

## Effect of Hydrotropic Compounds on the Self-Organization and Solubilization Properties of Cationic Surfactants

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**Abstract**—The effect hydrotropic additives (salts of aromatic acids and choline chloride) have on the micelle-forming properties (the critical concentrations of micelle formation and the Krafft temperature) of cationic surfactants, and on the solubilization capability of mono- and dicationic surfactants toward such hydrophobic compounds as a Sudan I spectral probe and curcumin natural dye, is considered. The factors that govern solubilization capacity, e.g., the structure of the head group of surfactants, the nature of the solubilize and hydrotropic additives, and the pH of the medium are determined.

**Keywords:** cationic surfactants, hydrotropes, micelle formation, solubilization

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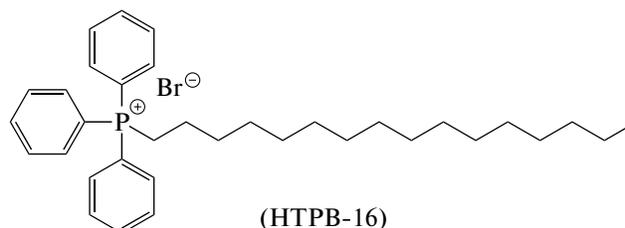
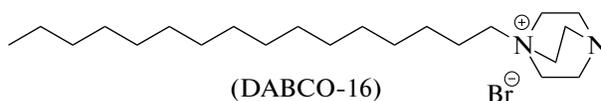
### INTRODUCTION

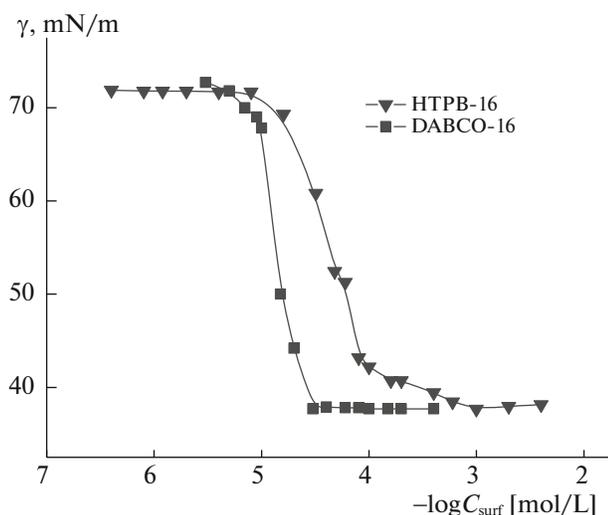
Supramolecular systems based on amphiphilic compounds find wide application in different fields of nano- and biotechnology, including catalysis and the food and cosmetics industries [1–4]. One of the most important properties of solutions of surfactants is their capacity to enhance the solubility of hydrophobic compounds (e.g., drugs, spectral probes, additives, stabilizers) in water. This is due to the ability of amphiphilic molecules to aggregate above a specific concentration referred to as the critical micelle concentration (CMC) and to form nanosized aggregates, particularly micelles. A hydrophobic cavity in the composition of micelles allows us to use them as nanocontainers that improve the solubility of nonpolar compounds in water. An additional effect can be achieved by introducing hydrotropic additives that can modify the aggregation and functional activity of micellar systems, including their solubilization properties [5–10].

There is no strict classification of hydrotropic compounds in the literature [5–7]; they include both non-ionic substances (derivatives of alcohols, phenols, and amines) and organic electrolytes that can increase the solubility of nonpolar molecules in water. Even though the solubilizing action of hydrotropic compounds has been reliably determined empirically, the mechanism behind the effect and the specific character of their

solubilization properties in molecular and micellar systems remain unclear and require additional investigation.

In [11–15], we studied homological series of mono- and dicationic surfactants and showed the considerable effect the structure of head groups has on the solubilization, catalytic, and antimicrobial properties of micellar systems. In this work, we studied the effect hydrotropic additives (salts of aromatic acids and choline chloride) have on the aggregation properties and their solubilizing activity toward hydrophobic dyes of cationic surfactants with such sterically hindered head groups as 4-aza-1-hexadecyl-1-azoniabicyclo[2.2.2]octane bromide (DABCO-16) and hexadecyltriphenylphosphonium bromide (HTPB-16), the formulas of which are presented below:





**Fig. 1.** Dependence of the surface tension of aqueous solutions of cationic surfactants on their concentration when there is 1 mM sodium salicylate at 25°C.

