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Adsorption of a Cationic Surfactant, Miramistin, from Aqueous Solutions on the Surface of Highly Dispersed Silica

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Abstract—The adsorption of a universal antiseptic agent, the cationic surfactant miramistin, on the surface of highly dispersed silica has been studied. It has been shown that, when miramistin is adsorbed from acidic premicellar solutions, the main contribution to miramistin binding with the surface is made by hydrogen bonding between amide groups of surfactant molecules and silanol groups of silica, which is, at higher pH values, accompanied by ionic interaction between positively charged quaternary nitrogen atoms of miramistin and negatively charged dissociated silanol groups. In the case of adsorption from a micellar solution, an increase in the surface concentration of miramistin is almost independent of solution pH, because the second layer is predominantly formed due to hydrophobic interactions.

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INTRODUCTION

Highly dispersed silica (HDS) is being increasingly used as an enterosorbent; as a composite component and carrier of drugs of both synthetic and herbal origins; and for excretion of toxic, ballast, and other pathogenic substances and microorganisms [1, 2]. The simultaneous presence of an adsorbent and a drug in a human organism necessitates investigation of the general regularities of sorption interactions in such systems and a pharmacokinetic account of them.

Today, surfactant-based drugs are becoming increasingly popular. A cationic surfactant, benzyldimethyl[3-(myristoylamino)propyl]ammonium chloride, is one of the most efficient therapeutic agents, which is known under the trade name Miramistin and used as a broad-spectrum antiseptic agent with pronounced antimicrobial, antifungal, and antiviral effects [3]. Only the pharmaceutical properties of miramistin and its application in medicine have been considered in the literature, while information concerning its physicochemical properties is absent. Note that the knowledge of the regularities of cationic surfactant adsorption on highly dispersed silicas is of great importance for the development of formulations and the technology of medical preparations, while theoretical interest in this problem is associated with the fundamental problems relevant to the study of the adsorption mechanisms, as well as the influence of different factors on the formation and the structure of adsorption layers [4, 5].

The goal of this work was to study the regularities of miramistin adsorption from aqueous solutions on HDS at different concentrations and pH values of the solutions.

EXPERIMENTAL

Highly dispersed silica A-300 (specific surface area of 300 m^2/g, *GOST* (State Standard) 14922-77, produced by the pilot plant of the Institute of Surface Chemistry, National Academy of Sciences of Ukraine, Kalush) was used as a sorbent. Miramistin is an odorless white powder (t_m= 177°C), which is readily soluble in water, chloroform, and ethanol. Stock solutions of miramistin (Infamed) were prepared by dissolving precisely weighted portions of the substance in distilled water and diluted to required concentrations before use. The pH values of the solutions were preset in a range of 2–8 using phosphate buffers (pH 4.8–7.8) [6], to which hydrochloric acid or sodium hydroxide solutions were added to obtain more acidic or alkaline solutions.

Miramistin adsorption from aqueous solutions on the surface of HDS was studied under static conditions; for this purpose, a weighted portion of the adsorbent (m, g) was added to a specified volume (V, mL) of a corresponding miramistin solution with concentration C_0 (M) at ratio V/m = 200 mL/g and the mixture was stirred until the equilibrium was established (≈2 h at 20°C). Then, the adsorbent was separated by centrifugation for 15 min at 8000 rpm and dried in air. After adsorption, miramistin concentration C in equilibrium solutions was determined using calibration curves, which were preliminarily obtained for each miramistin concentration at a given pH value of the equilibrium solution. The adsorption value (a, mol/g) was calculated by the following equation:

$$a = (C_0 - C)V/1000m.$$

The IR spectra of initial miramistin and miramistin adsorbed on the HDS surface were measured with a

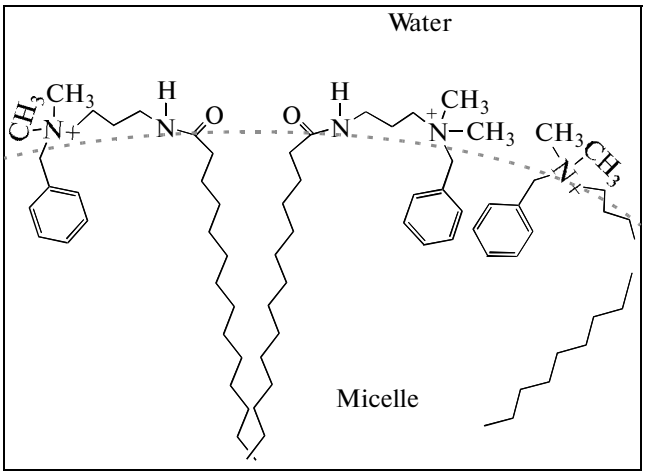

Fig. 1. Arrangement of miramistin molecules in a micelle.

