

## VOLTAMMETRIC DETERMINATION OF ANTI-MALARIAL DRUG AMODIAQUINE AT A BORON-DOPED DIAMOND ELECTRODE SURFACE IN AN ANIONIC SURFACTANT MEDIA

Sara Kurdo Kamal, Yavuz Yardim

<sup>1</sup> Department of Analytical Chemistry, Faculty of Pharmacy, Van Yuzuncu Yil University, 65080 Van, Turkey  
yavuzyardim2002@yahoo.com

In this study, the electrochemical determination of the amodiaquine (ADQ) drug was evaluated using an electrochemically pretreated boron-doped diamond (BDD) electrode due to the enhanced surface activity. The cyclic voltammogram results of ADQ were given as single reversible and diffusion-controlled peaks at +0.48 V for the oxidation peak and +0.05 V for the reduction peak (vs. Ag/AgCl) in Britton-Robinson (BR) buffer at pH 8.0. The peak potential and current signals of ADQ were evaluated at the surface of the BDD electrode using instrumental parameters to develop a simple method for ADQ detection. Also, the effect of an anionic surfactant, sodium dodecyl sulfate (SDS), on the adsorption applicability of the BDD electrode significantly increased the stripping voltammetric determination of ADQ. Under the optimal conditions chosen and employing square-wave adsorptive stripping voltammetry at the BDD electrode, ADQ was determined at + 0.34 V (vs. Ag/AgCl) at the open-circuit condition in BR buffer at pH 8.0 in the presence of  $2 \cdot 10^{-4}$  mol l<sup>-1</sup> SDS. Furthermore, analytical parameters showed the linear relationship for ADQ determination in the concentration range of 0.1–20.0 µg ml<sup>-1</sup> ( $2.2 \cdot 10^{-7}$  –  $4.3 \cdot 10^{-5}$  mol l<sup>-1</sup>), with a detection limit of 0.03 µg ml<sup>-1</sup> ( $6.5 \cdot 10^{-8}$  mol l<sup>-1</sup>). The proposed approach can be applied to determine ADQ in water samples.

**Keywords:** amodiaquine; antimalarial drug; surfactant; boron-doped diamond electrode; voltammetry

### ВОЛТАМЕТРИСКО ОПРЕДЕЛУВАЊЕ НА АНТИМАЛАРИЧНИОТ ЛЕК АМОДИАКИН СО УПОТРЕБА НА ДИЈАМАНТСКА ЕЛЕКТРОДА ШТО СОДРЖИ ПРИМЕСИ НА БОР НА ЕЛЕКТРОДНАТА ПОВРШИНА МОДИФИКУВАНА СО АНЈОНСКИ СУРФАКТАНТ

Во рамките на оваа студија извршено е електрохемиско определување на антималяричниот лек амодиакин (ADQ) со употреба на електрохемиски третирана дијамантска електрода што содржи примеси на бор (BDD-електрода). Цикличните волтамограми на амодиакин беа преликани во единичен хемиски реверзибилен и дифузиски контролиран процес со пик на +0,48 V во оксидациона насока и со редукциски пик позициониран на +0,05 V (во однос на потенцијалот од референтната Ag/AgCl електрода) во Бритон-Робинсонов пуфер со pH = 8,00. Потенцијалите и струите на пиковите од волтаметрискиот сигнал на ADQ беа евалуирани на површината на BDD-електрода со примена на инструментални параметри што овозможуваат примена на едноставен метод за квантитативно определување на ADQ. Притоа беше утврдено дека присуството на анјонски сурфактант натриум додецил сулфат (SDS) влијае врз адсорпцискиот потенцијал на BDD-електродата, при што присуството на SDS придонесува за значително зголемување на содржината на ADQ со примена на т.н. „стрипинг“ волтаметрија. Со примена на оптимални услови и со употреба на квадратно-бранова адсорптивна стрипинг волтаметрија на BDD-електрода, определувањето на ADQ беше извршено на + 0,34 V при отворено електрично коло во Бритон-Робинсонов пуфер со pH од 8,00 и во присуство на  $2 \cdot 10^{-4}$  mol l<sup>-1</sup> SDS. Аналитичките параметри покажаа линеарна зависност од концентрацијата на ADQ во подрачјето на концентрации на ADQ од 0,1 до 20,0 µg ml<sup>-1</sup> ( $2,2 \cdot 10^{-7}$  –  $4,3 \cdot 10^{-5}$  mol l<sup>-1</sup>), со граница

