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STUDIES ON ELECTROCHEMICAL BEHAVIOUR OF THIOMERSAL

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Though its application rises several problems, thiomersal has remained up to the present one of the most frequently utilized conservants in the composition of different serobacteriological preparations (1, 2), on the basis of its energetic bacteriostatic, respectively bactericidal effect (3). Since during its conservation thiomersal undergoes a gradual decomposition, which may lead to unwanted reactions, it is indispensable to elaborate adequate qualitative and quantitative methods, the requirements in this connection being pretentious enough. To determine the decomposition degree of thiomersal is often applied the Szász' method (4), based either on the appearance of colloidal mercury, or on the determination of the mercury (II) ion concentration, originating from the decomposition of this compound. Nevertheless, this method does not measure directly the thiomersal concentration, which may be possible for instance by means of the bound mercury.

Based on our earlier results concerning the polarographic and chronopotentiometric particularities of carbon-mercury bond, interesting both from the analytical point of view and that of mechanism and kinetics, as well as of chemical structure (5—9), we have examined the applicability of this manysided and useful method for investigation of thiomersal. In the case of this compound some particularities appear, which to the present are unknown in other depolarizers and which have a notable theoretical importance and direct analytical employment. The thiomersal molecule has a number of bonds, respectively groups which in principle may be polarographically active. Taking into account the electronegativities of the participant atoms in the reaction center, it is apparent that the largest degrees of ionicity are attached to the S—Hg and Hg—C bonds. Since the sulfur atom participates in the conjugated system of the benzene ring and carboxyl group, the most polarizated bond is S—Hg.

Experimental

The measurements were carried out according to the manner described in our other papers, e.g. in (10). By recording the polarograms of thiomersal in different background electrolyte solutions, especially in 0.1 M KNO_3, we obtained voltamperometric curves containing several waves (Fig. 1), from which the first is anodic, i.e. it appears under the zero line of galvanometer, the others — two or three, depending on conditions — being cathodic waves.
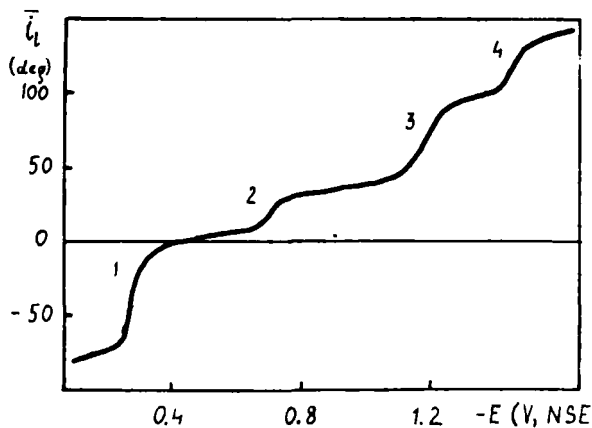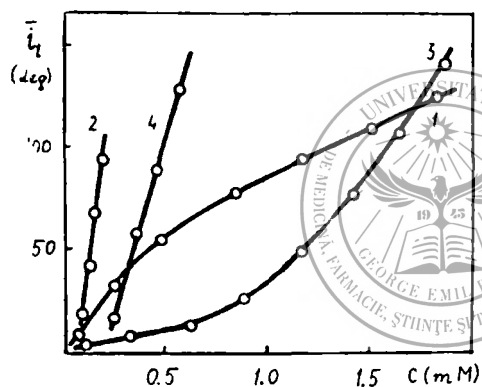
Results and discussion

The curves $\bar{i}_1$ vs. c for each polarographic waves are illustrated in Fig. 2.

