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Theoretical Description for Firocoxib Cathodic Electrochemical Determination in Meat and Milk

Volodymyr V. Tkach [1,*], Tetiana V. Morozova [2], Sílvio C. de Oliveira [3], Valerii P. Domnich [4], Vira V. Kopiika [4], Yana G. Ivanushko [5], Igor G. Biryuk [5], Tetiana B. Sykyrytska [5], Jarem R. Garcia [6], Necdet Karakoyun [7], Petro I. Yagodynets [1,*], Zholt O. Kormosh [8,*], Karina V. Palamarek [9], Iryna R. Loshenyuk [9], Konon L. Bagrii [9], José Inácio Ferrão da Paiva Martins [10], Inesa M. Khmeliar [11], Lesya O. Kushnir [11], Rostyslav O. Sabadyshyn [11], Dmytro L. Lysytsia [11], Riboba G. Sharipova [12], Sabina Nasirova [12], Markhabo R. Rakhmatova [12], Vazira Z. Jalalova [12], Yulia M. Honchar [13], Alla V. Grekova [14], Ianina F. Burdina [14], Viktoria O. Khrutba [2]

1 Chernivtsi National University, 58000, Kotsyubyns´ky Str. 2, Chernivtsi, Ukraine
2 National Transport University, 02000, Omelianovych-Pavlenko Str. 1, Kyiv, Ukraine
3 Federal University of Mato Grosso do Sul, Av. Sen. Felinto. Müller, 1555, C/P. 549, 79074-460, Campo Grande, MS, Brazil
4 Zaporizhzhia National University, 69600, Zhukovsky Str. 66, Zaporizhzhia, Ukraine
5 Bukovinian State Medical University, 58001, Teatralna Sq., 9, Chernivtsi, Ukraine
6 State University of Ponta Grossa, Av. Gal. Carlos Cavalcanti, 4748, 84030-900, Ponta Grossa, PR, Brazil
7 Yüzüncü Yil University of Van, Bardakçı, 65090, Tuşba/Van, Türkiye
8 Volyn National University, 43000, Voli Ave., 13, Lutsk, Ukraine
9 Chernivtsi Institute of Trade and Economics of Kyiv National University of Trade and Economics, 58001, Central Sq. 6, Chernivtsi, Ukraine
10 Engineering Faculty of the University of Porto, 4200-465, Rua Dr. Roberto Frias, s/n, Porto, Portugal
11 Rivne State Basic Medical Academy, 33000, Mykola Karnaukhov Str., 53, Rivne, Ukraine
12 Abu Ali Ibn Sino Bukhara State Medical Institute, 705018, Navoi Str., 1, Bukhara, Uzbekistan
13 Kyiv National University of Trade and Economics, 02156, Kyoto Str. 21, Kyiv, Ukraine
14 Odesa National Medical University, 65000, Valikhovsky Ln. 2, Odesa, Ukraine
* Correspondence: nightwatcher2401@gmail.com (V.V.T.); ved1988mid@rambler.ru (P.I.Y.); zholt1971@ukr.net (Z.O.K.);

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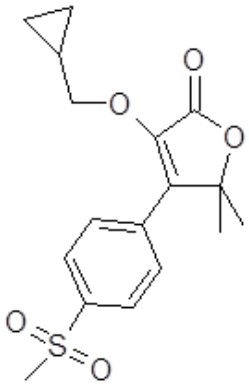
Abstract: In this work, the possibility of firocoxib electrochemical determination in meat and milk has been theoretically described. The electroanalytical process is performed at the cathode, providing an efficient method. The analysis of the corresponding model, using linear stability theory and bifurcation analysis, has confirmed that the conducting polymer can serve as an efficient electrode modifier for the electrochemical determination of firocoxib. As for oscillatory and monotonic intabilities, they will depend on the nature of the monomer used to yield the conducting polymer.

Keywords: firocoxib; food security; veterinary drug; electrochemical sensors; conducting polymers; electrochemical oscillations; stable steady-state.

1. Introduction

Firocoxib (Figure 1) [1–4] is a veterinary anti-inflammatory and analgesic drug that acts as a selective COX inhibitor. It was the first COX inhibitor approved for use in horses (Equioxx) and dogs (Previcox).



feasible.

Figure 1. Firocoxib.

