

Measurement of the Critical Micelle Concentration of Ionic-Nonionic Mixed Micelles by the First Derivative Absorption Spectrum Method

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In anionic-nonionic and cationic-nonionic mixed surfactant systems, when two surfactants below their individual critical micelle concentrations (cmc) were mixed, the formation of mixed micelles was confirmed and the cmc values were measured by the first derivative absorption spectrum (FDAS) method, the solubilization method (with Sudan Red dye) and the surface tension method (Wilhelmy plate method). From plots of the mole fraction normalized with respect to cmc ($=[[\text{sodium dodecyl sulfate (SDS)}]/\text{cmc}_{\text{SDS}}]/[[\text{SDS}]/\text{cmc}_{\text{SDS}} + [\text{heptaethylene glycol dodecyl ether (HED)}]/\text{cmc}_{\text{HED}}]$ where $[\text{SDS}]$ (or $[\text{HED}]$) is the concentration of SDS (or HED), and cmc_{SDS} (or cmc_{HED}) is the cmc of SDS (or HED)) on the abscissa against the sum of concentrations corresponding to the cmc ($=[\text{SDS}]_{* \text{HED}}/\text{cmc}_{\text{SDS}} + [\text{HED}]_{* \text{SDS}}/\text{cmc}_{\text{HED}}$ where $[\text{SDS}]_{* \text{HED}}$ (or $[\text{HED}]_{* \text{SDS}}$) is the concentration of SDS (or HED) in the cmc of mixed micelles of SDS-HED binary systems) on the ordinate, obtained by the FDAS method and the surface tension method, the boundary line between the regions forming mixed micelles and the regions of monomer was obtained. The results obtained are compared and the usefulness of the methods is discussed.

Keywords first derivative absorption spectrum; critical micelle concentration; wavelength shift; solubilization; alkylparaben; sodium dodecyl sulfate; heptaethylene glycol dodecyl ether; mixed micelle; cetyl trimethylammonium bromide; octaethylene glycol dodecyl ether

When surfactants are utilized, it is usually desirable to use the smallest amount possible from the viewpoints of toxicity, cost, and ease of handling. Lowering of the toxicity or cost and improvement of the ease of handling are important considerations in the preparation of emulsions, microemulsions, aqueous solutions of micelles, dissolution of chemical agents, *etc.* in the field of pharmaceuticals.

At present, surfactants are often used as binary or multi-component mixed systems, and many reports have appeared on mixed micelle systems.¹⁻¹⁸⁾ However, in many cases, where binary mixed surfactant systems have been used, one or both of the surfactants have been used at concentrations above the critical micelle concentration (cmc). Little work has been done on the use of two surfactants at concentrations below their cmc values or on the measurement of the cmc values of binary mixed micelle systems.

In the present work, we examined anionic-nonionic and cationic-nonionic mixed surfactant systems. When two surfactants below their individual cmc values were mixed, formation of mixed micelles was confirmed by the first derivative absorption spectrum (FDAS) method,^{19,20)} the solubilization method using a water-insoluble dye (Sudan Red) and the surface tension method (Wilhelmy plate method). Further, the cmc values of mixed micelles were measured by the FDAS method and the surface tension method, and the boundary line between the regions forming mixed micelles and the regions of monomer was obtained.

Experimental

Materials Propyl *p*-hydroxybenzoate (propylparaben) and cetyl trimethylammonium bromide (CTAB, minimum 99%) were obtained from Nakarai Chemicals, Ltd. (Nakarai), Sudan Red (Sudan III), sodium hydroxide (NaOH, minimum 95%), and butyl alcohol (BuOH, minimum 99.0%) and molecular sieves (3A1/8, 5A1/8) were obtained from Wako Pure Chemical Ind., Ltd. (Wako), and heptaethylene glycol dodecyl ether (HED) and octaethylene glycol dodecyl ether (OED) were obtained from Nikko Chemicals Company, Tokyo, Japan. These chemicals were used as received. Sodium dodecyl sulfate (SDS, minimum 99%; Nakarai) was purified by the method of Iwai *et al.*²¹⁾ Briefly, a mixed solution of SDS (10 g), ethyl alcohol (EtOH, minimum 99.5%; Wako) dehydrated by the

