The importance of the active complexes of 6 - mercaptopurine with Bi(III) with regards to kinetics and electrode mechanism changes in the presence of non-ionic surfactants

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ABSTRACT

The presence of mixed adsorption layers affects the mechanism and kinetics of irreversible Bi(III) ions electroreduction process in $2 \, mol \cdot dm^{-3}$ chlorates(VII). Triton X-100 and Tween 80 change the dynamics of the catalytic activity of 6-mercaptopurine (6MP) on Bi(III) ions electroreduction with the tendency of inhibition. Above the critical micelle concentration of Triton X-100 and Tween 80, the irreversibility of Bi(III) ions electroreduction decrease to the size comparable to the irreversible reduction of Bi(III) in $2 \, mol \cdot dm^{-3}$ chlorates(VII) which can be associated with the electrode surface blocking by formed hemispherical surface micelles. It was proved that the unstable complexes of Bi – 6MP or mixed Bi – 6MP – TritonX-100 and Bi – 6MP – Tween 80 intermediating in electrons transfer, play a significant role in the multi-stage mechanism of the electrode process. The hydration shell and composition of active complexes change as well. The obtained regularities indicate that in this case confirmed changes in entropy are a decisive factor.

1. Introduction

The development of industry, and the degradation of the environment, as well as the specific lifestyle of man, contribute to a new occurrence; which are diseases of civilization. Among them, tumorous diseases which are difficult to diagnose and treat are quite frequent. One of the systemic treatment methods is chemotherapy, based on drugs acting on the cellular cycle, but it has been shown that this therapy is toxic for the whole organism. Knowledge of electrochemical properties of anti-neoplastic drugs is essential with regards to more profound understanding of their metabolic path or in vivo redox processes. Therefore, it is necessary to investigate the mechanism of their actions and search for new systems of controlled drugs release mechanism, which can be used for monitoring any patient's health condition.

Based on the above, the studies on the kinetics and mechanisms of any electrode's process in the presence of 6-mercaptopurine, the drug used in the anti-neoplastic chemotherapy, mainly in marrow and lymphoblastic leukaemia's [1–3], seem to be by all means justified.

Because 6-mercaptopurine is the natural purine derivative, whose therapeutic efficiency depends upon a series of bio-chemical transformations [4]. The mechanism of the drug's biological activity is complex and can involve modulation of cellular metabolism in several ways.

The first pathway is the incorporation of active nucleotides into replicating nucleic acids and the second the action as a pseudo-feedback inhibitor of de novo purine nucleotide synthesis [5].

The results of previous studies clearly indicated to the key role of active complexes involved in the transition of electrons in the electrode process [6]. It has been shown that the process of Bi(III) ion electroreduction in the presence of amino acids and Zn(II) ion electroreduction in the presence of sodium 1-decanesulfonate [7] are controlled for all the chlorate(VII) concentrations studied by the reaction kinetics of the formation of active complexes preceding electron transfer. The active Bi – Mt. and Bi – Hg(SR)$_2$ complexes are located inside the adsorption layer [8–10]. The composition of the complex changes after the transfer of consecutive electrons.

Using Bi(III) ions as a depolariser enables observations of changes of reaction kinetics towards its acceleration by 6-mercaptopurine according to the "cap-pair" rule [8]. However, the addition of surface active substances Triton X-100 and Tween 80 to the supporting electrolyte will probably affect a change of dynamics of the catalytic

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process of drug action on Bi(III) ions electroreduction towards inhibition. This is evidenced by the studies on the inhibiting effect of non-ionic *N*-octanoyl-*N*-methylglucamine and *N*-decanoyl-*N*-methylglucamine [11] on the kinetics of Zn^{2+} ion electroreduction on a mercury electrode.

The application of voltametric techniques (SWV, CV, DC), as well as electrochemical impedance spectroscopy (EIS) will allow the determination of the kinetic and thermodynamic parameters which in turn, will define the 6-mercaptopurine catalytic effect and also their correlation in the presence of Triton X-100 and Tween 80 [12].

