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Micelle Formation of Polyoxyethylene Cholesteryl Ether in Water

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The critical micelle concentrations and the micellar weights of polyoxyethylene cholesteryl ether, $C_{27}H_{46}(OCH_2CH_2)_nOH$ (Chol EO$_n$, $n=25$ and 30) and polyoxyethylene dihydrocholesteryl ether, $C_{27}H_{48}(OCH_2CH_2)_nOH$ (Dichol EO$_n$, $n=30$) were determined by surface tension measurement and membrane osmometry. The critical micelle concentration (cmc) values and the micellar weights of these surfactants are similar in magnitude to those of nonionic surfactants of ethylene oxide adduct type with an alkyl or aralkyl group as a lipophilic group. On the basis of these results, it was concluded that these nonionic surfactants form the usual type of large micelles in water in contrast to the cases of cholic acids and their conjugates which form small aggregates in the relatively high concentration range.

Keywords——nonionic surfactant; polyoxyethylene cholesteryl ether; critical micelle concentration; surface tension; micellar weight; membrane osmometry

Polyoxyethylene cholesteryl ether is a kind of nonionic surfactant containing a cholesteryl group and a polyoxyethylene group as a lipophilic and a hydrophilic group, respectively, in the molecule. This type of surfactant solubilizes steroidal hormones in aqueous solution[1] and has been used in the cosmetic industry to increase the transepidermal absorption of various compounds. However, few studies have been done on the solution properties of polyoxyethylene cholesteryl ether.

On the other hand, surfactants with a flat and bulky lipophilic group, such as cholic acids and their conjugates, form micelles with small aggregation numbers in the relatively high concentration range (cmc −0.13 M),[2] being stacked side by side,[3,4] while the usual nonionic surfactants, such as polyoxyethylene alkyl or aralkyl ethers form spherical or ellipsoidal micelles with large aggregation numbers.[5]

Thus, we investigated the critical micelle concentration's (cmc's) and micellar weights of polyoxyethylene cholesteryl ethers by means of measurements of surface tension and osmotic pressure in aqueous solutions.

Experimental

Materials——Polyoxyethylene cholesteryl ether with average numbers of ethylene oxide units of 25 and 30 (Chol EO$_{25}$ and Chol EO$_{30}$), and polyoxyethylene dihydrocholesteryl ether with an average number of ethylene oxide units of 30 (Dichol EO$_{30}$) were synthesized by Nikko Chemical Co. using the reaction of ethylene oxide gas and cholesterol or dihydrocholesterol in a suitable solvent. Therefore all these surfactants have the poisson distribution of ethylene oxide chain lengths, and the average degree of polymerization was determined from the increase in weight of the reaction mixture. These surfactants are white waxy solids and were used without purification. These surfactants were dissolved in water purified by distillations and deionization.

Determination of cmc——Determination of cmc was performed by the measurement of surface tension at various concentrations. The surface tension was measured by the drop weight method described elsewhere.[6] Surface tension of the solution (γ) was calculated from the observed volume of the drop (V) and the radius of the capillary tube (r) using Eq. 1.

$$\gamma = \frac{V\rho g F}{r} \tag{1}$$

where ρ, g and F are the density of the solution, the acceleration due to gravity and the correction factor of Harkins and Brown,[7] respectively. Experimental determination of surface tension was precise to ±0.2 dyn cm^{-1}.

Determination of Micellar Weight——Osmotic pressure (π) was measured at various concentrations with an electronic membrane osmometer munufactured by Knauer Co., Ltd. Micellar weight (M_w) was calculated from Eq. 2.

$$M_w = \frac{RT}{\pi/C(C\rightarrow 0)\rho} \tag{2}$$

where C and ρ are the concentration in g/100 ml and the density of the solution, respectively. R and T have the usual meanings. In this experiment, ρ was assumed to be unity because of fairly low concentration of the solution. Experimental error in the determination of M_w was within ±10%.

Results and Discussion

Figure 1 shows plots of the surface tension *vs.* logarithm of concentration of Chol EO_{30} at various temperatures. Surface tension decreases with increase of $\log M$ and the concentration at the break point of each curve is regarded as the cmc, which is given in Table I together with the thermodynamic parameters of micellization, adsorbed amount (Γ) and adsorbed area of molecule (A) at the cmc. Free energy (ΔG°_m), enthalpy (ΔH°_m) and entropy (ΔS°_m) were calculated from Eqs. 3, 4 and 5.

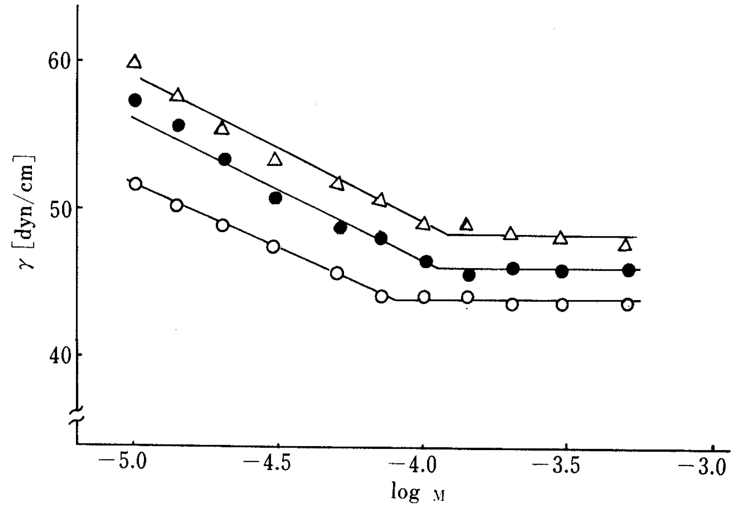

Fig. 1. Surface Tension *vs.* Concentration Curves for Chol EO_{30} at Various Temperatures

△, 15 °C; ●, 25 °C; ○, 35 °C.

