

Full Paper

The Mathematical Description of Allopurinol Electrochemical Determination, Assisted by $\text{VO}_2^+/\text{VO}^{2+}$ Redox Pair in Acidic Solutions

Volodymyr V. Tkach,^{1,2,*} Yana G. Ivanushko,¹ Iryna L. Kukovs'ka,¹ Lyudmyla V. Romaniv,¹ Svitlana M. Lukanova,¹ Sílvio C. de Oliveira,² Gleison A. Casagrande,² Reza Ojani³ and Petró I. Yagodynets¹

¹*Chernivtsi National University, Ukraine*

²*Universidade Federal de Mato Grosso do Sul, Brasil*

³*University of Mazandaran, Islamic Republic of Iran*

*Corresponding Author, Tel.: +380506400359; Fax: +5521991809675

E-Mail: nightwatcher2401@gmail.com

Received: 21 February 2017 / Accepted: 2 March 2018 / Published online: 31 March 2018

Abstract- The possibility of allopurinol electrochemical detection, assisted by pervanadyl-vanadyl redox pair, has been evaluated from the theoretical point of view. The correspondent mathematical model has been developed and analyzed by means of linear stability theory and bifurcation analysis. It was shown that the steady-state stability in this system is maintained easily. The electroanalytical process is diffusion-controlled. The oscillatory behavior in this system is more probable than for general case, due to the presence of electrostatic and DEL-influencing factors.

Keywords- Allopurinol, Pervanadyl-vanadyl redox pair, Electrochemical sensors, Electrochemical oscillations, Steady-state stability

1. INTRODUCTION

The use of chemically modified electrodes [1–7] provides the possibility of flexible electrochemical analysis of different substances. Its advantages are precision, exactitude, rapidity and sensibility of the analysis and also the electrode affinity to the analyte.

Among the materials, possibly used as electrode modifiers for electroanalytical systems there are different vanadium compounds, generally containing tetra- and pentavalent vanadium compounds for anodic processes and bi- and trivalent vanadium for cathodic processes (but with exceptions) [8–10]. The pervanadyl VO_2^+ and vanadyl VO^{2+} are frequently used not only in electroanalytical processes, but also in purely chemical analytical determinations [11–13].

On the other hand, allopurinol is a uric acid derivative, structural isomer of hypoxanthine. Allopurinol inhibits xanthine oxidase, an enzyme that converts oxypurines to uric acid. By blocking the production of uric acid, this agent decreases serum and urine concentrations of uric acid, thereby providing protection against uric acid-mediated end organ damage in conditions associated with excessive production of uric acid, i.e. the massive cell lysis associated with the treatment of some malignancies [14-16]. It is specifically used to prevent gout, prevent specific types of kidney stones, and for the high uric acid levels that can occur with chemotherapy. It may be also used for treatment the treatment of primary or secondary uric acid nephropathy, with or without the symptoms of gout, as well as chemotherapy-induced hyperuricemia and recurrent renal calculi [15].

Nevertheless, its use may be conjugated with side effects, like fever, sore throat, headache with a severe blistering, peeling, red skin rash, pain or bleeding while urination, or even urination less frequent the usual or not at all, severe tingling, numbness, pain, muscle weakness and less serious effects, like vomiting, diarrhea, drowsiness or headache [17-19]. Moreover, its use during pregnancy has not been well studied [20]. So the development of a rapid, efficient and cheap method if its quantification is really an actual task, and electrochemical methods may be applied to it [21–23].

For now, no work has been published, referring to the allopurinol electrochemical detection, assisted by vanadium derivatives, but, in these, this process is possible. Nevertheless, the introduction of new electroanalytical techniques may confront the problems like:

- the indecision in the modifier mechanism of action;
- the compatibility of the modifier with the tissue or biological object (some modifiers, used *in vitro* may be non-compatible with *in vivo* sensing);
- the presence of electrochemical instabilities, accompanying both electrochemical reactions of vanadium compounds [24], and electrochemical oxidation and electrooxidative polymerization of organic molecules [25-28].

