Bile Salt-Induced Vesicle-to-Micelle Transition in Catanionic Surfactant Systems: Steric and Electrostatic Interactions

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The vesicle-to-micelle transition (VMT) was realized in catanionic surfactant systems by the addition of two kinds of bile salts, sodium cholate (SC) and sodium deoxycholate (SDC). It was found that steric interaction between the bile salt and catanionic surfactant plays an important role in catanionic surfactant systems that are usually thought to be dominated by electrostatic interaction. The facial amphiphilic structure and large occupied area of the bile salt are crucial to the enlargement of the average surfactant headgroup area and result in the VMT. Moreover, bile salts can also induce a macroscopic phase transition. Freeze−fracture transmission electron microscopy, dynamic light scattering, isothermal titration calorimetry, and absorbance measurements were used to follow the VMT process.

Introduction

Self-assembled aggregates, such as vesicles and micelles, have attracted much attention from a fundamental perspective[1] as well as for their widespread applications.[2−4] In particular, aggregates that undergo a transition between vesicles and micelles are of special interest because they offer great promise in drug-delivery systems. The formation and transition of self-assembled aggregates greatly depend on electrostatic, van der Waals, hydrophobic, and steric interactions and their delicate balance.[5,6] Many efforts were made to elucidate the weak interactions, which advanced the comprehension and control of the self-assembly processes.[5,6] However, systematic research is still necessary to obtain a better understanding of these weak interactions.

Recently, catanionic surfactant systems, which have various kinds of self-assembled structures and peculiar phase behaviors,[7−9] have attract an increasing amount of attention. It is believed that the electrostatic interactions, especially electrostatic attractions between oppositely charged surfactant headgroups, are crucial to the aggregate transition in this kind of system. Accordingly, most of aggregate transition-related studies focused on the electrostatic interactions, for example, the influences of surfactant composition,[7] pH,[10] salts,[11,12] and heavy metal ions.[13] However, our previous work indicated that the aggregate transition is induced not only by electrostatic interactions but also by hydrophobic interactions under certain conditions.[3] This gave us a hint that it is possible to identify other kinds of weak interactions that are comparable to or even surpass electrostatic interactions in catanionic surfactant systems.

Bile salts, which are different from conventional "head-and-tail" amphiphiles, are well-known facial amphiphiles that are composed of a rigid steroid skeleton with a polar face and a nonpolar face (Chart 1).[14] After entering the conventional amphiphile aggregates, owing to this specific facial structure, bile salt molecules lie flat at the aggregate surface between headgroups of the conventional amphiphile. In turn, the large steroid skeleton of the bile salt forces these headgroups apart from each other, which is referred to as steric interactions between the bile salt and amphiphile.[15,16] Hence the addition of a bile salt to the amphiphile aggregates usually increases the average headgroup area (referred to as the steric effect of a bile salt) and transforms these aggregates into highly curved ones (e.g., a bile salt-induced liposome-to-micelle transition).[17] On the basis of this viewpoint, herein we introduced bile salts into catanionic surfactant systems and studied the steric and electrostatic interactions as well as their effects on the aggregate transition.

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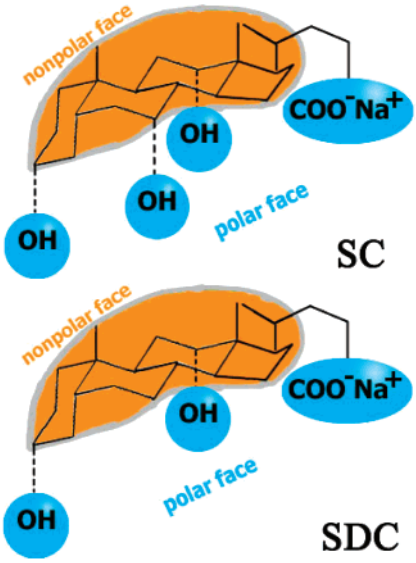
Chart 1. Molecular Structures of Sodium Cholate (SC) and Sodium Deoxycholate (SDC)[a]



[a] The facial amphiphilic structures of the bile salt are highlighted.

In contrast to a liposome formed by neutral or negative phospholipids, the catanionic vesicle is governed by electrostatic attractions that tend to reduce the average surfactant headgroup area and benefit the vesicle formation. Besides these already existing electrostatic attractions, the addition of a bile salt will bring about extra electrostatic interactions, especially steric interactions, between the negative bile salt and catanionic surfactant. The combined contributions of these factors will determine the aggregate transition in the catanionic surfactant/bile salt mixed systems. Thus, the present study on the aggregate transition is closely related to the steric and electrostatic interactions, which will advance the fundamental understanding of these weak interactions. Besides, catanionic surfactant systems have plentiful phase behaviors, for example, an aqueous surfactant two-phase (ASTP) behavior.[18] It is possible to utilize a bile salt to induce a macroscopic phase transition in catanionic surfactant systems.

Experimental Section

Materials. Dodecyltriethylammonium bromide (DEAB) and dodecyltrimethylammonium bromide (DTAB) were prepared by reactions of 1-bromododecane with triethylamine/trimethylamine, followed by recrystallizing five times from ethanol/acetone. Sodium laurate (SL) was prepared by neutralizing the lauric acid with NaOH in ethanol. Then the solvent was removed, and sodium laurate was vacuum dried. Lauric acid was recrystallized five times from ethanol/water. The purities of the surfactants were examined, and no minimum was found in the surface tension curves. Sodium dodecyl sulfate (SDS) and sodium dodecylbenzene sulfonate (SDBS) were purchased from Acros Organics Co. and used as received. Sodium cholate (SC) and sodium deoxycholate (SDC) were purchased from Fluka Co. and used as received. The water that was used was redistilled from potassium permanganate.

