

Adsorption of Lipoic Acid on the Surface of Silver: The Kinetics of the Formation and Structure of Self-Assembled Monolayers

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Abstract—The kinetics of lipoic acid adsorption on the surface of silver is studied by the methods of quartz crystal microbalance and wetting. The multilayer nature of adsorption is established. The optimal conditions for the formation of a mono- and bilayer of lipoic acid on a solid surface are determined. The results obtained make it possible to predict the use of silver nanoparticles as carriers of lipophobic drugs in biomedical applications.

Keywords: lipoic acid, adsorption, quartz crystal microbalance, wetting, surface energy

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Monolayers of thiols and disulfides with various terminal functional group, self-organizing on the surfaces of metals, have been studied for more than 40 years [1–3]. Interest in their study is related to the possibility of obtaining systems with the desired properties using such monolayers, on which charge transport, as well as biological, chemical, and photochemical activity, depend. Complexation of terminal groups of alkanethiols with ions of transient metals allows obtaining ion-selective electrodes and fixed catalysts—metal complex surfaces [4, 5]. However, adsorption of thiols and disulfides on the surface of nanoparticles of precious metals, specifically silver, can be used for the transport delivery of water insoluble sulfur-containing drugs into a living organism during the treatment and diagnosis of various illnesses [6–8]. The delivery must be realized in a bioavailable form, which is determined by solubility of a drug in water and its ability to penetrate cell membranes. Since most drugs are poorly soluble in water, the transport problem can be solved using nanosized carriers including solid ones. In turn, the efficiency of immobilization of a drug on a solid carrier is mostly determined by its adsorption of the surface of the carrier [8].

EXPERIMENTAL

The kinetics of adsorption of lipoic acid (LA) on the surface of silver was studied. Lipoic acid (1,2-ithioland-3-pentanoic acid) is water insoluble cyclic disulfide, which possesses antioxidation properties (Fig. 1). LA is also used as an antidepressant and is included into the composition of many vitamin com-

plexes. Bioavailability of LA when administered orally constitutes ~30% [9].

In this study, we used lipoic acid manufactured by Sigma-Aldrich (purity $\geq 98.0\%$ (HPLC), molecular mass $M = 206.33$ g/mol). Adsorption of LA from its solutions in methanol was determined at a concentration of $c = 10^{-3}$ M depending on the contact time of the surface of silver with the solution. According to the reference data, this concentration is optimal for studying the kinetics of adsorption of ethyl mercaptans from solutions on a solid surface, which allows revealing different stages of the formation of an adsorption layer on the substrate [10].

Adsorption of LA on the surface of silver was determined using our complex methodology developed earlier, which includes measurement of adsorption on the surface of metal using the highly sensitive quartz crystal microbalance technique contact angles of various liquids for controlling the formation of the adsorption layer on a solid surface (estimation of degree the surface was filled, as well as the determination of the predominant orientation of molecules in the adsorption layer and surface energy of the modified layers) on the same samples [11, 12].

Quartz crystal microbalance (QCM) is a direct gravimetric method, which is physically based on the

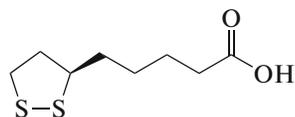


Fig. 1. Structural formula of lipoic acid.

fact that the oscillation frequency f of a quartz plate of the resonator (sensor of piezoquartz microbalance) depends on the amount of substance m applied to its surface. At a uniform distribution of the substance by the resonator surface, the dependence of the oscillation frequency of the microscale sensor on the mass of the applied substance is determined by the equation of Sauerbrey, a scientist whose classical work underlies the study of adsorption layers using the QCM method [13]:

$$\Delta f = -C_f \Delta m, \quad (1)$$

where Δf is the change of frequency (Hz), Δm is the change of mass per unit area (g/cm^2) of the sensitive part of the resonator (the surface of the electrode), and C_f is the coefficient of mass sensitivity, which is found computationally and is determined by the properties of the quartz and self oscillation frequency of the resonator f_0 . As a rule, piezoelectric resonators are made in the form of a thin disk ($d = 5\text{--}16$ mm) from quartz crystal, on each side of which electrodes from various metals (gold, silver, aluminum, chromium, platinum) are formed by thermal spraying. The mass-sensitive area of the quartz plate is limited by the area of the electrode. High sensitivity (up to 10^{-12} g) of the QCM allows measuring adsorption in the domain of small concentrations of the solutions. The correctness of the PM method when measuring the adsorption of a surfactant on solid surface is confirmed by other adsorption determination methods [11, 14].

