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Thermodynamic and elastic fluctuation analysis of langmuir mixed monolayers composed by dehydrocholic acid (HDHC) and didodecyldimethylammonium bromide (DDAB)

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ABSTRACT

The physicochemical and elastic properties of Langmuir mixed monolayers composed by dehydrocholic acid (HDHC) and didodecyldimethylammonium bromide (DDAB) were evaluated. The experiments were performed with a constant surface pressure penetration Langmuir balance based on Axisymmetric Drop Shape Analysis (ADSA).

The behavior of such amphiphiles in monolayer was clearly non-ideal and would be seriously influenced by the amount of HDHC molecules present. The presence of bile acid type molecules caused the monolayer be more condensed (A_c diminution) and the intermolecular attractive interactions be stronger (high ε_0 values). This fact would be related to H-bond formation between water and carboxilate and carbonile groups in the cholesteric ring and agreed with the existence of laterally structured microdomains at the monolayer (determined by the analysis of the first virial coefficient, $b_0 < 1$, of the state equation). The miscibility of both surfactants in the monolayer, their high bulk hydrophobicity ($\pi_c > 35\,\mathrm{mJ\,m^{-2}}$) just with the obtained negative values of the free energy of mixing ΔG_{mix}, and the excess second virial coefficient $(b_1)^{\mathrm{E}}$ obtained allows us to infer that net attractive interaction existed between HDHC and DDAB molecules at the monolayer and that mixed systems would be able to be used in the formulation of supramolecular assemblies.

1. Introduction

Bile salts with their rigid ring structures are in many respects unusual surfactants, and are usually described as having both a hydrophilic and a hydrophobic faces. The physical chemistry of bile salts micellization has been, and still is, an active area of research. The high specificity and capacity for bile salts transport systems during their enterohepatic circulation might form the basis of a current research on drug–bile acids delivery for specific drug targeting to the liver and for improving the intestinal adsorption of poorly adsorbed or non-adsorbed drugs, such as peptides [1,2]. A variety of techniques have been employed to gain more insight into the structure/size/shape of bile salts aggregates. Several studies which involved the interactions of such surfactants in mixtures with cationic amphiphiles have been performed and different types of supramolecular assemblies have been obtained [3]. Swanson-Vethamuthu et al. [4] have studied the behavior of sodium cholate (NaC, with three hydroxyl groups on the hydrophobic face) and sodium desoxycholate (NaDOC, with two hydroxyl groups) in combination with C_{16}TAB and C_{16}TAC. In such mixed systems NaC gave mixed micelles that decrease monotonously in size, whereas NaDOC induced a transition to rod-like micelles, at close to equimolar concentration a separation into two phases occurred [4]. According to that, the aim of this article is the evaluation of the physicochemical and elastic properties of Langmuir mixed monolayers composed by a bile salt type (dehydrocholic acid, HDHC) and a double tailed cationic surfactant (didodecyldimethylammonium bromide, DDAB) as a previous step in their use as structural units for the construction of new delivery systems. The selection of both amphiphiles was because of their biocompatibility [5,6] and of their packing parameters [7].

Although a bilayer cannot simply be considered to consist of two independent monolayers, the head group–water interface in the two systems may be sufficiently similar to make monolayers

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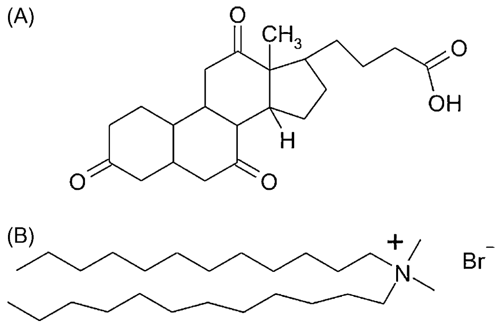

Fig. 1. Surfactant molecular structures: (A) dehydrocholic acid (HDHC) and (B) didodecyldimethylammonium bromide (DDAB).

effective bilayers surrogates [8,9]. Spread monolayers could be considered the simplest model to get molecular information and hence the first step to understand the properties and the behavior of selected molecules in future arrangements which can lead to promising materials with biological and medical applications.

2. Experimental

2.1. Materials

Dehydrocholic acid (HDHC) was from Dr. Theodor Schuchardt (Munich) and didodecyldimethylammonium bromide (DDAB) was obtained from Sigma. Both compounds were of analytical grade (99% pure) and were used as purchased, as a reference their structures are shown in Fig. 1.