Sample Preparation. Catanionic surfactant mixtures were prepared by mixing the single surfactant solutions directly in a test tube. Then the desired amount of a concentrated bile salt solution (0.1 or 0.5 M) was added to the tube by a microsyringe. After the samples were stirred for several minutes, they were thermostated at 25 °C for at least 24 h to reach equilibrium. The effective pK_a values of bile salts in the studied catanionic surfactant systems were determined to be between 4.3 and 4.8 by pH titration. In DEAB/SDS/SC or SDC and DTAB/SDBS/SC solutions, pH values were between 6.4 and 6.8 without adjusting. In DTAB/SL/SC solution, the pH was adjusted to 9.2 by 10 mM $Na_2B_4O_7 \cdot 10H_2O$ to control the hydrolysis of SL. In all of these cases, the percentages of ionized SC or SDC are higher than 99%.

Absorbance Measurements. Absorbance measurements were carried out at 500 nm with a Beijing Purkinje General TU-1810 spectrophotometer whose temperature was controlled at 25.0 °C.

Freeze−Fracture Transmission Electron Microscopy (FF-TEM). Samples for transmission electron microscopy were prepared by freeze−fracture replication according to standard techniques. Fracturing and replication were carried out in a high-vacuum freeze-etching system (Balzers BAF-400D). Replicas were examined in a JEM-100CX electron microscope.

Dynamic Light Scattering (DLS). Dynamic light scattering measurements were made using a spectrometer of standard design (ALV-5000/E/WIN Multiple Tau Digital Correlator) and a Spectra-Physics 2017 200 mW Ar laser (514.5 nm wavelength). The scattering angle was 90°, and the intensity autocorrelation functions were analyzed by the CONTIN method. The temperature was held at 25.0 °C by an external thermostat.

Isothermal Titration Calorimetry (ITC). The calorimetric measurements were conducted with a TAM 2277-201 microcalorimetric system (Thermometric AB, Jarfalla, Sweden) with a stainless steel sample cell of 1 mL at 25.00 °C. The cell was initially loaded with 0.8 mL of the DEAB/SDS (molar ratio 42/58, C_{total} = 10 mM) aqueous solution. The concentrated SC or SDC solution was injected into the sample cell via a 250 μL Hamilton syringe controlled by a 612 thermometric Lund pump. The system was stirred at 50 rpm with a gold propeller. The observed enthalpy (ΔH_{obs}) was obtained by integration over the peak of each injection in the plot of heat flow P against time t.

Zeta Potential Measurements. Zeta potentials were measured using a temperature-controlled "zetasizer 2000" (Malven Instruments Co.) zeta potential analyzer at 25.0 °C.

Surface Tension Measurements. Surface tension measurements were conducted using the drop volume method[19] at 25.0 °C. To provide constant ionic strength, all solutions were prepared with a buffer of 0.08 M NaBr and 0.01 M $Na_2B_4O_7 \cdot 10H_2O$, which kept the pH of the solution at 9.2 and controlled the hydrolysis of SC or SDC. The adsorbed amount of surfactant (Γ_∞) was calculated according to the Gibbs adsorption equation because the ionic strength and [Na^+] were kept constant[20]

$$\Gamma_\infty = \frac{-\mathrm{d}\gamma}{2.303RT\,\mathrm{d}\log C} \quad (1)$$

where γ is the surface tension in mN m^{-1}, C represents the total concentration of surfactants, including bile salt when it is present, Γ_∞ is the saturated adsorption in mol m^{-2}, dγ/d log C is the slope of corresponding dashed line in Figure S1 (Supporting Information), T is the absolute temperature, and R = 8.314 J mol^{-1} K^{-1}. Then the average minimum area per surfactant molecule (A_{min}) in nm^2 is obtained from the saturated adsorption by

$$A_{min} = \frac{10^{18}}{N_A \Gamma_\infty} \quad (2)$$

where N_A is Avogadro's number. The average headgroup area of the catanionic surfactant/bile salt mixture (i.e., a in Table 1) is approximately equal to the corresponding A_{min}.

Model Calculations for the Calculated Average Headgroup Area a_c. Our assumption is that bile salt molecules lie flat at the aggregate surface between headgroups of the catanionic surfactant in catanionic surfactant/bile salt mixed systems. On the basis of this assumption and the fact that most bile salt charges are screened in

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such systems, it is reasonable to take the limiting areas of cholic acid,[21] 1.5 nm^2, and deoxycholic acid,[22] 1.2 nm^2, as the occupied areas of SC and SDC, respectively. Now, we can roughly estimate the a_c after bile salt addition by simply averaging the areas of catanionic surfactant and bile salt against their molar ratio. For example, according to the a of DEAB/SDS (molar ratio 3/1, 0.26 nm^2, in Table 1) and the occupied area of SC (1.5 nm^2), the a_c of DEAB/SDS/SC (molar ratio 3/1/2) is 0.67 nm^2 ($0.26 \times 2/3 + 1.5/3$ nm^2). The agreement between calculated a_c and experimental a (Table 1) supports our assumption. The calculated values are a little larger than the experimental values (Table 1) because the contribution of the electrostatic attractions between the bile salt and excess cationic surfactant was neglected in the calculations.