The mentioned problems may only be solved by means of an analysis of a mathematical model, capable to describe adequately the electroanalytical system. By modeling it is also capable compare the behavior of this system with that for the similar ones without any experimental essay.

So, the goal of this work is the mechanistic theoretic analysis of the possibility of allopurinol vanadyl/pervanadyl-assisted electrochemical quantification. In order to achieve it, we realize the specific goals:

- suggestion of the mechanism of the electroanalytical reaction consequence, leading to the appearance of analytical signal;
 - development of the balance equation mathematical model, correspondent to the electroanalytical system;
 - analysis and interpretation of the model in terms of the electroanalytical use of the system;
 - the seek for the possibility of electrochemical instabilities and for the factor, causing them;
- the comparison of the mentioned system's behavior with the similar ones [29 – 35].

2. SYSTEM AND ITS MODELING

In order to simplify the comprehension of the electroanalytical process, we make a brief description of some details of the reaction mechanism.

As in [21–23], the allopurinol electrooxidation may be realized in acidic solutions with the pH=3. In these conditions, the pentavalent vanadium exists in the form of pervanadyl ion, as the decavanadates are transformed to pervanadyl by the reaction:

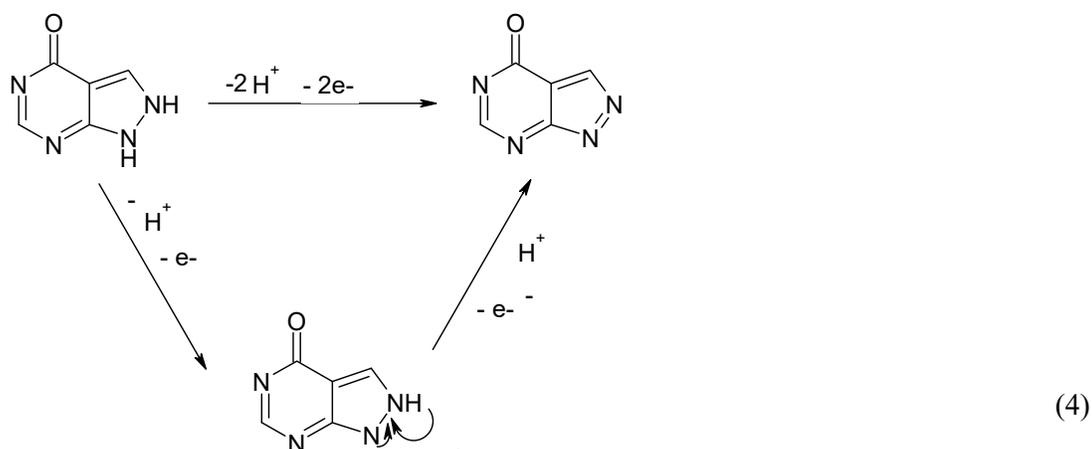


In the presence of allopurinol, the electroanalytical process will be realized according to:



In which Ao stands for allopurinol oxidized form.

The general mechanism for allopurinol electrooxidation may be described as:



So, in order to describe mathematically the allopurinol electrochemical detection, assisted by $\text{VO}_2^+/\text{VO}^{2+}$ redox pair, we introduce three variables:

a – allopurinol concentration in pre-surface layer;

v – the vanadyl coverage degree on the anode;

h – the protons' concentration in the pre-surface layer.

To simplify the modeling, we suppose that the reactor is intensively stirred, so we may neglect the convection flow. Also we suppose that the supporting electrolyte is in excess, so we may neglect the migration flow. Also we suppose that the concentrational distribution on pre-surface layer is linear, and the layer thickness is constant, equal to δ .

