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# Measurement of the Critical Micelle Concentration of Nonionic Surfactants by the First Derivative Absorption Spectrum Method

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The absorption maximum of a drug in surfactant solution often shifts at surfactant concentrations above the critical micelle concentration (cmc). The first derivative absorption spectrum (FDAS) was used to evaluate the wavelength shift and to measure the cmc of surfactants.

The cmc's of heptaethylene glycol dodecyl ether (HED), octaethylene glycol dodecyl ether (OED) and sodium dodecyl sulfate (SDS) obtained by the FDAS method were $1.2 \times 10^{-4}$, $1.4 \times 10^{-4}$ and $7.6 \times 10^{-3}$ M, respectively. These cmc values were higher than those obtained by the surface tension method (the Wilhelmy plate method) because of the difference of the positions where the values were estimated on the curve (see text). In the measurement of cmc by the FDAS method, less sample and a shorter time are needed, and the reproducibility of this method is satisfactorily high. Though the FDAS method can be utilized for ionic and nonionic surfactants, it is particularly effective for nonionic surfactants, while the previous methods for cmc measurement of nonionic surfactant are generally cumbersome and time-consuming.

It was found that the degree of shift-length increased with increasing alkyl chain length of alkylparabens (or alkyl gallates). Therefore, it seems that the use of alkylparabens (or alkyl gallates) of greater alkyl chain length is most convenient in the determination of cmc values by the FDAS method.

**Keywords**——first derivative absorption spectrum; critical micelle concentration; wavelength shift; alkylparaben; alkyl gallate; solubilization; nonionic surfactant; heptaethylene glycol dodecyl ether; octaethylene glycol dodecyl ether; sodium dodecyl sulfate

## Introduction

The critical micelle concentration (cmc) is an important parameter of surfactants, and many methods (more than 20) are available for determining it.[1] However, many of these methods suffer from poor reproducibility, difficult procedure, requirement for a large amount of sample, *etc.* In the case of nonionic surfactants, the cmc is generally difficult to measure[2] because it is very low, and the surface tension method has been applied most frequently.

The absorption spectrum of a drug dissolved in a micellar solution showed shifts of the maximum absorption wavelength compared with that in aqueous solution, and we have utilized this effect for determining the cmc of surfactants. In this method, the first derivative absorption spectrum (FDAS) is used to evaluate the wavelength of the absorption maximum, and so the method is called the FDAS method.[3,4]

Measurement of cmc by employing changes in the absorption spectrum of a dye (dye absorption spectrum method)[5-10] has been reported, and the FDAS method is similar. The differences between the FDAS method and the dye absorption spectrum method are as follows. In the former, only the change of the wavelength of the drug is utilized, and the first derivative absorption spectrum is used. Therefore, a smaller change of the absorption spectrum can be detected by the FDAS method. In addition, the region of measurement is

200—900 nm. Thus the identification limit of metachromasy is broadened. In this paper, a comparison is made between the cmc values of nonionic surfactants obtained by the FDAS method and those obtained by the surface tension method, and the characteristics and the usefulness of the FDAS method are discussed.

## Experimental

**Materials**——Methyl *p*-hydroxybenzoate (methylparaben), ethyl *p*-hydroxybenzoate (ethylparaben), propyl *p*-hydroxybenzoate (propylparaben) and butyl *p*-hydroxybenzoate (butylparaben) were obtained from Nakarai Chemicals, Ltd., 3,4,5-trihydroxybenzoic acid ethyl ester (ethyl gallate) and 3,4,5-trihydroxybenzoic acid propyl ester (propyl gallate) were obtained from Wako Pure Chemical Ind., Ltd., 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 Chemicals, Ltd.) was purified by the method of Iwai *et al.*11) The purity was confirmed by the surface tension values of over 38 dyn/cm and the absence of a minimum in the surface tension–concentration curve.

**Measurement of Absorption Spectra**——A Hitachi 557 dual-wavelength double-beam spectrophotometer (557) equipped with a Haake F2C thermostat (F2C) was used. Measurement conditions were as follows: temperature 25 °C, scale expansion 4 times, scan speed 12 nm/min, slit width 2 nm, scale of absorption spectra from 0 to 1.

**Measurement of the cmc of Ionic and Nonionic Surfactant Solution at 25 °C by the Surface Tension Method (the 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 (each the average of the relative values multiplied by the correction factor) were obtained by the least-squares method.