Results and Discussion

VMT in the Dodecyltriethylammonium Bromide/Sodium Dodecyl Sulfate (DEAB/SDS, Molar Ratio 42/58, C_{total}= 10 mM) System Induced by Bile Salt. Before bile salt addition, vesicles are major aggregates in this DEAB/SDS solution, which is proved by the bluish appearance of the solution, spherical structures in the FF-TEM micrograph (Figure 1), and dominant peak at 70 nm in the DLS plot (Figure 3A). Open circles in Figure 2A show the variation of absorbance with the increase in SC concentration. With the addition of SC, the absorbance decreases slightly, followed by a sharp drop, and then reaches a constant value at last. The absorbance curve can be divided into three regions according to the two clear inflection points. In the beginning stage of SC addition, the absorbance decreases slightly (Figure 2A), and the aggregate size distribution in Figure 3B is almost the same as that in Figure 3A. These observations are reasonable because most SC molecules will dissolve in water as free molecules and can hardly influence vesicles at such a low [SC]. Thus, the first region is assigned as the vesicle region. With the further addition of SC, the absorbance decreases remarkably (Figure 2A), and the micelle peak becomes comparable with the vesicle peak (Figure 3C). This indicates that quite a few SC molecules enter vesicles and cause a considerable number of vesicles to transform into micelles. The second region is assigned as the coexisting region of vesicles and micelles. Finally, after the SC concentration reaches a critical value of 4.8 mM, the absorbance remains constant (Figure 2A), and the vesicle peak disappears (Figure 3D), which suggests that nearly all of the vesicles have turned into micelles. The third region is assigned as the micelle region. As to the addition of SDC to the same DEAB/SDS solution, a similar absorbance variation was observed (open circles in Figure 2B). At [SDC] = 2.5 mM, vesicles have been completely transformed into micelles (Figure 3E).

Microcalorimetry is a powerful tool for investigating the physical and chemical processes accompanied by the release or uptake of heat. In particular, ITC has advantages in characterizing the aggregate transition because of its high sensitivity.[23] To investigate the transition process further, ITC measurements were carried out to measure the observed enthalpy ΔH_{obs} with the titration of concentrated SC or SDC solution into DEAB/SDS (molar ratio 42/58, C_{total} = 10 mM) solution. For the addition of SC to the solution, as shown in Figure 2A (filled circles), the boundaries of the peak in the calorimetric curve coincide exactly with the inflection points of the absorbance curve. In the vesicle region, the absolute value of ΔH_{obs} is small and undergoes only a moderate change, in accordance with the small influence of SC on vesicles at such a low [SC]. In the coexisting region of vesicles and micelles, the appearance of significant exothermic peaks corresponds to the fact that a considerable number of vesicles transform into micelles. The exothermic enthalpies are caused by the transition from the mixed vesicles of DEAB, SDS, and SC to mixed micelles, namely, the vesicle disruption and micelle formation. In the micelle region, the absolute value of ΔH_{obs} is small and remains nearly constant, indicating that no obvious aggregate transition occurs. That is to say that the vesicles have

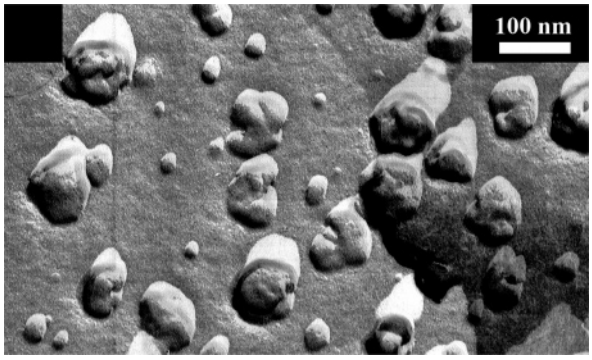

Figure 1. FF-TEM micrograph of the DEAB/SDS (molar ratio 42/58, C_{total} = 10 mM) solution without bile salt.

