Electrochemical properties of some 1,2,4-triazole derivatives

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Nitrogen-rich heterocyclic systems, particularly 1,2,4-triazole derivatives, are attractive sources of functionally diverse compounds and promising modifiers for electrochemical sensors. Ionometry, as a branch of potentiometric analysis, focuses on developing highly selective ion-selective electrodes (ISEs) capable of providing direct assessment of ion activity or ionogenic forms of analytes in solution. β-Estradiol is a biologically important steroid hormone; its quantification is relevant for pharmaceutical analysis. Schiff bases as membrane electroactive components represent a viable strategy to enhance sensor selectivity.

The aim of the study was to create and study the electrochemical characteristics of an ISE with a plasticized membrane based on 5-(3-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol with lipophilic ionogenic additives of various nature – tetraoctylammonium bromide (TOABr) and sodium tetraphenylborate ($NaB(C_6H_5)_4$, NaBPh).

Materials and methods. The electroactive Schiff base was synthesized by condensation of 2-hydroxy-5-(phenyldiazenyl)benzaldehyde with 5-(3-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol in n-butanol (2 h reflux, 12 h standing), followed by purification (DMF recrystallization) and structural confirmation by elemental analysis and ^{1}H NMR (DMSO-d_6, 400 MHz). A PVC membrane (0.2 g) was prepared containing 2 wt.% electroactive compound, 0.5 wt.% ionogenic additives (NaBPh or TOABr), polyvinyl chloride (PVC; one-third of the mass), and nitrophenyloctyl ether (two-thirds) as plasticizer, using tetrahydrofuran as the casting solvent. Potentiometric measurements were performed at 20–25 °C (Ezodo PL-700PV) versus an Ag/AgCl reference electrode. Calibration was carried out in the 10^{-2}–10^{-4} M β-estradiol range (1000–10 ppm) with reproducibility control every 2 h.

Results. The use of plasticized PVC membranes and a solid-contact configuration was justified to improve potential stability and minimize drift. The presence of azo and azomethine fragments in the modifier implies a dual-pathway electroanalytical process. A mathematical model incorporating diffusion supply and electrode surface coverage by reduction products was proposed; linear stability analysis using the Routh–Hurwitz criterion indicated a broad parameter region where a stable steady state is attainable, enabling formation of an interpretable analytical signal. The detection limit is associated with monotonic instability, whereas potential oscillatory behavior is expected beyond the analytical working range.

Conclusions. A plasticized PVC-based ISE incorporating a triazole-derived Schiff base and ionogenic additives (NaBPh / TOABr) was proposed for potentiometric β-estradiol determination; theoretical analysis supports its electroanalytical feasibility and controllable steady-state operation.

Keywords: 1,2,4-triazole derivatives, ionometry, ion-selective electrode.

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Електрохімічні властивості деяких похідних 1,2,4-тріазолу

О. А. Бігдан, С. О. Федотов, А. С. Гоцуля

Азотовмісні гетероциклічні системи, зокрема похідні 1,2,4-тріазолу, становлять значний інтерес як джерело функціонально різноманітних сполук і перспективних модифікаторів електрохімічних сенсорів. Іонометрія як складова потенціометричного аналізу орієнтована на створення високоселективних іон-селективних електродів (ІСЕ), здатних забезпечувати пряме оцінювання активності іонів / іоногенних форм аналіту в розчинах. β-Естрадіол – біологічно значущий стероїдний гормон, контроль вмісту якого актуальний для фармацевтичного аналізу; застосування шифових основ як електрод-активних компонентів мембран є перспективним підходом до підвищення селективності сенсорних систем.

Мета роботи – створити та дослідити електрохімічні характеристики ІСЕ з пластифікованою мембраною на основі 5-(3-фторфеніл)-4-аміно-1,2,4-тріазол-3-тіолу з ліпофільними іоногенними добавками різної природи – тетраоктиламоній бромідом (TOABr) і натрій тетрафенілборатом ($NaB(C_6H_5)_4$, NaBPh).