In this work we used quartz resonators of AT cut with silver electrodes 200 nm thick and with a self oscillation frequency of $f_0 = 5$ MHz. For such a resonator the coefficient of mass sensitivity $C_f = 2.27 \times 10^6 f_0^2 = 56.75 \times 10^6$, $\text{Hz cm}^2/\text{g}$ [11, 12]. The electrode surface area is ~ 0.5 cm^2 .

Adsorption was measured as follows. Firstly we measured the self-frequency of oscillations f_0 of the resonators until a constant value f_0 . Then the resonators were kept for various periods of time (from 1 min to 24 h) in solutions of lipoic acid in methanol (10^{-3} M), after which the samples were washed several times in methanol and dried in air for 2 h. After drying the oscillation frequency f of the resonators with the adsorption layer of lipoic acid were measured. The constant value of f was established after 2 h. Then adsorption value Γ (g/cm^2) was calculated by the equation

$$\Gamma = -1.76 \Delta f \times 10^{-8}, \quad (2)$$

using the quantity $\Delta f = f - f_0$ (during the adsorption of a substance on the surface of the microscale sensor, its oscillation frequency decreases). The oscillation frequency of the resonators was measured using the electron-counter frequency meter ChZ 54 in a thermostatic chamber at 20°C with an accuracy of ± 1 Hz. The adsorption determination accuracy constitutes

$\pm 10^{-8}$ g/cm^2 or (accounting for the molecular mass of LA) ± 0.5 mol/m^2 .

A sufficiently large surface area of the resonator electrodes (~ 0.5 cm^2) allows measuring contact angles on the same samples, using which it is possible to obtain information about the state of the solid surface (degree of filling with adsorption layer and predominant orientation of molecules in it, specific free surface energy of the modifying layers) [15, 16].

In this study we measured advancing contact angles θ_a when applying a water droplet on the surface using a microsyringe and the receding contact angles θ_r when bringing an air bubble to the surface in water. The volume of the droplet (bubble) was 2 μL . The hysteresis value of the contact angles $\Delta\theta = (\theta_a - \theta_r)$ at a different degree of filling of the surface of silver with the adsorption layer characterizes the degree of homogeneity of the substrate [17]. The contact angles were measured in closed cuvettes at room temperature for 2–3 droplets (bubbles).

The degree of filling of the surface of silver with the adsorption layer of LA was calculated based on the theory of wetting of heterogeneous surfaces by the Rebinde–Cassie–Baxter equation, according to which the value of the contact angle θ on the heterogeneous surface is determined by the relation [16, 17]

$$\cos\theta = X \cos\theta_1 + (1 - X) \cos\theta_2, \quad (3)$$

where θ_1 and θ_2 are the contact angles of water on homogeneous surfaces of types 1 and 2; X and $(1 - X)$ is the fraction of area occupied by regions 1 and 2 respectively. In the calculation of $X \theta_1 = 10^\circ$ was taken as the contact angle of water on the monolayer of thiol with the terminal carboxylic groups [18] and $\theta_2 = 70^\circ$ was taken as the contact angle of water on the initial surface of the silver electrodes of the quartz resonators.

The specific free surface energy σ_{sv} of the surface of silver modified by the adsorption layers of LA accounting for the contribution of dispersive (σ_{sv}^d) and nondispersive (σ_{sv}^p) components $\sigma_{sv} = \sigma_{sv}^d + \sigma_{sv}^p$ [19] was calculated based on the molecular theory of wetting in the Owens–Wendt–Kaelble approximation [20] using the contact angles θ_1 and θ_2 of the two test liquids (water and methylene iodide, CH_2I_2) with the known values of the surface tension $\sigma_{lv}(1)$ and $\sigma_{lv}(2)$, as well as its dispersive σ_{lv}^d and polar σ_{lv}^p components [21] (table 1). The calculation was carried out by solving the set of Eqs. (4) [19]:

$$\begin{aligned} \sigma_{lv}(1 + \cos\theta_1) &= 2(\sigma_{lv(1)}^d \sigma_{sv}^d)^{1/2} + 2(\sigma_{lv(1)}^p \sigma_{sv}^p)^{1/2}; \\ \sigma_{lv}(1 + \cos\theta_2) &= 2(\sigma_{lv(2)}^d \sigma_{sv}^d)^{1/2} + 2(\sigma_{lv(2)}^p \sigma_{sv}^p)^{1/2}. \end{aligned} \quad (4)$$

The accuracy of the determination of the surface energy (σ_{sv}) was ± 0.8 mJ/m^2 .