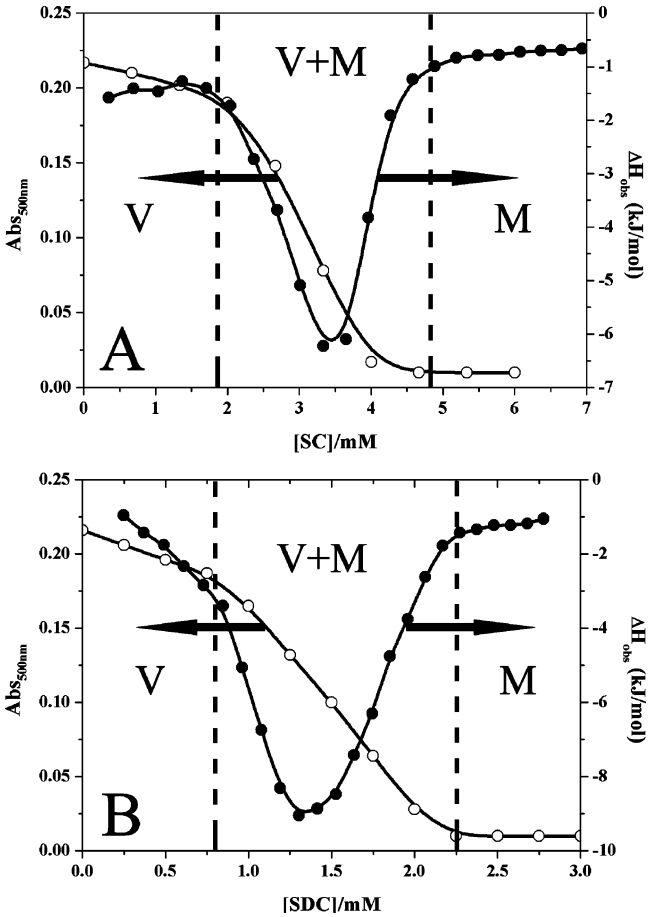

Figure 2. (Open circles) Variation in absorbance in the DEAB/SDS (molar ratio 42/58, C_{total} = 10 mM) system with various concentration of SC (A) or SDC (B). (Filled circles) Calorimetric titration curves of concentrated SC (A) or SDC (B) solution in DEAB/SDS (molar ratio 42/58, C_{total} = 10 mM) solution against the final bile salt concentration. V, vesicle region; M, micelle region; V + M, vesicle and micelle coexisting region. Dashed lines are the boundaries of these regions.

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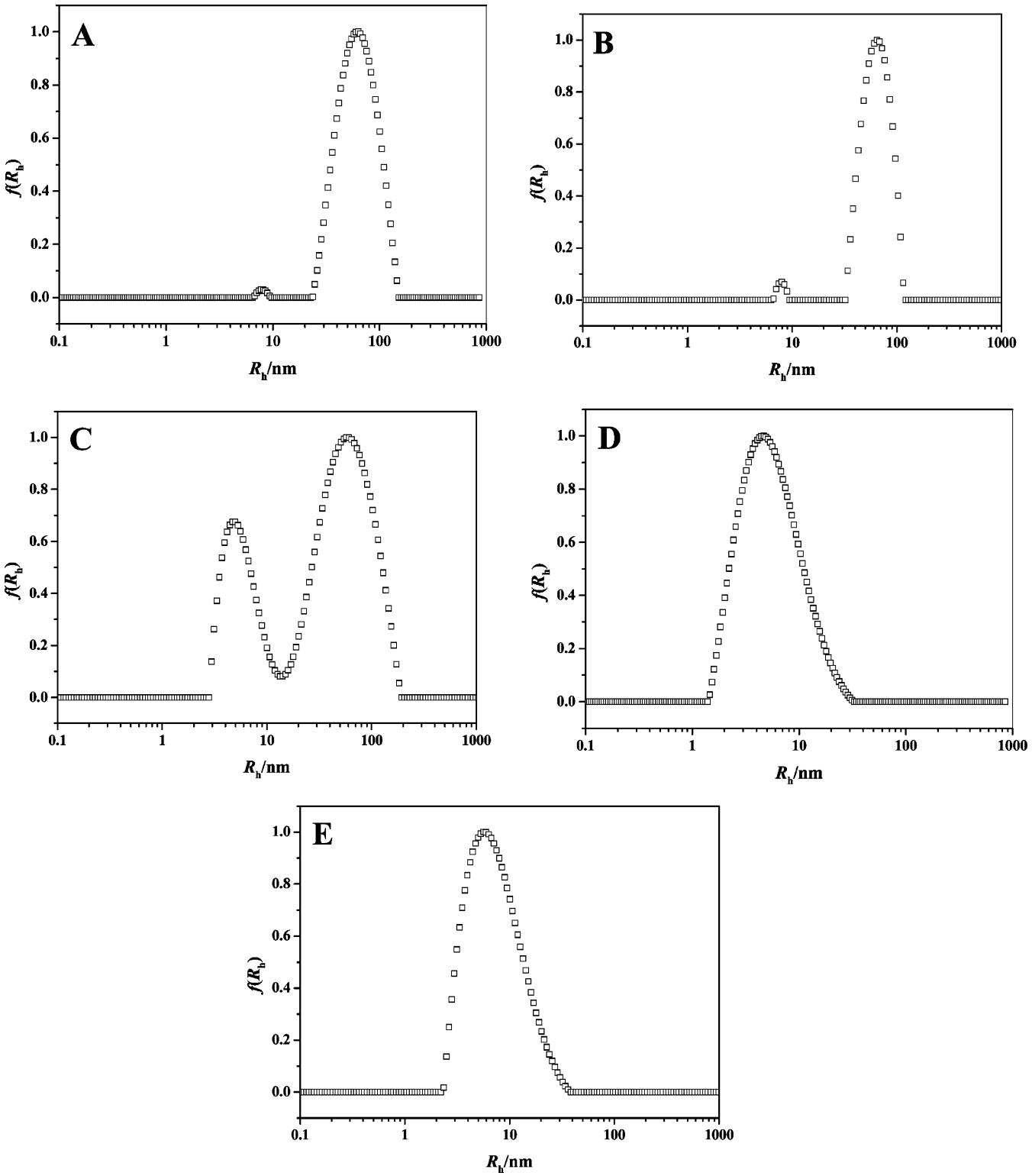

Figure 3. Hydrodynamic radius (R_h) distributions in the DEAB/SDS (molar ratio 42/58, C_{total} = 10 mM) system with different bile salt concentrations. (A) Without bile salt. (B) [SC] = 1.5 mM. (C) [SC] = 3.5 mM. (D) [SC] = 6 mM. (E) [SDC] = 2.5 mM.

transformed into the micelles completely. As to another facial amphiphile, SDC, a similar result was observed when it was added to the same DEAB/SDS solution (filled circles in Figure 2B). Combining the results of absorbance, DLS, and ITC measurements, we can draw the conclusion that SC and SDC can induce VMT in the DEAB/SDS (molar ratio 42/58, C_{total} = 10 mM) system. In this anionic surfactant-rich system, the bile salt-induced VMT may come from the steric and electrostatic effects of bile salt because both the electrostatic repulsion (between negative bile salt ions and excess DS^-) and the steric interaction (between bile salt and catanionic surfactant) tend to enlarge the average headgroup area, promoting micelle formation.