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Матеріали і методи. Електрод-активну шифову основу синтезовано конденсацією 2-гідрокси-5-(фенілдіазеніл)бензальдегіду з 5-(3-фторфеніл)-4-аміно-1,2,4-тріазол-3-тіолом у *н*-бутанолі (нагрівання 2 год, витримування 12 год) з подальшим очищенням (перекристалізація з ДМФ) і підтвердженням будови даними елементного аналізу та ^{1}H ЯМР (DMSO-d_6, 400 МГц). Мембрану на основі полівінілхлориду (ПВХ; 0,2 г) формували з 2 мас.% електрод-активної сполуки, 0,5 мас.% іоногенних добавок (NaBPh або TOABr), ПВХ (1/3 маси) та нітрофенілоктилового етеру (2/3 маси) з використанням тетрагідрофурану як розчинника. Потенціометричні вимірювання здійснили при 20–25 °C (Ezodo PL-700PV) відносно Ag/AgCl; калібрування виконали в діапазоні 10^{-2}–10^{-4} M β-естрадіолу (1000–10 м. ч.) з періодичним контролем відтворюваності (кожні 2 год).

Результати. Обґрунтовано доцільність пластифікованих ПВХ-мембран і конструкції solid-contact для мінімізації дрейфу потенціалу. Встановлено, що наявність у модифікаторі азо- та азометинового фрагментів зумовлює можливість двоканального перебігу електроаналітичного процесу. Запропоновано математичну модель, що враховує дифузійний підвід аналіту й адсорбційне покриття електрода продуктами відновлення; аналіз лінійної стійкості (критерій Рауса–Гурвіца) підтвердив наявність широкої області параметрів зі стабільним стаціонарним режимом, що сприятливий для формування інтерпретованого аналітичного сигналу. Межа виявлення пов’язана з монотонною нестійкістю, а можливі осциляції очікуються за межами робочого діапазону.

Висновки. Запропоновано ІСЕ з пластифікованою ПВХ-мембраною на основі тріазольної шифової основи та іоногенних добавок NaBPh / TOABr для потенціометричного визначення β-естрадіолу. Теоретичні результати підтверджують електроаналітичний потенціал системи та керованість стаціонарного режиму.

Ключові слова: похідні 1,2,4-тріазолу, іонометрія, іонселективний електрод.

Актуальні питання фармацевтичної і медичної науки та практики. 2026. Т. 19, № 2(51). С. 143-150

The need to introduce new highly effective and low-toxic drugs into practice is constantly growing in the modern world. As a result, the creation of new original molecules is an actual task of native pharmaceutical science. Analyzing the literature, it is necessary to note the special role of nitrogen-rich heterocyclic systems, which are widely represented [1,2]. A separate large group of substances belongs to 1,2,4-triazole derivatives, which for many years have attracted scientists of various directions [3,4]. The modern trend remains the possibility of combining 1,2,4-triazole with various pharmacophoric substituents, which can be oriented according to different positions of this heterocycle [5,6].

Ionometry is a modern, constantly developing direction of the potentiometric method of analysis. The main task of the method is the development, study and application of various ion-selective electrodes (ISE), reversible and selective for various cations and anions. Ion-selective electrodes provide direct information about the activity of ions in the solution of the analyzed object and function according to the mechanism of ion transport, and the sufficiently high selectivity of the electrode ensures the permeability of the membrane for one or a limited number of ions due to the introduction of an electrode-active compound [7,8]. Due to the different sizes and shapes of anions, the task of creating selective potentiometric sensors for their determination is very urgent.

A successful solution can be the use of heterocyclic compounds as active components of the membrane, such as 1,2,4-triazoles, 1,3,4-oxadiazoles, metalloporphyrins, porphyrazines, phthalocyanines, etc. [9].

There are many 1,2,4-triazole derivatives that are used as corrosion inhibitors to inhibit the corrosion of steel and copper [7,8]. In some of our publications, we theoretically described the possibility of using 1,2,4-triazole derivatives as electrode active compounds [10,11,12]. Triazoles can be in different tautomeric forms, the influence of such tautomeric forms on electrochemical properties can be significant. The use of 1,2,4-triazole derivatives as an electrode-active component of ISE membranes is a new and promising task [13,14,15].

β-Estradiol is an estrogenic steroid hormone and the main female sex hormone. It is involved in the regulation of the estrous and menstrual female reproductive cycle. Estradiol is responsible for the development of secondary sex characteristics in women, such as breasts, enlarged hips, and the female-associated pattern of fat distribution. It is also important in the development and maintenance of female reproductive tissues such as the breast, uterus, and vagina during puberty, adulthood, and pregnancy. It also has important effects on many other tissues, including bone, fat, skin, liver and brain.