It is possible to show that the behavior of this system will be described by a tridimensional balance equation set, represented as:

$$\begin{cases} \frac{da}{dt} = \frac{2}{\delta} \left(\frac{\Delta}{\delta} (a_0 - a) - r_2 - r_h \right) \\ \frac{dv}{dt} = \frac{1}{G} (r_2 - r_3) \\ \frac{dh}{dt} = \frac{2}{\delta} \left(\frac{D}{\delta} (h_0 - h) + r_3 - r_2 - r_h \right) \end{cases} \quad (5)$$

In which D is the diffusion coefficient of protons, Δ is the diffusion coefficient of allopurinol, a_0 and h_0 are correspondent bulk concentrations, r_2 and r_3 are the reaction rates of the reactions (2) and (3), and r_h is the reaction rate of the protonic attack on allopurinol.

The correspondent reaction rates may be calculated as:

$$r_2 = k_2 a (1 - v)^2 h^2 \exp(\alpha v) \quad (6)$$

$$r_3 = k_3 v \exp\left(\frac{F\alpha v}{RT}\right) \quad (7)$$

$$r_h = k_h a h \quad (8)$$

In which the parameters k are correspondent reaction rate constants, $F=N_{Ae}$ is the Faraday number, α is the variable, relating the ion configuration change to DEL potential slope, related to the zero-charge potential, R is the universal gas constant, and T is the absolute temperature.

In general, the system's behavior will resemble that of the similar systems [29–35]. Nevertheless, the presence of DEL-influencing chemical stage will contribute strongly to the steady-state stability, and this contribution will be discussed below.

3. RESULTS AND DISCUSSION

In order to investigate the steady-state stability of the system with the electrochemical detection of allopurinol, assisted by pervanadyl-vanadyl redox pair, we analyze the equation set (5) by means of linear stability theory. The Jacobi functional matrix steady-state members may be described as:

$$\begin{pmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{pmatrix} \tag{9}$$

in which:

$$a_{11} = \frac{2}{\delta} \left(-\frac{A}{\delta} - k_2(1-v)^2 h^2 \exp(\alpha v) - k_h h \right) \tag{10}$$

$$a_{12} = \frac{2}{\delta} (2k_2 a(1-v) h^2 \exp(\alpha v) - \alpha k_2 a(1-v)^2 h^2 \exp(\alpha v)) \tag{11}$$

$$a_{13} = \frac{2}{\delta} (-k_h a) \tag{12}$$

$$a_{21} = \frac{1}{G} (k_2(1-v)^2 h^2 \exp(\alpha v)) \tag{13}$$

$$a_{22} = \frac{1}{G} \left(-2k_2 a(1-v) h^2 \exp(\alpha v) + \alpha k_2 a(1-v)^2 h^2 \exp(\alpha v) - k_3 \exp\left(\frac{F\alpha v}{RT}\right) + \alpha k_3 v \exp\left(\frac{F\alpha v}{RT}\right) \right) \tag{14}$$

$$a_{23} = \frac{1}{G} (2k_2 a(1-v)^2 h \exp(\alpha v)) \tag{15}$$

$$a_{31} = \frac{2}{\delta} (-k_2(1-v)^2 h^2 \exp(\alpha v) - k_h h) \tag{16}$$

$$a_{32} = \frac{2}{\delta} (2k_2 a(1-v) h^2 \exp(\alpha v) - \alpha k_2 a(1-v)^2 h^2 \exp(\alpha v) + k_3 \exp\left(\frac{F\alpha v}{RT}\right) - \alpha k_3 v \exp\left(\frac{F\alpha v}{RT}\right)) \tag{17}$$

$$a_{33} = \frac{2}{\delta} \left(-k_h a - 2k_2 a(1-v)^2 h \exp(\alpha v) - \frac{D}{\delta} \right) \tag{18}$$

Observing the expressions (10), (14) and (18), it is possible to observe that the *oscillatory behavior* for this system is possible. Moreover, it is more probable than for the simplest systems with the electrochemical detection of different compounds [29–35], as there is more than one process influencing the double electric layer.