VMT in DEAB/SDS (Molar Ratio 75/25, C_{total}= 10 mM) System and Other Catanionic Surfactant Systems Induced by Bile Salt. As mentioned above, bile salt-induced VMT may arise from the steric and electrostatic effects of bile salt in the anionic surfactant-rich vesicle system (DEAB/SDS, molar ratio 42/58, C_{total} = 10 mM, zeta potential −56 mV). It is hard to know the different contributions of the steric effect and the electrostatic effect in such case. To compare the steric interactions

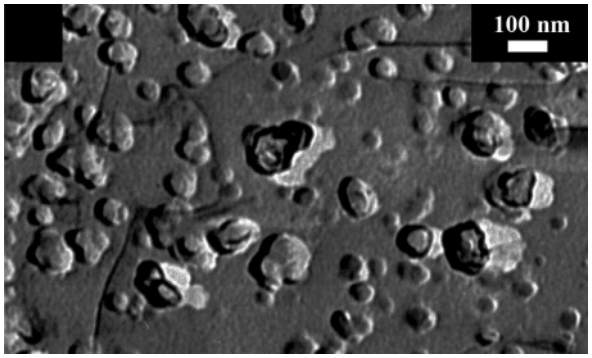

Figure 4. FF-TEM micrograph of the DEAB/SDS (molar ratio 75/25, C_{total} = 10 mM) solution without bile salt.

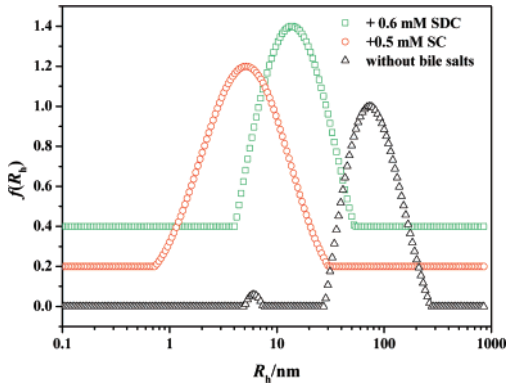

Figure 5. Hydrodynamic radius (R_h) distributions in the DEAB/SDS (molar ratio 75/25, C_{total} = 10 mM) system with different bile salt concentrations.

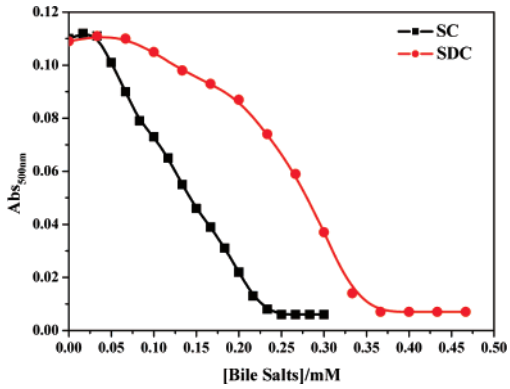

Figure 6. Variation in absorbance with varied bile salt concentration in the DEAB/SDS (molar ratio 75/25, C_{total} = 10 mM) system.

with electrostatic attractions directly, further investigations were performed in the cationic surfactant-rich vesicle system (DEAB/SDS, molar ratio 75/25, C_{total} = 10 mM, zeta potential 32 mV). Before bile salt addition, vesicles are major aggregates in the solution, which is verified by TEM (Figure 4) and DLS (Figure 5) results. After the addition of SC or SDC, the absorbance of the solution decreases remarkably (Figure 6) and the vesicle peak disappears in DLS plots (Figure 5), indicating that the bile salt transforms vesicles into the micelles. It is worth noting that, besides the already existing electrostatic attractions between DEA^+ and DS^-, the addition of negative bile salt ions to vesicles with excess DEA^+ will bring about extra electrostatic attractions. In other words, the mixed vesicles get closer to neutral ones. Usually, aggregates in catanionic surfactant systems with less excess charge will turn into aggregates with less-curved structures, such as vesicles, lamellae, or precipitation.[7] However, only VMT was found after bile salt addition, which opposites the effect of

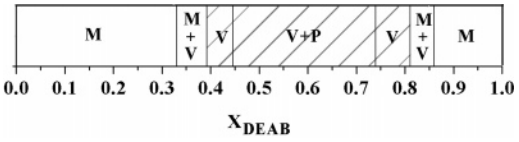

Figure 7. Phase diagram of DEAB/SDS with C_{total} = 10 mM and varying X_{DEAB} ($X_{DEAB} = C_{DEAB}/C_{total}$) at 25 °C. M, micelle region; M + V, micelle and vesicle coexisting region; V, vesicle region; V + P, vesicle and precipitation coexisting region. The shadowed area is the effective region of the bile salt. This phase diagram is redrawn from ref 3.

electrostatic attractions and reveals that electrostatic interactions do not play a predominant role in this case. Because the observed VMT is in line with the steric effect of bile salt, it is supposed that the steric interactions between the bile salt and catanionic surfactant overcome both the already existing and the extra electrostatic attractions, dominating this aggregate transition.