At the moment, some methods of electrochemical determination of steroid hormones have already been developed. Moreover, its chemical composition suggests that it could be determined by electrodes using Schiff bases and their complexes, which are very popular in electroanalysis.

Aim

Thus, the aim of our work was to create and study the electrochemical characteristics of an ion-selective electrode with a plasticized membrane based on 5-(3-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol with lipophilic ionogenic additives of various nature – tetraoctylammonium bromide (TOABr) and sodium tetraphenylborate ($NaB(C_6H_5)_4$, NaBPh).

Materials and methods

5-(3-Fluorophenyl)-4-amino-1,2,4-triazole-3-thiol was synthesized by us earlier and its physicochemical properties were described earlier [14], other reagents, including 2-hydroxy-5-(phenyldiazenyl)benzaldehyde, β-estradiol (E8875-250MG) were purchased from Sigma Aldrich (Germany) and used without further purification. ^{1}H NMR spectra were recorded at Enamine (Kyiv, Ukraine) on a Varian Mercury 400 spectrometer (400 MHz) in DMSO-d_6. Research drug – “Guna-beta-estradiol” drops or. 30 ml each in a bottle cap. (Odesa, Ukraine), was purchased in a retail pharmacy chain.

A mixture of 0.57 g (0.0025 mol) of 2-hydroxy-5-(phenyldiazenyl)benzaldehyde with 0.53 g (0.0025 mol) of

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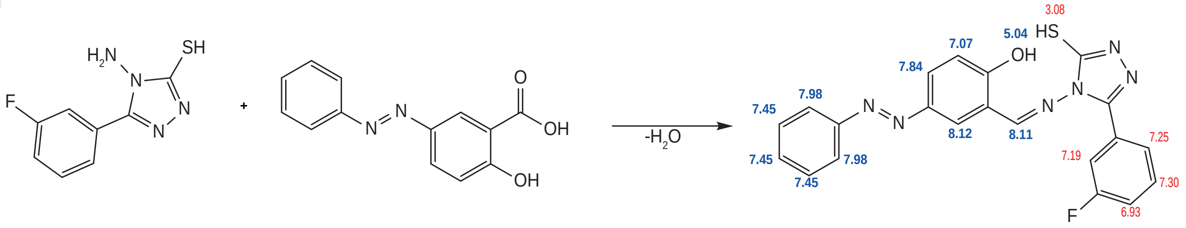

Fig. 1. Obtaining the Schiff base by the condensation method.

5-(3-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol in 20 ml of butan-1-ol is refluxed for 2 hours. The reaction mixture was kept at room temperature for 12 hours *(Fig. 1)*. The precipitate was filtered off and washed with diethyl ether, obtaining 0.43 g of Schiff's base (MP >250 °C, crystallized from DMF). Found: C: 60.56 %, H: 3.43 %; N: 20.04 %; $C_{21}H_{15}FN_6OS$. Calculated: C: 60.42 %, H: 3.38 %; N: 20.13 %.

Results

Liquid membranes are a solution of an electrode-active component in an organic solvent immiscible with water, held by a porous partition. Unlike solid membranes, where active centers are fixed in space by the forces of chemical bonding, in liquid membranes organophilic active components are mobile in the membrane phase.

Close to liquid are plasticized membranes obtained as a result of the introduction of active components into an inert, for example, polyvinyl chloride matrix. Its elasticity and mechanical strength is caused by the presence of plasticizers – esters of phthalic, phosphoric, sebacic and other acids. The use of a plasticized membrane allows you to completely abandon the internal liquid reference electrode. In this case, the platinum, silver or copper wire is covered with a film of polyvinyl chloride containing AK membranes and a plasticizer. The liquid active phase can also be fixed on the graphite surface. ISEs obtained in this way, in the design of which there is no liquid system of the reference electrode, are called solid-contact. An important role in forming the potential of such electrodes is played by the material of the current collector.

The use of a fundamentally new electrode modifier requires a priori mechanistic theoretical analysis of the electroanalytical system. This will help us solve problems such as: instability in the interaction of the electrode with the analyte and its role in the electroanalytical system; the possibility of electrochemical instabilities in similar systems with electrooxidation of various organic molecules, including electrochemical polymerization.