**Measurement of the cmc of Ionic and Nonionic Surfactant Solution by the FDAS Method**——The 557 spectrometer equipped with the F2C thermostat was used. Titration was performed at 25 °C (or 35 °C) by adding portions (1—100 μl) of a $2.2—4.2\times10^{-3}$ M stock solution of HED (or $2.2—2.3\times10^{-3}$ M OED, or $268.9—350.8\times10^{-3}$ M SDS) to 2000 μl of 51.5—90.4 μM alkylparaben (or 106.0—110.7 μM alkyl gallate) solution and to 2000 μl of aqueous solution (control). We directly read the wavelength of the absorption maximum of the difference absorption spectrum (for example, propylparaben–HED solution and HED solution) from the first derivative absorption spectrum. Measurement conditions were as follows: scale expansion 20 times, scan speed 6 nm/min, derivative width ($\Delta\lambda$) 5, slit width 2 nm, scale of absorption spectra from +0.5 to −0.5 or from +0.3 to −0.3.

## Results and Discussion

### Measurement of the cmc by the Surface Tension Method

Figures 1A and 2 show the results of cmc determination of HED and OED solutions at 25 °C by the surface tension method ($9.0\times10^{-5}$ and $9.9\times10^{-5}$ M). Figure 1B shows the variation of surface tension of HED solution containing 55.9 μM propylparaben at 25 °C. The surface tension values were lower than those of HED solution, but the cmc was $8.8\times10^{-5}$ M. These results show that the concentration of propylparaben used in the FDAS method does not significantly affect the cmc value of HED.

### Measurement of the cmc by the FDAS Method

Figure 3 shows the effect of HED (HED concentration above the cmc) on the absorption spectrum of propylparaben as an example. The maximum absorption wavelength and the absorbance of propylparaben shift in HED solution. With the aid of the first derivative absorption spectrum, the maximum absorption wavelength can be determined accurately.12) We utilized this approach to measure the shift of the maximum absorption wavelength. Figure 4 illustrates the first derivative absorption spectra obtained from propylparaben, and shows the effect of the concentration of surfactant or drug on the wavelength shift. The wavelength shift depends on the concentration of surfactant (Fig. 4A), but does not depend on the concentration of drug (Fig. 4B). Figure 5 shows that the maximum absorption wavelength of propylparaben in aqueous solution (Fig. 5A) is the same as that in HED solution below the cmc (Fig. 5C), while that in HED solution above the cmc shifts to longer wavelength (Fig.

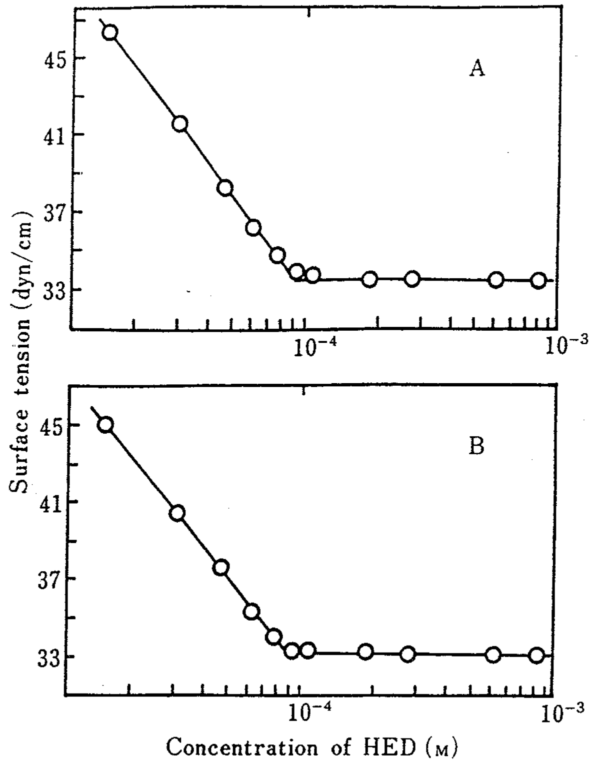

Fig. 1. Determination of cmc of HED Solution at 25 °C by Surface Tension Measurement

A, in $H_2O$; B, in 55.9 μM propylparaben solution.