Figure 7 shows the phase diagram of DEAB/SDS systems at C_{total} = 10 mM with the variation of X_{DEAB} ($X_{DEAB} = C_{DEAB}/C_{total}$). Our previous work[3] reported that some organic additives, such as *n*-butylbenzene and *n*-hexane, induce only the micelle-to-vesicle transition (MVT) in limited micelle regions near the boundaries between the M and M + V regions in Figure 7. However, VMT induced by bile salt can take place in the entire vesicle region. Furthermore, even the precipitation and vesicles in the V + P region can be completely turned into micelles by bile salt. The effective region of bile salt ranges from X_{DEAB} = 0.39 to 0.82 (shadow area in Figure 7). These results demonstrate that SC and SDC are effective additives for transforming catanionic vesicles into micelles and the steric effect of bile salt is powerful even in catanionic surfactant systems.

Further work demonstrates that the bile salt-induced VMT can also be found in other catanionic surfactant systems, such as dodecyltrimethylammonium bromide/sodium dodecylbenzene sulfonate (DTAB/SDBS), cetyltrimethylammonium bromide/sodium octyl sulfate (CTAB/SOS), and DTAB/sodium laurate (SL). For example, the results of TEM (Figure 8A) and DLS (Figure 8C) suggest that the predominant aggregates are vesicles in DTAB/SDBS (molar ratio 75/25, C_{total} = 10 mM) solution, which agrees with the literature.[24] With SC addition, as expected, the absorbance decreases from 0.178 to 0.005 (Figure 8B) and the peak in the DLS plot shifts from 80 to 3 nm (Figure 8C), which clearly shows the SC-induced VMT. It is suggested that the bile salt can generally be used to turn vesicles into micelles in catanionic surfactant systems.

Mechanism for VMT in Catanionic Surfactant Systems Induced by Bile Salt. In general, the transformation of self-assembled aggregates depends on the variation of weak interactions.[5,6] In particular, for surfactant systems, the average surfactant headgroup area is usually thought to be sensitive to the variation of weak interactions when the molecular structure of the surfactant does not change.[25] Thus, surface tension measurements were carried out to get information about the influence of bile salt on the average headgroup area, *a*. Table 1 shows that *a* increases greatly after the addition of bile salt to cationic surfactant-rich systems. For DEAB/SDS and DTAB/SDBS, the values of *a* are 0.26 and 0.29 nm^2, respectively, whereas for DEAB/SDS/SC, DEAB/SDS/SDC, and DTAB/SDBS/SC, the values of *a* are 0.56, 0.37, and 0.63 nm^2, respectively. As mentioned in the Introduction, three factors should be taken into consideration to interpret this *a* enlargement: (1) the already existing electrostatic attraction between oppositely charged surfactant ions, (2) the steric

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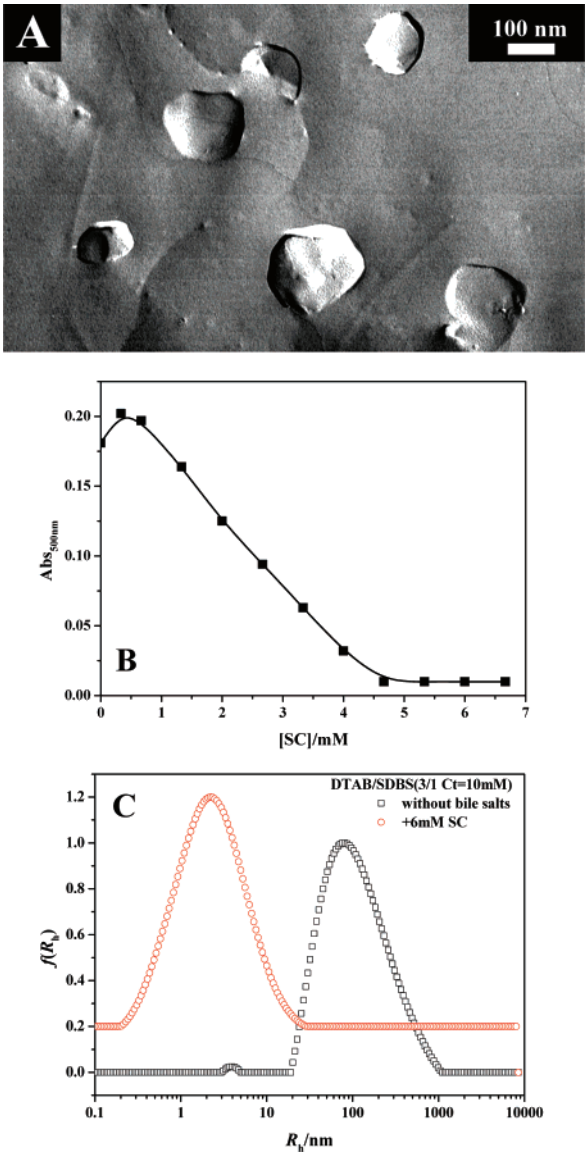

Figure 8. (A) FF-TEM micrograph of the DTAB/SDBS (molar ratio 75/25, C_{total} = 10 mM) system without bile salt. (B) Variation in absorbance with varied SC concentration in DTAB/SDBS (molar ratio 75/25, C_{total} = 10 mM) system. (C) Hydrodynamic radius (R_h) distributions in the DTAB/SDBS (molar ratio 75/25, C_{total} = 10 mM) system with different SC concentrations.