на детекција од  $0,03 \mu\text{g ml}^{-1}$  ( $6,5 \cdot 10^{-8} \text{ mol l}^{-1}$ ). Предложениот метод може да се употреби за определување на содржината на ADQ во примероци на вода.

**Клучни зборови:** amodiaquine (амодиакин); антimalаричен лек; сурфактанти; дијамантска електрода што содржи примеси на бор; волтаметрија.

## 1. INTRODUCTION

Malaria is one of the oldest and most widespread human infectious African diseases. It is considered one of the most fatal illnesses.<sup>1</sup> Africa accounts for the highest rates of infection and mortality, with nearly 94 % of the total malaria cases and deaths globally, particularly in the sub-Saharan Africa.<sup>2</sup> Every two minutes, a child dies from the disease.<sup>3</sup> To this day, malaria is the leading cause of death in developing countries, infecting, on average, around 220 million people every year.<sup>4</sup> The world witnessed 229 million malaria cases, which resulted in 409,000 deaths, in 2019 alone.<sup>2</sup> This disease is caused by parasitic protozoans in the genus *Plasmodium*, which are transmitted between vertebrate hosts by female mosquitoes in the genus *Anopheles*, which act as carriers.<sup>5</sup> *Plasmodium falciparum* is one of the six infecting species and is responsible for almost 90 % of all malaria infections.<sup>6</sup> This disease is life threatening but can be cured when diagnosis is made at an early stage with the use of the right eradication therapy, based largely on the type of infecting species and severity, age, and general health of the patient.<sup>7</sup>

Amodiaquine (ADQ), known as 4-[(7-chloroquinolin-4-yl)amino]-2-(diethylaminomethyl) phenol, is a Mannich base 4-aminoquinoline anti-malarial pro-drug and is largely converted to the active metabolite desethylamodiaquine. It was FDA approved in 1948. ADQ differs from other types of quinolines such as chloroquine in that it has the same 7-chloroquinoline ring system but has a Mannich base side chain that contains a *p*-hydroxyaniline aromatic ring, which changes the pKa, the lipophilicity, and the flexibility of the side chain.<sup>8</sup> ADQ is therapeutically effective, treating malaria as well as chloroquine-resistant *Plasmodium falciparum* malaria infections. In the past, ADQ was used as a prophylaxis for malarial diseases but was found to be linked with severe cases of acute hepatitis and agranulocytosis associated with long-term use and thus was used as prophylaxis.<sup>7</sup> Therefore, in 2006, the World Health Organization (WHO) recommended artemisinin-based combination therapy (ACT) as global first-line treatments for uncomplicated *P. falciparum* malaria. Five ACTs are recommended by the

WHO, including Artesunate-Amodiaquine which is considered one of the best treatments to improve the efficacy and prevent the development of resistance against Artesunate. This is due to the fact that Artesunate has an extremely rapid effect (in vitro studies show complete growth inhibition of all parasite stages within 2–4 h of exposure) and a short half-life, while the ADQ metabolite has a long half-life of several weeks.<sup>9</sup> The mechanism of action of ADQ is targeting ferriprotoporphyrin (IX), also known as Heme, the toxic byproduct of hemoglobin. In other words, the drug inhibits the glutathione-dependent destruction of ferriprotoporphyrin IX in the malaria parasite, leading to the accumulation of this harmful peptide that compromises the parasite's survival.<sup>7,10</sup>