Although its use in human medicine is prohibited, residues of firocoxib and its metabolites may still occur in horse meat and milk products [5–9]. Such products are widely consumed in Turkic countries, including Türkiye, Azerbaijan, and particularly Kazakhstan, Kyrgyzstan, Turkmenistan, and Uzbekistan. In Kastamonu, Türkiye, horse and donkey milk are even used in the preparation of traditional yogurts and cottage cheeses. Consequently, if the animals have been treated with firocoxib, the drug may be present in these meat and dairy products. This makes detecting firocoxib in such matrices an important challenge [10–14], for which electrochemical methods may provide valuable analytical solutions.

Given the drug's molecular structure, cathodic detection appears particularly suitable due to the presence of strongly electron-accepting groups, although anodic approaches are also feasible. In this case, the use of a conducting polymer capable of providing and mediating the electrochemical reduction of firocoxib for analytical purposes as an electrode modifier may make the electroanalytical process more rapid and efficient [15–18]. Moreover, conducting polymers are pH-flexible and can adapt to the pH of the concrete medium (biological liquid or food product).

Therefore, in this work, we describe the electrochemical determination of firocoxib on CP-modified electrodes in milk and meat. In this work, based on the suggestions and analyses of the mechanism and the corresponding mathematical model, we investigate the practical use of the electrochemical process and compare its behavior with that of similar electroanalytical processes [19–21].

2. Materials and Methods

Given that the firocoxib molecule contains highly electron-accepting moieties, we expect the cathodic process to be more suitable for firocoxib determination. Moreover, in mildly acidic media, corresponding to meat and milk, this process will become even more convenient (Figure 2).

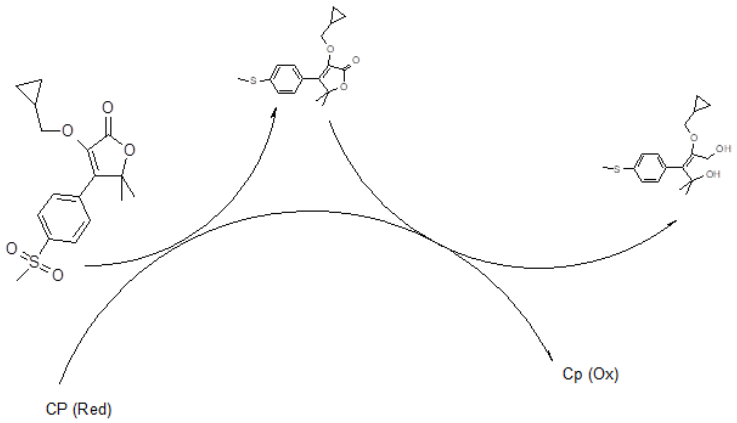


Figure 2. The scheme for firocoxib.

Therefore, considering certain assumptions [19–21], the electroanalytical process will be described by the equation set (1):

$$\begin{cases} \frac{df}{dt} = \frac{2}{\delta}\left(\frac{\Phi}{\delta}(f_0 - f) - r_1\right) \\ \frac{df*}{dt} = \frac{2}{\delta}(r_1 - r_2) \\ \frac{dp}{dt} = \frac{1}{V}(r_1 + r_2 - r_3) \end{cases} \quad (1)$$

Herein, f is firocoxib pre-surface layer concentration, Φ is its diffusion coefficient, f_0 is its bulk concentration, f* is the concentration of the first reduction product, p is the polymer surface coverage degree, P is its maximal surface concentration, and the parameters r are the corresponding reaction rates, calculated as (2 – 4):

$$r_1 = k_1 f(1-p)\exp(ap) \quad (2)$$

$$r_2 = k_2 f*(1-p)\exp(bp) \quad (3)$$

$$r_3 = k_3 p \exp\left(-\frac{nF\varphi_0}{RT}\right) \quad (4)$$

Herein, k denotes the corresponding reaction rate; a and b describe the DEL influence of the polymer transformation; in the case of high ionicity, n is the number of electrons transferred during the elementary act of the electroanalytical process; and F is the Faraday constant. φ_0 is the potential slope, referred to as the zero-charge potential, R is the universal gas constant, and T is the absolute temperature.

Considering that firocoxib isn't highly ionized during the electrochemical determination, the steady-state stability and oscillatory instability will depend highly on the monomer nature. The conducting polymer will be an efficient electrode modifier for firocoxib determination, as shown below.

