

The Theoretical Description of Risperidone Electrochemical Determination on Copper Sulfide Nanoparticles

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Abstract: The possibility for risperidone electrochemical determination in an alkaline medium on copper sulfide nanoparticles has been evaluated. The analysis of the correspondent mathematical model confirms the efficacy of the copper (II) sulfide nanoparticles for risperidone electrochemical determination in an alkaline medium despite the influence of the ionic form transformation, provoking the oscillatory behavior.

Keywords: risperidone; electrochemical sensor; copper sulfide nanoparticles; electrochemical oscillations; stable steady-state.

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1. Introduction

Risperidone (Figure 1) [1–4] is an atypical antipsychotic drug developed by Johnson and Johnson. It is used for the treatment of bipolar syndrome, depressive psychosis, obsessive-compulsive syndrome, and even schizophrenia. It is popularly known as mentioned in the House M.D. series.

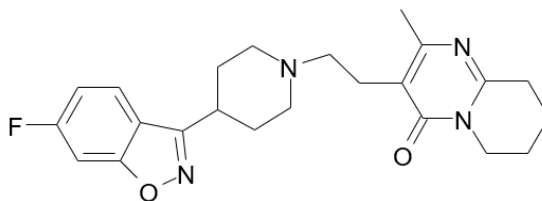
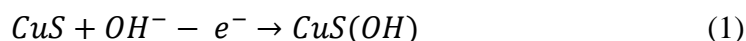


Figure 1. Risperidone.

Being the dopamine antagonist [5–9], its side effects include movement disorder, dizziness, malign neuroleptic syndromes, weight gain, and augmented suicide risks; the reason why the determination of risperidone concentration is actual, and the electrochemical methods may be an efficient method for it [10–12].

Either cathodic or anodic routes are possible for risperidone electrochemical determination. In the case of the anodic route, electrochemical oxidation may be caused by strong oxidants. These oxidants may be anode modifiers or may be formed on the electrochemical stage *in situ* [13–15].

In the last case, copper (II) sulfide nanoparticles may be used in the basic medium as a source for an aggressive oxidant –copper(III) sulfohydroxide (1):



It will thereby oxidize risperidone by N-oxidation and phenolization mechanism, preceded, in an alkaline medium, by risperidone hydrolysis. All of the stages deal with the ionic form transformations, affecting the double electric layer (DEL) ionic force and related electrochemical and electrophysical properties. These influences may affect the sensorial and electroanalytical properties of the sensors [14–17] and may be detected during the theoretical mechanistic investigation of the process.

For this reason, we mechanistically investigate the system's behavior by correspondent and adequate balance differential equation, which will be thereby analyzed by linear stability theory and bifurcation analysis to detect the steady-state stability requirements, like the oscillatory and monotonic instability conditions. Also, the behavior of the system will be compared with that of similar ones [18–21]. The abovementioned statements describe the general aim and specific objectives of this work.

2. Materials and Methods

In an alkaline medium, risperidone is firstly hydrolyzed by either fluorine atom and amide group, yielding the carboxylate ion and phenolic group correspondently. This form thereby reacts with the *in situ* formed trivalent copper sulfohydroxide, which either yields Noxide or phenolizes the aromatic ring and is followed by quinonic compound formation. The polymerization scenario isn't discarded either (Figure 2).

