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The effect of the supporting electrolyte on the voltammetric determination of the veterinary drug nitroxinil

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ABSTRACT

In this work, a new approach for the determination of the veterinary drug nitroxinil is presented, and its electrochemical behavior is investigated as well as voltammetric determination based on its oxidation signal is proposed. A glassy carbon electrode (GCE) was used as an electrochemical sensor for the determination of this compound, and a square–wave voltammetric (SWV) technique with the optimized parameters was applied for the quantification of nitroxinil. The effect of the supporting electrolytes, such as Britton–Robinson buffer solution (BRBS), citrate buffer solutions (CBS), and hydrochloric acid–potassium chloride buffer solutions (HCl–KClBS), on the SWV determinations of nitroxinil was investigated, and the experiments showed that the supporting electrolyte has a significant effect on the nitroxinil determination. The highest analytical SWV response of nitroxinil was obtained in acidic medium of the investigated supporting electrolytes, *i.e.* in the BRBS at pH 2.0, the CBS at pH 2.0, and the HCl–KClBS at pH 1.8. The corresponding current at *ca.* +1.3 V *vs.* Ag/AgCl/3 mol L^{-1} KCl reference electrode increased linearly with the concentration of nitroxinil within two linear dynamic ranges (LDR) in each supporting electrolyte solution. The lowest limit of detection (LOD) and quantification (LOQ) for nitroxinil were achieved in the BRBS at pH 2.0 (LOD = 0.28 μmol L^{-1} and LOQ = 0.93 μmol L^{-1}). In addition, the analytical parameters obtained from calibration curves indicated the best sensitivity in the BRBS at pH 2.0 (0.124 μA L $μmol^{-1}$). Cyclic voltammetric (CV) experiments showed that the electrode reaction of nitroxinil is irreversible (oxidation peak at *ca.* +1.3 V) and diffusion–controlled in each supporting electrolyte solution.

1. Introduction

Veterinary drugs are extensively used in the prevention and the treatment of animal diseases (bacterial infections) in livestock farming and in the enhancement of the rate of growth and the efficiency of feed [1,2]. The use of these drugs is commonly accepted in veterinary medicine, however, despite all of the advantages, the veterinary drugs could be easily accumulated in animal tissues, and hence, could lead to the presence of residues from these substances in animal food products (meat, milk, and eggs) [3]. In addition, the veterinary drugs could cause risks to human health (toxic effects, hypersensitivity, and allergic reactions) [2,3] or encourage the spread of drug–resistant pathogenic bacterial strains [1,3]. To protect human beings against these effects, the European Union (EU) and other regulatory authorities worldwide have established maximum residue limits (MRLs) for the veterinary drugs in various products including honey, milk or eggs. In addition, several harmful veterinary drugs were banned due to the undesirable effect on the human health [4].

Nitroxinil is a substituted halogenated phenolic veterinary drug (flukicide and nematicide anthelmintic) used on cattle, sheep, and goats [5]. It is used in the prophylaxis and the treatment of adult and late immature stages of liver fluke, a few gastrointestinal roundworm species and myiasis caused by the sheep nasal bot fly [6–9]. Nitroxinil inhibits oxidative phosphorylation in mitochondria what disturbs the ATP production, thus, impairing the parasites motility and presumably also other processes [8]. The European Commission has set MRLs for nitroxinil in bovine and ovine muscle (400 μg kg^{-1}), kidney (400 μg kg^{-1}), fat (200 μg kg^{-1}), liver (20 μg kg^{-1}), and milk (20 μg kg^{-1}) [10].

Available literature data showed that several analytical methods have been developed for the nitroxinil determination, and the main methods for its quantification described in the literature are based on the chromatography [6–8,11–14]. Nitroxinil has been also determined using optical biosensing technique [15]. The electrochemical methods for determination of nitroxinil on dropping mercury electrode (DME) in combination with direct current polarography (DCP) have been described in

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the second half of the 20th century [16–18] and at the beginning of the 21st century [9]. The determination of nitroxinil was also performed using differential pulse adsorptive cathodic stripping voltammetry (DPAdCSV) and square–wave adsorptive cathodic stripping voltammetry (SWAdCSV) with hanging mercury drop electrode (HMDE) as a working electrode, and the nitroxinil quantification was based on the nitro group ($-NO_2$) electroreduction [9]. The limits of detection (LOD) obtained using HMDE are very low (1.3×10^{-8} mol L^{-1} for DPAdCSV and 8.4×10^{-10} mol L^{-1} for SWAdCSV), however, due to the high toxicity of mercury, there is a necessity and need to determine biologically active compounds using an environmentally friendly electrodes [19]. Although nitroxinil has been determined by means of the voltammetric technique (reduction of nitroxinil) [9], a procedure for its voltammetric determination based on its oxidation signal using an environmentally friendly electrode has not been reported up to date. Therefore, the square–wave voltammetric (SWV) procedure for the nitroxinil determination based on the electrooxidation of nitroxinil using the glassy carbon electrode (GCE) is presented for the first time in this paper. In addition, the effect of supporting electrolyte on the SWV determination of nitroxinil is described.