## EXPERIMENTAL

1-Hexadecyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide (DABCO-16) was synthesized according to the procedure in [16]. Commercial samples of hexadecyltriphenylphosphonium bromide, choline chloride, and hydrophobic probes (Sudan I and curcumin) from Acros Organics (99% of the main substance) were used in each experiment. All solutions were prepared with bidistilled water obtained on a Direct-Q 5 UV unit (specific resistance of the water, 18.2 M $\Omega$  cm at 25°C).

The surface tension of the solutions was determined on a K6 tensiometer (KRÜSS) according to the du Noüy ring procedure in a thermostated cell. Specific electric conductivity ( $\chi$ ,  $\mu\text{S}/\text{cm}$ ) of the systems was measured on an InoLab Cond 7110 conductivity meter. The values of the CMC corresponded to the points of the change in slope in the property–concentration graphs of surfactant dependence.

To determine the Krafft temperature, solutions of surfactants with concentrations that greatly exceeded the CMC were used. The solutions were cooled until a precipitate of the surfactant formed, and the electric conductivity of the supernatant was measured by heating the solution.

The solubilizing ability of the micellar systems was determined spectrophotometrically. The spectra were recorded on a Specord 250 Plus spectrophotometer in the range of 250 to 700 nm using quartz cells 0.5 and 1 cm thick. Such hydrophobic probes as Sudan I (1-phenylazo-2-naphthol) and curcumin (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) were used as solubilizates.

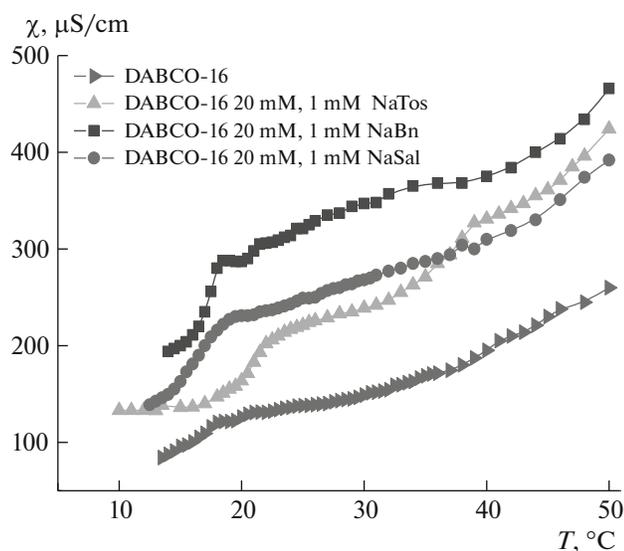
Molar extinction coefficient ( $\epsilon$ ) of the solubilizates in the investigated solutions was found from the value of absorbance  $D$  of a sample determined at the fixed concentration  $C$  of the hydrophobic probes in their absorption maxima according to the equation  $\epsilon = D/LC$ . To estimate solubilization capability, a series of solutions containing a specific concentration of a surfactant in the range of 0 to 10 mM was prepared. An excess of a crystalline dye was added to each, vigorously stirred for two hours, and then kept for two days to obtain saturated solutions. The undissolved residue was filtered off, and the absorption spectra of the filtrate were recorded. The concentration of the dye in the sample was estimated from the obtained values of the absorbance of the solutions in the absorption maximum, allowing for the extinction coefficient of the dye.

## RESULTS AND DISCUSSION

The use of hydrotropic electrolytes is an effective technique that not only allows us to improve the solubility of useful substances but also to vary the properties of cationic micelles. The so-called salt effect depends on the nature of the counterions. It is known that have the strongest effect is produced by organic counterions that are capable of effectively interacting with cationic head groups, thereby reducing the surface potential of micelles and changing such quantitative parameters as the CMC, hydrodynamic radius, and aggregation numbers [1, 17]. In contrast to mineral salts (e.g., metal halides), organic electrolytes can change the size, shape, and structural and phase characteristics of systems at low concentrations, since they have much greater affinity for micellar surfaces than small hydrophilic ions with high charge density. Because of this, the displacement of halide ions from the Stern layer and an increase in the degree of bonding between counterions are observed upon an increase in the concentration of organic electrolytes.

