

## Effect of Urea Derivatives on the Critical Micelle Concentration of Polyoxyethylated Nonionic Surfactant

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**Abstract** □ The critical micelle concentrations (CMCs) of aqueous solutions of a nonionic surfactant, polyoxyl 23 lauryl ether in the presence of various concentration of urea and its derivatives were measured. The CMC of the surfactant increased in proportion to the concentration of the additives, and the CMC-raising activities increased with more and longer alkyl groups substituted in urea. The CMC shift values were successfully correlated with the cloud point shift values and the protein-denaturing activities of the additives, respectively. These results suggest that the micelle formation, clouding of the surfactant and the protein denaturation are a closely related phenomenon, and a common mechanism is operating which might be the hydrophobic interaction.

**Keywords** □ Critical micelle concentration, urea, nonionic surfactant.

The effects of additives on the solution properties of polyoxyethylated nonionic surfactants have been of continuing interest for investigating the interactions among the surfactant, solvent and the additives<sup>1-5</sup>. An aqueous solution of a polyoxyethylated nonionic surfactant has characteristic properties; micelle formation and clouding phenomena. In addition to the critical micelle concentration (CMC), polyoxyethylated nonionic surfactants have a upper consolute temperature called the cloud point. Higher solubility in cold than hot water leads to reversible phase separation on heating, and the solutions turn quite cloudy at that temperature<sup>6,7</sup>.

The presence of a third component in the surfactant/water system may often have dramatic effects on the physical characteristics of solution. In general, two classes of interactions may be distinguished. The first affects the micellar properties by the surfactant/solvent interactions. Compounds in this category include electrolytes, urea and cosolvents. The second class of interactions affects the micellar properties through the incorporation of the additives into the micelle. Problems pertinent to the second class include comicellization of other surfactants and the solubilization of nonsurface-active compounds, as well as the effect of essentially non-

polar solubilizates on micellization.

The influence of electrolyte addition on the solution properties of polyoxyethylated nonionic surfactants has been the subject of many studies<sup>8-12</sup>. The electrolytes usually lowered the cloud point and the CMC of surfactants. In some cases, they rather increased the cloud point and the CMC. Their effects were adequately understood in terms of well-known salting-out and salting-in phenomena in aqueous solutions. It is generally accepted that added electrolytes cause electrostriction of water and increase internal pressure of the solution, and salt out the surfactant. The order of effectiveness of electrolytes in lowering the cloud point and the CMC is in line with a decrease in the lyotropic number of the ions<sup>13</sup>, and a change in the lyotropic number of the anions has a larger effect on the lowering of the cloud point and the CMC than those of the cations<sup>8</sup>.

Some studies have suggested the possibility that changes in water structure are an important factor in the effect of additives on the micellar properties of surfactants. Water-structure formers usually lower the cloud point and the CMC, and water-structure breakers rather increase the cloud point and the CMC<sup>3</sup>. Among the water-structure breakers, urea

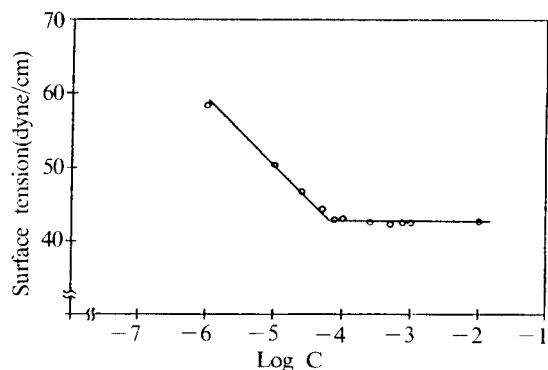


Fig. 1. Surface tension versus log molar concentration, C for aqueous solution of  $C_{12}E_{23}$  at 25°C.

and its derivatives have been of great concern<sup>14-16</sup>) They are known as good protein denaturants.

