The theoretical description for the use of the vanadium (III) oxyhydroxide for letrozol electrochemical determination

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Abstract

The VO(OH)-assisted letrozole electrochemical determination has been analyzed and evaluated by theoretical point of view. The electrochemical determination is realized by a cathodic process, in which vanadium (III) oxyhydroxide plays the role of active substance and proton-electron transfer mediator. The correspondent mathematical model has been analyzed and evaluated by means of linear stability theory and bifurcation analysis. It was shown that VO(OH) may be an excellent electrode modifier for the letrozole electrochemical determination in neutral and mildly acidic pH conditions. The oscillatory behavior in neutral media is less probable than in acidic media.

Keywords: letrozole, electrochemical sensors, chemically modified electrodes, vanadium (III) oxyhydroxide, stable steady-state.

Introduction

Letrozole (Fig. 1) is an aromatase inhibitor, used in the treatment of different types of breast cancer [1 – 4]. From the chemical point of view, it is a triazolic derivative, containing two cyanic moieties:
Fig. 1. Letrozole

Besides of its use as an anti-cancer drug, it is used also in the treatment of the infertility, as an ovarian stimulation [5 – 6]. It has less side effects than clomiphene and gives less chances of multiple gestation. Nevertheless, besides of its direct action as anti-cancer and reproductive drug, it possesses different dose-related adverse effects [7 – 10], like arthralgia, fatigue. Its excessive use in females may provoke the ovarian hyperstimulation syndrome [9 – 10]. Its lasting use may provoke osteoporosis [11]. Thus, the development of the methods for its determination is really actual [12 – 14], and the development of the electrochemical methods would be an interesting solution for this problem.

Recently, some methods for Letrozole electrochemical determination have been developed [15 – 18]. The electroanalytical process has been realized via a cathodic reaction, including the reduction of the latter cyanic groups. This leads to the supposition that the vanadium (III) oxyhydroxide, a trivalent vanadium compound with the electrochemical behavior, strongly inclined to the reductive properties, and stable in the pH range 3<pH<14, could also be used as a modifier.

For now, only one experimental work concerning the use of VO(OH) as an electrode modifier is known [19]. Nevertheless, the electroanalytical use of VO(OH) has been theoretically predicted in [20] for nitrite determination in acidic media. Nevertheless, the development of principally electroanalytical processes may confront some problems, like:

- The indecision about the mechanism of electrochemical action of the electrode modifier with the analyte;

- The possibility of the appearance of electrochemical instabilities, characteristic for the electrosynthesis and action of CoO(OH), a similar compound [21 – 22].

These problems may be solved, if the experimental essays are preceded by an a priori theoretical investigation of the electroanalytical system. So, the goal of our work is to investigate theoretically the possibility of benzodiazepines electrochemical quantification, assisted VO(OH). 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 superposition of the general case of letrozole electrochemical reduction and the case of VO(OH)-assisted electroanalytical 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 [23 – 28].

**System and its modeling**

*The general scheme* for the electroanalytical process in neutral media may be described as on the Fig. 2:

![Diagram of the electroanalytical process](image)

**Fig. 2. The scheme of the electroanalytical process**

For the neutral media and the absence of the interfering substances, capable to compromise the stability of the analyte and the modifier, the electroanalytical process will be described by two variables:

- $c$ - the letrozole concentration in the pre-surface layer;
- $v$ – the vanadium oxyhydroxide surface coverage degree.

To simplify the modeling, we suppose that the reactor is intensively stirred, so we can neglect the convection flow. Also we assume that the background electrolyte is in excess, so we can neglect the migration flow. The diffusion layer is supposed to be of a constant thickness, equal to $\delta$, and the concentration profile in it is supposed to be linear.
Taking this into account, we may represent the balance equation set as:

\[
\begin{aligned}
\frac{dc}{dt} &= \frac{2}{\delta}\left(\frac{\Delta}{\delta}(c_0 - c) - r_1\right) \\
\frac{d\nu}{dt} &= \frac{1}{G}(r_2 - r_1)
\end{aligned}
\]  

(1)

In which \(\Delta\) is the diffusion coefficient, \(c_0\) is benzodiazepines’ bulk concentration, \(G\) is VO(OH) maximal surface concentration and the parameters \(r\) are correspondent reaction rates, which may be calculated as:

\[
\begin{aligned}
r_1 &= k_1 cv^8 \\
r_2 &= k_2 (1 - \nu) \exp\left(-\frac{F\phi_0}{RT}\right)
\end{aligned}
\]  

(2), (3)

in which the parameters \(k\) are correspondent reaction rate constants, \(F\) is the Faraday number, \(\phi_0\) is the DEL potential slope in the double, related to the zero-charge potential, the parameters \(\beta\) and \(\rho\) describe the surface influences of the VO(OH) dissolution and its influence to the DEL capacitances, \(R\) is the universal gas constant and \(T\) is the absolute temperature.

