Base-Catalyzed Hydrolysis of Acetylcholine Chloride in the Presence of Cationic and Nonionic Surfactants

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(Received July 15, 1985)

The base-catalyzed hydrolysis of acetylcholine chloride (Ach) in the presence of cationic and nonionic surfactants was investigated. The rate of hydrolysis of Ach was determined by following the disappearance of Ach spectrometrically. At a constant pH of 9.0, addition of dodecyltrimethylammonium chloride (DTAC) at concentrations below the critical micelle concentration results in a large decrease in the apparent rate constant for the hydrolysis of Ach, k_{app}. The plot of k_{app} against the concentration ratio of DTAC to Ach ($C_{DTAC}/[D]_0$) gives a break point at $C_{DTAC}/[D]_0=1$. This is considered to be due to the formation of 1:1 complex between Ach and DTAC. In the presence of heptaoxyethylene dodecyl ether (HED)–DTAC mixed micelles, k_{app} decreases with the mole fraction of DTAC, in contradistinction to the usually presupposed electrostatic effect. This is because Ach molecule penetrates into the micellar phase and is shielded from the attack by OH^- for hydrolysis. The decrease of k_{app} has been successfully interpreted on the basis of the data on the distribution of Ach between the micellar and aqueous phases.

A number of studies[1–7] on the hydrolysis of acetylcholine chloride (Ach) have been carried out, particularly in relation to the effect of pH and temperature, salt effect, and the enthalpy of hydrolysis of Ach. Nogami et al.[8] have revealed the influence of sodium dodecyl sulfate (SDS), a surfactant, on the hydrolysis of Ach. The reaction in the presence of surfactants is also interesting from the viewpoint of micellar catalysis. No kinetic analysis of the hydrolysis in the presence of SDS has, however, been carried out yet.

A kinetic study on the base-catalyzed hydrolysis of Ach in the presence of anionic and nonionic surfactants has been reported in our previous paper,[9] in which the relevant rate constant is explained well by taking into consideration both the distribution of Ach between the aqueous and micellar phases and the electrostatic effect operating on the micelle surface.

In this paper, we report a further kinetic study on the base-catalyzed hydrolysis of Ach in the presence of a cationic surfactant and mixed micelles composed of cationic and nonionic surfactants; this study has been conducted by taking into account both the accurate critical micelle concentration (cmc) of surfactant in the presence of Ach[10] and the distribution of Ach between micellar and bulk phases.[11]

Experimental

Materials. Acetylcholine chloride (Ach) and heptaoxyethylene dodecyl ether (HED) are the same as those used for our previous paper.[9] Dodecyltrimethylammonium chloride (DTAC) obtained from Nakarai Chemicals Co. was purified as previously described.[10,11]

Method of Measurement. The rate of hydrolysis of Ach was obtained as the disappearance rate of Ach at pH 9.0 and 25 °C. The concentration of Ach was determined spectrometrically as previously described.[9,11]

Results

Effect of DTAC Concentration on the Hydrolysis of Ach. The apparent rate constant for the hydrolysis, k_{app}, is defined as

$$k_{app} = \frac{1}{t}\ln\frac{[D]_0}{[D]}, \tag{1}$$

where $[D]_0$ and $[D]$ are the concentrations of Ach at the beginning and at time t, respectively. Plots of $\ln([D]_0/[D])$ vs. t are shown in Fig. 1, where the percent hydrolyzed of Ach is also included on the right side of the ordinate. In all cases, good proportionality is observed. The hydrolysis of Ach in the presence of DTAC can, therefore, be characterized as a first order reaction. The relation between the rate constant evaluated from the slope shown in Fig. 1 and the concentration of DTAC is shown in Fig. 2. In Fig. 2, each curve has a break point and this point

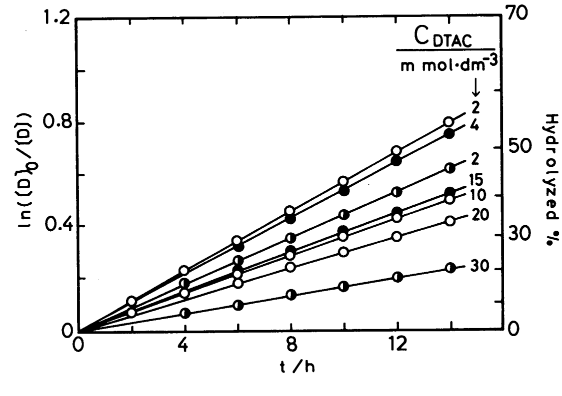

Fig. 1. Hydrolysis of Ach in the presence of DTAC. $\ln([D]_0/[D])$ vs. time.
Concentration of Ach $[D]_0$: ◑ 3, ○ 5, ● 10 mmol dm^{-3} pH: 9.0.