The limiting current-concentration correlation for the first wave, in small concentrations, is approximately rectilinear ($<c> = mM$, $<\bar{i}_1> = deg$):

$$\bar{i}_1 = (15.58 \pm 0.82)\, c + (10.7 \pm 2.5) \quad deg$$
$$n = 6; \; r = 0.995; \; s_0 = \pm 3.2 \; deg$$

From this relationship it is relevant that the Ilkovič equation is not satisfied mainly as a consequence of an adsorption process on the electrode surface. This assumption is proved if — for the whole studied concen-

tration series (order of mM) — the statistical calculations are performed according to the Langmuir isotherm:

$$a = a_\infty \frac{c}{c+k}$$

studying the linearity of the $c \, \bar{\iota}_l$ vs. c correlation. The regression line equation thus obtained is significantly linear:

$$\frac{c}{\bar{\iota}_l} = (0.00260 \pm 0.00015) \, c + (0.161 \pm 0.014) \quad \text{mM deg}$$

$$n = 10; \; r = 0.987; \; s_0 = \pm 0.029 \quad \text{mM deg}$$

The current character is verified from the dependence of the limiting current on the pressure of the mercury column. In the case of the anodic wave the following regression equation is obtained (T = 293 K, <h> = = cm):

$$\lg \bar{\iota}_l = (0.812 \pm 0.029) \lg h - (0.100 \pm 0.050),$$
$$n = 7; \; r = 0.997; \; s_0 = \pm 0.012$$

respectively

$$i_l = 0.79 \, h^{0.81}$$

The exponent $0.81 > 0.50$ likewise suggests the contribution of adsorption process to the overall electrochemical reaction.

In dealing with the dependence of the half-wave potential on the height of the mercury column, the changes are not significant; they are of order of mV, if the mercury column height varies between 30 and 90 cm. The same absence of significant changes is observed studying this parameter as a temperature function ($E_{1/2} = - 0.247 \pm 0.005$ V, NSE).

The half-wave potential considerably depends on the depolarizer concentration. When the half-wave potential is plotted as a function of thiomersal concentration an excellent linear correlation is obtained:

$$E_{1/2} = - (0.0974 \pm 0.0054) \lg c - (0.575 \pm 0.017) \quad \text{V}$$
$$n = 7; \; r = - 0.992; \; s_0 = \pm 0.0043 \quad \text{V}$$

This dependence — namely, the shift of the half-wave potential with about 100 mV, when the concentration varies 10 times — emphasizes that the electrode process is succeeded by a chemical reaction, with a high probability by a dimerization. Since the reaction takes place rapidly and practically without activation energy, as the potential determining step remains the diffusion transport, the activation barrier of which ($\triangle H_{tr} - = 5.6$ kcal mole) falls in the waited interval. The temperature coefficient of the current ($+1.56 \, \%$ deg) corroborates this conclusion.

The cathodic waves have some essentially different features.

The first polarographic wave, recorded in this domain, is characterized by a linear i_l vs. c correlation:

$$\bar{\iota}_l = (63.4 \pm 4.1) \, c - (30.4 \pm 12.5) \quad \text{deg,}$$
$$n = 6; \; r = 0.992; \; s_0 = \pm 16 \quad \text{deg}$$

nevertheless, the corresponding straight line does not pass through the origin. As a consequence, the transport is also carried out by other pro-

cesses than the diffusion. This statement is verified as well by the correlation lg i_l vs. lg h, given in the following form:

$$lg\ \bar{i}_l = (0.2318 \pm 0.0080)\ lg\ h - (1.292 \pm 0.016),$$
$$n = 7;\ r = 0.996;\ s_0 = \pm\ 0.037$$

respectively

$$i_l = 19.59\ h^{0.23}$$

The low value of the exponent (0.23<0.50) suggests a considerable kinetic contribution to the studied process.

At the second wave, the concentration dependence of the limiting current is represented by a parabola (Fig. 2, curve 3). Accordingly, the appropriate double logarithmic regression equation can be written:

$$lg\ \bar{i}_l = (0.960 \pm 0.099)\ lg\ c + (5.56 \pm 0.35),$$
$$n = 10;\ r = 0.960;\ s_0 = \pm\ 0.08$$

respectively

$$\bar{i}_l = 3.63 \times 10^5\ c^{0.96}$$

The half-wave potential of the second cathodic wave also depends on the concentration:

$$E_{1/2} = -(0.0725 \pm 0.0073)\ lg\ c - (1.445 \pm 0.025)\quad V$$
$$n = 10;\ r = -0.962;\ s_0 = 0.013\quad V$$

The susceptibility of the electrode process to the depolarizer concentration is much more reduced than in the previous cases: when the thiomersal concentration increases with an order, its half-wave potential is shifted with about 70 mV in the direction of more negative potentials.