Table 1. Calculated Average Headgroup Area a_c, Average Headgroup Area *a*, Packing Parameter *p*, and Aggregate Type in Different Systems

system (molar ratio)	a_c $(nm^2)^a$	a $(nm^2)^b$	p	aggregate type
DEAB/SDS (3/1)		0.26	0.70	vesicle
DEAB/SDS/SC (3/1/2)	0.67	0.56	0.32	micelle
DEAB/SDS/SDC (3/1/2)	0.57	0.37	0.49	micelle
DTAB/SDBS (3/1)		0.28	0.62	vesicle
DTAB/SDBS/SC (3/1/2)	0.69	0.63	0.29	micelle

[a] Calculated values. See the Experimental Section for details of model calculations. [b] Experimental values based on adsorption data in Figure S1. See the Experimental Section.

interaction between the bile salt and catanionic surfactant, and (3) the extra electrostatic interaction between the negative bile salt and catanionic surfactant (i.e., the attraction when the cationic surfactant is in excess and repulsion when the anionic surfactant is in excess). In the cationic surfactant-rich case, factors of 1 and 3 tend to reduce *a*, and factor 2 tends to increase *a*. The resultant *a* enlargement (Table 1) indicates that the steric interaction is so powerful that it overcomes not only the already existing electrostatic attraction but also the extra electrostatic attraction. Such a strong steric effect of bile salt may come from its large occupied area (i.e., 1.5 nm^2 for SC[21] and 1.2 nm^2 for SDC,[22] which are 3 to 4 times larger than the headgroup area of a conventional surfactant). As to the anionic surfactant-rich case, the *a* enlargement can be expected because factors of 2 and 3 tend to increase *a*.

The geometry rule[25] has been widely used to explain the transformations of organized assemblies where *p* is a packing parameter: $p < 1/2$ for micelles and $1/2 < p < 1$ for vesicles or lamellar structures. *P* is defined as v/al, where v is the surfactant tail volume, l is the tail length, and a is the average headgroup area. After being added to the catanionic surfactant vesicle solution, bile salt will participate in vesicles and, in turn, influence vesicles. In the former process, hydrophobic interaction is essential (i.e., the hydrocarbon moiety of bile salt prefers the hydrophobic environment in aggregates). In the latter process, steric interaction plays a key role and increases *a* greatly as mentioned above. As a result, *p* decreases, and vesicles turn into micelles. Furthermore, packing parameter *p* can be calculated from v/al, where *a* is the experimental value in Table 1 and v/l equals a constant value,[26] 0.18 nm^2. Before the addition of bile salt, the values of *p* are larger than 0.5, corresponding to vesicles, whereas after the addition of bile salt the values of *p* are smaller than 0.5, corresponding to micelles (Table 1). These results are in good agreement with our interpretation.

In addition, Table 1 also demonstrates the calculated average headgroup area a_c, which is based on the assumption that bile salt molecules lie flat on the aggregate surface. The coincidence between calculated a_c and experimental *a* supports our assumption, which is also supported by the results of ^2H NMR[15] and SANS[16] in phospholipid/bile salt mixed systems. Combining the results of adsorption and calculation data, we can propose the corresponding mechanism in Scheme 1. After being added to the catanionic surfactant solution, the bile salt is incorporated into vesicles as a result of its hydrophobicity. In vesicles, bile salt molecules lie flat on the vesicle surface between the headgroups of the catanionic surfactant and enlarge the distance between catanionic surfactant headgroups, promoting micelle formation. The steric interaction surpasses the electrostatic attraction and dominates the aggregate transition in this case. The facial amphiphilic structure and large occupied area of the bile salt are responsible for its strong steric effect and are critical to the VMT. These results imply that the steric effect of bile salt may be used to render a transition in weak interaction-based self-assembled aggregate systems.

Bile Salt-Induced Macroscopic Phase Transition in DTAB/SL System. It is widely accepted that the microstructures in the solution are closely related to the macroscopic phase behavior. Here, we try to exploit a bile salt, which can render a microstructure transition, to induce a macroscopic phase transition in the catanionic surfactant/bile salt mixed system. The formation of an aqueous surfactant two-phase (ASTP) in a DTAB/SL (molar ratio 58/42, C_{total} = 80 mM, pH 9.2) system is typical and well studied.[18] The upper phase is bluish and contains a large number of aggregated vesicles, which is shown in Figure 9A. Correspondingly, the peak at 200 nm in the DLS plot (Figure 10) can be assigned to vesicle aggregation. With the addition of 15

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(26) Kraack, H.; Ocko, B. M.; Pershan, P. S.; Sloutskin, E.; Deutsch, M. *Science* **2002**, *298*, 1404. The diameter (*d*) of a hydrocarbon tail is 0.48 nm. We assumed the hydrocarbon tail to be a cylinder with $v/l = l\pi(d/2)^2/l = 0.18$ nm^2.

