Changes in the Fraction of Uncomplexed Cyclodextrin in Equilibrium with the Micellar System as a Result of Balance between Micellization and Cyclodextrin−Surfactant Complexation. Cationic Alkylammonium Surfactants

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A study was carried out on the basic hydrolysis of *m*-nitrophenylacetate in mixed systems made up of trimethylalkylammonium micelles and α- or *β*-cyclodextrin (CD). The surfactants used enabled us to vary the length of the hydrocarbon chain between 8 and 18 carbon atoms. In all cases the existence of a significant concentration of uncomplexed CD was observable in equilibrium with the micellar system. Contrary to expectations, the concentration of uncomplexed CD increased together with the hydrocarbon chain of the surfactant. This result was interpreted as a consequence of the balance between the complexation processes of the surfactant monomers by the CD and its autoassociation to form micelles. We have found the existence of a linear dependence between the percentage of uncomplexed CD and the inverse of the critical micellar concentration of the surfactant, indicating that, as the tendency toward micellization increases, so too does the percentage of the uncomplexed CD. The results obtained indicate that the concentration of uncomplexed α-CD in equilibrium with the micellar system is always lower than that of *β*-CD, which has been interpreted as a consequence of the greater tendency of the α-CD to form CD-surfactant complexes with a stoichiometry of 2:1. One of the main consequences of this study is that the critical micellar concentration of the mixed CD-surfactant systems cannot be used directly to obtain the stoichiometry of the CD-surfactant complexes, since the micellization occurs without the complexation ability of the CD having been saturated.

Introduction

The study of the mixed cyclodextrin−surfactant systems has aroused great interest in recent years due to its numerous applications. For example the evaporation of perfumes from detergent powders is inhibited by complexation with cyclodextrins.[1] In aqueous solutions, the complexed perfumes are displaced from the cyclodextrin (CD) cavity by the surfactant molecules. The extent of this displacement varies largely with the chemical nature and/or steric factors of the competing molecules. Tensides and cyclodextrins are also used in combination in skin and hair lotions to decrease the skin irritation of the tensides and to lengthen the deodorizing action. Hence surfactants are ideal guests which allow a systematic study of complexation with cyclodextrins since both their hydrophobic and hydrophilic moieties can be systematically changed.[2]

The majority of the studies carried out on these mixed systems are focused on analyzing the stoichiometry of the CD-surfactant complexes, and the calculation of their complexation constants. For this purpose, authors use mainly surfactant concentrations that are smaller than those corresponding at the start of the micellization process. In a few cases, the surfactant concentration has varied in such a way that results can be obtained for surfactant concentrations both below and above the micellization point. Previous work in our laboratory we have applied a kinetic method, the basic hydrolysis of the *m*-nitrophenylacetate (*m*-NPA), to study the mixed systems *β*-CD-TTABr (TTABr is tetradecyltrimethylammonium bromide), *β*-CD-TTAOH (TTAOH is tetradecyltrimethylammonium hydroxide), and *β*-CD−SDS (SDS is sodium dodecyl sulfate) using surfactant concentrations obtained prior to and after the micellization process. The results obtained[3] allowed us to indicate some characteristics of mixed CD-surfactant systems.

(a) For surfactant concentrations lower than the micellization point, we can establish complexation equilibrium between the *m*-NPA and the surfactant with the cyclodextrin. As the surfactant concentration increases we reach a situation in which the concentration of uncomplexed surfactant monomers in equilibrium with the CD is sufficient for the micellization process to begin.

(b) The critical micelle concentration has been found to shift to higher values in the presence of CD, while the concentration of free monomers remains basically the same,[4] slightly increases,[5] or slightly decreases[5,6] depending on the surfactant. At the micellization point an appreciable concentration of uncomplexed CD must exist, $[CD]_f$, which will increase along with the total concentration of CD present in the medium.

(c) Once the micellization process has begun, no type of interaction will be established between the CD and the micellar system,[7,8] regardless of the type of charge which the micellar surface carries.

In this article we will present a systematic study of the basic hydrolysis of the *m*-NPA in mixed systems[9] made up of micelles of octyltrimethylammomium bromide (C_8TAB), decyltrimethylammonium bromide (C_{10}TAB), dodecyltrimethylammonium bromide (C_{12}TAB), tetradecyltrimethylammonium bromide (C_{14}TAB), hexadecyltrimethylammonium chloride (C_{16}TACl), and octadecyltrimethylammonium chloride (C_{18}TACl) and cyclo-

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dextrins (α-CD and *β*-CD). With the aim of comparing the nature of the headgroup of the surfactant, we have also carried out a limited number of experiments using hexadecylpyridinium chloride (CTPyCl). The results obtained show that contrary to expectations[10] the concentration of uncomplexed CD in equilibrium with the micellar system increases together with the length of the hydrocarbon chain of the surfactant.[11] The main implications of this result are of crucial importance in the use of CDs as transfer agents of hydrophobic substances[1] and in the determination of the stoichiometry of the CD-surfactant complexes.

Method

The surfactants and *β*-CD (α-CD is a Cyclolab product) were supplied by Sigma in the highest available purity and used without further purification. To check the purity of the surfactants we performed both conductometric and surface tension measurements of cmc, obtaining results consistent with literature values. *m*-Nitrophenyl acetate (*m*-NPA) was synthesized by reacting *m*-nitrophenol with acetic anhydride in pyridine.[12] Owing to the low solubility of *m*-NPA in water, its stock solutions were prepared in acetonitrile. The percentage of acetonitrile in the reaction mixtures was always lower than 1% (v/v). CD solutions were made taking into account that commercial *β*-CD has a H_2O content of 8 mol mol^{-1} and commercial α-CD has 6 mol mol^{-1}.

Under the alkaline conditions used, all CD will have been deprotonated (to give −1 anion), since $pK_a^{\alpha-CD} = 12.33$ and $pK_a^{\beta-CD} = 12.2$.[13] All hydroxyl ion concentrations given were obtained by subtracting the CD concentration from that of NaOH. The reaction kinetics were monitored by measuring the absorbance of the resulting nitrophenoxide at 400 nm, using an Applied Photophysics DX17MV sequential stopped-flow spectrophotometer thermostated at 25.0 ± 0.1 °C. The substrate concentration used was always approximately 2.0×10^{-4} M and that of hydroxyl ion higher than 0.1 M. The absorbance−time data of all kinetic experiments were fitted by first-order integrated equations, and the values of the pseudo-first-order rate constants k_{obs} were reproducible to within 3%.