The interaction of urea and its derivatives with nonionic surfactants is of interest because the denaturation of proteins bears some resemblance to the clouding phenomenon of nonionic surfactants. The previous publications in this series described the effect of protein denaturants on the cloud point of nonionic surfactants<sup>16,17</sup>). The present study extended the effect of alkyl derivatives of urea on the CMC of a nonionic surfactant. In this study, the effects of alkyl derivatives of urea on the critical micelle concentration of polyoxyethylated nonionic surfactant were measured, and correlations between the effects of the alkyl derivatives of urea on the CMC and the cloud point and protein-denaturing activities of urea derivatives were sought to elucidate the interaction between polyoxyethylated nonionic surfactants and alkyl derivatives of urea.

## EXPERIMENTAL

### Materials

Polyoxyl 23 lauryl ether, also called Brij 35 and abbreviated as  $C_{12}E_{23}$ , was obtained from Sigma Chemical Company (St. Louis, MO., USA.), and used without further purification. Urea and its derivatives were obtained from Fluka Chemical Corporation (Buchs, West German), and used as received. All other chemicals were reagent grade. Water was double distilled.

### Measurement of critical micelle concentrations

The surface tension of solutions was measured

Table I. The critical micelle concentration of  $C_{12}E_{23}$  in water in the presence of urea and its derivatives at 25°C<sup>a</sup>

Additive	Conc.	CMC $\times 10^5$ (mol/l)			
		0.2 M	0.5 M	1.0 M	2.0 M
Urea		8.8	9.1	9.4	9.7
Methylurea		9.4	9.4	11.1	15.2
1,3-Dimethylurea		10.4	12.1	13.7	33.0
Ethylurea		11.0	14.0	16.0	22.3
Tetramethylurea		12.5	17.4	31.1	84.1

<sup>a</sup>The CMC of the blank  $C_{12}E_{23}$  solution was  $8.0 \times 10^{-5}$  mol/l.

by means of a DuNuoy tensiometer. The platinum ring was calibrated by measuring the surface tension of twice distilled water at 25°C. Three measurements were made for the surface tension of each solution. The precision of the measurements was within  $\pm 0.3$  dyne/cm. In the plot of surface tension vs. logarithm of the concentration of the surfactant, the intersection point between the nearly horizontal segment above the CMC and the nearly straight line below the CMC was taken as the CMC of the surfactant.

## RESULTS AND DISCUSSION

### Effect of urea derivatives on the CMC of $C_{12}E_{23}$

A typical plot of the surface tensions vs. logarithm of the concentrations of  $C_{12}E_{23}$  in water was illustrated in Fig. 1. It clearly showed a breaking point, which was taken as the CMC. The CMC of  $C_{12}E_{23}$  in water at 25°C was  $8.0 \times 10^{-6}$  mol/l, and this value agreed with the values already reported<sup>9</sup>). The CMCs of  $C_{12}E_{23}$  in water in presence of different concentrations of urea and its alkyl derivatives were measured in this way, and the results were listed in Table I. It shows that urea and all urea derivatives tested in the experiment raised the CMC of the surfactant in proportion to their concentration. The effectiveness of the urea derivatives in raising the CMC was in the order that the more alkyl radicals are substituted in urea, the stronger their activities. This trend is in accord with their effects on the cloud point of polyoxyethylated nonionic surfactants.

The effect of urea on the solution properties of

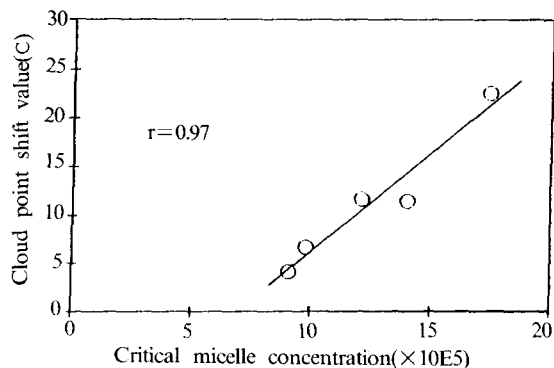


Fig. 2. Cloud point shift values of urea and its derivatives versus their CMC shift values.