Besides of the influences of the electrochemical reaction, characteristic for the similar systems, another process causing the oscillatory behavior is linked with the DEL influences of the chemical process, conjugated with ionic configuration change. Mathematically, these factors may be expressed by the positivity of the parameter α , and, consequently, of the elements $\alpha k_2 a(1-v)^2 h^2 \exp(\alpha v)$ and $\alpha k_3 v \exp\left(\frac{F\alpha v}{RT}\right)$. The oscillations are expected to be frequent and of little amplitude.

In order to investigate the *steady-state stability* in this system, we apply the Routh-Hurwitz stability criterion to the equation set (5). In order to avoid the cumbersome expressions, we introduce new variables, so the Jacobian determinant will be described as:

$$\frac{4}{\delta^2 G} \begin{vmatrix} -\kappa_1 - \Xi - \xi & \Sigma & -P \\ \Xi & -\Sigma - \Omega & \Lambda \\ -\xi & \Sigma + \Omega & -P - \Lambda - \kappa_2 \end{vmatrix} \tag{19}$$

Opening the brackets, we obtain the steady-state stability requirement in the form of:

$$(-\kappa_1 - \Xi - \xi)(\Sigma P + \Omega P + \Sigma \kappa_2 + \Omega \kappa_2) + \Xi(\Sigma \Lambda + \Sigma \kappa_2 - \Omega \Pi) - \xi(\Sigma \Lambda - \Sigma P - \Omega P) < 0 \tag{20}$$

After the rearrangement of (20) with the annihilation of the elements with equal module and opposed signs, the requirement will be rewritten as:

$$(-\kappa_1 - \varepsilon - \xi)(\Sigma P + \Omega P + \Sigma \kappa_2 + \Omega \kappa_2) - \varepsilon(\Sigma P + 2\Omega P + \Omega \kappa_2 - \Sigma \Lambda) - \xi(\Sigma \Lambda + \Sigma \kappa_2 + \Omega \kappa_2) < 0 \quad (21)$$

This condition is satisfied with warranty, in the absence or fragility of DEL influences of electrochemical and chemical reactions reaction. The stability is realized in a vast parameter region. From the electroanalytical point of view it is correspondent to the linear dependence between anodic current and allopurinol concentration, so it is possible to confirm that the process will be electroanalytically efficient.

When the allopurinol concentrations are relatively small, and/or the electrode is relatively big the diffusion is kinetically the slowest process, and the electroanalytical process will be diffusion controlled. Yet, when the analyte concentration values are higher, and the electrode is relatively small, the reaction (2) will be, kinetically, slower than the diffusion, and this reaction will control the electroanalytical process.

In the case of the equality of destabilizing and stabilizing influences of electrochemical reaction, the *monotonic instability*, correspondent to the detection limit, is realized, and its condition for this system will be presented as:

$$(-\kappa_1 - \varepsilon - \xi)(\Sigma P + \Omega P + \Sigma \kappa_2 + \Omega \kappa_2) - \varepsilon(\Sigma P + 2\Omega P + \Omega \kappa_2 - \Sigma \Lambda) - \xi(\Sigma \Lambda + \Sigma \kappa_2 + \Omega \kappa_2) = 0 \quad (22)$$

In the case of the possible solubilization of pervanadyl-cation, the reactions of its formation and reduction are accompanied by surface phenomena and they are responsible for the oscillatory behavior.

4. CONCLUSION

The theoretical investigation for the pervanadyl-vanadyl redox pair-assisted electrochemical detection of allopurinol let us conclude that:

- Pervanadyl may serve as an excellent anode modifier for allopurinol electrochemical reduction.
- The steady-state in the system is easy to maintain. The linear dependence between the allopurinol concentration and electrochemical parameter (current) is maintained in the vast concentration range, due to steady-state stability.
- The process is diffusion-controlled, but in relatively concentrated analyte solution may be kinetically controlled.

- The oscillatory behavior in the system is possible, being caused not only by influences of the electrochemical reaction on DEL capacitances, but also by the influences of the chemical stage, leading to the positive callback.
- The oscillations are expected to be frequent and of small amplitude.

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