Results

1. Basic Hydrolysis of the *m*-NPA in the Presence of α-CD and *β*-CD. Although the hydrolysis of acyl esters in particular phenyl acetates in the presence of CD is one of the most thoroughly studied processes,[13−16] we have studied the influence of the CD concentration on the basic hydrolysis of the *m*-nitrophenylacetate with the aim of obtaining a greater coherence in the experimental results. The cyclodextrins catalyze the basic hydrolysis of phenyl acetates by aryl transfer of the ester to the ionized hydroxyl group of the CD.[17] The reaction takes place within an inclusion complex in which the phenyl group of the ester resides in the hydrophobic cavity of the CD. As a result, the efficiency of the CD for the rupture of the ester, relative to the reaction with the hydroxide ion, is generally greater for phenyl acetates with substitution in the *meta*-position since they allow the phenyl group to be orientated within the cavity with a geometry which is very suitable for the acyl group transfer.

Rate constants for hydrolysis of *m*-NPA, k_{obs}, were obtained over a range of [CD] (Figure 1). Saturation kinetics[13−15,17−19] were observed with *β*-CD, which may be ascribed to reactions of the *m*-NPA in aqueous medium (k_w, Scheme 1A) and reaction via an CD-*m*-NPA complex (k_{CD}, Scheme 1B).[16]

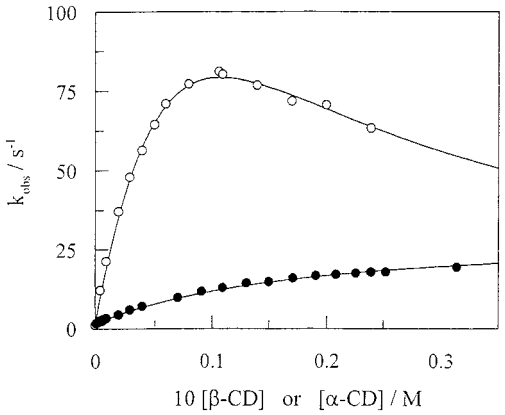
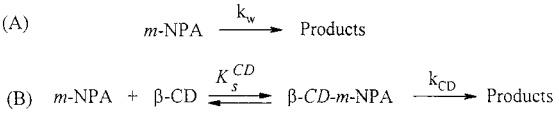


Figure 1. Influence of cyclodextrin concentration upon the pseudo first-order rate constant, k_{obs}, for hydrolysis of *m*-NPA. [NaOH] = 0.165 M; T = 25 °C. (●) 10[*β*-CD] and (○) [α-CD].

SCHEME 1



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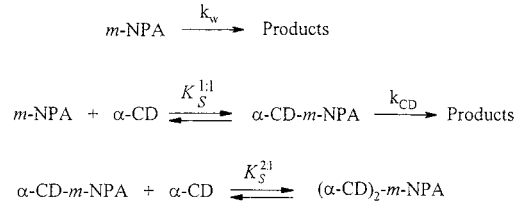


These two processes lead to the dependence of k_{obs} on [*β*-CD] expressed by eq 1.

$$k_{obs} = \frac{k_w[HO^-] + k_{CD}K_s^{CD}[\beta\text{-CD}]}{1 + K_s^{CD}[\beta\text{-CD}]} \qquad (1)$$

Equation 1 gave excellent fit to the observed data from which were obtained the parameters $k_{CD} = (31 \pm 2)$ s^{-1} and $K_S^{CD} = (54 \pm 5)$ M^{-1}. The value of the uncatalyzed rate constant, $k_w = (9.0 \pm 0.1)$ M^{-1} s^{-1}, has been previously determined in the absence of *β*-CD.

The hydrolysis of *m*-NPA in the presence of α-CD shows a different behavior. Rate constants deviate at high [α-CD] (see Figure 1) suggesting the onset of 2:1 ((α-CD)$_2$-*m*-NPA) binding.[20] The decrease in k_{obs} at high [α-CD] can be accommodated by the equilibrium formation of a nonproductive 2:1 complex (Scheme 2) in which case eq 1 is replaced by eq 2.

$$k_{obs} = \frac{k_w[OH^-] + K_S^{1:1}k_{CD}[\alpha - CD]}{1 + K_S^{1:1}[\alpha - CD] + K_S^{1:1}K_S^{2:1}[\alpha - CD]^2} \qquad (2)$$

Fitting this equation to the data gave the following rate and equilibrium constants: $k_{CD} = (280 \pm 30)$ s^{-1}, $K_S^{1:1} = (7 \pm 1)$ M^{-1}, and $K_S^{2:1} = (12 \pm 2)$ M^{-1}. The value of the uncatalyzed rate constant, $k_w = (9.0 \pm 0.1)$ M^{-1} s^{-1}, has been previously determined in the absence of α-CD.

2. Basic Hydrolysis of the *m*-NPA in the Presence of Cationic Micelles. A number of kinetic models[21] have been developed to analyze the acceleration observed in reactions of lipophilic substrates and anionic nucleophiles in the presence

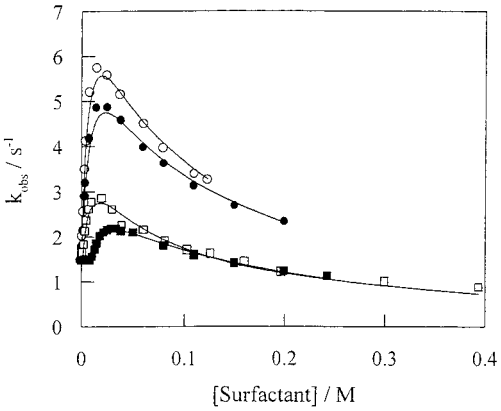


Figure 2. Influence of surfactant concentration upon the pseudo-first-order rate constant, k_{obs}, for hydrolysis of *m*-NPA. [NaOH] = 0.165 M; T = 25 °C. (○) C_{18}TACl, (●) C_{16}TACl, (□) C_{14}TAB, and (■) C_{12}TAB. The curves were obtained by fitting eq 3 to the experimental results (parameters in Table 1).

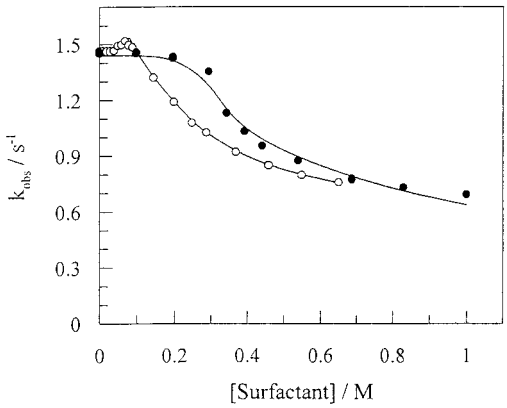


Figure 3. Influence of surfactant concentration upon the pseudo first-order rate constant, k_{obs}, for hydrolysis of *m*-NPA. [NaOH] = 0.165 M; T = 25 °C. (○) C_{10}TAB and (●) C_8TAB. The curves were obtained by fitting eq 3 to the experimental results (parameters in Table 1).

of cationic surfactants quantitatively. In most cases, the pseudophase-ion-exchange model[21−23] utilizing the k_{obs} vs surfactant-concentration profiles works fairly well and gives access to the micellar reagent concentrations and rate constants. The interfacial ion exchange and the binding constant of the substrate are the key factors at the origin of micellar catalysis since it is now recognized[21,24] that accelerations in surfactant solutions arise not because of an increase in the micellar rate constants, k_m, as compared to those in water, k_w, but because of large reagent concentrations in the small interfacial volume in which the reaction occurs.