A number of analytical methods have been applied for the determination of ADQ in various samples, such as high-performance liquid chromatography (HPLC),<sup>11–14</sup> liquid chromatography/mass spectrometry (LC/MS),<sup>15</sup> nuclear magnetic resonance (NMR),<sup>16</sup> fluorimetry,<sup>17</sup> conductometry,<sup>18</sup> spectrophotometry,<sup>19</sup> potentiometry,<sup>20</sup> and capillary electrophoresis.<sup>21–23</sup> It is agreed that the analytical methods provide high precision and sensitivity to the analysis. However, they require long hours, prolonged extraction methods, skilled personnel for operation, and expensive equipment. On the other hand, electroanalytical techniques provide wide application areas for analysis in terms of sensitivity, ease of use, and different alterations to electrodes to obtain suitable chemical selectivity. One of the most commonly used analytical approaches is voltammetry; it can be used as a means of complementary electrochemical analysis or an alternative to the analytical methods of analysis, with advantages of low-cost equipment, little to no prior treatment, rapid analysis, and rapid, reproducible, and sensitive detection of analytes with redox active groups.<sup>24–26</sup>

According to the literature, five studies have been reported on electroanalytical techniques for quantitative analysis of ADQ in which different types of modified electrodes have been used, such as hemin-modified carbon paste electrode (CPE) using square wave voltammetry (SWV),<sup>27</sup> multi-walled carbon nanotubes (MWCNT)-polymethyl orange modified glassy carbon electrode using dif-

ferential pulse voltammetry (DPV),<sup>28</sup> polyvinyl chloride (PVC) membrane sensors using potentiometry,<sup>20</sup> pencil graphite electrode (PGE) using DPV,<sup>29</sup> and poly(calcein)-modified pencil graphite electrode using DPV.<sup>30</sup>

Literature has shown that the use of surfactants enhances the analytical results in the field of electrochemistry and analytical chemistry. In electrochemistry, aside from the main function of surfactants in enhancing solubility (forming micelles), the decrease in liquid surface tension between two immiscible solutions, adsorption of surfactants on electrodes, and micelle aggregates can significantly change the redox potential, amplify the oxidation peak potential, and enhance the electron transfer kinetics process, selectivity, and sensitivity of the electrochemical analysis.<sup>31–33</sup> Numerous studies have been conducted using electroanalytical techniques with boron-doped diamond (BDD) electrodes for the purpose of testing an analyte with its opposite charged surfactant. This aided in the adsorption of the analyte to the surface of the electrode.<sup>34–42</sup>

The selection of the working electrode is essential in the fabrication of an electrochemical sensor because the electrode type significantly affects the sensitivity, cost, stability, and selectivity.<sup>29,43</sup> The BDD electrode is a chemically modified, innovative electrode material that offers a wide range of work in the electrochemistry field. It provides high functioning properties and results when compared with other types of electrodes. This distinctive electrode offers remarkable features, such as wide potential working window (both cathodic and anodic direction), low background current, low signal-to-noise ratio, large surface-to-volume ratio, and reproducible electrochemical analysis.<sup>44–46</sup>

To the best of our knowledge, the BDD electrode has not yet been used in the voltammetric determination of ADQ. The aim of the study is to develop a simple voltammetric procedure for the determination of ADQ using the BDD electrode in the presence of the anionic surfactant SDS and apply it to measure ADQ levels in tap water samples.