The studies will develop the current knowledge about the kinetics and mechanisms of electrode processes in which chemical stages play an essential role, which in turn can target therapy connected with determination and getting to know the mechanisms of controlled drugs release.

2. Experimental

2.1. Reagents and chemicals

The solutions were thermostatted at 298°K (if not stated otherwise) and de-aerated using nitrogen. $2 \, mol \cdot dm^{-3}$ chlorates(VII) were used as a supporting electrolyte. The concentration of Bi(III) ions in the studied solution was $1 \cdot 10^{-3} \, mol \cdot dm^{-3}$. The $1 \cdot 10^{-3} \, mol \cdot dm^{-3}$ Bi(III) solution in chlorates(VII) was prepared dissolving the weighed amount 0.2425 g of 99.999% $Bi(NO_3)_3 \cdot 5H_2O$ in a small amount of supporting electrolyte using the ultrasound bath. Then it was filled up with the $2 \, mol \cdot dm^{-3}$ chlorates(VII) solution to $500 \, dm^{-3}$. Additionally, the solutions containing 6-mercaptopurine (Fluka), Triton X-100 (Sigma-Aldrich) and Tween 80 (Sigma-Aldrich) prepared just before the measurements were applied in the investigations. There were used the following ranges of concentrations of organic substances: 6MP from 0.1 to $10 \cdot 10^{-3} \, mol \cdot dm^{-3}$, Triton X-100 and Tween 80 from $1 \cdot 10^{-6}$ to $1 \cdot 10^{-3} \, mol \cdot dm^{-3}$. The investigations were carried out in the systems:

- Bi(III) – the inhibitor (Triton X-100 or Tween 80),
- Bi(III) – the catalyst (6-mercaptopurine),
- Bi(III) – the catalyst – the inhibitor.

2.2. Instrumentation and measurement procedure

The electrochemical experiments were performed with a μAutolab Fra 2/GPES (Version 4.9) frequency response analyser (Eco Chemie, Utrecht, Netherlands), in a three – electrode cell containing: a dropping or hanging mercury–electrode with a controlled increase rate and a constant drop surface ($0.014740 \, cm^2$), as a working electrode (MTM Poland); Ag/AgCl (3 M saturated solution of NaCl) as a reference electrode and a platinum spiral, as an auxiliary electrode.

In the DC polarography, square – wave voltametry (SWV) and cyclic voltametry (CV), the optimal experiment operating conditions were as follows: step potential 2 mV for DC, pulse amplitude 20 mV, frequency 120 Hz and step potential 2 mV for the SWV, and scan rate 5–1000 mV s^{-1} and step potential 5 mV for the CV. The impedance data were collected at 36 frequencies in the range from 100 to 100,000 Hz within the faradaic potential region with 10 mV intervals.

The values of diffusion coefficients (D_{ox}) necessary for the calculation of kinetic parameters of the Bi(III) ion electro-reduction in the studied solutions were determined based on the Ilkovič equation for the boundary current controlled by diffusion [13].

The values of formal potential (E_f^0), transfer coefficient (α) and standard rate constants (k_s) were determined as in the paper [13].

The activation polarisation resistances (R_A) were determined using the electro-chemical impedance spectroscopy for E_f^0 and from the dependence $Z' = f(\omega Z'')$ or $Z' = f(Z'')$ [13], where Z' is the real and Z'' is the imaginary part of the cell impedance.

From the charge – transfer resistance values [13] as a function of DC

potential, the values of the apparent rate, constant (k_s), of the Bi(III) electro-reduction in the studied systems were obtained. The details are described elsewhere.