2. Experimental

2.1. Reagents

To obtain a stock solution of nitroxinil (1.0×10^{-3} mol L^{-1}), an appropriate amount of an analytical standard of nitroxinil (VETRANAL®, Merck) was dissolved in acetone (p.a. purity, Avantor, Poland). The prepared solution was constantly kept in a refrigerator when not used. Britton–Robinson buffer solution (BRBS) in the pH range of 2.0–10.0, citrate buffer solutions (CBS) in the pH range of 1.5–4.0, and hydrochloric acid–potassium chloride buffer solutions (HCl–KClBS) in the pH range of 1.0–2.2 were used as supporting electrolytes for purposes of this work. For the preparation of the BRBS, H_3BO_3, H_3PO_4, and CH_3COOH (all components at the concentration of 0.04 mol L^{-1}) were mixed with water, and pH of BRBS was adjusted with NaOH (0.2 mol L^{-1}). The CBS (0.1 mol L^{-1}) were prepared by addition of $Na_3C_6H_5O_7$ (0.1 mol L^{-1}) to HCl (0.1 mol L^{-1}). The HCl–KClBS were prepared by adding HCl (0.2 mol L^{-1}) to KCl (0.2 mol L^{-1}). All reagents used to prepare the above–mentioned supporting electrolyte solutions were purchased in Avantor (Poland), and solutions were prepared in triply distilled water. In order to clean and polish the GCE surface, alumina powder (Al_2O_3, micron sizes of 0.05 μm and 0.3 μm, Buehler, USA) was used.

2.2. Instruments

Electrochemical measurements were undertaken with an EmStat^3 potentiostat (Palm Instruments B.V., the Netherlands) driven by a PSTrace software (version 4.2) in combination with a M164D electrode stand (MTM Anko Instruments, Poland). A standard three–electrode configuration was used, where commercially available glassy carbon electrode (GCE, diameter of 3 mm, Basi®, USA) served as a working electrode, a silver chloride electrode (Ag/AgCl/3 mol L^{-1} KCl, Mineral, Poland) was used as a reference electrode, and a platinum wire (Pt, 99.99%, The Mint of Poland, Warsaw, Poland) was applied as a counter electrode.

All pH values were assessed using Orion Star pH–meter (A111, Thermo Scientific, the Netherlands) equipped with an Orion pH electrode (9157BNMD Triode 3–in–1 pH/ATC Probe, Thermo Scientific, the Netherlands).

2.3. Preparation of working electrode surface

Firstly, the GCE surface was polished with alumina (0.3 μm and 0.05 μm, respectively) on a polishing cloth to obtain a mirror–like appearance. Subsequently, GCE was rinsed thoroughly with triply distilled water. Further, GCE was cleaned in 0.1 mol L^{-1} H_2SO_4 using cyclic voltammetry in the potential range from −0.35 V to +1.5 V at the scan rate of 100 mV s^{-1} (10 scans), and then, the GCE was washed again with deionized water. This procedure was repeated prior to each set of measurements.

2.4. Voltammetric procedures

The evaluation of analytical performance was performed in three different supporting electrolyte solutions with the optimized pH values, *i.e.* in the BRBS at pH 2.0, the CBS at pH 2.0, and the HCl–KClBS at pH 1.8, using a square–wave voltammetry (SWV). The SWV measurements were carried out in the potential range from +0.2 V to +1.45 V with the following optimized parameters: an amplitude of 40 mV, a frequency of 50 Hz, and a step potential of 4 mV. After the optimization of the experimental conditions, a calibration curve was constructed. The consecutive additions of the nitroxinil stock solution (1.0 mmol L^{-1}) were made directly into the voltammetric cell containing 10.0 mL of the supporting electrolyte, the working solutions were mixed for 30 s after each addition of nitroxinil stock solution, and the SW voltammograms were recorded. Each concentration from the calibration curve was measured in quadruplicate. The nitroxinil peak current (I_p) was evaluated from the baseline–corrected SW voltammograms. The results were evaluated in a 95% confidence interval. The limits of detection (LOD) and limits of quantification (LOQ) for nitroxinil were calculated from the calibration curves as 3 and 10 times the standard deviation of the intercept divided by the slope of the calibration curve [20].

The cyclic voltammetry was applied for the investigation of nitroxinil electrochemical behavior on the GCE. The CV study was carried out in the potential range from +0.2 V to +1.45 V at the scan rate range of 10–400 mV s^{-1} in selected supporting electrolyte solutions with the optimized pH values.

3. Results and discussion

3.1. Supporting electrolyte optimization

It is well known that the supporting electrolyte is used to increase the conductivity of the solution, reduce the Ohmic drop effect, eliminate the migration of electroactive species towards the electrodes through electrostatic attractions, and maintain a constant ionic strength and pH [21]. In addition, the type of the supporting electrolyte and its pH can have a major influence on the electrochemical behavior of electroactive organic compound, *i.e.* its peak current, peak potential, as well as peak shape [22,23]. Thus, in this work, various supporting electrolytes with different pH values, such as the BRBS (pH 2.0–10.0), the CBS (pH 1.5–4.0), and the HCl–KClBS (pH 1.0–2.2), were tested. The peak currents of nitroxinil (47.6 μmol L^{-1}) in the abovementioned supporting electrolyte solutions were recorded with the GCE using SWV, and the obtained results are given in Fig. 1. As it can be seen in Fig. 1A, nitroxinil is oxidized in each tested supporting electrolyte. The decrease of the nitroxinil peak height with increasing pH value of BRBS was observed, and the highest SWV response of nitroxinil in the BRBS was achieved in acidic medium (pH 2.0), therefore, the effect of other acidic media on the SWV responses of nitroxinil was also tested. When the CBS were served as the supporting electrolytes, the maximum current response was obtained at pH 2.0. As regards HCl–KClBS, the best analytical response was recorded at pH 1.8. As it can be seen from the Fig. 1B, the nitroxinil peaks were recorded at very similar potentials, and similar current intensities were observed in each selected pH of the supporting electrolytes.

Moreover, the obtained results showed that the peak potentials (E_p) shifted towards less positive values with increasing pH values (Fig. 1C), indicating that protons participate in the electrode reaction [24]. The