THE POSSIBILITY OFNALBUPHIN CoO(OH)-ASSISTED ELECTROCHEMICAL DETECTION AND ITS MATHEMATICAL DESCRIPTION

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Abstract. The possibility of nalbuphin electrochemical determination over a CoO(OH)-modified electrode has been studied 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 CoO(OH) may be applied as an efficient electrode modifier in the detection of nalbuphin in neutral and lightly alkaline media. The electrochemical response has to be clear and easy to interpret. The possibility of the oscillatory and monotonic instabilities has also been verified.

Keywords: nalbuphin, chemically modified electrodes, cobalt (III) oxyhydroxide, electrochemical detection, stable steady-state.

Introduction. The use of chemically modified electrodes (CME) is a very important step in electroanalytical chemistry [1–4]. Compared to the bare electrodes, they have some advantages, like, rapidity, low cost, precisity, exactity, flexibility, versatility in use and affinity between the electrode modifier and the analyte. On the other hand, nalbuphine is a semi-synthetic opioid pain-relieving drug, used as an analgesic to relieve the moderate and severe pains. It is an agonist at kappa opioid receptors and an antagonist or partial agonist at mu opioid receptors [5]. Nalbuphine is the only opioid analgesic that is not a controlled substance in the United States. In Ukraine it is included in the first aid box of the sanitary instructors. In Brazil it is sold as Nubain and is commercialized only to hospitals. It may be used as a supplement to balanced anesthesia, for preoperative and postoperative analgesia, and for obstetrical analgesia during labor and delivery [5–8]. Its plasma half-life is about 5 hours and in clinical studies the duration of analgesic activity has been reported to range from 3 to 6 hours [9]. Its excess can create side effects, like dizziness, drowsiness, feeling of constant movement of self or surroundings, nausea, relaxed and calm sensation of spinning, slumber, sweaty, clammy skin, vomiting, rarely, dry mouth and headache [10–14]. So, the development of an efficient and rapid method for its quantification is, without a doubt, an actual problem [15–17]. In the work [18] an electroanalytical process for naphlubine electrochemical detection on PtCo nanostructure has been suggested. The sensor has shown efficient selectivity in the presence of diclofenac. Nevertheless, its modifier contained platinum, with may enhance the cost of its use, so the cobalt (III) oxyhydroxide CoO(OH), seen by many researchers as a substitute to titanium dioxide [19] and yet used in the detection of ascorbic acid [20], oxalic acid [20–21], phenolic and hydroquinonic compounds [22], which are oxidized in the similar conditions, may be an interesting alternative. On the other hand, its electroanalytic properties’ investigation has only begun, and a CoO(OH)-assisted electrochemical oxidation may confront the problems like: the induction 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 electrochemically instabilities, accompanying both electrochemical synthesis of cobalt (III) oxyhydroxide [23–24], 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 to 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 nalbuphine CoO(OH)-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].

System and its modeling. In general, the mechanism of CoO(OH)-assisted nalbuphine electrochemical oxidation in neutral media may be described as:

![Fig. 1 Nalbuphine CoO(OH)-assisted oxidation mechanism](http://www.ajphsci.com)

and it is accomplished, while compared with the similar systems [29 – 35], by dimerization. In this system we may introduce three variables: c – nalbuphine concentration in the pre-surface layer; c² - nalbuphine radical-cation concentration in the pre-surface layer; θ – CoO surface concentration. Nevertheless, if the radical-cations do not provoke side reactions on the surface or in the solution, the variable c² is easily eliminated, and the system will be bivariant with the variables c and θ. This case will be described in this system.
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. It’s also supposed that at the beginning of the reaction CoO covers the entire electrode surface. It’s possible to show that the two-dimensional mathematical model for this case will be described as:

$$\begin{align*}
\frac{dc}{dt} &= \frac{2}{\delta} \left( \frac{\Delta}{\delta} (c_0 - c) - r_1 \right) \\
\frac{d\theta}{dt} &= \frac{1}{G} (r_1 - r_2)
\end{align*}$$

Eq. [1]

In which $\Delta$ is the diffusion coefficient, $c_0$ is nalturbine bulk concentration, $G$ is CoO maximal concentration and $r_1$ and $r_2$ are the reaction rates of the electroanalytical process stages, shown on the Fig. 1, which may be calculated as:

$$r_1 = k_c c^2 (1 - \theta)^2$$

Eq. [2]

$$r_2 = k_2 \theta \exp \left( \frac{2F\gamma \theta}{RT} \right)$$

Eq. [3]

In which the parameters $k$ are reactions’ rate constants, $F$ is Faraday number, $\gamma$ is the parameter describing the influence of the electrochemical process on double electric layer (DEL) capacitance, $R$ is the universal gas constant, and $T$ is the solution absolute temperature. Contrariwise to the CP-based systems [32–35], in which the radical coupling influenced the polymer composition and properties, leading to surface instabilities, in this system, it gives less impact, which will be discussed below.