Figure 2 shows the results obtained from studying the variation of k_{obs} with the [surfactant] in the basic hydrolysis of *m*-NPA. We obtained the typical behavior of the catalysis of the basic hydrolysis processes of hydrophobic substrates by cationic micelles. On comparing the results obtained with various micellar systems C_{12}TAB, C_{14}TAB, C_{16}TACl, and C_{18}TACl, we observe that the catalytic effect increases together with the length of the hydrocarbon chain of the surfactant. Hence the relationships k_{obs}^{max}/k_w present the following dependence on the nature of the surfactant 3.89; 3.29; 1.93 and 1.47 for C_{18}TACl, C_{16}TACl, C_{14}TAB, and C_{12}TAB, respectively. As mentioned previously, this catalytic effect is determined fundamentally by two factors: as the length of the hydrocarbon chain of the surfactant increases, so too does its hydrophobicity and hence the association constant of the *m*-NPA to the micellar system must also increase. Likewise as the length of the hydrocarbon chain of the surfactant increases, the critical micellar concentration, cmc, decreases, and therefore so too does the concentration of nonreactive counterions in equilibrium with the micellar system when the micellization process begins. Another factor which determines the catalytic effect observed is the difference between the exchange constants of the nonreactive counterions and the ion OH^-. However, the values of the exchange constants,[25] K_{OH}^{Br} and K_{OH}^{Cl}, are sufficiently close to ensure that their influence on the catalytic effect is small.

Figure 3 shows the effect of the micelles of C_{10}TAB and C_8TAB on k_{obs} in the basic hydrolysis of *m*-NPA. The catalytic effect of C_{10}TAB micelles is very small, k_{obs}^{max}/k_w = 1.06, whereas in the case of C_8TAB micelles we only observe an inhibitory effect. This behavior is due fundamentally to the high values of the critical micellar concentration, cmc = 5.8×10^{-2} M and cmc = 0.27 M, for the C_{10}TAB and C_8TAB, respectively. These values of the cmc give rise to the fact that the concentration of Br^- ions in equilibrium with the micellar system is 5.7×10^{-2} and 0.27 M at the beginning of the micellization process. This high concentration of nonreactive counterions is the cause of the disappearance of the catalytic effect exerted by the cationic micelles on the basic hydrolysis of *m*-NPA.

Application of the micellar pseudophase formalism with an ionic exchange allows us to obtain the following expression for k_{obs}

$$k_{obs} = \frac{k_w[HO^-]_w + (k_m K_s^m - k_w) m_{OH}[D_n]}{1 + K_s^m[D_n]} \qquad (3)$$

where the association constant of the *m*-NPA to the cationic micelles, K_s^m, the concentration of HO^- ions in the micellar surface, m_{OH}, and the concentration of micellized surfactant, D_n, are defined in a traditional way.[21,23,26,27] The critical micellar concentration has been obtained on the basis of kinetic measurements like the minimum concentration of surfactant needed to detect a clear catalytic effect (in the case of the micelles of C_{12}TAB, C_{14}TAB, C_{16}TACl, and C_{18}TACl). In the micelles of C_{10}TAB and C_8TAB, the absence of the catalytic effect has meant that the cmc are determined on the basis of conductivity measurements in the presence of a constant concentration of NaOH, [NaOH] = 0.165 M. The values obtained for the cmc are shown in Table 1. As we can see, the values of the cmc are lower than those shown by the micellar systems of the pure surfactants and agree with the influence of salts on the micellization process.[28] These values are compatible with others obtained in similar conditions.[29]

The values of m_{OH} were obtained by the application of the ionic exchange formalism.[21,23,26]

$$m_{OH}^2 - m_{OH}\left[\frac{[HO^-]_T + K_{OH}^X[Br^-]_T}{(K_{OH}^X - 1)[D_n]} - \beta\right] - \left[\frac{\beta[HO^-]_T}{(K_{OH}^X - 1)[D_n]}\right] = 0 \qquad (4)$$

To resolve eq 4 we have used K_{OH}^{Br} and K_{OH}^{Cl} values previously obtained in our laboratory.[25]

The simultaneous resolution of the eqs 3 and 4 for the results presented in Figures 2 and 3 (curves shown in Figures 2 and 3) allows us to obtain the values of the association constants of the *m*-NPA at the cationic micelles and the values of k_m (parameters in Table 1). The values of the association constants

TABLE 1: Compilation of Kinetic Parameters Obtained for the Basic Hydrolysis of the m-NPA in Different Cationic Micellar Systems in the Absence and Presence of β-CD: [NaOH] = 0.165 M, and T = 25 °C

surfactant	$[\beta\text{-CD}]_{tot}$/M	cmc_{app}/M	$[\beta\text{-CD}]_f$/M	cmc_{real}/M	K_S^m/M^{-1}	k_m/s^{-1}
C_8TAB				0.27	18 ± 6	31 ± 2
	1.00×10^{-2}	0.28	2.83×10^{-4}		21 ± 3	34 ± 1
$C_{10}TAB$				5.8×10^{-2}	23 ± 4	14.4 ± 0.3
	1.00×10^{-2}	6.80×10^{-2}	2.96×10^{-4}		25 ± 4	14.9 ± 0.3
$C_{12}TAB$				1.0×10^{-2}	32 ± 2	11.2 ± 0.1
	1.00×10^{-2}	1.90×10^{-2}	4.15×10^{-4}		31 ± 4	12.6 ± 0.3
$C_{14}TAB$				1.20×10^{-3}	63 ± 4	10.0 ± 0.2
	1.00×10^{-2}	1.00×10^{-2}	8.04×10^{-4}		76 ± 3	14.4 ± 0.1
$C_{16}TACl$				3.0×10^{-4}	59 ± 2	17.6 ± 0.2
	1.00×10^{-2}	6.50×10^{-3}	2.64×10^{-3}		59 ± 5	21.3 ± 0.3
$C_{18}TACl$				2.0×10^{-4}	82 ± 3	18.8 ± 0.3
	1.00×10^{-2}	4.50×10^{-3}	4.03×10^{-3}		73 ± 10	25.3 ± 0.5