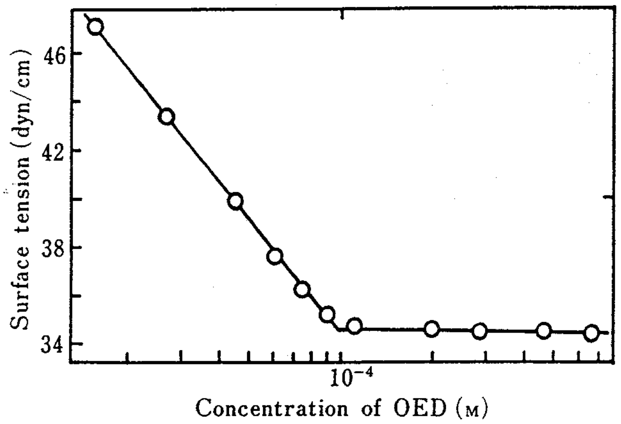

Fig. 2. Determination of cmc of OED Solution at 25 °C by Surface Tension Measurement

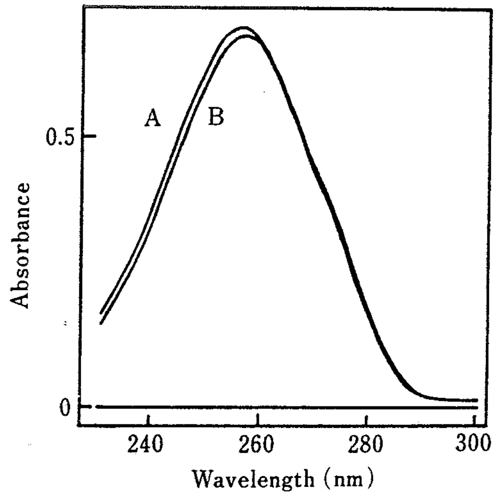

Fig. 3. Effect of HED on the Absorption Spectra of 47.0 μM Propylparaben at 25 °C

A, in $H_2O$; B, in $8.1 \times 10^{-4}$ M HED solution.

5B). The cmc was determined from the lowest concentration of surfactant where the shift was recognized by the FDAS method. The changes of the wavelength of the absorption maximum are shown in Fig. 6. In Fig. 6, the cmc is at the intersection (about 7.5 mM). In this experiment, we measured in detail at concentrations around the cmc, and read directly the wavelength of the absorption maximum from the difference absorption spectrum. This method allowed the detection of a wavelength shift above 0.1 nm (this corresponded to 1 mm shift-length on the recorded chart).

The cmc values obtained by the FDAS method and the surface tension method are shown in Table I. The cmc of HED obtained by the FDAS method was $1.2 \times 10^{-4}$ M with most of the drugs. The cmc value obtained by the FDAS method is higher than that obtained by the surface tension method. The difference is attributable to the measuring techniques. In

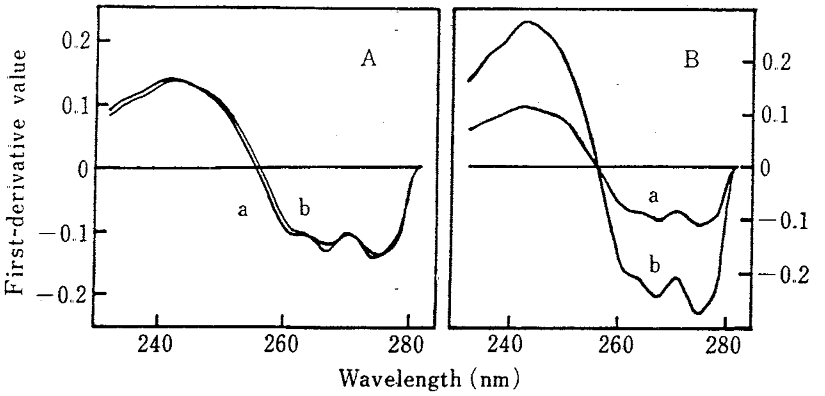

Fig. 4. First Derivative Absorption Spectra of Propylparaben at 25 °C

A, HED: a = 0 mM, b = 8.1 × $10^{-4}$ M; propylparaben: a = b = 47.0 μM.
B, HED: a = b = 6.4 × $10^{-4}$ M; propylparaben: a = 37.2 μM, b = 93.0 μM.

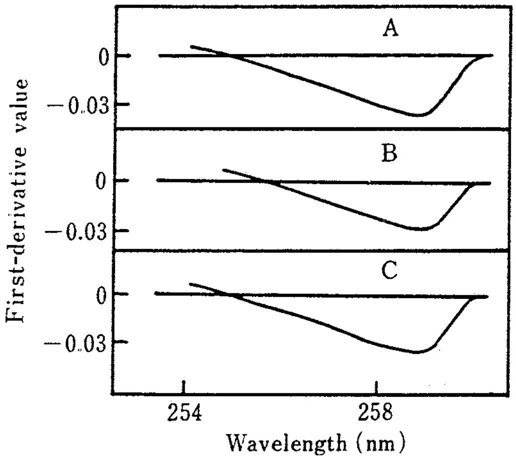

Fig. 5. First Derivative Absorption Spectrum of 55.8 μM Propylparaben at 25 °C

A, in $H_2O$; B, in 7.7 × $10^{-4}$ M HED solution; C, in 6.2 × $10^{-5}$ M HED solution.