## 2. EXPERIMENTAL

### 2.1. Chemicals

ADQ (as dihydrochloride dehydrate salt, ReagentPlus<sup>®</sup> 99.73 %) in its pure form was supplied from ChemScene LLC (USA) and used for analysis without further purification. The stock solution of ADQ of 1.0 mg ml<sup>-1</sup> (adjusted by the supplied form) and all other solutions were prepared by dissolving in deionized water using the

Millipore Milli-Q system (Millipore, resistivity  $\geq$  18.2 M $\Omega$  cm) and stored in cylindrical tubes under refrigeration to prevent degradation while not in use. Britton-Robinson (BR) buffer (0.04 mol l<sup>-1</sup>, pH 2.0–11.0) was prepared by using analytical-grade reagents (boric, acetic, and orthophosphoric acids) and purified water. The stock solution of ADQ was diluted prior to use with a supporting electrolyte at selected pH for the preparation of working solutions in calibration studies and the sample analysis. The surfactants tested were of the anionic type, sodium dodecyl sulfate (SDS, 90%, Merck), non-ionic type (Tween 20), and cationic type, cetyltrimethylammonium bromide (CTAB, 99 %, Sigma). Stock solutions ( $1 \times 10^{-2}$  mol l<sup>-1</sup>) of SDS and Tween 20 were prepared in water, while a water-methanol mixture (90:10, v/v) was used for CTAB. All voltammetric measurements were performed three times under working conditions.

### 2.2. Apparatus and measurements

The comprehensive electrochemical measurements were done using  $\mu$ Autolab type III (Metrohm Autolab B.V., The Netherlands), operated through GPES software (Version 4.9). Cyclic voltammetry (CV) and square-wave voltammetry (SWV) techniques were implemented for the primary studies to investigate the ADQ electrochemical behaviour. Square-wave adsorptive stripping voltammetry (SW-AdSV) was used in the presence of surfactants for the development of an electroanalytical method and quantification of ADQ in the samples. The resultant peak signals in the square wave (SW) voltammograms were corrected using the Savicky-Golay algorithm to smooth out the signals and baseline corrected by a moving average algorithm (peak width of 0.01 V).

All voltammetric measurements were performed in a three-electrode conformation single compartment glass cell (volume of 10 ml) maintained at  $25 \pm 1$  °C. This cell consisted of a commercially available BDD working electrode (with a diameter of 3 mm and boron content of 1000 ppm, Windsor Scientific Ltd., UK), a platinum wire auxiliary electrode, an Ag/AgCl reference electrode (3 mol l<sup>-1</sup> NaCl, model RE-1, BAS, USA). A pH meter (model WTW inoLab pH 720 m) with a combined glass-reference electrode was used for the pH value measurements.

At the beginning of each laboratory day, the surface of the BDD working electrode was pre-treated electrochemically using CV or SWV to ensure sensitivity and repeatable measurements. Anodic activation (+1.8 V for 180 s) followed by cathodic activation (-1.8 V for 180 s) was applied in

0.5 mol l<sup>-1</sup> H<sub>2</sub>SO<sub>4</sub> as recommended in the literature.<sup>33,47,48</sup> Afterwards, a mechanical cleaning step was performed following the two activation steps and also between every individual measurement taken. In this manner, the surface of the electrode was gently rubbed against a smooth damp polishing cloth manually in a circular steady pattern for less than a minute and then rinsed with deionized water.

To begin with, the CV technique was employed to study the electrode reaction mechanism and overall electrochemical behaviour of ADQ. Later, SW-AdSV was used to investigate the most suitable optimization conditions, such as the supporting electrolyte at different pH values, surfactant content, accumulation period, surface pretreatment, interfering compounds, practical application, and calibration for ADQ determination.

For quantification of ADQ using SW-AdSV, a three-electrode setup was immersed in a voltammetric cell containing the required aliquot of the ADQ working solutions and BR buffer at pH 8 in the presence of 2·10<sup>-4</sup> mol l<sup>-1</sup> SDS. The selected pre-concentration potential (open-circuit condition) was applied while the solution was stirred at 500 rpm. Following a fixed rest period (10 s) for the solution to reach equilibrium, anodic scanning was applied from 0.0 to +1.3 V in the alkaline solution. This protocol was utilized for the successive measurement for each analytic parameter. All measurements were performed in triplicates, and the determination of ADQ in the samples was made in accordance with the standard addition method.