Theoretical research makes it possible to solve the mentioned problems in the development of an ion-selective electrode. The research includes the development and analysis of a mathematical model capable of adequately describing the electroanalytical system. Since the compound contains two electrochemical centers – a diazo group and a "Schiff bond", the electroanalytical process can occur according to two parallel mechanisms using an azo group *(Fig. 2)*, in which "Estr" means an oxidized fragment of β-estradiol or through an azomethine fragment *(Fig. 3)*.

In both cases, the original Schiff base is restored at the electrochemical stage. So, considering the above statements, in order to theoretically describe the behavior of the system, we introduce three variables: c – concentration of estradiol in the pre-surface layer; θ4 is the degree of anode coverage by the reduction product in *Fig. 2*; θ5 is the degree of anode coverage by the reduction product in *Fig. 3*.

To simplify the simulation, let's assume that the reactor is intensively stirred, so the convection flow can be neglected. We also assume that the background electrolyte is in excess, so the migration flow can be neglected. The thickness of the pre-surface layer is assumed to be constant, equal to δ, and the analyte and alkali concentration profile is linear. It can be shown that the behavior of the system will be described by the following tripartite system:

$$\left\{\begin{array}{l} \frac{dc}{dt} = \frac{2}{\delta}\left(\frac{\Delta}{\delta}(c_0 - c) - r_{41} - r_{51}\right) \\ \frac{d\theta_4}{dt} = \frac{1}{G_4}(r_{41} - r_{42}) \\ \frac{d\theta_5}{dt} = \frac{1}{G_5}(r_{51} - r_{52}) \end{array}\right|$$

where c_0 is the molar concentration of estradiol; Δ is the diffusion coefficient; θ4 and θ5 are maximum concentrations of reduction products; r are the rates of the corresponding chemical and electrochemical stages associated with *Fig. 1–3*, which can be described as follows:

$$r_{41} = k_{41}c(1 - \theta_4 - \theta_5)$$

$$r_{51} = k_{51}c(1 - \theta_4 - \theta_5)$$

$$r_{42} = k_{42}\theta_4 exp\left(\frac{2F\varphi_0}{RT}\right)$$

$$r_{52} = k_{52}\theta_5 exp\left(\frac{2F\varphi_0}{RT}\right),$$

where k – are the corresponding rate constants; F – is the Faraday number; φ_0 – is the slope of the potential associated with the potential of zero charge; R – is the universal gas constant; T – is absolute temperature.

Although compared to the simple case, the behavior in this electroanalytical process will be efficient. To investigate the

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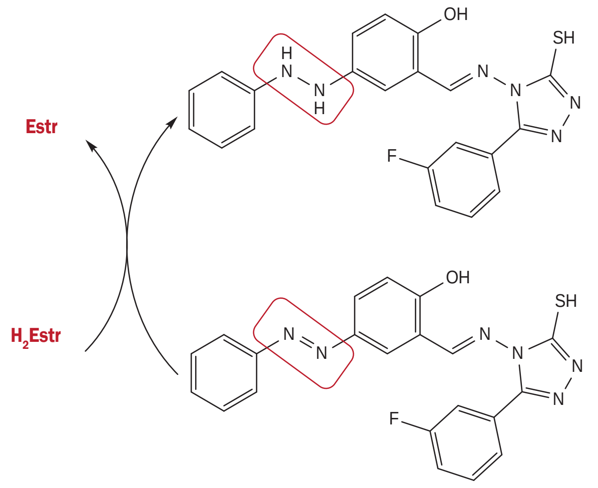

Fig. 2. Scheme of the electroanalytical process involving the azo group.