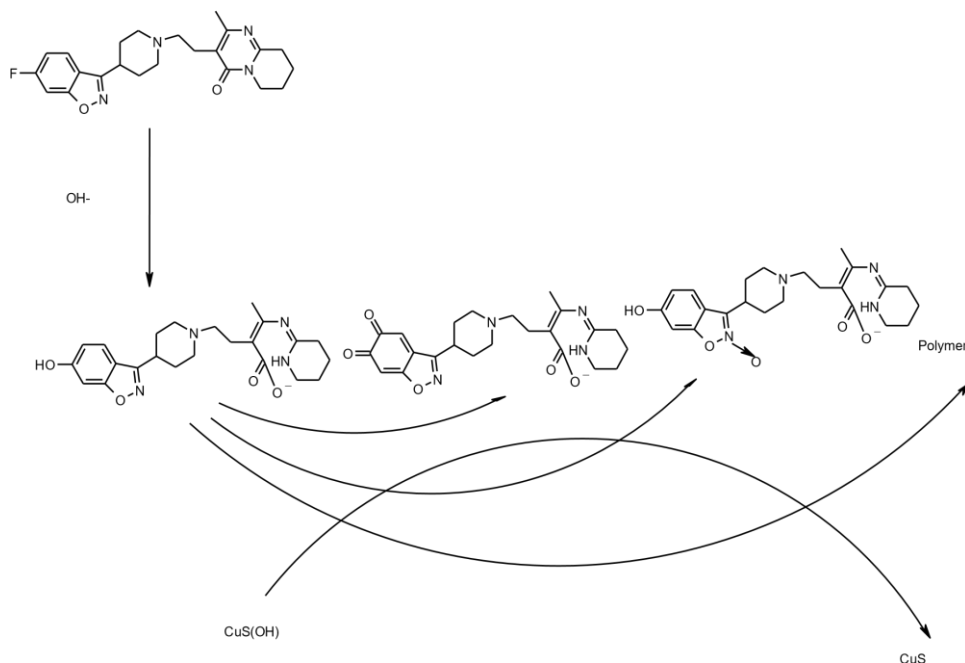


Figure 2. Schematic representation of risperidone electrochemical determination.

For this reason, taking some assumptions [25–28], we describe the potentiostatic behavior of this system by a trivariate balance differential equation-set (1):

$$\begin{cases} \frac{d\rho}{dt} = \frac{2}{\delta} \left(\frac{P}{\delta} (\rho_0 - \rho) - r_h \right) \\ \frac{d\rho^*}{dt} = \frac{2}{\delta} (r_h - r_{r1} - r_{r2} - r_p) \\ \frac{dc}{dt} = \frac{1}{c} (r_{r1} - r_{r2} - r_p - r_o) \end{cases} \quad (1)$$

This is very similar to the pyriproxyfen electrochemical determination described earlier in an alkaline medium.

Herein, ρ stands for the risperidone pre-surface concentration, ρ_0 stands for risperidone bulk concentration, P is its diffusion coefficient, ρ^* is the pre-surface concentration in the pre-surface layer, c is copper sulfide nanoparticles surface coverage degree, C is its maximal surface concentration, and the parameters r stand for the correspondent reaction rates, calculated as (2–6).

$$r_h = r_h \rho \exp(-a\rho) \quad (2)$$

$$r_{r1} = k_1 \rho * (1 - c)^2 \exp(-b\rho *) \quad (3)$$

$$r_{r2} = k_2 \rho * (1 - c)^2 \exp(-b\rho *) \quad (4)$$

$$r_p = k_p \rho *^n (1 - c)^{2n-2} \exp(-b\rho *) \quad (5)$$

$$r_o = k_o c \exp\left(\frac{F\varphi_0}{RT}\right) \quad (6)$$

Herein, the parameters k stand for the correspondent reaction rate constants, a and b are the parameters relating the DEL electrochemical and electrophysical properties with the ionic forms transformations, n is the polymer chain length, F stands for the Faraday number, φ_0 is the zero-charge related DEL potential slope, R is the universal gas constant, and T is the solution absolute temperature.

The ionic exchange and phenolate form transformations highly affect the DEL ionic force, leading to its cyclic changes and resulting in oscillatory behavior. Nonetheless, copper (II) sulfide nanoparticles may serve as an efficient electrode modifier for risperidone electrochemical determination, as shown in the next section.

3. Results and Discussion

To investigate the behavior of the system with the risperidone determination on CuS nanoparticles, we analyze the balance differential equation set (1), considering the algebraic relations (2–6) by means of linear stability theory. The steady-state Jacobian matrix members may be described as:

$$\begin{pmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{pmatrix} \quad (7)$$

Herein:

$$a_{11} = \frac{2}{\delta} \left(-\frac{P}{\delta} - k_h \exp(-\alpha\rho) + \alpha k_h \rho \exp(-\alpha\rho) \right) \quad (8)$$

$$a_{12} = 0 \quad (9)$$

$$a_{13} = 0 \quad (10)$$

$$a_{21} = \frac{2}{\delta} (k_h \exp(-\alpha\rho) - \alpha k_h \rho \exp(-\alpha\rho)) \quad (11)$$

$$a_{22} = \frac{2}{\delta} \left(-k_1(1-c)^2 \exp(-b\rho^*) + bk_1\rho^* (1-c)^2 \exp(-b\rho^*) - k_2(1-c)^2 \exp(-b\rho^*) + bk_2\rho^* (1-c)^2 \exp(-b\rho^*) - nk_p\rho^*{}^{n-1} (1-c)^{2n-2} \exp(-b\rho^*) + bk_p\rho^*{}^n (1-c)^{2n-2} \exp(-b\rho^*) \right) \quad (12)$$