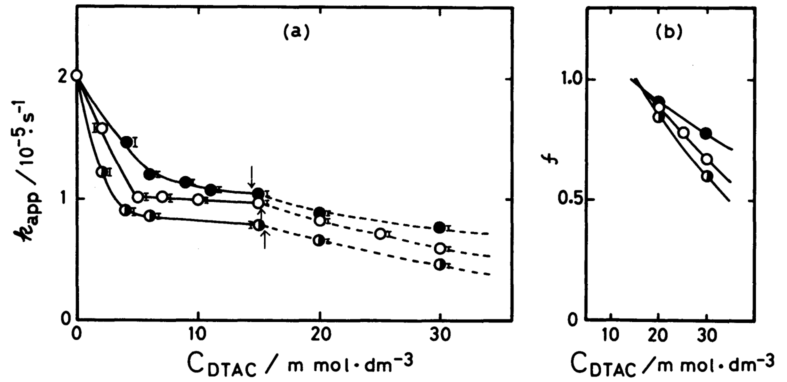

Fig. 2. Effect of DTAC on apparent rate constant for hydrolysis of Ach, k_{app}, with varying concentration of Ach (a) and distribution of Ach (b).[11]
$[D]_0$: ◑ 3, ○ 5, ● 10 mmol dm^{-3}. pH: 9.0.
Dotted line: theoretical curve for the rate in the aqueous phase expected from the distribution ratio shown in Fig. 2(b).

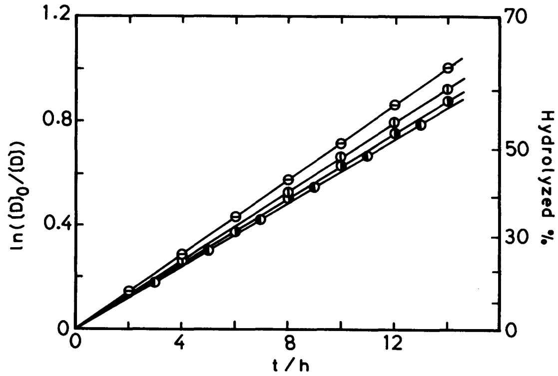

Fig. 3. Hydrolysis behavior of Ach in the presence of DTAC-HED mixed micelle ($X_{DTAC}=0.2$).
ln ($[D]_0/[D]$) vs. time.
Concentration of surfactants: ⊖ 2, ⦶ 10, ◑ 20, ◐ 30 mmol dm^{-3}. pH: 9.0. $[D]_0$: 5 mmol dm^{-3}.

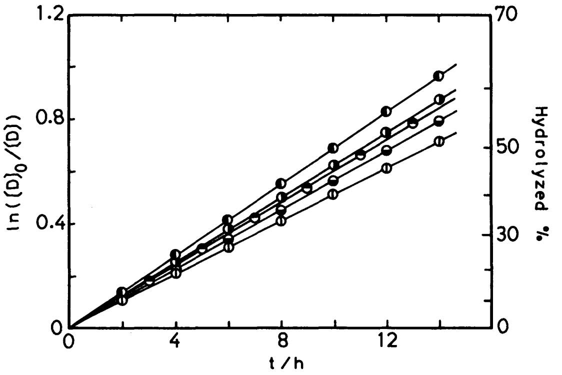

Fig. 5. Hydrolysis behavior of Ach in the presence of DTAC-HED mixed micelle systems.
ln ($[D]_0/[D]$) vs. time.
Mixed micelle systems at the total surfactant concentration of 20 mmol dm^{-3}: ◐ $X_{DTAC}=0.1$, ◑ $X_{DTAC}=0.2$, ◒ $X_{DTAC}=0.4$, ◓ $X_{DTAC}=0.6$, ⦶ $X_{DTAC}=0.8$. pH: 9.0. $[D]_0$: 5 mmol dm^{-3}.