It will be shown below that in neutral media the behavior will be less dynamic than in acidic media.

Results and discussion

In order to describe the behavior of the system with leterzole electrochemical detection, assisted by VO(OH), we analyze the equation set (1) by means of the linear stability theory. The steady-state Jacobian functional matrix elements for this system may be described as:

\[
\begin{pmatrix}
 a_{11} & a_{12} \\
 a_{21} & a_{22}
\end{pmatrix}
\]  

(4)

in which:

\[
\begin{aligned}
a_{11} &= \frac{2}{\delta}\left(-\frac{\Delta}{\delta} - k_1(v^8)\right) \\
a_{12} &= \frac{2}{\delta}(-8k_1cv^7) \\
a_{21} &= \frac{1}{G}(k_1v^8) \\
a_{22} &= \frac{1}{G}\left(-k_2 \exp\left(-\frac{F\phi_0}{RT}\right) - jk_2(1 - \nu) \exp\left(-\frac{F\phi_0}{RT}\right) - 8k_1cv^7\right)
\end{aligned}
\]  

(5), (6), (7), (8)

The main conditions for bivariant systems are described in the Table 1:
Table 1. The main conditions for bivariant systems.

In order to simplify the analysis of the matrix, we introduce new variables, so the matrix determinant will be described as:

\[
\frac{2}{\delta G} \begin{vmatrix} -\kappa & -\zeta & -\Omega \\ \zeta & -\chi - \Omega \\ -\chi - \Omega \end{vmatrix} \tag{9}
\]

It is possible to see that in this system the oscillatory behavior in this system is less probable than in acidic media, as the only factor, responsible for its appearance is the DEL influence of the electrochemical stage, leading to the periodic change of DEL capacitances. It is typical either for this electroanalytical process, or for the similar ones [21 – 24]. Yet in strongly acidic solutions, the surface and capacitance effect of the VO(OH) dissolution:

\[
\text{VO(OH)} + 3\text{H}^+ \rightarrow \text{V}^{3+} + 2\text{H}_2\text{O} \tag{10},
\]

which occurs in low pH values and without redox process, may also be responsible for the oscillatory behavior. These influences (as it will be described below) are typical for the parameter values beyond the detection limit.

The steady-state stability condition for a two-dimensional system may be described as: Tr J<0, Det J>0. For this system, it will be rewritten as:

\[
\begin{cases}
-\kappa - \zeta - \chi - \Omega < 0 \\
\kappa \chi + \kappa \Omega + \zeta \chi + 2\zeta \Omega \chi > 0
\end{cases} \tag{11}
\]

If j is possible, describing the absence or fragility of DEL influences of the electrochemical stage, the condition (11) is satisfied warrantedly. Really, if j is possible, the left side of the first inequation will obtain more negative values, and the steady-state will be stable.

As there are no substances, capable to compromise the stability of the analyte and/or electrode modifier, the stable steady-state will be correspondent to the linear dependence between benzodiazepines’ concentration and electrochemical parameter. So, it is possible to conclude that in lightly and moderately acidic solutions, the electroanalytical process will be efficient. As the reactions occur by relatively rapid manner, the electroanalytical process is diffusion-controlled.
The monotonic instability in this system is possible, being caused by the equality between the stabilizing influences and the destabilizing ones of the electrochemical process influences on DEL. It is correspondent to the detection limit and its condition may be described as:

\[
\begin{align*}
-\kappa - \xi - X - \Omega < 0 \\
\kappa X + \kappa \Omega + \xi X + 2\xi \Omega A = 0
\end{align*}
\] (11)

It is also possible to prepare the CP – VO(OH) composite, in order to use the mediated electron transfer. In this case, the presence of a polymer may make the system more stable and more efficient. The conducting polymer, besides of the VO(OH) nanoparticles stabilization, will effectuate the role of the mediator.

**Conclusion**

The analysis of the possibility of the VO(OH)-assisted letrozole electrochemical determination let us conclude that:

- VO(OH) may serve as an excellent modifier for letrozole quantification. The vanadium(III)oxyhydroxide acts as an active substance in neutral and mildly acidic solutions;
- In these conditions, the stable steady-state is maintained easily. The system is electroanalytically efficient. The electroanalytical process is diffusion-controlled;
- The oscillatory behavior in this system is possible, being caused by the unique factor of capacitance influences in double electric layer, capable to be realized beyond the detection limit.

**References**

2. D. Xe, X. Ma, OncoTargets Ther., 9(2016), 1077
7. J. Younus, L. Kligman, Curr. Oncol., 17(2010), 87
17. M. Aydin, B. Yilmaz, E. Alcin et al., Neuroscience, 151(2008), 186
27. V. V. Tkach, I. L. Kukovska, Ya. G. Ivanushko et al., TecnoAlimentar, 14(2018), 10