use of molecular sieves (400 ml), water (100 ml), NaOH (5 g) and about 25 ml of activated charcoal (heated for 30 min; Wako) was allowed to stand overnight. The mixed solution was filtered through a Millipore® filter (0.22 µm). BuOH was added, and then the solvent was evaporated off. The crystalline product was recrystallized from dehydrated EtOH. The crystals obtained were washed with ethyl ether (minimum 99.5%; Wako) dehydrated by molecular sieves for 40 h in a Soxhlet extractor. The purity was confirmed by the surface tension value of over 38 dyn/cm and the absence of a minimum in the Surface tension-concentration curve.

Measurement of the cmc of Ionic-Nonionic Mixed Surfactant Solution at 30°C (or 35°C) by the FDAS Method A Hitachi 557 dual-wavelength double-beam spectrophotometer equipped with a Haake F2C thermostat was used. Titration was performed by adding portions (1—100 µl) of a stock solution of 0.80—32.0 mM SDS—0.0138—0.345 mM HED (or 0.10—4.05 mM CTAB—0.017—0.43 mM OED) to 2000 µl of 51.5—104.7 µM propylparaben solution and to 2000 µl of aqueous solution (control). We obtained the difference absorption spectra (for example, between propylparaben-SDS-HED solution and SDS-HED solution) from the first derivative absorption spectrum and read the wavelength of the absorption maximum. Measurement conditions were as follows: scale expansion 20 times, scan speed 12 nm/min, derivative width ($\Delta\lambda$) 5, slit width 2 nm, scale of absorption spectra from +0.7 to -0.3 or from +0.5 to -0.5.

Measurement of the cmc of Ionic-Nonionic Mixed Surfactant Solution by the Solubilization Method Mixed surfactant solutions (20 ml; 10—20 different concentration ratios) containing Sudan Red (water-insoluble dye) were shaken for 37 h, and the solutions were filtered through a Millipore® filter (0.22 µm). The absorbances of the filtrates were measured at 420—560 nm by using a Hitachi U-2000 dual-wavelength double-beam spectrophotometer.

Measurement of the cmc of Ionic-Nonionic Mixed Surfactant Solution at 30°C (or 35°C) by the Surface Tension Method (Wilhelmy Plate Method) A Kyowa Kagaku CBVP surface tensiometer (A-1) equipped with a Tokyo Rikakikai thermostat and a glass plate was used. Each measurement was repeated at least three times, and two straight lines in the plots of absolute values (the relative values multiplied by the correction factor) on the ordinate against logarithm of surfactant concentration on the abscissa were obtained by the least-squares method.

Results and Discussion

Confirmation of Mixed Micelle Formation and Determination of the cmc of Mixed Micelles by the FDAS Method The shift of the maximum absorption wavelength of a chemical agent (propylparaben in this report) in a micelle solution is utilized for the FDAS method. The

TABLE I. Volume Ratio of Mixed Solutions

	A	B	H ₂ O	Total
MIX-C	25	1	24	50
MIX-G	50	7	43	100
MIX-K	10	3	7	20
MIX-N	2	1	1	4
MIX-P	1	1	0	2
MIX-Q	1	2	1	4
MIX-T	1	4	3	8
MIX-U	1	5	4	10
MIX-V	1	10	9	20
MIX-Y	1	40	39	80

A, B: A-B system.