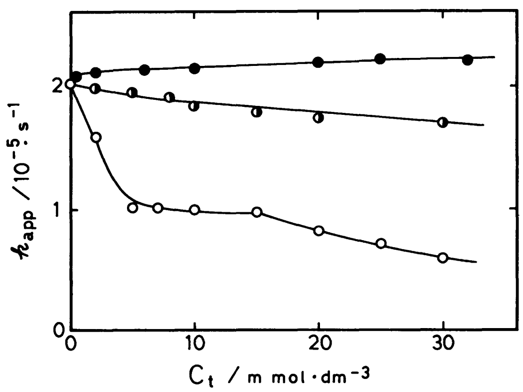

Fig. 4. Effect of surfactants on k_{app}.
Surfactants: ● HED alone,[9] ○ DTAC alone, ◑ HED-DTAC mixed system ($X_{DTAC}=0.2$). pH: 9.0. $[D]_0$: 5 mmol dm^{-3}.

is found to correspond to the cmc of DTAC in the presence of Ach: 14.4, 15.2, and 15.5 mmol dm^{-3} for Ach at 10, 5, and 3 mmol dm^{-3}, respectively.[10] The value of k_{app} decreases largely at the lower concentration region and again above the cmc.

We have carried out the present experiment very carefully. Therefore, the conclusion that the break points actually exist, may be drawn in conjunction with the experimental error (note that the error for the three measurements of hydrolysis rate is within ±1.5%, that for the distribution of Ach between the micellar and aqueous phases[11] being within ±2.0%) and the solubilization into the micelle.

Effect of DTAC-HED Mixed Micelles on the Hydrolysis of Ach. For the case of the presence of DTAC-HED mixed micelle ($X_{DTAC}=0.2$) with

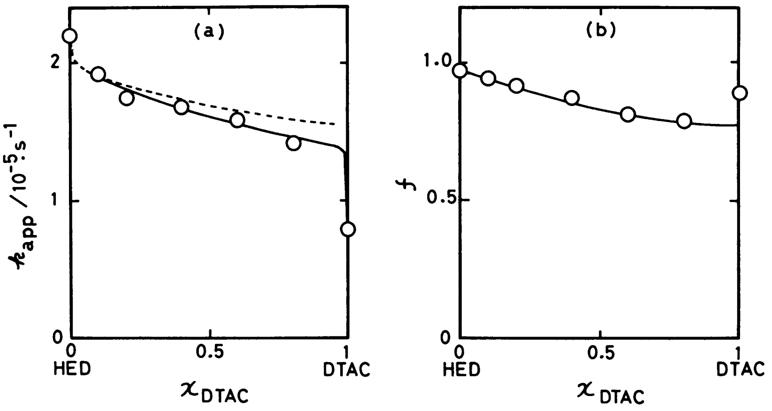

Fig. 6. Effect of HED–DTAC mixed systems on k_{app} (a) and distribution of Ach (b).[11]
(a) solid line: experimental curve.
dotted line: theoretical curve for the rate in the aqueous phase expected from the distribution ratio shown in Fig. 6(b).
(b) $f=[D_f]/[D_t]$, $[D_t]=[D_f]+[D_m]$
Total concentration of surfactants: 20 mmol dm^{-3}. pH: 9.0. $[D]_0$: 5 mmol dm^{-3}.

varying concentration, values of ln ($[D]_0/[D]$) for Ach of $[D]_0=5$ mmol dm^{-3} are plotted in Fig. 3 against t according to Eq. 1.

The values of k_{app} obtained from the plots shown in Fig. 3 are plotted in Fig. 4 against the total concentration of surfactants, C_t. The values of k_{app} in the presence of HED alone[9] and of DTAC alone are shown together in Fig. 4. In the presence of DTAC-HED mixed micelle ($X_{DTAC}=0.2$), no break point, unlike the case of DTAC alone, can be found because the value of cmc is as low as 0.1 mmol dm^{-3} for this system in the presence of 5 mmol dm^{-3} Ach.

On the other hand, the effect of the composition of DTAC-HED mixed systems at a total concentration of 20 mmol dm^{-3} was also examined. Plots of ln ($[D]_0/[D]$) vs. t are shown in Fig. 5, and the values of k_{app} obtained from Fig. 5 are given in Fig. 6(a). The value of k_{app} decreases with the mole fraction of DTAC.

Discussion

Effect of Concentrations of Ach and DTAC on the Hydrolysis of Ach. It is found from Fig. 2 that k_{app} decreases greatly in the lower concentration region below the cmc and that the inclination becomes the steeper, the lower the concentration of Ach. Therefore, the values of k_{app} are plotted against the concentration ratio of DTAC to Ach, ($C_{DTAC}/[D]_0$), in Fig. 7, and it is found that all the three curves in Fig. 2 give the same curve that has a break point at $C_{DTAC}/[D]_0=1$. This would indicate that Ach is stabilized by the formation of 1:1 complex with DTAC, because the attack of OH$^-$ is suppressed. Furthermore, k_{app} decreases again above the point corresponding to the cmc. Ach would form a complex with free ions of DTAC, and the complex would be solubilized into the micelle above the cmc.