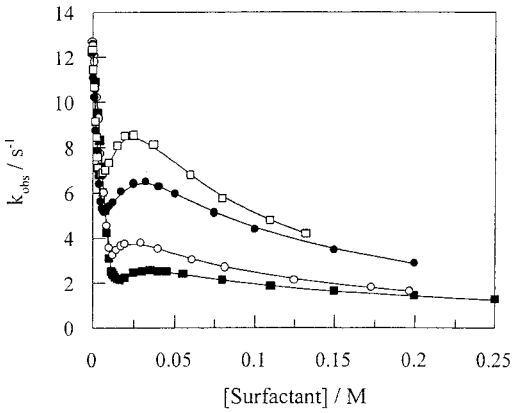


Figure 4. Influence of surfactant concentration upon the pseudo first-order rate constant, k_{obs}, for hydrolysis of *m*-NPA in the presence of β-CD. $[\beta\text{-CD}] = 1.00 \times 10^{-2}$ M; [NaOH] = 0.165 M; T = 25 °C. (■) $C_{12}TAB$, (○) $C_{14}TAB$, (●) $C_{16}TACl$, and (□) $C_{18}TACl$. The curves were obtained by fitting eq 5 to the experimental results (parameters in Table 1).

present a linear dependence between the logarithm of K_S^m and the number of carbon atoms of the surfactant (not shown). This behavior is well documented in the literature as a consequence of the increase in hydrophobicity of the surfactant as the length of the hydrocarbon chain.[26] The values of k_m do not present any clear variation, probably due to the uncertainty of their determination, as a consequence of the small catalytic effect exerted by these micellar systems on the basic hydrolysis of the *m*-NPA and the small influence of the polarity of the medium on this reaction.

3. Basic Hydrolysis of the *m*-NPA in the Presence of Mixed CD−Surfactant Systems. Previous studies[3,30] carried out in our laboratory have allowed us to characterize the kinetic behavior of the mixed CD−surfactant systems. Figure 4 shows the behavior observed in studying the influence of the surfactant concentration on k_{obs} in the basic hydrolysis of *m*-NPA in the presence of a constant concentration of β-CD, $[\beta\text{-CD}] = 1.0 \times 10^{-2}$ M. It can be observed that the value of the rate constant, k_{obs}, extrapolated to zero surfactant concentration is in agreement with the values obtained in the absence of the surfactant (Figure 1). The initial decrease of k_{obs}, as the surfactant concentration increases until it reaches a minimum value, is due to the complexation of the monomers of the surfactant with the β-CD displacing the *m*-NPA and losing the catalytic effect. The basic hydrolysis path of the *m*-NPA catalyzed by the β-CD. Subsequently an increase of k_{obs} occurs as the surfactant concentration increases, passing through a maximum and a subsequent inhibition that is compatible with the behavior of cationic micelles in the basic hydrolysis of hydrophobic substrates.

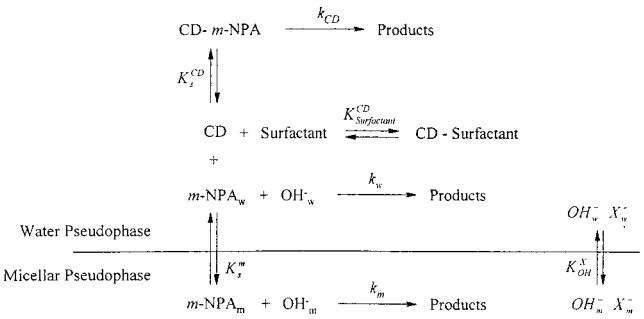
With the surfactants C_8TAB and $C_{10}TAB$ (not shown) we can observe a reduction of k_{obs} as the surfactant concentration increases until reaching a limit value where k_{obs} is independent of the surfactant concentration. A later increase in the surfactant concentration produces a new reduction of k_{obs}. The absence of a maximum in the curves k_{obs} vs [surfactant] is explained in a similar way to the behavior observed in the absence of β-CD.

The surfactant concentration at the minimum in the curve k_{obs} vs [surfactant] is taken as the onset of micellization and equal to cmc_{app}.[31] The values of cmc_{app} are displaced to lower surfactant concentrations as the length of the hydrocarbon chain increases. Hence the surfactant concentration in the minimum of the curve will be 0.28, 6.8×10^{-2}, 1.9×10^{-2}, 1.0×10^{-2}, 6.5×10^{-3}, and 4.5×10^{-3}M for C_8TAB, $C_{10}TAB$, $C_{12}TAB$, $C_{14}TAB$, $C_{16}TACl$, and $C_{18}TACl$, respectively, in the presence of a constant concentration of β-CD, $[\beta\text{-CD}] = 1.0 \times 10^{-2}$ M. This behavior is related to the known effect of complexation of the surfactant monomers and with the increase in the critical micellar concentration of the surfactants as the length of its hydrocarbon chain decreases.

The catalytic efficiency of the various mixed systems, $k_{obs}^{max}/k_{obs}^{min}$, could be identified with the catalytic efficiency which the simple micellar systems present. However the relationship $k_{obs}^{max}/k_{obs}^{min}$ remains practically constant as the length of the hydrocarbon chain of the surfactant varies: $k_{obs}^{max}/k_{obs}^{min} = 1.19$, 1.16, 1.25, and 1.25 for $C_{12}TAB$, $C_{14}TAB$, $C_{16}TACl$, and $C_{18}TACl$. This result contrasts with the values of $k_{obs}^{max}/k_w = 1.47$, 1.93, 3.29, and 3.89 for the same surfactants. This loss of catalytic efficiency of the surfactant could be explained as a consequence of the complexation of the surfactant monomers by the CD. This complexation displaces the critical micellar concentration and, hence, increases the concentration of non-reactive counterions at the point of micellization. However, in the case of the $C_{18}TACl$ the critical micellar concentration increases from 2.0×10^{-4} to 4.5×10^{-3} M. It is difficult to see how this increase in the $[Cl^-]$ can explain why the catalytic effect exerted by this micelle passes from 389% to 125%. Therefore, there must exist another factor responsible for the loss of the catalytic effect, and we can suggest that this may be the presence of uncomplexed β-CD. The results obtained on studying the mixed α-CD−surfactant systems present a similar behavior to the systems β-CD−surfactant.

A quantitative interpretation of the experimental behavior observed can be carried out by means of the formalism of the micellar pseudophase with an ionic exchange. In the basic hydrolysis of *m*-NPA we must consider the existence of three simultaneous reaction paths: the reaction of the free substrate in aqueous medium; the reaction of the complexed substrate with the CD and the reaction of the substrate associated with

SCHEME 3



the micelle with the OH^- ions present in the micellar surface (see Scheme 3).