Table 1. Characteristics of test liquids, contact angles, and specific free surface energy of adsorption layers of LA on the surface of silver

Surface tension of test liquids σ_{lv} , mJ/m ²			
Liquid	σ_{lv}	σ_{lv}^d	σ_{lv}^p
H ₂ O	72.6	21.8	50.8
CH ₂ J ₂	50.8	2.3	48.5
Contact angles θ , deg			
monolayer		bilayer	
θ (H ₂ O)	15	40	
θ (CH ₂ J ₂)	10	20	
Surface energy σ_{sv} , mJ/m ²			
σ_{sv}^d	35.2	35.6	
σ_{sv}^p	35.9	25.9	
σ_{sv}	71.1	61.5	

This approach is widely used for determining the surface energy of solid bodies, adsorption layers of surface-active agents on solid substrates, self-organized monolayers of organic molecules on a solid surface, and organic films [12, 17, 22].

RESULTS AND DISCUSSION

On the surface of silver electrodes advancing and receding contact angles constituted 70° and 68°, respectively. The observable insignificant hysteresis of wetting ($\Delta\theta = (\theta_a - \theta_r) = 2^\circ$) indicates the purity and homogeneity of the surface of the silver electrode.

According to studies of adsorption kinetics of alicyclic disulfides on the surface of metals, the process of the formation of monolayers on solid surface can be conventionally split into two stages: first, the Langmuir adsorption on the surface, and second, the structuring of the layer on the surface when alkyl chains are lined up in a certain order (ordering of the monolayer). At the same time, depending on the type of ligand and solution concentration, the duration of the first stage may last from 1 min to more than 1 h; and for the second stage, dozens of hours [10].

Lipoic acid is adsorbed on the surface of silver due to the disulfide fragment included in the five-member cycle (Fig. 1). The interaction results in the formation of a covalent bond Me–S with the simultaneous breaking of the S–S bond in the disulfide cycle of LA [2].

The dependence of the LA adsorption on the surface of silver on the time of the contact with the solution is presented in Fig. 2. At $t < 10$ min, no noticeable self organization of the disulfide on the surface of silver was found (Table 2): the microscale sensor does

not detect changes in the frequency of its oscillations. This means that there is an incubation period, during which the adsorption of LA on the surface of silver does not occur or it is extremely small (less than the sensitivity limit of the method when measuring adsorption in these conditions). At $t \geq 10$ min, the adsorption increases, the kinetic curve has an inflection point at $t = 3$ h, and it reaches a plateau at $t = 5$ h, which indicates the polylayer nature of the adsorption (Fig. 2).

It can be assumed that the monolayer filling of the surface of silver with disulfide ends 3 h later after the contact of the solid surface with the solution. At $t = 3$ h the value of the adsorption of LA $\Gamma = 6.7 \times 10^{-6}$ mol/m², which corresponds to the value of the area per molecule

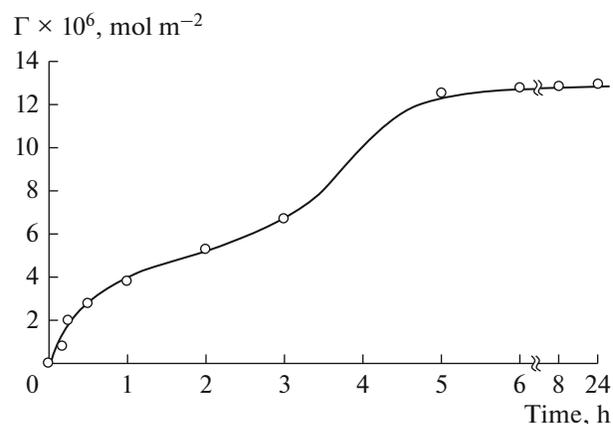
**Fig. 2.** Dependence of adsorption of LA on the surface of silver on time.