The electrochemical process is in this case irreversible, too.

The effect of the temperature also furnishes precious data about the nature of the electrode process:

$$lg\ i_l = -(542.035 \pm 0.018 \frac{1}{T} + (3.14 \pm 0.58),$$
$$n = 7;\ r = -0.997;\ s_0 = \pm 0.0054$$

from which $\triangle H_{tr} = 4.96$ kcal mole, in accordance with a preponderently diffusion transport in the respective step.

The temperature change affects the half-wave potential values, too:

$$E_{1/2} = -(120.5 \pm 6.8)\frac{1}{T} - (0.745 \pm 0.022)\ V,$$
$$n = 7;\ r = -0.992;\ s_0 = \pm 0.0021\ V$$

this latter parameter varying with about $+$ 1 mV, when the temperature increases by one degree.

The last cathodic wave may be characterized as well — between certain limits — by a linear $\bar{i}_l$ vs. c correlation:

$$i_l = (1.71 \pm 0.36) \times 10^5\ c - (21 \pm 8)\ deg$$
$$n = 4;\ r = 0.960;\ s_0 = \pm 13\ deg$$

Since the corresponding straight line does not pass through the origin, furthermore, the half-wave potential depends considerably on the logarithm of concentration:

$$E_{1/2} = -(0.769 \pm 0.016) \lg c - (4.160 \pm 0.053) \quad V,$$
$$n = 4; \; r = -0.9996; \; s_0 = \pm 0.017 \quad V$$

as well as the value of activation energy (17.6 kcal/mole), calculated from the temperature dependence of the limiting current:
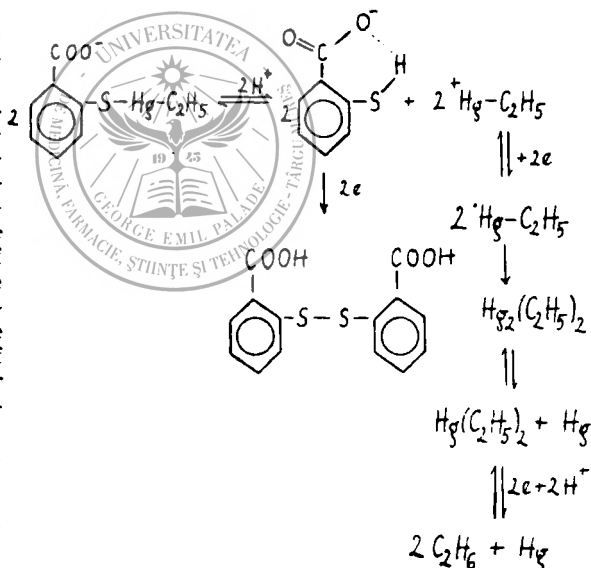
$$\lg \bar{i}_1 = -(1.93 \pm 0.14)\frac{1}{T} + (7.41 \pm 0.47)$$
$$n = 7; \; r = -0.986; \; s_0 = \pm 0.043$$

exceeds much the limits characteristic of diffusion process (about 6 kcal/mole), it follows that the electrochemical reaction is kinetically hindered.

On the basis of our experimental results, as well as on that of some data obtained from the special literature about the polarographic behaviour of organic compounds of mercury (11), we propose the following mechanism for the electrochemical reaction:

This mechanism agrees with the results of different chemical, pharmacological and microbiological investigations described in the literature (1, 2), demonstrating the formation of colloidal mercury in the reductive decomposition of thiomersal. On the other hand, some authors (12) suppose that the binding of the thiomersal — or its hydrolysis product — to the protein molecules responds for the appearance of certain allergical reactions, revealing the formation of a chemical bond between the sulfhydryl groups of proteins and the ethyl-mercury (II) group arising from dissociation of thiomersal. These data explain the appearance of the anodic wave of this depolarizer, especially if we take into account that as a consequence of protonation of the thioanion the possibility of its

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chelation with the carboxylate ion arises (13), promoting the considered process.

The complex electrochemical reaction described here is — as we believe — the first in this respect in special literature regarding to the polarography of elementorganic compounds, completing our knowledge about both theoretical and applied chemistry and electrochemistry.

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