On the basis of this mechanism we can obtain the following expression for the rate constant.

$$k_{obs} = \frac{k_w[HO^-] + (k_m K_s^m - k_w) m_{OH}[D_n] + k_{CD} K_s^{CD}[CD_f]}{1 + K_s^m[D_n] + K_s^{CD}[CD_f]} \quad (5)$$

To resolve this equation it is necessary to obtain the concentration of uncomplexed CD in equilibrium with the micellar system, as well as the values of m_{OH} and D_n.

3.1. Concentration of Uncomplexed CD. The calculation of the concentration of uncomplexed CD, $[CD_f]$ for each surfactant concentration is difficult due to the great disparity of the values of the equilibrium complexation constants between CD and surfactants.[32] In previous studies we have obtained the $[CD_f]$ by means of a simulation process supposing that the complex formed between the β-CD and the C_{14}TAB presents a stoichiometry of 1:1. An analysis of the values of the cmc_{app} presented previously seems to suggest the existence of CD−surfactant complexes with stoichiometry 1:1 and 2:1. The existence of both types of complexes would imply the simulation of the two complexation constants, the values of which should be closely connected.

Therefore, we have calculated the concentration of $[CD_f]$ on the basis of the values of k_{obs} for surfactant concentrations below the cmc_{app}. The experimental results k_{obs} obtained on studying the influence of the concentration of β-CD on k_{obs} in the basic hydrolysis of the *m*-NPA in the absence of surfactants lead to a kinetic saturation behavior, eq 1. This equation can be regrouped to obtain the values of the $[\beta - CD_f]$ in the experiments carried out in the presence of surfactants using the values of $k_w = (9.0 \pm 0.1)\ M^{-1}\ s^{-1}$, $k_{CD} = (31 \pm 2)\ s^{-1}$, and $K_s^{CD} = (54 \pm 5)\ M^{-1}$ obtained previously.[3A]

$$[\beta - CD_f] = \frac{k_w[OH^-] - k_{obs}}{k_{obs} K_s^{CD} - k_{CD} K_s^{CD}} \quad (6)$$

The advantage of this method of calculation the $[\beta - CD_f]$, compared with others used previously, is that it is not necessary to assume any stoichiometry for the complex CD−surfactant.

For the mixed α-CD−surfactant systems we can calculate the $[\alpha\text{-CD}]_f$ in a similar way, obtaining the following equation.

$$k_{obs} K_S^{1:1} K_S^{2:1}[\alpha - CD]_f^2 + (k_{obs} K_S^{1:1} - k_{CD} K_S^{1:1})[\alpha - CD]_f + (k_{obs} - k_w[OH^-]) = 0 \quad (7)$$

Using the values $k_{CD} = (280 \pm 30)\ s^{-1}$, $K_S^{1:1} = (7 \pm 1)\ M^{-1}$, $K_S^{2:1} = (12 \pm 2)\ M^{-1}$, and $k_w = (9.0 \pm 0.1)\ M^{-1}\ s^{-1}$, we can calculate the $[\alpha\text{-CD}]_f$ for each value of k_{obs}.

In Tables 1 and 2 we present the values of $[\beta\text{-CD}]_f$ and $[\alpha\text{-CD}]_f$ obtained at the beginning of the micellization process.

3.2. Kinetic Parameters. Fitting eq 5 to the experimental results it is necessary to know the concentration of OH^- in the micellar pseudophase, m_{OH}, which has been calculated from the eq 4 in the same way as the system in absence of CD. The micellar concentration has been evaluated kinetically considering that the minimum of the curve k_{obs} vs [surfactant] corresponds with the initiation of the micellization process, in such a way that the surfactant in the aforesaid minimum should correspond with the cmc_{app}. In the mixed systems, β-CD-C_8TAB and β-CD-C_{10}TAB the cmc_{app} has been determined by means of conductivity.

The kinetic model developed considers that the $[CD_f]$ remains constant once the micellization process has begun and there exists no type of interaction between the CD and the micellar system once this system has formed.[3] The curves traced in Figure 4 correspond with the fit of eq 5 to the experimental values of k_{obs}. Following the methodology used previously we have only optimized the parameters corresponding with the reaction in the micellar pseudophase, k_m and K_s^m. In Tables 1 and 2 we show the obtained values for these parameters in simple micellar systems and mixed CD-micelle systems. As we can observe, there exists a good agreement between the values of k_m and K_s^m obtained in the absence and presence of CD, which clearly indicates the validity of the model being applied.

Discussion

The results presented in the previous section allows us to confirm the validity of the kinetic model developed for mixed systems β-CD-C_{14}TAB when we apply it to other surfactants or CD systems. In what follows we will center our discussion on the existence of an appreciable concentration of uncomplexed CD in equilibrium with the micellar system[33] and in its main repercussions.

1. Variation of Uncomplexed CD Concentration with the Chain Length of the Surfactant. Table 3 shows the values of the % $\alpha\text{-CD}_f$ and % $\beta\text{-CD}_f$ in equilibrium with the micellar system as the length of the hydrocarbon chain of the surfactant varies. As shown, the percentage of uncomplexed CD in equilibrium with the micellar system increases together with the length of the hydrocarbon chain of the surfactant (see Figure 5). The increase in the concentration of uncomplexed CD in equilibrium with the micellar system causes the minimums of the curves k_{obs} vs [surfactant] to change to higher values of k_{obs} as the length of the hydrocarbon chain of the surfactant increases (see Figure 3). This dependency of the minimum value of k_{obs} on the nature of the surfactant must cause the loss of catalytic efficiency, $k_{obs}^{max}/k_{obs}^{min}$, of the mixed CD−surfactant systems. This result contrasts clearly with earlier behavior models of the mixed CD−surfactant systems. The traditional ideas on mixed CD−surfactant systems consider that the micellization process only begins once the complexation capacity of the CD has been saturated. This supposition implies the absence of uncomplexed CD in equilibrium with the micellar system. Our results indicate that this vision should be modified. We should consider that the complexation equilibrium of the surfactant by the CD and the autoassociation of the surfactant (micellization) take place simultaneously. The balance between both processes will be the cause of the existence of uncomplexed CD in equilibrium with the micellar system and its variation with the nature of the surfactant.