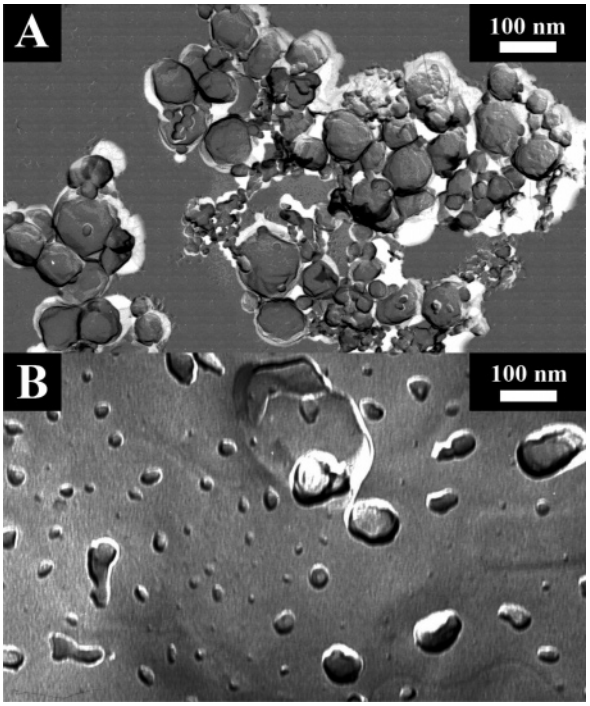
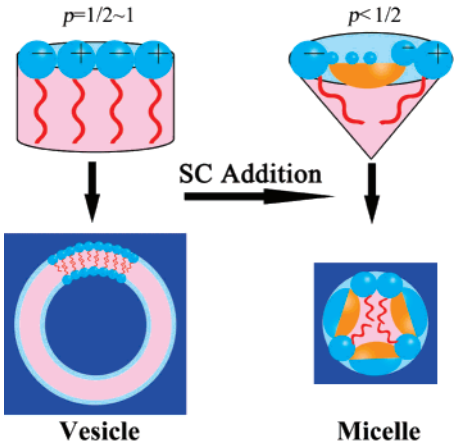


Figure 9. FF-TEM micrographs. (A) Upper phase of the DTAB/SL (molar ratio 58/42, C_{total} = 80 mM, pH 9.2) solution. Aggregated vesicles. (B) Homogeneous solution of DTAB/SL (molar ratio 58/42, C_{total} = 80 mM, pH 9.2) and [SC] = 15 mM. Separated vesicles.

Scheme 1. VMT in Catanionic Surfactant Systems Induced by SC[a]



[a] The situation for SDC is similar. Catanionic surfactants are shown as molecules with a spherical head and a flexible tail, whereas the SC is schematically represented following Chart 1.

mM SC, the two-phase solution turns into a homogeneous solution with a bluish appearance. The FF-TEM micrograph demonstrates that the aggregated vesicles become separated (Figure 9B), which is in accordance with the peak shift from 200 to 70 nm (Figure 10). Meanwhile, the micelle peak at 10 nm grows considerably (Figure 10), indicating that a moderate number of vesicles transform into micelles. When [SC] = 20 mM, the solution is transparent and homogeneous, and the vesicle peak disappears

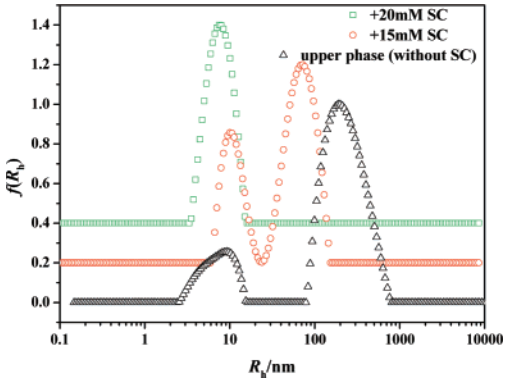


Figure 10. Hydrodynamic radius (R_h) distributions in DTAB/SL/SC systems.

(Figure 10), which means that vesicles completely transform into micelles. By combining the above results, it can be concluded that SC induces VMT and turns the ASTP into a homogeneous solution. Usually, the ASTP is ascribed to vesicle aggregation,[18] whereas the addition of SC decreases the number of vesicles and makes the density of vesicles too low to maintain aggregation. Therefore, the addition of bile salt can induce not only a surfactant aggregate transition but also a macroscopic phase transition.

Conclusions

Bile salt is found to be one kind of effective additive to transform vesicles into micelles not only in anionic surfactant-rich catanionic systems but also in cationic surfactant-rich ones. The facial amphiphilic structure and large occupied area of bile salt are crucial to this transition. The steric effect of bile salt is powerful and even surpasses the effect of electrostatic attractions in catanionic surfactant/bile salt mixed systems, which shows the potential to affect other kinds of weak interaction-based self-assembled aggregate systems. Moreover, it is interesting to find that beyond the microstructure transition the bile salt is also able to induce a macroscopic phase transition. Our studies on the catanionic surfactant/bile salt mixed systems may generally provide a simple, effective way to control the microstructure and macroscopic phase transition in surfactant systems, which will benefit the design and control of self-assembled structures. We hope that this work will promote a further understanding of weak interactions and advance the applications of bile salt in microstructure and macroscopic phase transitions.

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Supporting Information Available: Surface tension curves in catanionic surfactant/bile salt systems. This material is available free of charge via the Internet at http://pubs.acs.org.

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