TABLE I. cmc Values and Thermodynamic Parameters of Chol EO_{30} in Water at Various Temperatures

Temp. (°C)	cmc (M)	ΔG°_m (cal/mol)	ΔH°_m (cal/mol)	ΔS°_m (cal/mol·deg.)	Γ (mol/cm²)	A (Å²/molecule)
15	1.17×10^{-4}	−5.18	3.49	30.1	1.8×10^{-10}	92
25	1.12×10^{-4}	−5.39	3.74	30.6	1.7×10^{-10}	100
35	0.79×10^{-4}	−5.77	3.99	31.7	1.2×10^{-10}	140

$$\Delta G^{\circ}_{\mathrm{m}} = \boldsymbol{R}T \ln \mathrm{cmc} \tag{3}$$

$$\Delta H^{\circ}_{\mathrm{m}} = -\boldsymbol{R}T^2\left(\frac{d \ln \mathrm{cmc}}{dT}\right)_{\mathrm{p}} \tag{4}$$

and

$$\Delta S^{\circ}_{\mathrm{m}} = \frac{\Delta H^{\circ}_{\mathrm{m}} - \Delta G^{\circ}_{\mathrm{m}}}{dT} \tag{5}$$

where $\boldsymbol{R}$ and T have the usual meanings.
Γ and A are calculated from Eqs. 6 and 7.

$$\Gamma = -\frac{1}{2.203\ \boldsymbol{R}T}\left(\frac{\partial \gamma}{\partial \log M}\right) \tag{6}$$

and

$$A = \frac{10^{16}}{N\Gamma} \tag{7}$$

where N is the Avogadro number.

As can be seen in Fig. 1 and Table I, cmc values increase on lowering the temperature. Similar behavior was observed in aqueous solutions of polyoxyethylene alkanol ether.[8)] As shown in Table I, negative values of free energy changes on micellization originate from the large positive entropy changes, as with other nonionic surfactants.[8,9)] The positive values of enthalpy change indicate that the energy required for dehydration of the ether group and melting of the "iceberg" in the vicinity of the cholesteryl group is larger than the energy delivered on the association of the hydrophobic cholesteryl group in the micellization process. The large positive entropy changes mean that the entropy changes associated with the above-mentioned endo- and exothermic processes overcome the configurational entropy loss of the ethylene oxide chain on micellization.

The limiting adsorbed area of cholesterol in a monolayer film is about 41 Å^2.[10)] The A value of Chol EO$_{30}$ is more than twice that of cholesterol, indicating that the steric effect of the ethylene oxide chain is important on the alignment of the molecules of Chol EO$_{30}$ at the air-water interface. This idea is supported by the fact that the A value of nonylphenol with 30 ethylene oxide units is 101 Å^2 at 25 °C,[11)] and this value is nearly equal to that of Chol EO$_{30}$, though the cross-sectional area of the benzene ring (25 Å^2) is much smaller than that of the cholesteryl group. These results suggest that the adsorbed area of a nonionic surfactant molecule of ethylene oxide adduct type is determined mainly by the ethylene oxide chain length if the chain length is long enough.

The cmc value of Chol EO$_{30}$ is almost the same as that of Chol EO$_{25}$ and larger than that of Dichol EO$_{30}$. The cmc values of nonylphenol and dodecanol, each having 30 ethylene oxide

TABLE II. cmc Values, Micellar Weights and Aggregation Numbers of Polyoxyethylene Cholesteryl Ethers in Water

Compd.	cmc[a)] (M)	Micellar[b)] weight	Aggregation[b)] number
Chol EO$_{30}$	1.12×10^{-4}	1.5×10^{5}	90
Chol EO$_{25}$	1.15×10^{-4}	—	—
Dichol EO$_{30}$	0.79×10^{-4}	8.1×10^{5}	470

a) At 25 °C. b) At 23 °C.

units, are 1.8×10^{-4}[12] and 0.7×10^{-4} M[8], respectively. These cmc values are comparable to those of the surfactants listed in Table II, suggesting that the cholesteryl group has similar hydrophobic character to the dodecyl or nonylphenyl group.

Micellar weight was investigated by using a vapor pressure osmometer and membrane osmometer with a cellulose acetate membrane. It was difficult to detect the vapour pressure difference between pure water and aqueous nonionic surfactant solution in the concentration range of 0.0018—0.05 M by vapor pressure osmometry, indicating that formation of small aggregates, as observed in aqueous solutions of cholic acid, hardly takes place in aqueous solutions of polyoxyethylene cholesteryl ether. Thus, membrane osmometry was employed in the concentration range of 0.0058—0.03 M at 23 °C. Almost linear relations were obtained between π/C values and C. Micellar weights were calculated from the π/C values extrapolated to $C=0$. As can be seen in Table II, the micellar weights for Chol EO_{30} and Dichol EO_{30} are 150000 and 800000, respectively, which correspond to aggregation numbers of 90 and 470. The aggregation number of octylphenol with 9 ethylene oxide units is around 100[13] and that of dodecanol with 6 ethylene oxide units is around 300—500 depending on concentration.[14] Generally, micellar weight increases with the hydrophobicity of a surfactant molecule and cmc decreases with increase of hydrophobicity. Judging from the values of cmc and aggregation number of the surfactants, the dihydrocholesteryl group is more hydrophobic than the cholesteryl group. In any case, it is reasonable to conclude that polyoxyethylene cholesteryl ethers form the usual type of large micelles like other nonionic surfactants with ethylene oxide condensates as a hydrophilic group.

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