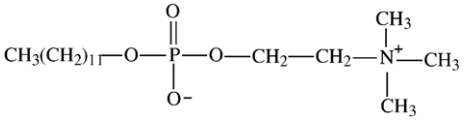

Fig. 1. Molecular structure of $C_{12}H_{25}PO^-{}_4C_2H_4N^+(Me)_3(C_{12}PC)$. The general formula for this series of biosurfactant studied is C_nP_mC, where $n=10$, 12, 14 and 16 and $m=2$, 4 and 6.

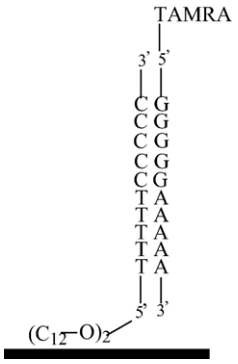

Fig. 2. An example of a DNA surfactant immobilised onto the surface via its hydrophobic C12 tails. Its DNA head strand is capable of binding to its complementary strand tagged with a TAMRA (denoting a rhodamine fluorescence label).

$C_{12}PO^-{}_4C_mN^+(Me)_3$ ($C_{12}P_mC$), where $m=2$, 4 and 6 (for the natural PC group $m=2$). No structural change was detected when m was increased from 2 to 4, but at $m=6$, the area per molecule was substantially increased, indicating the tilting of the zwitterionic head.

Solution aggregation of $C_{12}PC$ has been studied using molecular dynamic simulation by Tieleman et al. [23]. They showed that an ensemble consisting of 54 molecules and 1200 water molecules was sufficient to represent the entropically driven micellisation in water. Although micellisation is dynamic and its size varies, the number of water molecules n_w associated with each surfactant molecule was found to be around 22. This was broadly consistent with the experimental data for $C_{12}PC$ micelles obtained from quasi-elastic light scattering and analytical ultracentrifugation [24]. This value of n_w is close to the value of 25 obtained from the $C_{12}PC$ monolayer adsorbed at 0.073 mM (ca. 1/10 CMC) but is higher than the value of 15 obtained at the CMC. The differences must arise from the different packing and geometrical shapes between the planar and curved interfaces. A value much closer to n_w of $C_{12}PC$ was obtained for DPPC at the air/liquid interface by Brum and co-workers [19•]. Neutron reflectivity measurements at the liquid-condensed phase (LC) for this lipid indicate 14 water molecules at an area per molecule of 52 Å^2. However, more interesting is that they suggest a head thickness of 11.5 Å and conclude that the P–N dipole is close to the surface normal, an observation that is consistent with our results for $C_{12}PC$ at its CMC.

3. DNA surfactants

Paunov and his co-workers have reported the covalent attachment of one or two hydrophobic tails to the (3′- or 5′-) end of a single DNA strand [3••,25•]. The anchoring hydrophobe allows the DNA strand to be adsorbed or immobilised onto hydrophobic surfaces via hydrophobic affinity (Fig. 2). These authors have designed a novel approach for fabrication of DNA arrays based on microcontact printing of these DNA surfactants on solid substrate and the single DNA strands are effective for hybridisation with their complementary DNA strands. This new technology could be used for rapid production of genetic biochips and many other bioassays based on DNA base pairing.