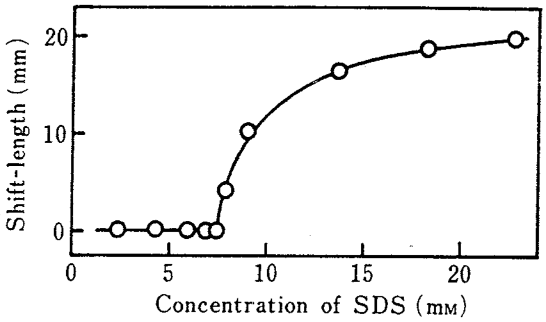

Fig. 6. Plots of SDS Concentration against Shift-Length of 55.8 μM Propylparaben at 25 °C

Fig. 7, the points determined by the surface tension method deviate from the straight line (A-C) before complete arrangement of molecules of the surfactant on the water surface, and follow the curve (B-D). However, the cmc value is obtained as the cross-point (C point: theoretical value) of the two straight lines. As this C is the value before micellar formation (premicellar region), a slightly lower value than the cmc is obtained. On the other hand, the cmc value by the FDAS method is obtained as the D point, namely at the point where the shifts are caused by the drug incorporated into the micellar phase after micelle formation. Since the cmc is the concentration of micelle formation, the cmc obtained from the FDAS method may be nearer to the true value.

The features of the FDAS method are as follows: 1) only a small amount of sample is needed for the measurement, 2) the titration method is used, 3) a short time is enough for measurement, 4) the wavelength of the absorption maximum is obtained directly from the crossing-point of the first derivative absorption spectrum and the base line and 5) high reproducibility is obtained. Moreover, this method has the advantages that it is possible to determine the cmc of ionic and nonionic surfactants, and the temperature of measurement can be precisely regulated.

In addition, the cmc values of a given surfactant obtained with different alkylparabens or alkyl gallates are the same, and the shift-length increases with increasing alkyl chain length of

TABLE I. The cmc of HED and OED at 25 or 35 °C[a]

| Surfactant | Drug | Surface tension method (M) | FDAS method (M) |
|---|---|---|---|
| HED | — | $9.0\times10^{-5}$ | — |
| HED | Methyl *p*-hydroxybenzoate | — | $13\times10^{-5}$ |
| HED | Ethyl *p*-hydroxybenzoate | — | $12\times10^{-5}$ |
| HED | Propyl *p*-hydroxybenzoate | $8.8\times10^{-5}$ | $12\times10^{-5}$ |
| HED | Butyl *p*-hydroxybenzoate | — | $12\times10^{-5}$ |
| HED | Ethyl gallate | — | $12\times10^{-5}$ |
| HED | Propyl gallate | — | $12\times10^{-5}$ |
| OED | — | $9.9\times10^{-5}$ | — |
| OED | Propyl *p*-hydroxybenzoate | — | $14\times10^{-5}$ |
| OED | Propyl *p*-hydroxybenzoate | — | [a] $18\times10^{-5}$ |
| SDS | — | $7.3\times10^{-3}$ | — |
| SDS | Methyl *p*-hydroxybenzoate | — | $7.6\times10^{-3}$ |
| SDS | Propyl *p*-hydroxybenzoate | — | $7.6\times10^{-3}$ |

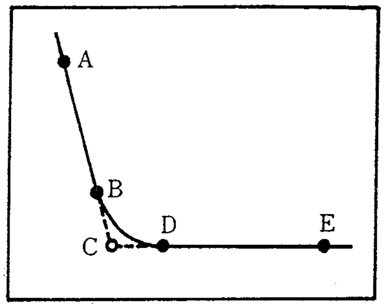

Fig. 7. Determination of cmc by Surface Tension Measurement

the alkylparabens (or alkyl gallates). Therefore, the order of suitability of alkylparabens for measurement of the cmc by the FDAS method is butyl->propyl->ethyl->methylparaben, and that of alkyl gallates is propyl->ethyl gallate, though the order is reversed from the standpoint of dissolution time for sample preparation.

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