The optimized parameters using SW for the sample analysis were as follows: frequency of 50 Hz, pulse amplitude of 50 mV, and step potential of 12 mV.

### 2.3. Sample preparation

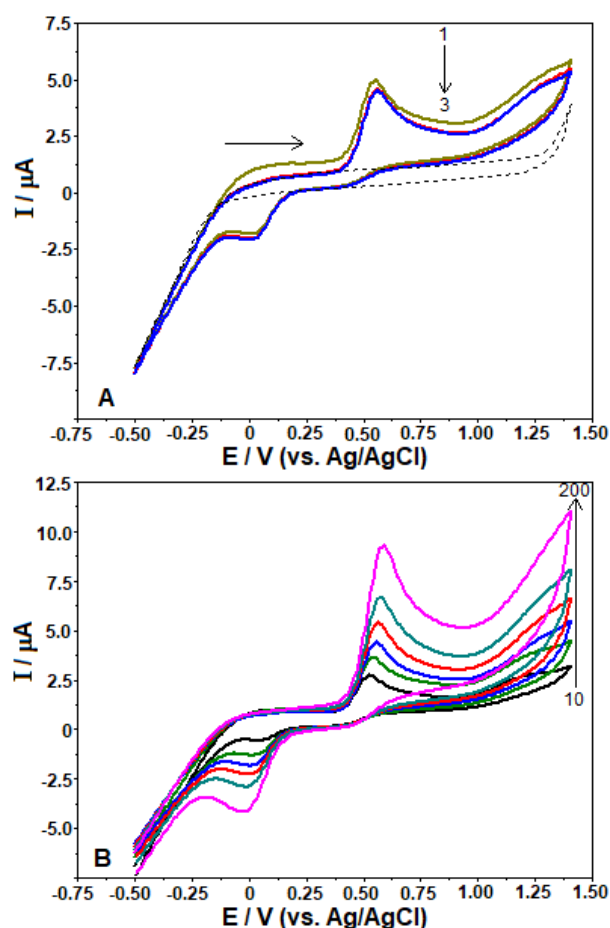
The tap water was sampled from the analytical laboratory (Van Yuzuncu Yil University, Faculty of Pharmacy, Van, Turkey), analyzed with no further pretreatment. The tap water sample (9 ml) was pipetted into a test tube and then spiked with the standard working solution of ADQ (1 ml of 1 mg ml<sup>-1</sup>). After mixing the test tube for 5 min, the sample (0.5 ml) was pipetted into an electrochemical cell and filled up to 10 ml with the selected supporting electrolyte (BR buffer at pH 8 in the presence of 2·10<sup>-4</sup> mol l<sup>-1</sup> SDS). The prepared solution was analyzed by the SW-AdSV technique. Then, respective volumes of the standard solutions of the compound were added to the mixture, and the analysis was undertaken. The ADQ content in the sample was determined by using the standard

addition method in which six standard additions were added. Consequently, SW-AdS voltammograms were recorded after each addition.

## 3. RESULTS AND DISCUSSION

### 3.1. Cyclic voltammetry on the BDD electrode

The CV technique was executed to study the reaction kinetic mechanism and overall electrochemical behavior of ADQ. The cyclic voltammogram showed the result of the redox behavior on the surface of the BDD electrode for 100 µg ml<sup>-1</sup> ADQ in BR buffer pH 8.0 without the presence of the surfactant. As shown in Figure 1A, at a scan rate of 100 mV s<sup>-1</sup>, the cyclic voltammogram recorded three successive readings and showed a quasi-reversible electron transfer. The oxidation system of ADQ displayed a pair of redox peaks, which might be related to the presence of a hydroxyl group.



**Fig. 1.** The repetitive CVs at the scan rate of 100 mV s<sup>-1</sup> for 100 µg ml<sup>-1</sup> amodiaquine (A) and CVs at different scan rates (10, 25, 50, 75, 100, and 200 mV s<sup>-1</sup>) for 100 µg ml<sup>-1</sup> amodiaquine (B) on the BDD electrode in BR buffer at pH 8.0.