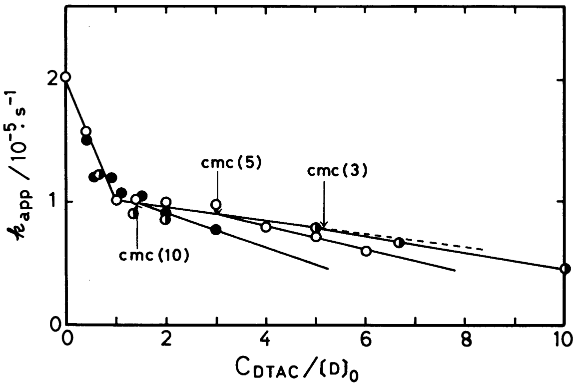

Fig. 7. Relation between k_{app} and concentration ratio of DTAC and Ach ($C_{DTAC}/[D]_0$).
$[D]_0$: ◑ 3, ○ 5, ● 10 mmol dm^{-3}.

The decrease of k_{app} above the cmc suggests that the rate of hydrolysis of Ach in the micellar phase is very small. This is considered to be due to the sequence that the acetyl group of Ach enters the palisade layer of the DTAC micelle[11] and is protected from the hydrolysis; hence the base-catalyzed hydrolysis of Ach in the DTAC micellar phase cannot be interpreted in terms of the electrostatic effect in contrast to the case[9] of Ach and sodium dodecyl sulfate.

Effect of DTAC-HED Mixed Micelles on the Hydrolysis of Ach. Ach is distributed between the micellar and bulk phases. The apparent rate constant, k_{app}, for the hydrolysis of Ach is, therefore, written as a sum of two terms

$$k_{\mathrm{app}} = k(f) + k(m), \tag{2}$$

where $k(f)$ and $k(m)$ are the rates of hydrolysis in the aqueous and micellar phases, respectively. Equation 2 is rewritten as follows by taking into account the distribution ratio f between the aqueous and micellar phases and the concentrations of $\mathrm{OH^-}$, $[\mathrm{OH^-}]_f$, and $[\mathrm{OH^-}]_m$:

$$\left.\begin{aligned} &k_{\mathrm{app}} = k_{2\,\mathrm{app}}[\mathrm{OH^-}]_f = k_{2f}f[\mathrm{OH^-}]_f + k_{2m}(1-f)[\mathrm{OH^-}]_m \\ &\text{or} \\ &k(f) = k_{2f}f[\mathrm{OH^-}]_f,\ k(m) = k_{2m}(1-f)[\mathrm{OH^-}]_m, \end{aligned}\right\} \tag{3}$$

where $[\mathrm{OH^-}]_f$ and $[\mathrm{OH^-}]_m$ are the concentrations of hydroxide ion, k_{2f} and k_{2m} are the second order rate constants for the hydrolysis of Ach in the aqueous and micellar phases, respectively, and f is the distribution ratio of Ach in the aqueous phase, that is, $f=[\mathrm{D}_f]/[\mathrm{D}_t]$ where $[\mathrm{D}_t]=[\mathrm{D}_f]+[\mathrm{D}_m]$ and $[\mathrm{D}_f]$ and $[\mathrm{D}_m]$ are the concentrations of Ach in the aqueous and micellar phases, respectively. When the total concentration of surfactants, C_t, is lower than the cmc, namely $C_t<\mathrm{cmc}$, Eq. 3 reduces to

$$k_{2\,\mathrm{app}} = k_{2f} \quad (\text{for } C_t<\mathrm{cmc}), \tag{4}$$

since $f=1$ and $[\mathrm{OH^-}]_m=0$.

The apparent rate constants for the hydrolysis of Ach in the presence of DTAC–HED mixed micelles are represented by the solid line in Fig. 6(a). The distribution ratios[11] of Ach in the aqueous phase, $f=[\mathrm{D}_f]/[\mathrm{D}_t]$, in the presence of DTAC–HED mixed micelles are given in Fig. 6(b).