TABLE 2: Compilation of Kinetic Parameters Obtained for the Basic Hydrolysis of the *m*-NPA in Different Cationic Micellar Systems in the Absence and Presence of α-CD: [NaOH] = 0.165 M, and $T = 25$ °C

surfactant	$[\alpha\text{-CD}]_{tot}$/M	cmc_{app}/M	$[\alpha\text{-CD}]_f$/M	cmc_{real}/M	K_S^m/M^{-1}	k_m/s^{-1}
$C_{10}TAB$				5.8×10^{-2}	23 ± 4	14.4 ± 0.3
	1.00×10^{-2}	6.80×10^{-2}	2.65×10^{-5}		16 ± 3	13 ± 1
$C_{12}TAB$				1.0×10^{-2}	32 ± 2	11.2 ± 0.1
	1.00×10^{-2}	1.90×10^{-2}	1.28×10^{-4}		29 ± 4	11.9 ± 0.3
$C_{14}TAB$				1.20×10^{-3}	63 ± 4	10.0 ± 0.2
	1.00×10^{-2}	9.50×10^{-3}	5.82×10^{-4}		66 ± 7	13.8 ± 0.3
$C_{16}TACl$				3.0×10^{-4}	59 ± 2	17.6 ± 0.2
	1.00×10^{-2}	6.30×10^{-3}	1.54×10^{-3}		59 ± 8	23.2 ± 0.5
$C_{18}TACl$				2.0×10^{-4}	82 ± 3	18.8 ± 0.3
	1.00×10^{-2}	4.50×10^{-3}	2.81×10^{-3}		78 ± 6	26.4 ± 0.6

TABLE 3: Values of the $[\alpha\text{-CD}]_f$ and $[\beta\text{-CD}]_f$ in Equilibrium with the Micellar System in the Presence of Different Surfactants[a]

surfactant	% α-CD_f	% β-CD_f
C_8TAB		2.83
$C_{10}TAB$	0.27	2.96
$C_{12}TAB$	1.28	4.15
$C_{14}TAB$	5.82	8.04
$C_{16}TACl$	15.4	26.4
$C_{18}TACl$	28.1	40.3

[a] In all cases the total concentration of CD is 1.00×10^{-2}M. [NaOH] = 0.165 M; $T = 25$ °C.

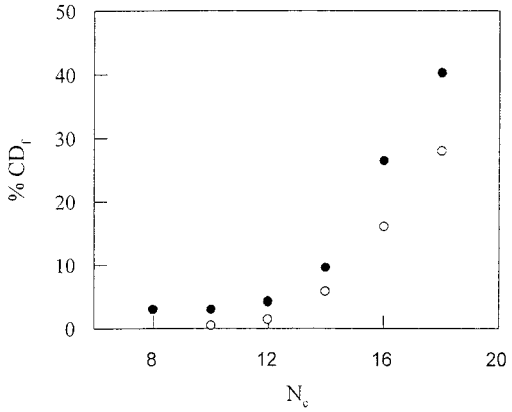


Figure 5. Variation of the percentage of uncomplexed CD in equilibrium with the micellar system according to the number of carbon atoms (N) of the hydrocarbon chain of the surfactant. (○) α-CD and (●) β-CD.

Traditional theories are based on the consideration that the association of substrates, which present a suitable geometry to the CD, increases along with the hydrophobic character of the substrate. In fact, the strength of CD−hydrocarbon chain interactions increases for the common water-soluble ionic surfactants as the length of the alkyl chains increases.[34] According to Tanford,[35] a fully extended alkyl chain consisting of four CH_2 groups can span the β-CD cavity, whereas Park and Song[36] indicate that eight CH_2 groups can be accommodated in the β-CD cavity if allowance is made for carbon chain coiling due to the occurrence of gauche links. Various authors have studied the variation of the CD−surfactant association with regard to the length of the hydrocarbon chain of the surfactant. Satake et al.[37] find that the capacity of complexes formation for sodium 1-alkanesulfonate increases together with the length of its hydrocarbon chain reaching a saturation value upward of 10 carbon atoms. The association constant of β-CD increases more rapidly than that of α-CD with increasing chain length but become also constant at $N = 10$. Other studies also indicate that on the basis of a determined length of the hydrocarbon chain of the surfactant, which depends on the type of surfactant

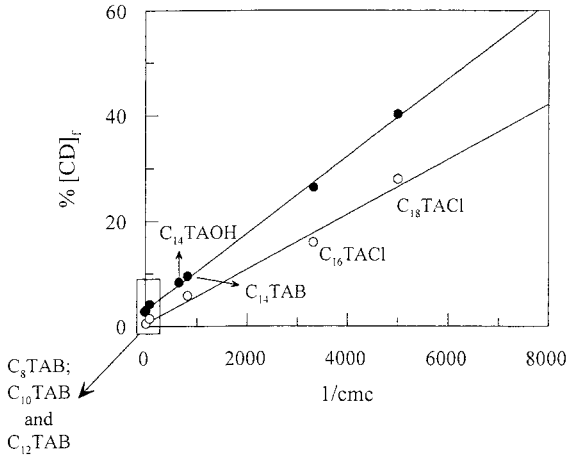


Figure 6. Variation of the percentage of uncomplexed CD in equilibrium with the micellar system according to the inverse of the critical micellar concentration of the surfactant. (○) α-CD and (●) β-CD.

used, deviations occur from the linearity indicating that the association constant CD-surfactant tends to reach a limit value.[36,38] Letellier et al.[39] have studied the complexation of several ammonium surfactants with β-CD showing that the binding constants for 1:1 CD-surfactant complexes fit a linear relation up to $N = 12$ carbon atoms; beyond that the K_1 binding constants tend to reach a limit value.

An increase in the hydrophobicity of the surfactant gives rise to an increase in its affinity to complex with the CD but simultaneously implies an increase in its tendency to micellize. The critical micellar concentration of a surfactant, cmc, can be considered as a measurement of its tendency to autoassociation. The value of the cmc is dependent on a large number of parameters. Usually the more surface active the amphiphilic monomer,[26] the higher is the tendency for micellization and, hence, the lower cmc of the micelle produced. Accordingly, the longer the total carbon chain length of the monomeric surfactant, the lower the cmc becomes. The number of carbon atoms, *N*, are empirically related to the logarithm of the cmc by[40] $\log cmc = A - BN$. The balance between the complexation processes of the surfactant by the CD and autoassociation (micellization) is responsible for the existence of uncomplexed CD and its variation with the nature of the surfactant.

The validity of our hypothesis is confirmed by Figure 6, where we represent the percentage of uncomplexed CD obtained with the different surfactants versus the inverse of the critical micellar concentration. We have used the cmc values of the surfactants obtained under the same experimental conditions as the kinetic study, [NaOH] = 0.165 M. If the percentage of uncomplexed CD is determined fundamentally by the tendency of the surfactants to micellize, it would be expected that the existence of a linear dependency between the % CD_f and 1/cmc.