polyoxyethylated nonionic surfactant has been studied intensively. It raised the cloud point and the CMC of nonionic surfactants in proportion to its concentration<sup>5,16,17</sup>. Up to now, the effects of urea have been mainly ascribed to the better hydration of the polyoxyethylene chain and weakened hydrophobic bonding of the hydrophobic chain through water-structure breaking of ureas. Another possibility has been suggested that urea binds directly with the hydrophobic moiety of the solute and reduces the hydrophobic binding<sup>16</sup>. Hydrophobic alkyl group is known as a water-structure former, and with increasing degree of alkylation, the urea derivatives should enhance the structure of water. By this logic, alkyl derivatives of urea should have raised the CMC less effectively than urea.

The results of this study strongly suggest that in the effect of urea derivatives on the CMC of the polyethylated nonionic surfactant, the water structure-breaking activity of urea derivatives are rather minor and other more important factors are operating. One of these might be the binding of urea derivatives with the hydrophilic and/or hydrophobic chain of the surfactant. Hydrophobic substituents of urea reinforce the binding between urea and the surfactant through hydrophobic interaction, and they might induce more strong hydration of the surfactant and raise the CMC.

**Correlations among the CMC shift values, the cloud point shift values and the protein denaturing activities**

The difference between the CMC of  $C_{12}E_{23}$  and the CMC of the surfactant in the presence of an additive was taken as the CMC shift value of the

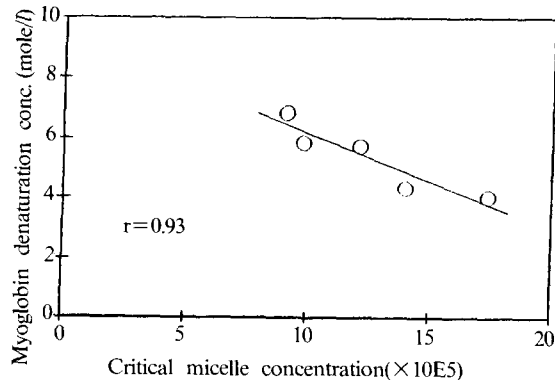


Fig. 3. Midpoint concentrations of urea and its derivatives for denaturing myoglobin versus the CMC shift values.

additive. These values of urea and its derivatives were found to be fairly well correlated with the cloud point shift values of the additives for 1% aqueous solution of Triton X-100 at 0.5 molar level of the additive as shown in Fig. 2 ( $n=5$ ,  $r=0.97$ )<sup>16</sup>. The CMC shift values were also successfully correlated with the concentrations of urea and its derivatives required to obtain the midpoint of the denaturation transition for sperm whale myoglobin ( $n=5$ ,  $r=0.93$ )<sup>18</sup>. It was shown in Fig. 3.

The successful correlations among these values strongly suggest that the micelle formation, clouding of polyoxyethylated nonionic surfactants and protein denaturation are closely related phenomena and a common mechanism is operating. A hydrophobic interaction should be the common factor in these three phenomena. The presence of urea or its alkyl derivatives in the aqueous solutions of the surfactant or protein weakens the hydrophobic interactions via its binding with the hydrophobic chains of the surfactant or protein, and the binding occurs more effectively with more alkyl-substituted urea derivatives. Han and his coworkers reported the percutaneous absorption-enhancing activities of urea derivatives<sup>19</sup>. Their absorption-enhancing activity is clearly in the order of the increasing the CMC of  $C_{12}E_{23}$ , although a quantitative correlation between these two sets of data has not been sought because of the difference of the concentration expression of the additives. This result suggests that urea and its derivatives might bind with the hydrophobic moiety of lipids and/or proteins via hydrophobic interaction and this binding

might induce the absorption-enhancing activity.

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