Figure 1 presents the comparative tensiometric data for micellar systems based on cationic surfactants with different structures of the head groups and the same alkyl radicals, DABCO-16 and HTPB-16. Without the additives, the values of the CMCs of these surfactants are 1.0 and 0.1 mM, respectively, while they fall to 0.3 and 0.07 mM, respectively, when there is 1.0 mM sodium salicylate. The weaker effect of the electrolytes in the case of the micelles of HTPB-16 is probably due to the bulk phenyl groups generating steric hindrances to the aromatic counterions' access to the positively charged phosphorous atoms.

The Krafft temperature is an important characteristic of micellar systems that determines the temperature region of aggregation. Since the alkylated salts of DABCO are a relatively new type of surface active substances, investigating their properties and the factors that govern their behavior in a solution is of undeniable theoretical and practical interest. Figure 2 presents the results from measuring the electric conductivity



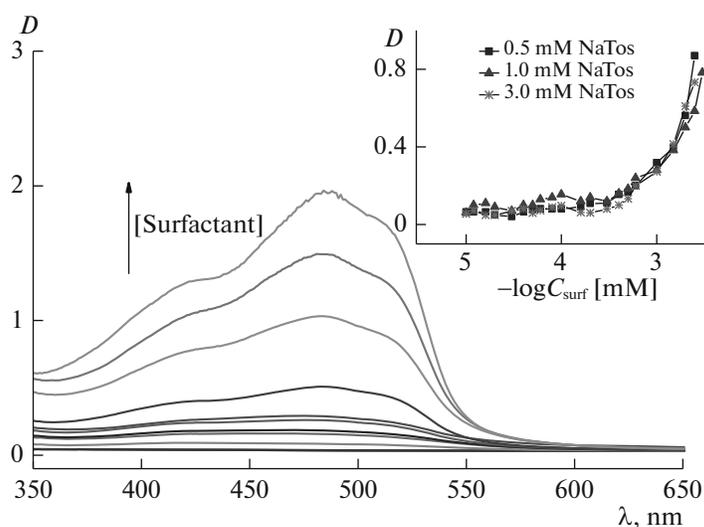
**Fig. 2.** Dependence of the specific electric conductivity of a solution of DABCO-16 (20 mM) on temperature with and without organic electrolytes.

ity of a solution of DABCO-16 in individual form and when there are sodium salts of aromatic acids with the below variation in the nature of the counterion: benzoate NaBn, tosylate NaTos, and salicylate NaSal. Varying the nature of the organic salts allows us to affect the composition of micelles (especially the qualitative and quantitative distribution of counterions in the Stern layer) and thus their properties. With electrolytes, there is a slight increase in the Kraft temperature, from 12 (with no additives) to 13, 14, and 18°C with 1 mM sodium salicylate, benzoate, or tosylate,

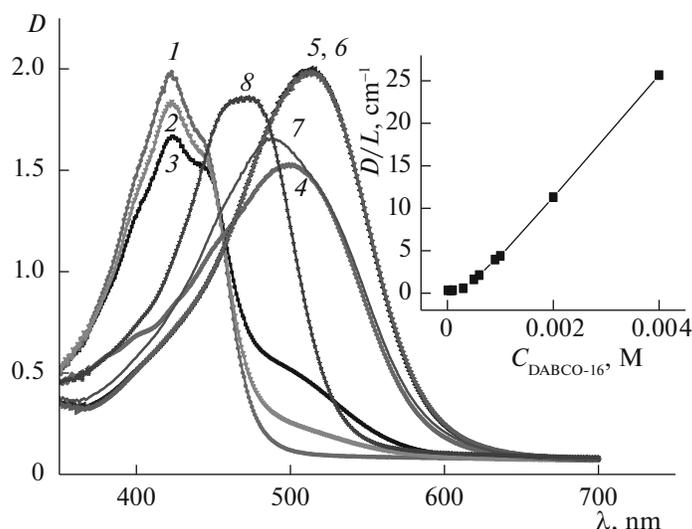
respectively. In light of the order of the change in the affinity of counterions for the micellar surface of cationic micelles ( $Bn < Tos < Sal$  [8, 9]), we may assume the change in the surface potential of aggregates is not the determining factor.