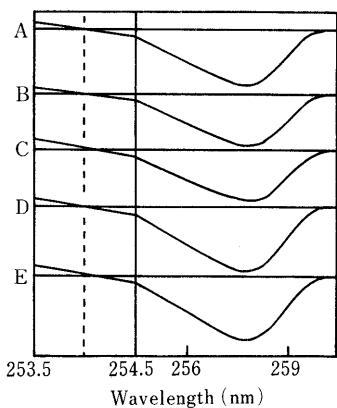


Fig. 1. First Derivative Absorption Spectra of Propylparaben

A, in H₂O (66.6 μ M propylparaben); B, in 2.9 mM SDS-0.031 mM HED solution (66.6 μ M propylparaben); C, 3.7 mM SDS-0.040 mM HED (66.6 μ M propylparaben); D, 0.30 mM CTAB-0.031 mM OED (91.8 μ M propylparaben); E, 0.36 mM CTAB-0.038 mM OED (91.8 μ M propylparaben).

lowest concentration at which the shift occurs is equal to the cmc value of the surfactant.²⁰ Some samples were prepared according to Table I. For example, in SDS-HED binary systems, 100 ml of MIX-N was a mixed solution of 50 ml of A (= 64.0 mM SDS), 25 ml of B (= 0.69 mM HED) and 25 ml of H₂O, and the concentrations of SDS and HED were 32.0 mM and 0.17 mM, respectively. Table I lists the mixing ratios of the various binary systems. In anionic-nonionic mixed surfactant systems (SDS-HED binary systems) and cationic-nonionic mixed surfactant systems (CTAB-OED binary systems), we confirmed the occurrence of shifts similar to that described above (Fig. 1). As the lowest concentration at which the shift occurred is lower than the cmc value of either surfactant, it is clear that mixed micelles are formed. The cmc values of mixed micelles of SDS-HED binary systems are summarized in Table II. Figure 2 shows plots of the sum of concentrations corresponding to the cmc ($=[\text{SDS}]_{*\text{HED}}/\text{cmc}_{\text{SDS}} + [\text{HED}]_{*\text{SDS}}/\text{cmc}_{\text{HED}}$ where $[\text{SDS}]_{*\text{HED}}$ (or $[\text{HED}]_{*\text{SDS}}$) is the concentration of SDS (or HED) in the cmc of mixed micelles of SDS-HED binary systems, and cmc_{SDS} (or cmc_{HED}) is the cmc of SDS (or HED)) on the ordinate against the mole fraction on the abscissa. However, this figure is not in a convenient form for comparison, and therefore we replaced the mole fraction by the mole fraction normalized with respect to cmc ($=[[\text{SDS}]/\text{cmc}_{\text{SDS}}]/[[\text{SDS}]/\text{cmc}_{\text{SDS}} + [\text{HED}]/\text{cmc}_{\text{HED}}]$ where $[\text{SDS}]$ (or $[\text{HED}]$) is the concentration of SDS (or HED)) on the abscissa (Fig.

TABLE II. The cmc of the SDS-HED System Determined by the FDAS Method at 35°C

	cmc		[SDS] _* HED/ cmc _{SDS} + [HED] _* SDS/ cmc _{HED}	Mole fraction	Mole fraction normalized with respect to cmc
	[SDS] _* HED (mM)	[HED] _* SDS (mM)			
MIX-C	6.7	0.0029	0.91	0.9995	0.97
MIX-G	5.8	0.0087	0.84	0.9985	0.91
MIX-N	4.3	0.023	0.77	0.995	0.73
MIX-P	3.3	0.035	0.75	0.989	0.57
MIX-Q	2.3	0.049	0.75	0.979	0.40
MIX-T	1.5	0.063	0.77	0.96	0.25
MIX-V	0.80	0.086	0.89	0.90	0.12
MIX-Y	0.23	0.099	0.93	0.70	0.033
SDS	7.6	—	1.00	1.00	—
HED	—	0.11	1.00	0	—

Concentration of source solution: A = 64.0 mM SDS, B = 0.69 mM HED.