If it is postulated that all DTAC molecules form mixed micelles with HED, the value of k_{2f} will be 2.02 $\mathrm{mol^{-1}\,dm^3\,s^{-1}}$ as obtained from the result[9] in the absence of surfactant. The values of $k(f)=k_{2f}f[\mathrm{OH^-}]_f$ are calculated and represented by the dotted line in Fig. 6(a), which indicates that the apparent rate of hydrolysis is nearly equal to the rate in the aqueous phase, implying that Ach in the micellar phase is not hydrolyzed with significant rate, i.e., $k_{2m}\approx 0$. This means that Ach molecules are bound so tightly to DTAC micelle[11] as to be prevented from hydrolysis. These are consistent with the result[11] that the binding constant for Ach to DTAC–HED mixed micelles increases, whereas f decreases with the mole fraction of DTAC in opposition to the expectation on the basis of the electrostatic repulsion between Ach cation and the mixed micelle caused to be charged positive by DTAC.

The small value of k_{app} in the presence of DTAC alone is due to both the existence of free DTAC and the occurrence of the interaction between Ach and DTAC in the aqueous phase.

The decrease of k_{app} with the mole fraction of DTAC is considered to be due to the decrease of f shown in Fig. 6(b). The deviation of the experimental result from the dotted line is considered to be due mainly to the existence of a small quantity of free DTAC in the aqueous phase. If the percentage of free DTAC to total added DTAC for the formation of mixed micelle is 5% at $X_{\mathrm{DTAC}}=0.8$, the value of k_{app} is expected to be $1.424\times10^{-5}\,\mathrm{s^{-1}}$ from the relationship between the rate constant and the concentrations of Ach and DTAC shown in Fig. 7, and the value thus obtained is consistent well with the experimental value; namely, when $(C_{\mathrm{DTAC}}/[\mathrm{D}]_0)\leqq 1$, the relation between k_{app} and $(C_{\mathrm{DTAC}}/[\mathrm{D}_f])$ is written as

$$k_{\mathrm{app}} = k^0_{\mathrm{app}} - 0.5\,k^0_{\mathrm{app}}\frac{C_{\mathrm{DTAC}}}{[\mathrm{D}_f]} \quad \left(\text{for } \frac{C_{\mathrm{DTAC}}}{[\mathrm{D}_f]}\leqq 1\right), \tag{5}$$

because the value of k_{app} at $(C_{\mathrm{DTAC}}/[\mathrm{D}_f])=1$ is equal to $(1/2)k^0_{\mathrm{app}}$ and the decrease of k_{app} is proportional to $(C_{\mathrm{DTAC}}/[\mathrm{D}_f])$ as can be seen in Fig. 7, where k^0_{app} is the value of k_{app} in the absence of free surfactant. By substituting $C_{\mathrm{DTAC}}=20\times0.8\times0.05=0.8$ ($\mathrm{mmol\,dm^{-3}}$), $[\mathrm{D}_f]=5\times0.785=3.925$ ($\mathrm{mmol\,dm^{-3}}$), and $k^0_{\mathrm{app}}=k^0(f)=2.02\times10^{-5}\times0.785=1.586\times10^{-5}$ ($\mathrm{s^{-1}}$), the value of k_{app} is obtained as $1.424\times10^{-5}\,\mathrm{s^{-1}}$.

We have reported[12] that all sodium dodecyl sulfate molecules will form mixed micelles with HED. Although we have not studied the DTAC–HED system, it is reported[13] that the formation of mixed micelle with cationic surfactant is harder than that with anionic surfactant. Therefore, the presence of a small quantity of free DTAC is reasonable.

Finally, the values of $k(f)(=k_{2f}f[\mathrm{OH^-}]_f)$ for the region above the cmc given by the dotted lines in Fig. 2(a) have been calculated by using the values of $k_{2\mathrm{app}}$ at the cmc as the values of k_{2f}. The dotted lines indicate that the apparent rate of hydrolysis decreases with decreasing value of f. This suggests that the complex formed between Ach and DTAC is solubilized into the micelle above the cmc. The existence of break point in Fig. 2(a) is, therefore, confirmed.

Conclusion

The apparent rate constant, k_{app}, for base-catalyzed hydrolysis of Ach is caused to decrease greatly by the presence of DTAC. This is considered to be due to Ach interacting with DTAC in the aqueous phase. In the presence of DTAC–HED mixed micelles, k_{app} decreases with the mole fraction of DTAC. The decrease of k_{app} is considered to be due to the sequence that the rate constant for the hydrolysis in the micellar phase is approximately zero and that the distribution ratio of Ach in the aqueous phase decreases with the mole fraction of DTAC. This sequence is, in turn, caused by the sequence that the Ach molecule penetrates into the micelle and is shielded from the attack by OH^- for hydrolysis. It is concluded that the base-catalyzed hydrolysis of Ach in the positively charged micelle is not interpreted in terms of the electrostatic effect, in contrast to the acid-catalyzed hydrolysis of Ach in the negatively charged micelle.

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