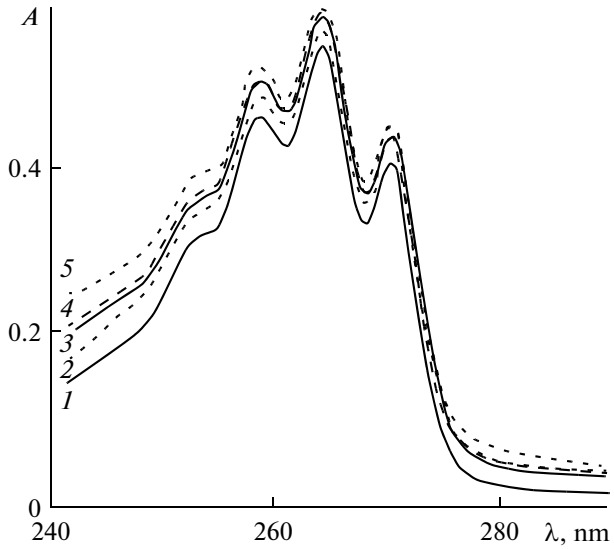

Fig. 2. Absorption spectra of miramistin at different solution pH values: (*1*) 3.0, (*2*) 6.0, (*3*) 7.0, and (*4*) 8.0. $C = 6.72 \times 10^{-4}$ M and $l = 2$ cm.

Thermo Nicolet Nexus FT-IR instrument (Germany) using HDS as a reference sample. The UV absorption spectra of the solutions were recorded using a Specord M-40 spectrophotometer (Carl Zeiss Jena, Germany). The influence of the background on analytical signal A obtained when measuring the absorption spectra of the examined solutions was eliminated by the method of heterochromatic extrapolation at two wavelengths [7]. The acidity of the solutions before and after the sorption was determined using a glass electrode of a Hanna instruments HI 221 universal ion meter.

RESULTS AND DISCUSSION

According to its structure, miramistin (Fig. 1) belongs to gemini-surfactants, i.e., a relatively new class of amphiphilic molecules that consist of two hydrophobic fragments and two hydrophilic polar groups, which are bonded to one another via a spacer. At present, such compounds are attracting increasing attention as efficient modifiers of interfacial properties. In particular, the presence of methylene chain as a spacer increases significantly the hydrophobicity of gemini-surfactants as compared to corresponding initial monomeric surfactants and, consequently, significantly decreases their critical micellization concentration (CMC) [8].

Unlike symmetric gemini-surfactants, such as the bis-quaternary ammonium salts ethonium and decamethoxine, the miramistin molecule is asymmetric. It has been established [9] that, in micelles of benzyl(3-acylaminopropyl)dimethylammonium, which has a similar structure, hydrophilic amide and quaternary ammonium groups are located on the surface, while hydrophobic tails (methylene chains and benzyl groups) are directed inside the micelles. The arrangement of miramistin molecules in a micelle is schematically represented in Fig. 1. It should be noted that the orientation of amide groups enables them to serve as active sites of hydrogen and coordination bonding.

Since there are no data concerning the physicochemical properties of miramistin, first of all, we studied its spectral characteristics. Figure 2 shows the electron spectra of miramistin at different solution pH values. All of the spectra have a band at 264 nm with a pronounced fine structure typical of benzene compounds; its position does not depend on solution pH, and the intensity slightly decreases in the acidic region. The calculated molar extinction coefficients of miramistin solutions (ε_{264}) decrease with an increase in their concentration (Fig. 3) and achieve a constant value at $C > 0.002$ M, with an inflection being observed in the curve at a concentration of 0.001 M that corresponds to the CMC of this surfactant.

Figure 4 shows the isotherm of miramistin adsorption from aqueous solutions on HDS. As the solution concentration increases to 1×10^{-3} M, its adsorption on the silica surface grows and reaches a plateau. A sharp inflection is observed in the isotherm at a concentration of 1×10^{-3} M, which corresponds to CMC.