The enthalpies of activation ($\Delta H^{\neq}$) for Bi(III) electroreduction in the studied systems were determined according to equation [14]:

$$\Delta H^{\neq} = R \frac{dlnk_s}{d\frac{1}{T}} \tag{1}$$

whereas the standard reaction entropy is (ΔS^0) [14]:

$$\Delta S^0_{Bi(III)/Bi(Hg)} = 2F \frac{dE_f^0}{dT} \tag{2}$$

3. Results and discussion

3.1. Kinetic measurements

The presence of both Triton X-100 and Tween 80 in the supporting electrolyte solution containing $1 \cdot 10^{-3} \, mol \cdot dm^{-3}$ Bi(III) indicates a decrease in the current of SWV peak of Bi(III) ions electroreduction, shift of the peak towards more negative potentials and simultaneous increase of the SWV peak width at half of its height (Fig. 1a, b). As a result, a decrease in reversibility of Bi(III) ions electroreduction in the presence of the studied surfactants is observed (currents of Bi(III) ions electroreduction peaks decrease both after introducing the examined surfactants to the solution and also with the increase of their concentration, at the same time the width of peaks at half their height is increased).

It should also be noted that the SWV peaks are deformed and ill-defined at the concentration above $1 \cdot 10^{-4} \, mol \cdot dm^{-3}$ for Triton X-100 and $5 \cdot 10^{-5} \, mol \cdot dm^{-3}$ for Tween 80. The concentrations are associated with the critical micelle concentration [15]. Above the critical micelle
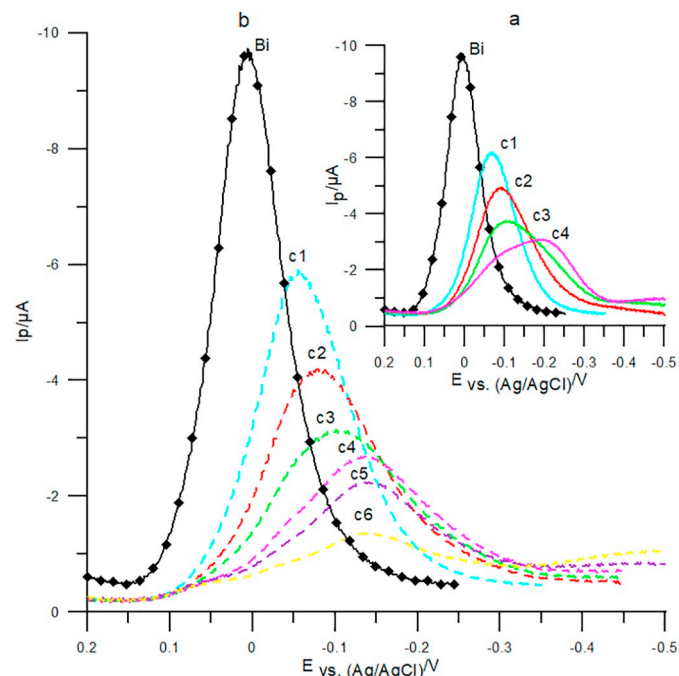
Fig. 1. a. The SWV peaks of $1 \cdot 10^{-3} \, mol \cdot dm^{-3}$ Bi(III) electroreduction in $2 \, mol \cdot dm^{-3}$ chlorates(VII) with various concentrations of Triton X – 100: (♦) 0, (—) $5 \cdot 10^{-6}$ (c1), (—) $1 \cdot 10^{-5}$ (c2), (—) $5 \cdot 10^{-5}$ (c3), (—) $1 \cdot 10^{-4}$ (c4) (in $mol \cdot dm^{-3}$).
b. The SWV peaks of $1 \cdot 10^{-3} \, mol \cdot dm^{-3}$ Bi(III) electroreduction in $2 \, mol \cdot dm^{-3}$ chlorates(VII) with various concentrations of Tween 80: (♦) 0, (---) $5 \cdot 10^{-6}$ (c1), (---) $1 \cdot 10^{-5}$ (c2), (---) $5 \cdot 10^{-5}$ (c3), (---) $1 \cdot 10^{-4}$ (c4), (---) $1.5 \cdot 10^{-4}$ (c5), (---) $2 \cdot 10^{-4}$ (c6) (in $mol \cdot dm^{-3}$).