3. Results and Discussion

Considering the equation set (1), like the algebraic relations (2 – 4), we describe the electrochemical behavior of this system using linear stability theory. The functional Jacobian matrix members may be exposed as (5):

$$\begin{pmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{pmatrix} \quad (5)$$

In which:

$$a_{11} = \frac{2}{\delta}\left(-\frac{\Phi}{\delta} - k_1(1-p)\exp(ap)\right) \quad (6)$$

$$a_{12} = 0 \quad (7)$$

$$a_{13} = \frac{2}{\delta}(k_1 f \exp(ap) - ak_1 f(1-p)\exp(ap)) \quad (8)$$

$$a_{21} = 0 \quad (9)$$

$$a_{22} = \frac{2}{\delta}(-k_2(1-p)\exp(bp)) \quad (10)$$

$$a_{23} = \frac{2}{\delta}(k_2 f * \exp(bp) - bk_2 f * (1-p)\exp(bp)) \quad (11)$$

$$a_{31} = \frac{1}{V}(k_1(1-p)\exp(ap)) \quad (12)$$

$$a_{32} = \frac{1}{V}(k_2 f * (1-p)\exp(bp)) \quad (13)$$

$$a_{33} = \frac{1}{V}\left(-k_1 f \exp(ap) + ak_1 f(1-p)\exp(ap) - k_2 f * \exp(bp) + bk_2 f * (1-p)\exp(bp) - k_3 \exp\left(-\frac{nF\varphi_0}{RT}\right) + jk_3 p \exp\left(-\frac{nF\varphi_0}{RT}\right)\right) \quad (14)$$

Herein, j represents the parameter describing the DEL influence of the electrochemical reduction process.

For example, in [19–21], the *oscillatory behavior* is possible in this process. Moreover, its probability will highly depend on the monomer and polymer ionicity. The more ionic the polymer, the more ionic the oscillatory behavior will become.

Observing the main diagonal elements (6), (10), and (14), we can conclude that, as they contain positive addenda, the positive callback they describe is possible. This callback is necessary for the Hopf bifurcation, corresponding to the oscillatory behavior. These addenda, capable of being positive, are $ak_1 f(1-p)\exp(ap) > 0$, if a>0, $bk_2 f * (1-p)\exp(bp) > 0$, if b>0 and $jk_3 p \exp\left(-\frac{nF\varphi_0}{RT}\right) > 0$, if j>0, but if the positivity of the last element, describing the DEL influences of the electrochemical stage, is more common, [19–21], the positivity of the first two of them, describing the DEL influences of the chemical stages, will be highly dependent on the ionicity of the monomer, chosen to produce conducting polymer. The non-ionicity of the monomer (and the polymer) will reset the parameters a and b to zero, thereby annihilating the corresponding addenda. Therefore, the oscillatory behavior will be caused by one factor for the non-ionic monomer and by three if an ionic monomer is used to yield the conducting polymer.

In the same manner, steady-state stability will also be influenced by the conducting polymer's ionicity. Applying the Routh-Hurwitz criterion and rewriting the Jacobian determinant as:

$$\frac{4}{\delta^2 P}\begin{vmatrix} -\varphi - \Xi & 0 & P \\ 0 & -T & Z \\ \Xi & T & -P - Z - \Omega \end{vmatrix} \quad (15)$$

We obtain the steady-state stability requirement in this system, expressed as (16):

$$\varphi(TP + T\Omega) + \Xi T\Omega > 0 \quad (16)$$

This describes a diffusion- and kinetically controlled process, in which the role of the kinetic factor increases with ionic monomer and decreases with non-ionic monomer. If the parameters a and b aren't nil, the parameters Ξ, T, Π, and Z may become negative, driving the left side of the inequation (16) to less positive values, making it possible for its cross to negative values, as mentioned below. Yet, in the case of a non-ionic monomer, the mentioned parameters will be warranted to be positive, widening the steady-state stability topological zone.

The steady-state stability of this system is reflected in the linear correlation observed between the electrochemical parameter and concentration. Therefore, using a non-ionic, or at

least less ionized, conducting polymer as an electrode modifier in firocoxib determination is recommended. Considering the mildly acidic pH of meat and milk, it is recommended to neutralize this influence with a background electrolyte.

The *detection limit* corresponds to the monotonic instability, in which the stable steady states have a margin of stability over the unstable states. Its condition is Det J = 0 or (17):

$$\varphi(TP + T\Omega) + \Xi T\Omega = 0 \quad (17)$$

As for the anodic route, it is also possible, but strong oxidants might be chosen as electrode modifiers: i) Cobalt oxyhydroxide in the presence of cobalt dioxide; ii) Copper sulfide nanoparticles in pair with trivalent copper; iii) Pentavalent bismuth compounds, created *in situ*.