TABLE 4: Values of the $[\beta\text{-CD}]_f$ in Equilibrium with the Micellar System in Different mixed β-CD-surfactant Systems, Using Different Concentrations of β-CD: [NaOH] = 0.165 M, and $T = 25$ °C

surfactant[a]	$[\beta\text{-CD}]_{tot}$/M	$[\beta\text{-CD}]_f$/M	% $\beta\text{-CD}_f$
C_{14}TAB	2.50×10^{-3}	3.39×10^{-4}	9.6
	5.00×10^{-3}	4.34×10^{-4}	8.7
	1.03×10^{-2}	1.01×10^{-3}	9.8
C_{14}TAOH	5.00×10^{-3}	4.02×10^{-4}	8.0
	1.00×10^{-2}	8.04×10^{-4}	8.0
	1.50×10^{-2}	1.30×10^{-3}	8.7
	2.50×10^{-2}	2.16×10^{-3}	9.0
CTPyCl	5.00×10^{-3}	1.41×10^{-3}	28.2
	1.00×10^{-2}	2.24×10^{-3}	22.4
C_{18}TACl	5.00×10^{-3}	2.00×10^{-3}	40.0
	1.00×10^{-2}	4.03×10^{-3}	40.3

[a] C_{14}TAB is tetradecyltrimethylammonium bromide, C_{14}TAOH is tetradecyltrimethylammonium hydroxide, CTPyCl is hexadecylpyridinium chloride, and C_{18}TACl is octadecyltrimethylammonium chloride.

This behavior can be verified experimentally in Figure 6 which shows that the CD-surfactant systems behave in a dynamic way where the micellization is the predominant factor for very hydrophobic surfactants, while the CD−surfactant complexation is the predominating factor for those surfactants with a negligible tendency to micellization.

In Table 4 we present the values of $[\beta\text{-CD}]_f$ obtained in previous studies in our laboratory.[3A] To achieve a greater coherence between our previous results and those shown in this study, the $[\beta\text{-CD}]_f$ has been recalculated by applying eq 6. In all cases the values of $[\beta\text{-CD}]_f$ are very near to those obtained previously through a process of simulation of the complexation constant of the monomers of the surfactant with the β-CD. It is important to point out that the $[\beta\text{-CD}]_f$ increases along with the total concentration of cyclodextrin present in the reaction medium. However, the percentage of uncomplexed CD remains approximately constant and independent of the total concentration of added β-CD. This result is consistent with the fact that the presence of uncomplexed cyclodextrin is derived from the existence of a balance between the complexation equilibrium of the surfactant by the cyclodextrin and the equilibrium of micellization.

2. Variation of Uncomplexed CD Concentration with the Headgroup of the Surfactant. The comparison of the results presented in Tables 3 and 4 allows us to study the possibility of changes in the % CD_f as the nature of the headgroup of the surfactant varies. A comparison of the % CD_f obtained with C_{14}TAB and C_{14}TAOH, two surfactants which are equal but with a different counterion, indicates that the % CD_f is independent of the nature of the counterion, in both cases a value of % $CD_f \cong 9$ being obtained. More significant would be the comparison of the hexadecylpyridinium chloride (Table 3) and the hexadecyltrimethylammonium chloride (Table 4). In the first case we obtain a mean value of % $CD_f \cong 25.3$. This value is perfectly comparable with the % $CD_f = 26.4$ obtained for the C_{16}TACl. The complexation of the surfactant monomers by the CD is due to the ability of CD to screen the hydrophobic moieties of surfactant molecules from contact with the surrounding aqueous media by the formation of an inclusion complex in which the hydrophobic chain of the surfactant is inserted into the CD cavity.

The absence of any dependence of the concentration of uncomplexed CD with the nature of the headgroup of the surfactant is, therefore, consistent with previous results existing in the literature which indicate that the CD-surfactant interaction is produced only through the hydrocarbon chain. For example, Letellier et al.[39] only find a very small variation between the association constant of alkylammonium and trimethylalkylammonium salts to β-CD. Christian et al.[33A] obtain the formation constants of the β-CD-surfactant complexes with stoichiometry 1:1 (K_1) and 2:1 (K_2) for mixed systems of β-CD-hexadecylpyridinium chloride ($K_1 = 48800\ M^{-1}$; $K_2 = 265\ M^{-1}$) and β-CD-hexadecyltrimethylammonium bromide ($K_1 = 65500\ M^{-1}$; $K_2 = 398\ M^{-1}$). More recently, Aicart et al.[41] have studied the complexation of dodecylethyldimethylammonium and dodecyltrimethylammonium bromides by cyclodextrins. They found that the substitution of a methyl group by an ethyl group in the polar head of the surfactant has no effect on the stoichiometry of the complex. The effect on the binding constant is small and much lower than that when the surfactant tail is lengthened by a methylene group.

3. Variation of Uncomplexed CD Concentration with the Nature of the CD. The results shown in the Tables 1 and 2 (Figures 5 and 6) indicate that the percentage of uncomplexed CD in equilibrium with the micellar system is lower for the systems formed by α-CD than β-CD. Hence, for a given surfactant we can observe that the quotient % $\beta\text{-CD}_f$/% $\alpha\text{-CD}_f$ is 10.9, 3.4, 1.38, 1.71, and 1.43 for C_{10}TAB, C_{12}TAB, C_{14}TAB, C_{16}TACl, and C_{18}TACl. It is significant that the % $\beta\text{-CD}_f$ is always greater than the % $\alpha\text{-CD}_f$ and that the difference becomes less as the length of the hydrocarbon chain of the surfactant increases.

Since we are always comparing pairs of equal surfactants, the difference in the percentage of uncomplexed CD should be due to the formation of α-CD-surfactant and β-CD-surfactant complexes. In the literature there exists an enormous disparity between the values of the complexation constants of the surfactants with the CD. For example,[32] the 1:1 complex formation constant between β-CD and sodium dodecyl sulfate (SDS), K_1, have been reported to range between 300−25600. For the interaction between α-CD and SDS, some determined only 1:1 complex formation constants, while others determined 1:1 and 2:1 complex formation constants, K_1 and K_2, or their product, K_1K_2. Because of the disparity of the results, we will only consider those studies in the literature, which involve a simultaneous analysis of the complexation of surfactants with α- and β-CD using the same experimental technique.

In general, the association constants between hydrocarbon surfactants and either α- or β-CD are of the same order of magnitude.[42] Hence Wyn-Jones et al.[2] have studied the complexation of surfactants with α- and β-CD. The values found for ($K_1 = 61000\ M^{-1}$; $K_2 = 7000\ M^{-1}$) and ($K_1 = 39750\ M^{-1}$; $K_2 = 3060\ M^{-1}$) for the complexation of the tetradecyltrimethylammonium bromide with α- and β-CD respectively show that the complexation with the α- is greater than with the β-CD. They find a similar result for the complexation of hexadecyltrimethylammonium bromide ($K_1 = 99200\ M^{-1}$; $K_2 = 20400\ M^{-1}$) and ($K_1 = 67700\ M^{-1}$; $K_2 = 9600\ M^{-1}$) with α- and β-CD, respectively. The same authors study the complexation of C_{12}TAB and sodium dodecyl sulfate with α- and β-CD[33A], finding values of ($K_1 = 17000\ M^{-1}$; $K_2 = 1000\ M^{-1}$) and ($K_1 = 18100\ M^{-1}$; K_2 not obtained) for the complexation of C_{12}TAB with α- and β-CD respectively and of ($K_1 = 21000\ M^{-1}$; $K_2 = 18000\ M^{-1}$) and ($K_1 = 21000\ M^{-1}$; $K_2 = 210\ M^{-1}$) for the complexation of sodium dodecyl sulfate with α- and β-CD, respectively.