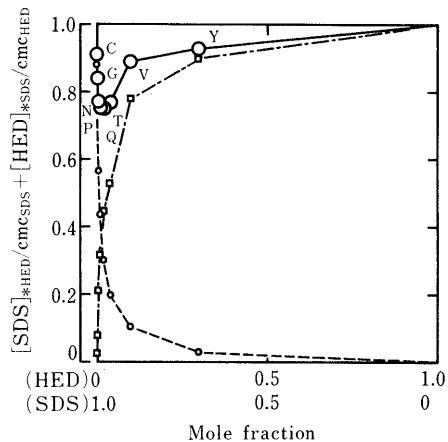


Fig. 2. Relationship between Sum of Concentrations Corresponding to cmc and Mole Fraction of SDS-HED Systems Determined by the FDAS Method

○, $[\text{SDS}]_{*\text{HED}}/\text{cmc}_{\text{SDS}} + [\text{HED}]_{*\text{SDS}}/\text{cmc}_{\text{HED}}$; ○, $[\text{SDS}]_{*\text{HED}}/\text{cmc}_{\text{SDS}}$; □, $[\text{HED}]_{*\text{SDS}}/\text{cmc}_{\text{HED}}$. Letters indicate the mixing ratio of components (see Table I, MIX-C = C).

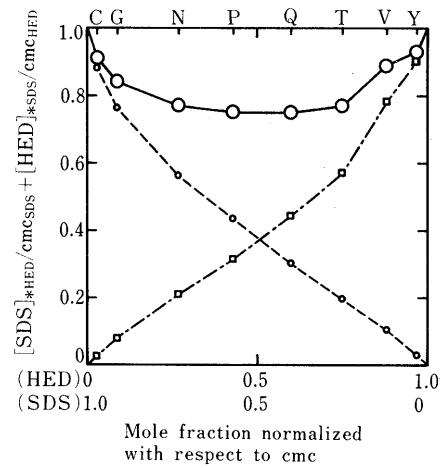


Fig. 3. Relationship between Sum of Concentrations Corresponding to cmc and Mole Fraction Normalized with Respect to cmc of SDS-HED Systems Determined by the FDAS Method

○, $[\text{SDS}]_{*\text{HED}}/\text{cmc}_{\text{SDS}} + [\text{HED}]_{*\text{SDS}}/\text{cmc}_{\text{HED}}$; ○, $[\text{SDS}]_{*\text{HED}}/\text{cmc}_{\text{SDS}}$; □, $[\text{HED}]_{*\text{SDS}}/\text{cmc}_{\text{HED}}$. Letters indicate the mixing ratio of components (see Table I, MIX-C = C).

3). This was also done in subsequent figures. Table III and Fig. 4 show the cmc of mixed micelles of CTAB-OED binary systems.

TABLE III. The cmc of the CTAB-OED System Determined by the FDAS Method at 30°C

	cmc [CTAB] _{*OED} (mm)	[CTAB] _{*OED} / cmc _{CTAB} + [OED] _{*CTAB} / cmc _{OED}	Mole fraction normalized with respect to cmc
	[OED] _{*CTAB} (mm)	[OED] _{*CTAB} / cmc _{OED}	
MIX-C	0.67	0.0028	0.86
MIX-G	0.61	0.0090	0.83
MIX-N	0.47	0.025	0.78
MIX-P	0.35	0.037	0.72
MIX-Q	0.25	0.053	0.72
MIX-T	0.16	0.068	0.72
MIX-V	0.086	0.082	0.74
MIX-Y	0.026	0.11	0.88
CTAB	0.80	—	1.00
OED	—	0.138	1.00

Concentration of source solution: A = 8.09 mM CTAB, B = 0.85 mM OED.

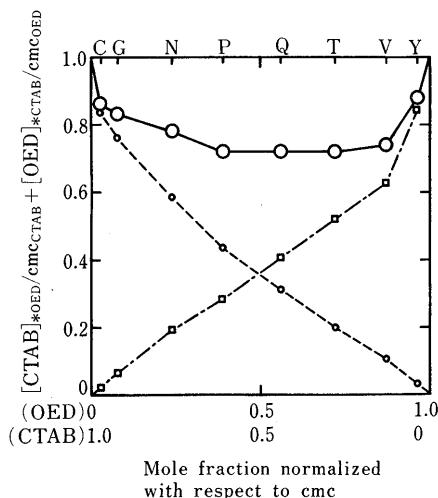


Fig. 4. Relationship between Sum of Concentrations Corresponding to cmc and Mole Fraction Normalized with Respect to cmc of CTAB-OED Systems Determined by the FDAS Method

○, [CTAB]_{*OED}/cmc_{CTAB} + [OED]_{*CTAB}/cmc_{OED}; □, [OED]_{*CTAB}/cmc_{OED}. Letters indicate the mixing ratio of components (see Table I, MIX-C = C).