The electrooxidative electroanalytical process for pirocoxib will be analyzed in our next work.

4. Conclusions

The analysis of the system using CP-assisted cathodic electrochemical determination of firocoxib indicates that the electroanalytical process is efficient. Although oscillatory behavior is more likely with ionic monomers and less likely with non-ionic ones, it does not destabilize the system much in the neutralized medium. As for the electroanalytical process, it is either diffusion or kinetically controlled, and the electroanalytical signal is easy to interpret. The role of the kinetic factor grows with the monomer ionicity.

Author Contributions

Conceptualization, V.V.T., T.V.M., S.C.O.; J.I.F.P.M., Y.G.I., P.I.Y. and K.V.P., methodology, V.V.T., T.V.M., J.I.F.P.M., Y.G.I., P.I.Y., M.V.K.; validation, V.V.T.; T.V.M.; S.C.O.; V.I.D.; V.V.K.; Y.G.I.; I.G.B.; T.B.S.; J.R.G.; N.K.; P.I.Y.; Z.O.K.; K.V.P.; I.R.L; K.L.B.; J.I.F.P.M.; I.M.K.; R.S.; D.L.L.; R. S.; S.N.; M.R.; V. J.; Y. M.H.; A.V.G.; I. F.B. and V. O. K. ; investigation, V.V.T.; T.V.M.; S.C.O.; V.I.D.;.; J.I.F.P.M.; I.M.K.; R.S.; D.L.L.; R. S.; S.N.; M.R.; V. J.; Y. M.H.; A.V.G.; I. F.B. and V. O. K.; resources, V V.V.T.; T.V.M.; S.C.O.; V.I.D.; V.V.K.; Y.G.I.; I.G.B.; T.B.S.; J.R.G.; N.K.; P.I.Y.; Z.O.K.; K.V.P.; I.R.L; K.L.B.; J.I.F.P.M.; I.M.K.; R.S.; D.L.L.; R. S.; S.N.; M.R.; V. J.; Y. M.H.; A.V.G.; I. F.B. and V. O. K..; data curation, V.V.T.; T.V.M.; S.C.O.; V.I.D.; V.V.K.; Y.G.I.; I.G.B.; T.B.S.; J.R.G.; N.K.; P.I.Y.; Z.O.K.; K.V.P.; I.R.L; K.L.B.; J.I.F.P.M.; I.M.K.; R.S.; D.L.L.; R. S.; S.N.; M.R.; V. J.; Y. M.H.; A.V.G.; I. F.B. and V. O. K.. ; writing—original draft preparation, V.V.T.; T.V.M.; S.C.O.; V.I.D.; V.V.K.; Y.G.I.; I.G.B.; T.B.S.; J.R.G.; N.K.; P.I.Y.; Z.O.K.; K.V.P.; I.R.L; K.L.B.; J.I.F.P.M.; I.M.K.; R.S.; D.L.L.; R. S.; S.N.; M.R.; V. J.; Y. M.H.; A.V.G.; I. F.B. and V. O. K.. ; writing—review and editing, V.V.T.; T.V.M.; S.C.O.; V.I.D.; V.V.K.; Y.G.I.; I.G.B.; T.B.S.; J.R.G.; N.K.; P.I.Y.; Z.O.K.; K.V.P.; I.R.L; K.L.B.; J.I.F.P.M.; I.M.K.; R.S.; D.L.L.; R. S.; S.N.; M.R.; V. J.; Y. M.H.; A.V.G.; I. F.B. and V. O. K. .; visualization, V.V.T.; T.V.M.; S.C.O.; V.I.D.; V.V.K.; Y.G.I.; I.G.B.; T.B.S.; J.R.G.; N.K.; P.I.Y.; Z.O.K.; K.V.P.; I.R.L; K.L.B.; J.I.F.P.M.; I.M.K.; R.S.; D.L.L.; R. S.; S.N.; M.R.; V. J.; Y. M.H.; A.V.G.; I. F.B. and V. O. K.; supervision, P.I.Y., Y.G. I., J.R. G., J. I. F. P. M..; project administration, V.V.T.. All authors have read and agreed to the published version of the manuscript.

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Data supporting the findings of this study are available upon reasonable request from the corresponding author.

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Conflicts of Interest

The authors declare no conflict of interest.

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