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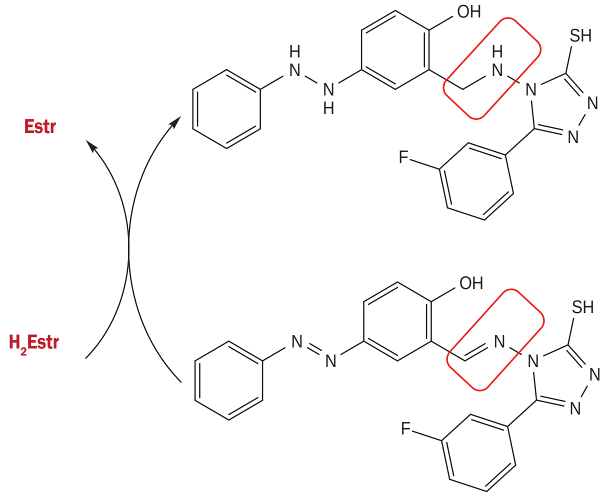

Fig. 3. Scheme of the electroanalytical process involving the azomethine fragment.

behavior of the electroanalytical process for the determination of estradiol using the new Schiff basis, we analyze a set of equations using the theory of linear stability. The members of the Jacobi functional matrix in the steady state will be described as follows:

$$a_{11} = \frac{2}{\delta}\left(-\frac{\Delta}{\delta} - k_{41}(1-\theta_4-\theta_5) - k_{51}c(1-\theta_4-\theta_5)\right)$$

$$a_{12} = \frac{2}{\delta}(k_{41}c + k_{51}c)$$

$$a_{13} = \frac{2}{\delta}(k_{41}c + k_{51}c)$$

$$a_{21} = \frac{1}{G_4}\left(k_{41}(1-\theta_4-\theta_5)\right)$$

Considering the expressions, it can be seen that the main diagonal of the Jacobi matrix contains two elements that can be positive and, as a result, describe a positive callback. This distinguishes this system from similar ones for which only one positive element can be possible.

The stationary stability criterion for dynamic systems is the so-called Raut–Hurwitz criterion. Opening the straight brackets of the determinant, applying to it the inequality resulting from the criterion, and considering that V + W = П, we can obtain the condition for the stability of the stationary mode:

$$-\kappa_1(\Omega W + VK + \Omega K) - \Xi(\Omega W + \Omega K - WK) -$$
$$- \Lambda(VK + \Omega K - \Omega V) < 0,$$

which is guaranteed to be satisfied if the parameters j and v are positive (which is realized in most cases). Therefore, the steady state is stable in a relatively large topological range of parameters, which from an electroanalytical point of view will mean that the system is electroanalytically efficient, since the relationship between the electrochemical parameter (in this case, the current) and the concentration of estradiol is linear, and the analytical signal is easy to interpret. The electroanalytical process in this case is mostly controlled kinetically, being diffusion controlled with the help of relatively large working electrodes.

The detection limit is determined by the realization of the monotonic instability, the corresponding saddle-node bifurcation, which separates stable steady states and unstable states. The condition of its appearance:

$$-\kappa_1(\Omega W + VK + \Omega K) - \Xi(\Omega W + \Omega K - WK) - \\ - \Lambda(VK + \Omega K - \Omega V) = 0.$$

The behavior of this system will be much less dynamic if the Schiff base is introduced into the conducting polymer as part of the macromolecule. Thus, both reduced forms will be present in the reduced macromolecules, which will reduce the number of variables to two.

The theoretical analysis of the electrochemical determination of estradiol using the new Schiff basis allows us to conclude that:

– it can be an excellent electrode modifier for estradiol quantification. The system is electroanalytically efficient because steady-state stability is easy to obtain and maintain;

– the electroanalytical process is mostly reaction-driven, being diffusion-driven if the working electrode is relatively large;

– possible oscillatory behavior in this system caused by the effect of two electrochemical steps on the electric double layer;

– the implementation of oscillatory behavior occurs beyond the limit of detection.

Development and preparation of the electrode. The total weight of the plasticized membrane was 0.2 g, the content of the electrode-active component (2-(((3-(3-fluorophenyl)-5-mercapto-4*H*-1,2,4-triazol-4-yl)imino)methyl)-4-(phenyldiazenyl)phenol) accounted for 2 wt.%, ionic additives – 0.5 wt.%, 1/3 of the total weight was the amount of polyvinyl chloride (PVC) and 2/3 – nitrophenyloctyl ether in the role plasticizer.