Confirmation of Mixed Micelle Formation and Determination of the cmc of Mixed Micelles by the Solubilization Method The solubilization method is one of the easiest methods for confirmation of micelle formation, and it is applicable to both ionic surfactant and nonionic surfactant systems. Therefore, it is desirable that the micelle formation in ionic–nonionic mixed surfactant systems should be confirmed by this method.

Figures 5A and 5B show the changes of absorbance of Sudan Red in SDS solution and in SDS-HED binary solution systems, respectively, determined by the solubilization method. In this method, the point of inflection (=the cmc of mixed micelles) was obtained graphically. The plot is suggestive of mixed micelle formation, because the concentration at the point of inflection of SDS-HED binary systems was lower than the cmc value of either surfactant alone. The cmc values of mixed micelles obtained by the solubilization method are listed in Table IV. These results agreed fairly well with the results obtained by the FDAS method.

Confirmation of Mixed Micelle Formation and Determination of the cmc of Mixed Micelles by the Surface Tension Method

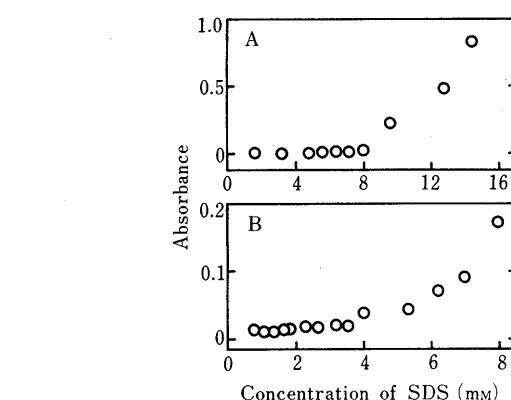


Fig. 5. Determination of cmc of SDS or SDS-HED Solution by the Sudan Red Solubilization Method

A, in SDS solution, wavelength 500 nm; B, in SDS-HED (MIX-P) solution, wavelength 500 nm.

TABLE IV. The cmc of the SDS-HED System Determined by the Solubilization Method

	[SDS] _{*HED}	[HED] _{*SDS}	Wavelength (nm)
MIX-N	4.0–4.8	0.021–0.026	480
MIX-P	3.5–4.0	0.038–0.043	420
MIX-Q	2.0–2.4	0.042–0.052	420
SDS	8.0—	—	480

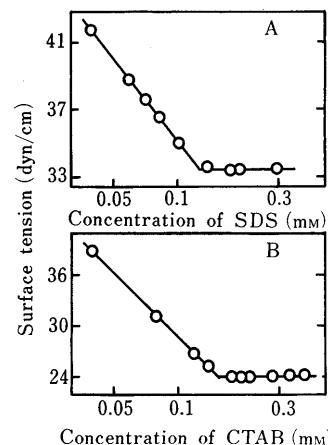


Fig. 6. Determination of cmc of SDS-HED or CTAB-OED Solution by Surface Tension Measurement (Logarithm of Surfactant Concentration on the Abscissa)

A, in SDS-HED (MIX-Y) solution at 35°C; B, in CTAB-OED (MIX-U) solution at 30°C.