The isotherm of miramistin sorption was also described using logarithmic coordinates ($\log a$–$\log C$), which, in particular, enabled us to study the isotherm in the region of low surface concentrations of the cationic surfactant (CS). The plotted curve (Fig. 5, curve *1*) consists of four linear portions. As a whole, the pattern of the resultant curve corresponds to the four-stage model (or the model of inverse orientation) described in the literature [5]. According to this model, which considers only electrostatic and hydrophobic interactions of CSs with adsorbent surfaces, adsorption is interpreted as follows. At stage I, SC monomers are adsorbed on silica due to electrostatic

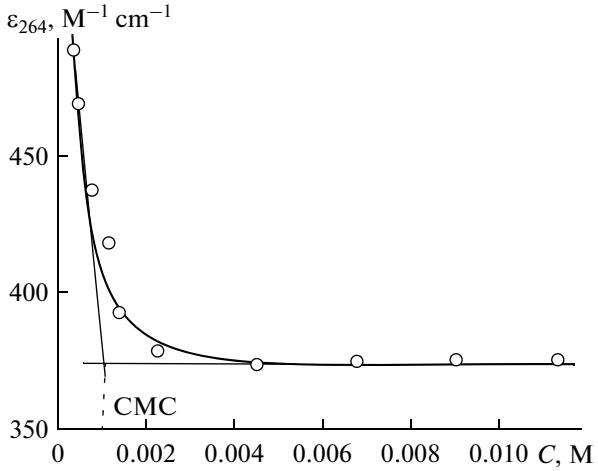

Fig. 3. Dependence of ε_{264} on miramistin concentration in aqueous solution.

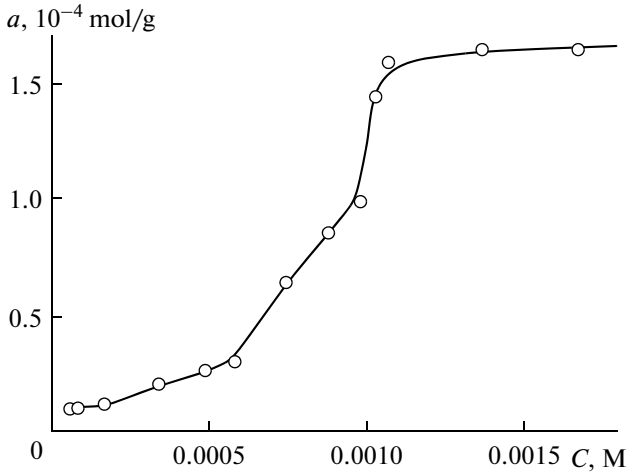

Fig. 4. Isotherm of miramistin adsorption from aqueous solutions on HDS.

interactions, while the hydrophobic hydrocarbon tails may interact with any hydrophobic region of the surface and acquire either horizontal or vertical orientation. At stage II, strong lateral interaction of adsorbed monomers gives rise to the formation of primary aggregates, which form hydrophobic surface regions. At stage III, the adsorption increases due to the growth of the structures that has been formed at stage II without an increase in the number of the aggregates on the surface. The presence of hydrophilic polar heads oriented toward the solution changes the surface hydrophilicity once more. The transition between stages II and III is associated with the neutralization of the surface charge. The formation of the adsorbed bilayer is completed at stage IV. A further increase in CS concentration in the solution does not enhance its concentration on the adsorbent surface.

However, the proposed model of adsorption does not take into account the value of solution pH and, consequently, the degree of dissociation of HDS silanol groups. We revealed experimentally that, when miramistin concentration in an initial solution is increased up to the CMC value, the pH values of equilibrium solutions decrease in the course of adsorption (Fig. 5, curve *3*) as compared with the initial ones (Fig. 5, curve *2*) and a plateau with pH 4 is observed at $C >$ CMC . Under these conditions (pH 4–6), the concentration of dissociated silanol groups $\equiv SiO^-$ is $\approx 3.5 \times 10^{-5}$ mol/g [10] and miramistin cations are adsorbed due to electrostatic interactions with the negative sites on a silica surface.

The reduction in miramistin solution pH as a result of adsorption is observed only for portions I and II of the isotherm, when the monolayer is being formed and silanol groups of the surface interact directly with CS; however, pH remains unchanged in regions III and IV, when the second layer is adsorbed (tail-to-tail). This concentration dependence of the solution pH shows that miramistin adsorption is accompanied by an exchange reaction between the protons of silanol groups and surfactant cations.