The problem of creating water-soluble preparations is extremely relevant in the field of biomedicine, since most medicines are barely soluble in water. The development of nanocontainers based on amphiphilic compounds, the properties of which are enhanced by the introduction of hydrotropic additives, thus has a pronounced applied component. Using micellar solutions of DABCO-16, we studied their ability for solubilization toward Sudan I dye (when there is sodium tosylate and choline chloride) and curcumin, a biologically active food colorant (when there is choline chloride) (Figs. 3 and 4). The solubilizing action of HTPB-16/choline chloride micellar systems toward Sudan I was also determined (Table 1).

Figure 3 shows the spectral data for Sudan I dye in the micelles of DABCO-16 when there is sodium tosylate. This spectral probe is characterized by intense absorption in the UV and visible spectral regions, which allows the quantitative determination of its concentration in solutions. In addition, the spectral characteristics of Sudan I dye in micellar solutions are quite well studied, allowing us to evaluate different systems comparatively. With the formation of micellar aggregates having nonpolar cores, there is bonding of the dye inside the aggregate, increasing its concentration in solution. It is registered spectrophotometrically using the absorption band in the visible spectral region (Fig. 3). This allows us to determine the value of the CMC from the dependence of absorbance  $D$  on concentration  $C_{surf}$  of the surfactant using the intercept on



**Fig. 3.** Absorption spectra of Sudan I in a DABCO-16–choline system (10 mM) upon an increase in the concentration of the surfactant in the range of 0–50 mM (25°C). The insert shows the dependence of the optical density of the absorption band of Sudan I at  $\lambda = 462$  nm on the concentration of the surfactant in a DABCO-16–sodium tosylate system.



**Fig. 4.** Absorption spectra of curcumin in aqueous solutions of DABCO (2 mM) at pH (1) 2.0, (2) 5.5, (3) 6.5, (4) 7.3, (5) 8.5, (6) 9.5, (7) 11.0, and (8) 12.8. The insert shows the dependence of the optical density of the absorption of saturated solutions of curcumin at  $\lambda = 422$  nm on the concentration of DABCO-16 when there is 10 mM choline chloride.

the abscissa. Value  $b$  of the slope of the  $D-C_{\text{surf}}$  dependences is proportionate to solubilizing capacity  $S$  of the micelles:  $S = b/\epsilon$ , where  $\epsilon$  is the extinction coefficient. In the micellar solutions of DABCO-16 in neutral media (pH 6.0), the value of  $\epsilon$  for Sudan 1 dye in the absorption maximum (462 nm) is  $8700 \text{ mol}^{-1} \text{ L cm}^{-1}$ . Our calculations using the data in Fig. 3 (insert) show that when there is sodium tosylate, the value of the CMC (1.0 mM for an individual solution of DABCO-16) changes within the series 0.67, 0.54, and 0.16 mM, while slope  $b$  changes from 190.0 (individual micelles of DABCO-16) to 363.2, 229.8, and 307.6 upon the introduction of 0.5, 1, and 3 mM sodium tosylate, respectively. This corresponds to the values of the solubilizing capacity: 0.0209, 0.0132, and 0.0177. The additions of organic hydrotropic compounds thus have a modifying action on the aggregates of DABCO-

16, increasing their aggregation activity and solubilizing capability.

The addition of choline chloride also changes the solubilization properties of DABCO-16, increasing them toward both Sudan I and curcumin (the insert in Fig. 4; Table 1). At the same time, the solubilization action toward Sudan I spectral probe is higher than with curcumin, due probably to the different natures of the dyes and the different localization in the aggregates. Sudan I belongs to the class of azo dyes of artificial origin, while curcumin is a natural dye of the class of polyphenols.

The considerable number of hydrophilic groups in a curcumin molecule can result in its localization in the peripheral region of the micellar core, while the more hydrophobic Sudan I molecules are probably localized in less polar zones. It should also be noted that choline chloride has a stronger effect on the solubility of Sudan I than sodium tosylate, due presumably to different mechanisms behind the actions of these hydrotrops. In contrast to the organic anion tosylate, which reduces the surface potential of micelles, a 2-hydroxyethyltrimethylammonium ion is positively charged and has no appreciable effect on the surface charge. At the same time, adding choline chloride lowers the CMC for both of the investigated cationic surfactants (Table 1). It should be noted that one of the mechanisms of the effect electrolytes have on the properties of aqueous solutions is probably due to their action on the properties of water, especially the effect they have on the hydrogen bond network [18].