Confirmation of Mixed Micelle Formation and Determination of the cmc of Mixed Micelles by the Surface Tension Method

The surface tension method is suitable to determine the cmc values of both ionic and nonionic surfactants. The results of the FDAS method were compared with those obtained by the surface tension method in the previous paper.²⁰

Figures 6A and 6B show the variations of the surface tension values of SDS-HED binary systems and CTAB-OED binary systems, respectively. In both binary systems, the surface tension values become lower with increase of the concentration (SDS-HED in 6A or CTAB-OED in 6B), and the point of inflection (=the cmc of mixed micelles) is lower than the cmc value of either surfactant alone. Again, this is suggestive of mixed micelle formation. Table V shows

TABLE V. The cmc of the SDS-HED System Determined by the Surface Tension Method (Wilhelmy Plate Method) at 35°C

	cmc		[SDS] _{*HED} /cmc _{SDS} + [HED] _{*SDS} /cmc _{HED}	Mole fraction normalized with respect to cmc
	[SDS] _{*HED} (mM)	[HED] _{*SDS} (mM)		
MIX-C	6.6	0.0028	0.94	0.96
MIX-G	5.2	0.0078	0.81	0.88
MIX-K	4.3	0.014	0.76	0.78
MIX-N	3.4	0.019	0.70	0.68
MIX-P	2.4	0.025	0.63	0.51
MIX-Q	1.6	0.034	0.63	0.35
MIX-T	0.93	0.040	0.62	0.21
MIX-V	0.45	0.048	0.65	0.096
MIX-Y	0.17	0.072	0.90	0.026
SDS	7.3	—	1.00	—
HED	—	0.082	1.00	—

Concentration of source solution: A = 32.0 mM SDS, B = 0.34 mM HED.

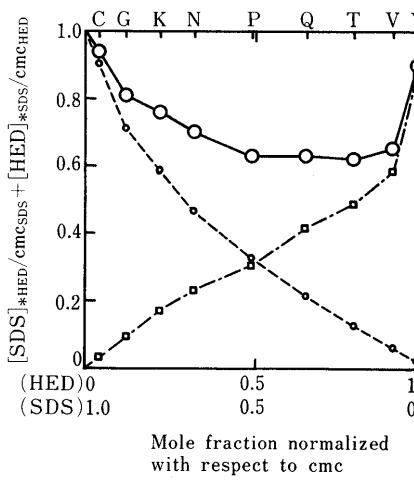


Fig. 7. Relationship between Sum of Concentrations Corresponding to cmc and Mole Fraction Normalized with Respect to cmc of SDS-HED Systems Determined by the Surface Tension Method

○, [SDS]_{*HED}/cmc_{SDS} + [HED]_{*SDS}/cmc_{HED}; □, [SDS]_{*HED}/cmc_{SDS}; □, [HED]_{*SDS}/cmc_{HED}. Letters indicate the mixing ratio of components (see Table I, MIX-C=C).

the cmc values of mixed micelles as determined by the surface tension method. Figure 7 shows the region in which mixed micelles are formed. However, as the surface tension values in binary mixed surfactant systems show rather nonlinear patterns, it is difficult to determine the cmc values accurately. In anionic-nonionic binary mixed surfactant systems, similar results have been reported by Ogino *et al.*¹²⁾ and Abe *et al.*¹³⁾ Consequently it seems that the surface tension method is not an appropriate one for determining the cmc values of mixed micelles.

When two surfactants were mixed at concentrations below their individual cmc values (anionic-nonionic and cationic-nonionic binary mixed surfactant systems), formation of mixed micelles was confirmed by three independent methods as described above. The regions of mixed micelle formation were obtained from the cmc values. It is clear that in the neighborhood of the boundary line of the

regions forming mixed micelles, as two surfactants at concentrations below their individual cmc values were mixed and the mixed micelles formed, the appearance of these mixed micelles depended upon the cooperation of both surfactants (=cooperative micelles). Few studies on measurement of the cmc values of mixed micelles have been done, probably because no effective determination methods have been available. For example, the electric conductivity method is difficult to apply in nonionic mixed surfactant systems, the surface tension method often gives inaccurate cmc values as discussed above, and the solubilization method shows poor reproducibility, as well as requiring a large amount of sample and a long time. In this study, we have shown that the FDAS method described in the previous paper²⁰⁾ is readily applicable to binary mixed surfactant systems, and does not suffer from the disadvantages associated with the other methods.

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