Tominaga et al.[32] study the complexation of tetradecyltrimethylammonium bromide by α- and β-CD. They find values of ($K_1 \cong 43000\ M^{-1}$; $K_2 \cong 3000\ M^{-1}$) and ($K_1 \cong 50000\ M^{-1}$;

K_2 not obtained) for its complexation by α- and β-CD. The difference in the association mode clearly reflects the difference in the internal diameter of the CD cavities. Because the internal diameter of the α-CD cavity (0.5 nm)[13,14,43] and the cross sectional diameter of the alkyl chain (0.45 nm) are so close, and the alkyl-chain length of the tetradecyltrimethylammonium ion (1.8 nm)[35] is long enough compared with the depth of the α-CD cavity (0.7−0.8 nm),[13,43] formation of the 2:1 complex is understood. In the case of β-CD, the inner diameter of the cavity (0.6−0.7 nm)[13,14,43] is too large and the fit of the β-CD and tetradecyltrimetilammonium bromide is too loose to form 2:1 complexes even though the alkyl chain length is long enough. It is of interest to note that there are indications of 2:1 β-CD−surfactant complexes when the alkyl chain length of the surfactant is longer.[36,33A]

Therefore, the studies existing in the literature indicate that the stability constants of the CD−surfactant complexes with α- and β-CD are similar, which means that the percentage of uncomplexed CD in equilibrium with the micellar system must be similar in both cases. However, the α-CD presents a greater tendency toward formation of CD-surfactant complexes with stoichiometry 2:1. The formation of these complexes with stoichiometry 2:1 must be the cause of the % $\alpha\text{-CD}_f$ being less than the % $\beta\text{-CD}_f$ in equilibrium with the micellar system. The quotient % $\beta\text{-CD}_f$/% $\alpha\text{-CD}_f$ decreases as the length of the hydrocarbon chain of the surfactant increases: 10.9, 3.4, 1.38, 1.71, and 1.43 for C_{10}TAB, C_{12}TAB, C_{14}TAB, C_{16}TACl, and C_{18}TACl. This variation would be compatible with the fact that the stability constants of the CD-surfactant complexes are close. With the α-CD the percentage of complexes with stoichiometry 2:1 is important even for short surfactant chains. With the β-CD the complexes with stoichiometries 2:1 begin to form in greater chains.

4. Repercussions on the Stoichiometries of the Complexes. The traditional vision of the mixed CD−surfactant systems indicated that the micellization only occurred once the complexation capacity of the CD has been saturated. Therefore, the concentration of the surfactant in the point of micellization would be cmc_{app} = [CD−surfactant] + [$surfactant_{Monomer}$] = [CD−surfactant] + cmc_{real}, where the cmc_{real} represents the concentration of free surfactant monomers in equilibrium with the micellar system. For long chain surfactants and in the presence of high CD concentrations it follows that $cmc_{app} \cong$ [CD−surfactant]. Therefore, the relationship $cmc_{app}/[CD]_{tot}$ should indicate the stoichiometry of the complex.

The results obtained in this study indicate the existence of an appreciable concentration of uncomplexed CD in equilibrium with the micellar system, especially as the length of the hydrocarbon chain of the surfactant increases. Therefore, the critical micellar concentration in the micellization point of the mixed systems will be defined as cmc_{app} = [CD−surfactant] + cmc_{real}. Therefore, the surfactant concentration complexed with the cyclodextrin (independently of the stoichiometry of the complex) will be given by [complexed surfactant] = $cmc_{app} - cmc_{real}$. The concentration of cyclodextrin complexed with the surfactant will be: [complexed CD] = $[CD]_{tot} - [CD]_f$. In this way the relationship between [complexed surfactant]/[complexed CD] will be given by $(cmc_{app} - cmc_{real})/([CD]_{tot} - [CD]_f)$. For very hydrophobic surfactants and in the presence of a high concentration of CD, it follows that $cmc_{app} \gg cmc_{real}$, in such a way that the relationship [complexed surfactant]/[complexed CD] must be approximately equal to [complexed surfactant]/[complexed CD] $\cong cmc_{app}/([CD]_T - [CD]_f)$. As the hydrophobic character of the surfactant increases the value of the cmc_{real} decreases but the $[CD]_f$ increases in such a way that the relationship $cmc_{app}/[CD]_T$ deviates from the relationship [complexed surfactant]/[complexed CD] making it impossible to use it to obtain the stoichiometry of the CD−surfactant complexes.

Conclusions

The results obtained in this study allow us to confirm the existence of an appreciable concentration of uncomplexed CD in equilibrium with the micellar system. Contrary to expectations, the percentage of uncomplexed CD increases along with the length of the hydrocarbon chain of the surfactant. This result is a consequence of the dynamic behavior which the mixed CD−surfactant systems present, where the concentration of uncomplexed CD is the result of the balance between the complexation processes of the surfactant with the CD and the autoassociation (micellization) processes of the surfactant.

The concentration of uncomplexed CD in equilibrium with the micellar system is independent of the nature of the headgroup of the surfactant. This result is consistent with the traditional hypothesis that the CD-surfactant interaction is established through the hydrocarbon chain. The comparison of the concentration of uncomplexed CD in mixed α-CD−surfactant and β-CD−surfactant systems shows that the percentage of uncomplexed CD is greater with β-CD than α-CD. This behavior has been interpreted as a consequence of the greater capacity of the α-CD to form CD-surfactant complexes with stoichiometries 2:1.

The existence of an important concentration of uncomplexed CD and its variation with the nature of the surfactant allows us to question the stoichiometry of the CD-surfactant complexes obtained from the surfactant concentration at the point of micellization, cmc_{app}.

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(9) The nomenclature C_8TAB, C_{10}TAB, C_{12}TAB, C_{14}TAB,C_{16}TACl, and C_{18}TACl is not the most usual to designate these surfactant molecules, but we think that it is the most suitable to identify the length of the hydrocarbon chain.

(10) As the hydrocarbon chain length increases its hydrophobicity would also increase and consequently the formation constant of the CD-surfactant complex. This increase of the equilibrium constant would imply a reduction in the concentration of free cyclodextrin in equilibrium with the micellar system once the latter has formed.

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