Table 2. Adsorption of lipioic acid on the surface of silver depending on time (t) of contact of the surface with the solution

Time(t)	5 min	10 min	15 min	30 min	1 h	2 h	3 h	5 h	6 h	8 h	24 h
$-\Delta f$, Hz	—	0.9	2.3	3.3	4.5	6.2	7.8	14.8	14.8	14.9	15.1
$\Gamma \times 10^8$, g/cm ²	—	1.6	4.1	5.8	7.9	10.9	13.7	26.0	26.0	26.2	26.6
$\Gamma \times 10^6$, mol/m ²	—	0.8	2.0	2.8	3.8	5.3	6.7	12.6	12.6	12.6	12.9

of LA in the adsorption layer $S_m = 1/(\Gamma N_A) = 0.26 \text{ nm}^2$, which is close in value to the area of disulfide (S–S) group. In this way, a saturated monolayer of LA is formed on the surface of silver. These results are in agreement with the calculation of the degree of filling of the surface of silver with disulfide (Table 3). At $t = 3 \text{ h}$, almost the entire surface of silver is filled with the adsorption layer and the degree of filling of the surface $X = 97\%$. This means that at $t = 3 \text{ h}$, a dense monolayer of lipioic acid is formed on the surface of silver and, at the same time, the outer part of the monolayer is formed by polar carboxylic groups, which are wetted by water: $\theta = 15^\circ$ (Table 1).

At $t > 3 \text{ h}$, a second layer of lipioic acid begins to form through the formation of hydrogen bonds between the terminal carboxylic groups of monolayer molecules on the surface of the silver and carboxy groups of the LA molecules in the solution (Fig. 3). The formation of the bilayer ends after 5 h and its outer part is formed by SH groups, which are wetted by water worse than carboxylic groups: the contact angle of water constitutes 40° (Table 1). These results are in agreement with the data of work [18]: the formation of bilayers as a result of the appearance of hydrogen bonds is established during the self organization of thiols with the terminal carboxylic and amino groups on the surface of gold. During the bilayer filling of the