Since an amide group is one of the two head groups of a miramistin molecule, the possibility of hydrogen bonding with the surface groups of silica should be taken into account. The IR spectroscopy data on the samples of initial miramistin and miramistin adsorbed on the HDS surface have confirmed the hydrogen bonding between functional amide groups NHCO and silanol groups ≡Si–OH of the surface during the adsorption in the studied systems, which is evident from the shift of the characteristic bands Amide I (C=O stretching vibrations) and Amide II (NH bending vibrations) (Fig. 6a) [11], as well as a reduction of

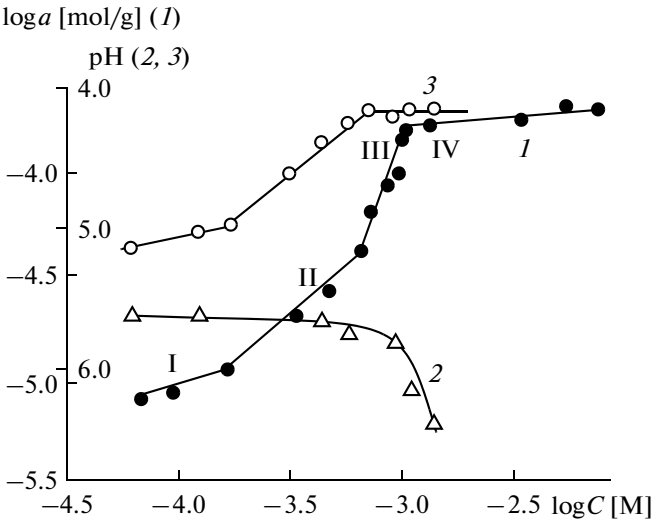

Fig. 5. Dependence of (*1*) adsorption and solution pH (*2*) before and (*3*) after miramistin adsorption on HDS on log*C*.

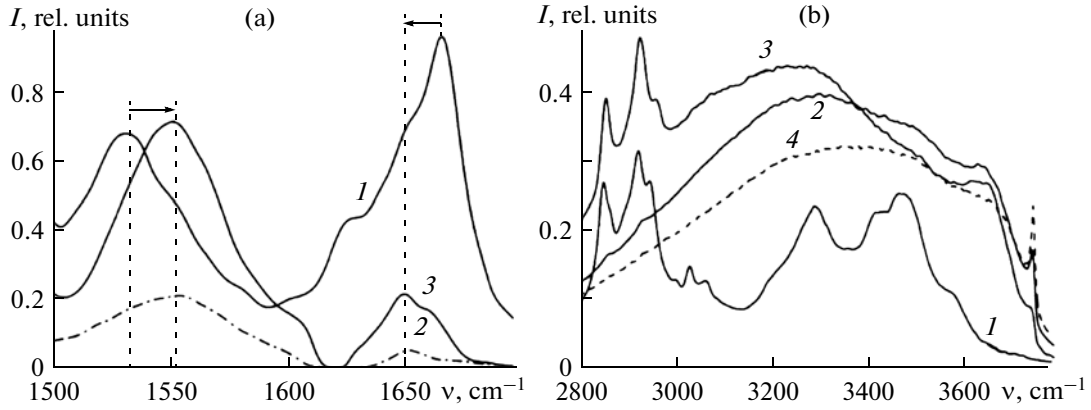

Fig. 6. The IR spectra of (*1*) initial miramistin and (*2–4*) miramistin adsorbed on HDS surface; a (mol/g) = (*2*) 1.0×10^{-5}, (*3*) 1.75×10^{-4}, and (*4*) 0.0. See text for explanations.

the intensity of the absorption band of free silanol groups (Fig. 6b).

Additional information concerning the mechanism of miramistin binding with the HDS surface was obtained by studying the pH dependence of miramistin adsorption (Fig. 7), since the solution acidity strongly influences the degree of silanol group dissociation. These experiments were performed with dilute premicellar miramistin solutions ($C_0 = 6.72 \times 10^{-5}$ M), from which it is adsorbed as a monomer mainly due to electrostatic interactions (portion I of the isotherm), and micellar solutions ($C_0 = 2.24 \times 10^{-3}$ M), in which hydrophobic interactions dominate (portion IV).