The membrane component was dissolved in tetrahydrofuran with constant stirring and left until the solvent completely evaporated. As an ionogenic additive – an ion exchanger, the anionic additive sodium tetraphenylborate, as well as a cationic additive – ionic liquid tetraoctylammonium bromide, were introduced into the membrane composition. The obtained membrane was fixed with the help of a special tip and a union nut to the cylindrical Teflon body of the electrode *(Fig. 4)*. The working surface of the membrane was approximately 0.5 cm^2. Potentiometric measurements were carried out at a temperature of 20–25 °C on an Ezodo PL-700PV laboratory device, relative to a silver chloride electrode. The potentiometric cell had the following form: Ag/AgCl/KCl sat./ads.pH//membrane//vnutr.p-n/AgCl/Ag. The internal solution was a mixture of 10^{-5} mol/l for analyte and 1 mol/l for KCl.

An aliquot (5–50 ml) of a diluted (10^{-3}–10^{-4} mol/l) analyte solution was placed in a potentiometric cell equipped with an ion-selective electrode, a reference electrode, and a magnetic stirrer, and with constant stirring, 10^{-3} (or 10^{-2}) mol/l titrant solution (2-((3-(3-fluorophenyl)-5-mercapto-4*H*-1,2,4-triazol-4-yl)imino)methyl)-4-(phenyldiazenyl)phenol) (in portions of 0.2–0.5 ml continuously with an adjustable speed) with simultaneous automatic recording of the EMF of the cell using a computer. The schematic diagram of the experimental setup for research is shown in *Fig. 5*. The pH of the solutions was measured with a glass pH electrode.

Sequence of work with an experimental ion-selective electrode:

1. With the help of serial dilution from the ready-made reference solution with a concentration of 0.1 M or 1000 ppm, we prepare three reference solutions. Reference solutions of β-estradiol should have concentrations of 10^{-2} M, 10^{-3} M and 10^{-4} M or 1000, 100 and 10 ppm.
2. Pour the most diluted solution (10^{-4} M or 10 ppm) into a beaker with a volume of 150 ml, place it on a magnetic stirrer and start stirring at a constant speed. Having made sure that the EZODO PL-700PV laboratory device is working, we lower the tip of the electrode into the solution. When the readings are set, we record the voltage value displayed on the digital display. We repeat similar manipulations with other concentrations of β-estradiol solution.
3. We construct a graph of the dependence of the voltage values displayed on the digital display (on the linear axis) on the concentration (on the logarithmic axis). It is necessary to check the calibration curve every 2 hours.

Discussion

The discussion of the obtained results indicates that the proposed membrane system constitutes a methodologically sound platform for the potentiometric determination of β-estradiol. The concept of this approach is based on combining the “liquid-like” mobility of the electroactive component with the mechanical stability of a plasticized PVC matrix, thereby ensuring both measurement reproducibility and technological suitability of the sensing element.

A decisive factor governing the functional properties of the membrane is the plasticizer, which generates an organophilic microenvironment of sufficient polarity. This microenvironment lowers the membrane resistance, accelerates the establishment of interfacial equilibria, and consequently improves the stability of potential generation. In contrast to solid membranes with immobilized active sites, plasticized PVC membranes maintain mobility of the electroactive species within the membrane phase, enhancing mass transport and promoting a stable distribution of the analyte at the membrane/solution interface. Moreover, this architecture provides a rationale for transitioning to solid-contact configurations without an internal liquid electrode, where the long-term potential stability may be substantially influenced by the current collector material.

The mechanistic features of the system are dictated by the nature of the modifier, i. e., the Schiff base, which contains two electrochemical centers (an azo group and an azomethine fragment). As a result, the interaction with β-estradiol may proceed via two parallel pathways, leading to the formation of

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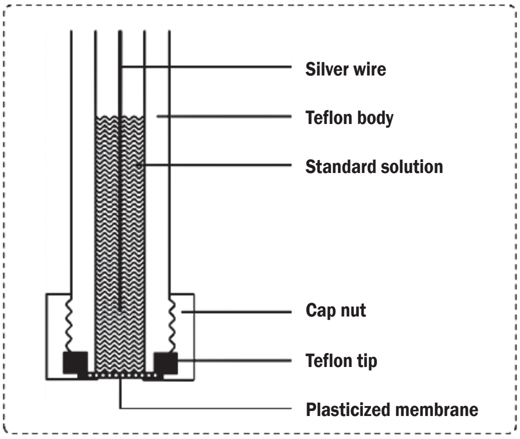

Fig. 4. Scheme of the structure of the liquid electrode.