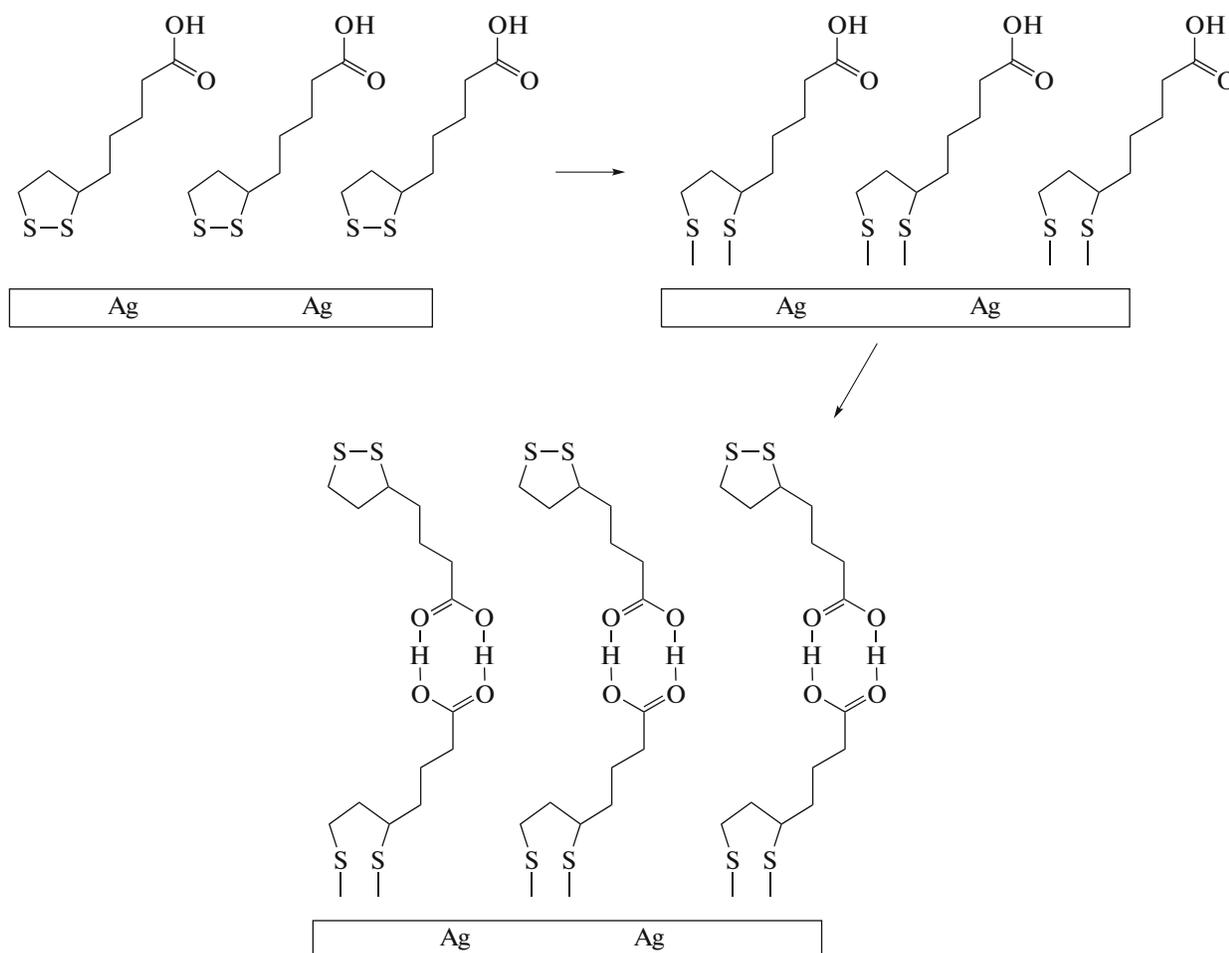

Fig. 3. Scheme of formation of adsorption layers of LA on the surface of silver (dashed line indicates hydrogen bonds).

Table 3. Contact angles of water on modified surface of silver at different times of its contact with the surface

Indicator	Ag	Contact angles θ , deg, at different contact times					
		10 min	15 min	30 min	1 h	2 h	3 h
θ_a	70	67	58	52	45	32	15
θ_r	68	55	51	47	42	30	14
$\Delta\theta = \theta_a - \theta_r$	2	12	7	5	3	2	1
X , %	0	8	30	42	58	78	97

surface of silver, the value of adsorption twice as much as the value of the limiting adsorption of LA during the multilayer filling of the substrate.

Table 3 presents the results of the measurements of water's contact angles (θ_a and θ_r) on the surface of the silver and calculation of the degree of its filling X with the adsorption layer with the increased time of the contact of silver with the LA solution. With the filling of the surface of silver with the adsorption layer hysteresis of the contact angles, $\Delta\theta = (\theta_a - \theta_r)$ decreases and approaches zero at a modification time of $t = 3$ h. The dependence $\Delta\theta(t)$ demonstrates the increased degree of homogeneity of the adsorption layers of LA during the transition from small modification degrees to the multilayer filling of the surface of silver. At the same time, as the monolayer is formed on the silver surface, the substrate is hydrophilized.

The specific free surface energy of the silver substrate during the mono- and bilayer filling of its surface with the adsorption layer of LA was calculated in the Owens–Wendt–Kaelble approximation (Eqs. (4), Table 1).

The surface energy of the adsorption layers of LA (mono- and bilayer) differs through the difference of the contributions of the polar component to its value, which is related to the different chemical nature of the terminal groups of the layers: polar carboxylic groups are better wetted than $-\text{SH}$ groups. However, in both cases a significant decrease in the specific free surface energy of silver occurs during the formation of adsorption layers, which according to the reference data constitutes 1140 mJ/m^2 [23].

CONCLUSIONS

The obtained results show that the surface of silver effectively adsorbs lipoic acid and, at the same time, a monolayer or even bilayer filling of the surface with the adsorption layer can be realized depending on the time of the contact with the modifying solution. These results can be in demand due to the wide-ranging application of nanoparticles of precious metals (Au, Ag) in medicine and pharmaceuticals as drug carriers in the diagnosis and treatment of illnesses [6, 7]. For the targeted delivery of drugs, it is possible to use ferromagnetic nanoparticles of silver of the core-shell type. Such magnetic nanoparticles were obtained with a

wide spectrum of metals [24]; however, silver and gold are the most suitable nanoparticles, which is determined by their bioavailability and the possibility of functionalization of the surface by sulfur-containing ligands [25].

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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