**Results and Discussions**

To investigate the behavior with CoO(OH)-assisted nalturbine electrochemical detection, we analyze the equation set (1) by means of linear stability theory and bifurcation analysis. The Jacobian functional matrix steady-state elements for it may be described as:

$$\begin{bmatrix}
a_{11} & a_{12} \\
a_{21} & a_{22}
\end{bmatrix}$$

Eq. [4]

$$a_{11} = \frac{2}{\delta} \left( \frac{\Delta}{\delta} - 2 k_c c(1 - \theta)^2 \right)$$

Eq. [5]

$$a_{12} = \frac{4}{\delta} (k_c c^2 (1 - \theta))$$

Eq. [6]

$$a_{21} = \frac{2}{G} (k_c c^2 (1 - \theta))$$

Eq. [7]

$$a_{22} = \frac{1}{G} \left( -k_c c(1 - \theta) - k_2 \theta \exp \left( \frac{2F\gamma \theta}{RT} \right) \right) k_2 \theta \exp \left( \frac{2F\gamma \theta}{RT} \right)$$

Eq. [8]

The oscillatory behavior is realized in the Andronov-Hopf bifurcation conditions $-$ Det $J > 0$, $Tr J = 0$, in which $Tr J = a_{11} + a_{22}$ and Det $J = a_{11} a_{22} - a_{12} a_{21}$. As the condition Det $J > 0$ is, generally, satisfied, the main one is that described as $Tr J = 0$. It may be satisfied, if at least one of the main diagonal elements is positive. The only main diagonal element, capable to be positive in this system, is

$$- k_2 \theta \exp \left( \frac{2F\gamma \theta}{RT} \right) > 0$$

positive if $\gamma < 0$, describing strong influences of the electrochemical processes on DEL. It is common for all similar systems [29-35]. The steady-state stability condition for a two-dimensional system may be described as: $Tr J < 0$, Det $J > 0$. In order to avoid the cumbersome expressions, we introduce new variables, so, the matrix determinant will be rewritten as:

$$\begin{vmatrix}
\frac{2}{G} & - \kappa - \Xi \left( - \Sigma - \Omega \right) \\
- \kappa - \Xi \left( - \Sigma - \Omega \right) & \Sigma
\end{vmatrix}$$

Eq. [9]

Opening the brackets, we obtain the steady-state condition as:

$$- \kappa - \Xi \left( - \Sigma - \Omega \right) < 0$$

Eq. [10]

And it is warranted to be satisfied in the case of the positivity of $\Omega$, describing the fragility of DEL influences of the electrochemical process. The process is diffusion-controlled, tending to be reaction-controlled in the case of the relatively small electrodes and relatively high analyte concentrations (see the Table).

<table>
<thead>
<tr>
<th>Analyte concentration</th>
<th>Electrode size</th>
<th>Steady-state stability defining process</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Small</td>
<td>Diffusion or reaction</td>
</tr>
<tr>
<td>High</td>
<td>Large</td>
<td>Reaction</td>
</tr>
<tr>
<td>Low</td>
<td>Large</td>
<td>Diffusion</td>
</tr>
<tr>
<td>High</td>
<td>Large</td>
<td>Diffusion or reaction</td>
</tr>
</tbody>
</table>

Tab. 1 The optimal conditions for nalturbine electroanalysis

For the electroanalytical effects the steady-state stability is correspondent to the linear dependence between the electrochemical parameter and analyte concentration, or, better saying, to the electroanalytical efficiency. It isn’t compromised even by radical recombination effects, if they do not provoke side reactions. 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:

$$- \kappa - \Xi \left( - \Sigma - \Omega \right) < 0$$

Eq. [11]

In the case of side reactions of radical cations, the variable $c^*$ can’t be eliminated, and the equation set used becomes triviant: it’s possible to mention that CoO(OH) may change its modification during the electroanalytical process. If so, an additional variable, describing another CoO(OH) modification coverage degree, is introduced, and the modification change effects strongly the system’s behavior. This system will be described in our next works.

**Conclusions.** From the theoretical investigation of the possibility of CoO(OH) – assisted nalturbine electrochemical detection it is possible to conclude that: CoO(OH) may serve as an excellent modifier for nalturbine quantification, despite of the presence of radical recombination. The stable steady-state is maintained easily, and the system is electroanalytically efficient; Depending on the electrode size and on analyte concentration, the process may be diffusion or reaction-controlled;
The oscillatory behavior in this system is possible, being caused by DEL influences of the electrochemical process; The mono-tonic instability in this system is also possible, being caused by the equality of the destabilizing influences in DEL to the stabilizing ones; The presence of side reactions of the cation-radicals and also modification changes in CoO(OH) may influence the system, making its behavior more complicated.

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