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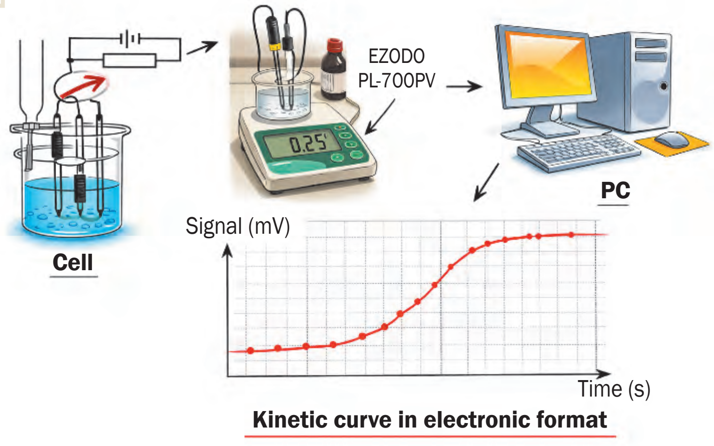

Fig. 5. Hardware design scheme.

two reduced surface forms. Competition between these forms for active electrode sites complicates the process dynamics; therefore, an adequate description requires accounting for both the analyte concentration in the near-surface layer and the surface coverage by the reduction products associated with each pathway.

The theoretical analysis was conducted under assumptions typical for potentiometric measurements: intensive mixing, an excess of supporting electrolyte, a constant diffusion-layer thickness, and a linear concentration profile. These conditions allow the contributions of diffusive analyte supply and the kinetics of surface stages to be separated and, accordingly, enable a formal stability analysis of the stationary regime. The Jacobian-matrix analysis suggests that the system may exhibit nonlinear effects due to the possible occurrence of two positive diagonal elements, which corresponds to positive feedback. In principle, this provides prerequisites for oscillatory regimes associated with the influence of two electrochemical stages on the electrical double layer.

Nevertheless, application of the Routh–Hurwitz criterion demonstrates that the stationary regime remains stable over a broad range of parameters. Therefore, under operating conditions one may expect a linear relationship between the analytical signal (EMF / current) and the β-estradiol concentration, along with an unambiguous interpretation of the results. In general, the process is predominantly reaction–kinetically controlled; however, with increased working surface area or under certain hydrodynamic conditions it may approach diffusion control. Within the framework of the model, the detection limit is associated with a monotonic saddle-node instability separating stable and unstable states, which reflects a loss of uniqueness or stability of the response as critical concentrations or parameters are approached. At the same time, any electrode-stage-induced oscillations are predicted to occur beyond the detection limit and therefore should not interfere with routine measurements within the working concentration range.

The experimental findings are consistent with the theoretical concept through a rational selection of membrane composition. A PVC / plasticizer ratio of 1:2, 2 wt.% of the electroactive component, and 0.5 wt.% of ionic additives correspond to conventional approaches for preparing plasticized PVC membranes. The use of sodium tetraphenylborate as an anion exchanger and tetraoctylammonium bromide as a cationic/ionic-liquid additive is expected to reduce membrane resistance, stabilize interfacial potentials, improve reproducibility, and decrease drift by optimizing charge balance and transport within the membrane phase.

An important procedural requirement is pH control and periodic verification of the calibration characteristic every 2 hours, which is consistent with possible slow membrane-conditioning processes and with the pH sensitivity of estradiol interactions with the membrane microenvironment. Further optimization may include standardization of preconditioning protocols and fine-tuning of membrane additives. A promising direction is also the immobilization of the Schiff base within a conducting polymer, which could reduce the number of dynamic variables and diminish the propensity of the system to instabilities.

Overall, the combined theoretical assessment and practical design choices for electrode fabrication and calibration support the use of the Schiff base as an effective modifier for the quantitative determination of β-estradiol, providing a stable stationary regime and the absence of practically significant oscillatory phenomena within the relevant concentration range.

Conclusions

1. Investigating the electrochemical properties of 1,2,4-triazole derivatives, the expediency of creating an ion-selective electrode based on 5-(3-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol for determining the concentration of β-estradiol.

2. For the first time, a study of the mechanism of electrochemical transformations based on an ion-selective electrode with 5-(3-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol was carried out, and the appearance of an analytical signal was revealed, which determines the possibility of determining the concentration of β-estradiol.

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