2.2. Apparatus and operation conditions

The experiments were performed with a constant surface pressure penetration Langmuir balance based on Axisymmetric Drop Shape Analysis (ADSA) [10]. The whole setup, including the image capturing, the micro-injector, the ADSA algorithm, and the fuzzy pressure control, is managed by a Windows integrated program (DINATEN). A solution droplet is formed at the tip of a capillary, which is outer one of an arrangement of two coaxial capillaries connected to the different branches of a micro-injector. These can operate independently, permitting one to vary the interfacial area by changing the drop volume, and to exchange the drop content by through flow. The software first detects the drop and with an appropriate calibration, transforms it into physical coordinates. Then the experimental drop profiles, extracted from digital drops micrographs, are fitted to the Young–Laplace equation of capillarity by using ADSA. This process is performed automatically, the liquid density difference and the local gravity being the only inputs and yielding as outputs the drop volume V, the interfacial tension γ and the surface area A in about 0.3–5 s for each picture, depending on the required precision. Area control uses a modulated fuzzy logic PID (proportional, integral and derivative control) algorithm and is controlled by changing the drop volume. During the experiment, the drop is immersed in a thermostated and vapor-saturated standard spectrophotometer cuvette (Hellma®) minimizing contamination and drop evaporation. The surface pressure is obtained from the relationship $\pi = \gamma_0 - \gamma$, where π is the surface pressure; γ and γ_0 are the surface tension of the subphase liquid covered with and without the monolayer. The setup is placed on a pneumatic vibration-damped optical bench table in a clean laboratory. All experiments were performed at $(25.0 \pm 0.1)\,^{\circ}\mathrm{C}$. Temperature was maintained by a thermostat bath with recycling water throughout all the experiment. The curves were highly reproducible: each experiment was done three times, the standard deviation [10c] on π and A was estimated to be $\pm 0.01\ \mathrm{mJ\,m^{-2}}$ and $\pm 0.005\ \mathrm{nm^2\,mole\,c^{-1}}$, respectively. Equation fitting was done from non-linear procedures using ORIGIN® computer package (release 7.0).

2.3. Monolayers

Spreading solutions of HDHC and DDAB and their mixtures were prepared dissolved in a methanol:chloroform mixture (1:4) to obtain solutions of $(7 \times 10^{-5}\ \mathrm{M})$ total concentration. Then an aliquot of 1.2 μL was spread on the surface using a microsyringe. Once the spreading solvent has evaporated (4 min were allowed) and consequently the amphoteric molecules were confined to a monomolecular film at the subphase–air interface, the program started the expansion until a volume of 25 μL at a rate of $0.2\ \mu\mathrm{L\,s^{-1}}$. When expansion was finished, the drop area was maintained constant for 118 s (the necessary time for the tested monolayers to reach the thermodynamic equilibrium) and then the compression started at the same rate of expansion process.

3. Theoretical methods

With the aim to analyze the response of the adsorbed molecules to interface compression [11] the static elasticity modulus (ε_0) has been estimated from the equilibrium relationship between interfacial pressure (π) and interfacial area (A):

$$\varepsilon_0 = \left| \left(\frac{d\pi}{d \ln A} \right)_{T_{eq}} \right| \tag{1}$$

On basis of the π–A dependencies, the two-dimensional compressibility C_s of a monolayer at a given molecular area, or equivalently at a given surface pressure, is defined as the partial change of the area strain with respect to the surface pressure, that is $C_s = -(1/A)(dA/d\pi)$. Its reciprocal is the area modulus C_s^{-1} and both are valuable tools which can be used to classify the monolayer physical state [12]. For an ideal monolayer, the compressibility is assumed to be additive with respect to the product ($C_{s,i}$, A_i, $i = 1, 2, 3, \ldots$, etc.). Thus, $C_{s,\mathrm{ideal}}$ is obtained as follows [13]:

$$C_{s,\mathrm{ideal}} = \left(\frac{1}{A_{\pi,\mathrm{ideal}}} \right) [(C_{s1}A_{\pi,1})X_1 + (C_{s2}A_{\pi,2})X_2] \tag{2}$$

where C_{s1} and C_{s2} are the compressibility of the pure DDAB and the pure HDHC monolayer at a specific surface pressure (π), respectively. However, the experimental data C_s obtained from π–A isotherm of the mixed monolayer is usually different from the ideal value. The change in compressibility due to the presence of HDHC ($\Delta C_{s,\mathrm{HDHC}}$) is as follows:

$$\Delta C_{s,\mathrm{HDHC}} = C_s - C_{s1} \tag{3}$$

The change in compressibility due to interaction non-ideality ($\Delta C_{s,\mathrm{real}}$) is as follows:

$$\Delta C_{s,\mathrm{real}} = C_s - C_{s,\mathrm{ideal}} \tag{4}$$

The interaction between amphiphilic molecules at the air-aqueous solution interface is composed by contributions of electrostatic, hydrophobic and hydration forces [14–17]. For mixed systems, we examined the influence of such forces, analyzing their effect on the collapse area values. An ideal mixed monolayer and a completely immiscible monolayer are absolute opposite. However, both follow Eq. (5). In an ideal mixed monolayer of components 1 and 2, the intermolecular force $F_{11} = F_{12} = F_{22}$ whereas in a completely immiscible monolayer $F_{11} \gg F_{12} \ll F_{22}$, where F_{12} represents the attractive forces between molecules of the two dissimilar components.