The degree of ion action is empirically described by Hofmeister series (lyotropic series), which distinguishes between so-called kosmotropic and chaotropic ions [19] with structuring or destructuring

**Table 1.** Aggregation characteristics and solubilization capacity of micellar solutions of DABCO-16 and HTPB-16 ( $C_{\text{surf}} = 2$  mM) with and without additions of choline chloride (pH 6.0, 25°C)

surfactant	$C_{\text{chol}}$ , mM	CMC, mM	Solubilization capacity	
			Sudan I	curcumin
DABCO-16	0	1.1	0.105	0.066
	1	0.80	0.139	0.082
	10	0.62	0.155	0.117
HTPB-16	0	0.10	0.085	—
	1	0.09	0.106	—
	10	0.05	0.117	—

For curcumin at pH 6.0,  $\lambda_{\text{max}} = 422$  nm, and  $\epsilon = 60\,500 \text{ mol}^{-1} \times \text{L cm}^{-1}$ .

**Table 2.** Solubilization capacity of micellar solutions of DABCO-16 toward curcumin, determined at various values of pH

pH	$\lambda_{\max}$ , nm	$\epsilon$ , $\text{mol}^{-1} \text{L cm}^{-1}$	$S$
2.0	422	60500	0.060
4.0	422	60500	0.061
6.0	422	60500	0.066
6.5	422	50400	0.064
7.3	501	47500	0.065
8.5	515	60500	0.072
9.5	515	60500	0.087
11.0	489	49200	0.088
12.8	470	55200	0.086

action on water, respectively. Choline chloride dissociates in water to ions with low charge density, due to which its influence on the process of micelle formation and the solubility of organic compounds can be felt as a result of compensation for electrostatic interactions between the head groups of surfactants, and through the salting-in and salting-out of hydrophobic substrates caused by the change in the structural characteristics of water [20].

Despite the higher micelle-forming activity of HTPB-16, the CMC of which is an order of magnitude lower than with DABCO-16, its solubilization properties towards Sudan I spectral probe are somewhat poorer: the maximum values of solubilization capacity are 0.155 and 0.117 for DABCO-16 and HTPB-16, respectively (Table 1). At the same time, the effect of choline has on the solubility of the dye is roughly the same for both cationic surfactants.

The second part of this work is devoted to estimating the additional factor that governs the solubility of curcumin: the pH of the solution. This dye contains conjugated double bonds and hydroxyl groups in the structure of the molecule, which determines their participation in the acid–base and tautomeric equilibria. Depending on the properties of the medium (especially its pH), curcumin can therefore exist in different forms, each of which has its own spectral characteristics and capacity for solubilization. In an acidic medium, the maximum of the absorption spectrum of curcumin in water lies in the region of 420–430 nm, while a bathochromic shift to the red region is observed in an alkaline medium. This is associated with the dissociation of the enol and phenol –OH groups and curcumin's transition from its neutral form to its anionic form [21]. Cationic surfactants affect the position of curcumin equilibrium. At a pH 9, the transition of DABCO-16, a dicationic surfactant, from water to solution is accompanied by a shift of the max-

imum of the absorption band, from 467 to 515 nm, in the spectra of curcumin. As an example, Fig. 4 presents the spectra of curcumin in micellar solutions of DABCO-16, recorded under conditions of a change in the pH of the medium. The spectral characteristics of this dye and the values of the solubilization capacity of solutions of DABCO-16 at pH 2–12 are presented in Table 2.

## CONCLUSIONS

The highest values of  $S$  are observed when  $\text{pH} > 8$ . Under these conditions, the anionic form of curcumin bonds more effectively with the positively charged groups of DABCO-16, due primarily to electrostatic interaction, which results in its intense solubilization. The phenolic hydroxyl groups in a curcumin molecule thus offers the possibility of additional control over its solubility by varying the pH of the medium.

Cationic surfactants exhibit high solubilization activity toward hydrophobic dyes, depending both on the structure of the head group of surfactants and the nature of the solubilizate. Additions of hydrotropic compounds and variations in the pH of the solution are additional factors that can enhance the solubilizing abilities of surfactants.

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