$$a_{23} = \frac{2}{\delta} \left(2k_1\rho^* (1-c) \exp(-b\rho^*) + 2k_2\rho^* (1-c) \exp(-b\rho^*) + (2n-3)k_p\rho^*{}^n (1-c)^{2n-2} \exp(-b\rho^*) \right) \quad (13)$$

$$a_{31} = 0 \quad (14)$$

$$a_{32} = \frac{1}{c} \left(k_1(1-c)^2 \exp(-b\rho^*) - bk_1\rho^* (1-c)^2 \exp(-b\rho^*) + k_2(1-c)^2 \exp(-b\rho^*) - bk_2\rho^* (1-c)^2 \exp(-b\rho^*) + nk_p\rho^*{}^{n-1} (1-c)^{2n-2} \exp(-b\rho^*) - bk_p\rho^*{}^n (1-c)^{2n-2} \exp(-b\rho^*) \right) \quad (15)$$

$$a_{33} = \frac{1}{c} \left(-2k_1\rho^* (1-c) \exp(-b\rho^*) - 2k_2\rho^* (1-c) \exp(-b\rho^*) - (2n-3)k_p\rho^*{}^n (1-c)^{2n-2} \exp(-b\rho^*) - k_o \exp\left(\frac{F\varphi_o}{RT}\right) + jk_o c \exp\left(\frac{F\varphi_o}{RT}\right) \right) \quad (16)$$

From the Jacobian main diagonal elements (9), (12), and (16), it is possible to conclude that the positive callback, necessary for the Hopf bifurcation, describing the oscillatory behavior, is possible, as the mentioned elements possess positive addendums.

In this system, the oscillatory behavior is more probable than in the simplest case, but either way, it is less probable than in the acidic medium. It is caused by two factors against one in the simplest case. Still, the DEL ionic force change factor is only manifested in the hydrolysis reactions, contrarily to other chemical stages. Also, the oscillatory behavior will be caused by the change of DEL and surface ionic force and conductivity in the electrochemical stage. Mathematically, it is manifested by the positivity of the elements $\alpha k_h \rho \exp(-\alpha\rho)$, if $\alpha > 0$, $bk_1\rho^* (1-c)^2 \exp(-b\rho^*)$, $bk_2\rho^* (1-c)^2 \exp(-b\rho^*)$, $bk_p\rho^*{}^n (1-c)^{2n-2} \exp(-b\rho^*)$, if $b > 0$ and $jk_o c \exp\left(\frac{F\varphi_o}{RT}\right) > 0$, if $j > 0$.

The oscillation frequency and amplitude will depend on the background electrolyte composition.

Avoiding the cumbersome expressions during the steady-state stability investigation using the Routh-Hurwitz criterion, we rewrite the Jacobian determinant as (17):

$$\frac{4}{\delta^2 C} \begin{vmatrix} -\kappa - \mathcal{E} & 0 & 0 \\ \mathcal{E} & -\Sigma & P \\ 0 & \Sigma & -P - \Omega \end{vmatrix} \quad (17)$$

And express the stability requisite by opening the straight brackets and applying the $\text{Det}J < 0$ condition, salient from the criterion, as (18):

$$-\Sigma\Omega(\kappa + \mathcal{E}) < 0 \quad (18)$$

The inequation (18) is warranted to be satisfied if the hydrolytic parameter \mathcal{E} and the electrooxidation parameter Ω are positive, which is characteristic of the wide majority of the real systems. Therefore, this inequation describes an efficient diffusion and kinetically controlled electroanalytical system.

Since no side reaction compromising the analyte and(or) modifier stability is realized in this system, the steady-state stability will correspond to the linear dependence between the electrochemical parameter and concentration, providing efficient analytical signal interpretation.

The detection limit is defined by monotonic instability, which depicts the margin between stable, steady states, and unstable states. It is described mathematically by the nullity of the Jacobian determinant, or (19):

$$-\Sigma\Omega(\kappa + \mathcal{E}) < 0 \quad (19)$$

Poly(risperidone) material may also be used for electroanalysis. It may be generally used to detect and immobilize chlorogenic compounds and in the proton-transfer mediation. This possibility may be important for risperidone recovery from pharmaceutical wastewater and will be evaluated in our next works.

4. Conclusions

From the analysis of the system with the electrochemical determination of risperidone over the copper sulfide nanoparticles composite, it is possible to conclude that the electroanalytical process is efficient. Although oscillatory behavior is possible, it is less probable than acidic solutions. As for the electroanalytical process, it is either diffusion or kinetically controlled, and the electroanalytical signal is easy to interpret. The risperidone polymer may be obtained from pharmaceutical wastewater and used in electroanalytical essays.

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Conflicts of Interest

The authors declare no conflict of interest.

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