The value of CS adsorption from the premicellar solution (Fig. 7, curve *1*) increases with pH, and the pattern of the curve correlates with the dissociation of silica silanol groups ($pK_{SiOH} = 7$ [10]). This finding confirms the conclusion that the main contribution to the CS adsorption on HDS from premicellar solutions

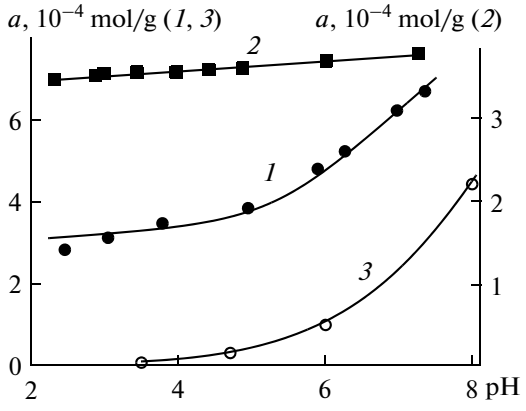

Fig. 7. The pH dependences of miramistin adsorption from (*1*) premicellar and (*2*) micellar solutions on HDS and (*3*) concentration of dissociated silanol groups [SiO^-] [10]. C = (*1*) 6.7×10^{-5} and (*2*) 2.24×10^{-3} M, m = 0.1 g, and V = 20 mL.

(portion I of the adsorption isotherm) is made by electrostatic interactions between the positively charged nitrogen atoms in miramistin molecules and negatively charged silanol groups.

However, unlike the bis-quaternary ammonium gemini-surfactants, ethonium and decamethoxine [12, 13], and cetyltrimethylammonium bromide [13], which begin to be adsorbed only at pH > 3, miramistin is efficiently adsorbed even at pH 2, because its molecules contain amide groups capable of hydrogen bonding with ≡SiOH groups of HDS.

Miramistin adsorption from micellar solutions is much more efficient, and this process is almost independent of solution pH (Fig. 7, curve *2*), because, during the formation of the second layer, the surface concentration increases mainly due to lateral interactions between the hydrophobic tails of miramistin molecules, with silanol groups of silica not being involved.

The study of the influence of the length of the hydrophobic tails of CSs on their orientation with respect to the adsorbent surface at low adsorption values (portion I of the isotherm) [14] has shown that tails consisting of eight methylene groups $(-CH_2-)_8$ do not interact with the silica surface and are most likely oriented normal to the surface. Longer hydrophobic groups of CSs $(-CH_2-)_{12}$ are nearly parallel to the surface. The same position can be supposed for methylene groups $(-CH_2-)_{13}$ of miramistin molecules at the early stages of adsorption. As for hydrophilic groups, in the case of absorption of the gemini-surfactant miramistin, positively charged quaternary nitrogen atoms are most likely located on the surface or very close to it and the shorter the spacer, the smaller the distance. In this case, the acidity of the neighboring silanol groups increases to reduce the solution pH at the early stages of miramistin adsorption (portions I and II of the isotherm) (Fig. 5, curve *3*).

The morphology of adsorbed layers of bis-quaternary ammonium gemini-surfactants at a silica–water interface was studied by Atkin et al. [15]. Observations

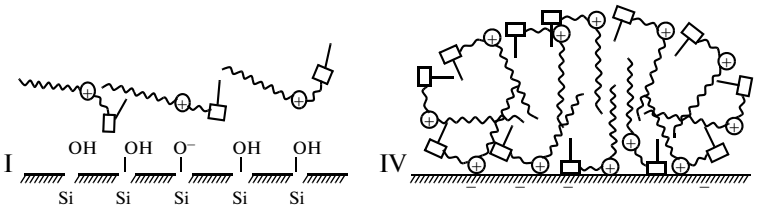

Fig. 8. Schematic representation of miramistin molecules adsorbed from dilute (portion I of the isotherm) and micellar (portion IV) solutions on HDS surface.

performed with a atomic force microscope showed that surfactants with the same lengths of the spacers and hydrophobic tails as those in miramistin formed planar ellipsoidal micelles at a solution concentration of ~2 CMC. Based on the listed experimental and literature data, miramistin adsorption in regions I and IV of the isotherm has been schematically represented in Fig. 8.

Thus, miramistin adsorption on HDS can be described according to the four-step model (inverse orientation model) of cationic surfactant adsorption on the surface of charged solids, which takes into account only electrostatic and hydrophobic interactions between a CS and an adsorbent surface.

At the same time, it should be emphasized that miramistin molecules contain amide groups capable of hydrogen bonding with silanol groups of silica, which results in rather efficient adsorption even at pH 2 in contrast to conventional quaternary ammonium cationic surfactant which begin to be adsorbed only at pH > 3.

Comparison between the patterns of the pH dependences of miramistin adsorption from premicellar and micellar solutions has demonstrated that the adsorption from premicellar solutions increases with pH and correlates with the dissociation of silanol groups of HDS, while, in case of adsorption from micellar solutions, this correlation is much weaker due to the domination of CS adsorption by the hydrophobic mechanism.

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