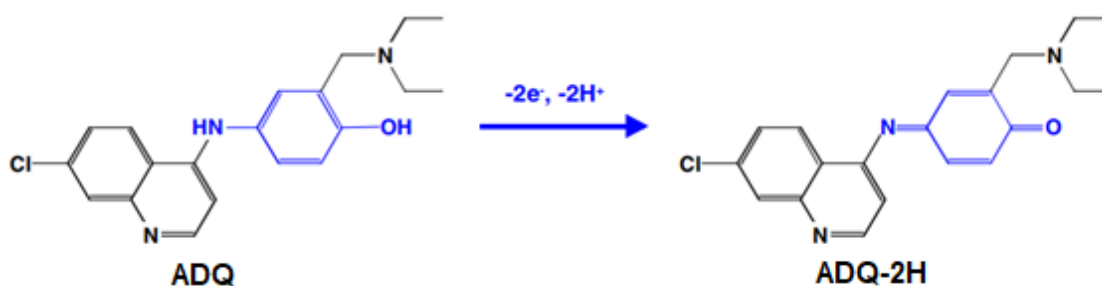
A: Arrow indicates order of the recorded scans; dashed lines represent background current

ADQ is converted by a two-electron oxidation reaction into the quinoneimine form (ADQ-2H), as can be seen in Scheme 1.<sup>49</sup> During the CV anodic scan from  $-0.50$  to  $+1.40$  V, ADQ exhibited a broad oxidation signal at about  $+0.48$  V. Similarly, in the cathodic scan (reverse scan), ADQ exhibited a broad reduction signal at about  $+0.05$  V. No important change was obtained in the second and third cycle of the three successive recordings, which might be due to the diffusion phenomenon that plays a major role on the electrode surface.

The effect of the potential scan rate ( $\nu$ ) on the oxidation peak current ( $i_p$ ) of  $100 \mu\text{g ml}^{-1}$  ADQ in BR buffer pH 8.0 was investigated by CV for the electrochemical determination of the electrode surface kinetics. As shown in Figure 1B, using a scan rate range of 10 to  $200 \text{ mV s}^{-1}$  ( $n = 6$ ), the oxidation peaks of ADQ slightly shifted toward more positive potential values with increased scan rate. Also, the oxidation peak current ( $i_p$ ) showed a linear relationship to the square root of the scan

rate ( $\nu^{1/2}$ ) using the equation  $i_p (\mu\text{A}) = 0.449 \nu^{1/2} (\text{mV s}^{-1}) - 0.043$ ,  $r = 0.995$ . To better understand the ADQ oxidation on the BDD electrode, plots were constructed between the  $\log i_p$  and  $\log \nu$ . In this case, a linear relationship was also achieved as follows:  $\log i_p (\mu\text{A}) = 0.467 \log \nu (\text{mV s}^{-1}) - 0.294$ ,  $r = 0.982$ . Moreover, the reduction peak current ( $i_p$ ) showed a linear relationship to the  $\nu^{1/2}$  as follows:  $i_p (\mu\text{A}) = 0.141 \nu^{1/2} (\text{mV s}^{-1}) + 1.839$ ,  $r = 0.989$ . Similarly, plots were constructed between the  $\log i_p$  and  $\log \nu$  of the reduction signal and a linear relationship was also attained as follows:  $\log i_p (\mu\text{A}) = 0.249 \log \nu (\text{mV s}^{-1}) - 0.147$ ,  $r = 0.943$ .

In conclusion, based on the obtained results, we can theorize that the electro-oxidation of ADQ is mainly controlled by a diffusion-based mechanism on the surface of the BDD electrode. A similar surface behavior has been reported for the voltammetric analysis of ADQ on various carbonaceous electrodes.<sup>28–30</sup>



**Scheme 1.** The proposed mechanism for the oxidation of amodiaquine (ADQ)

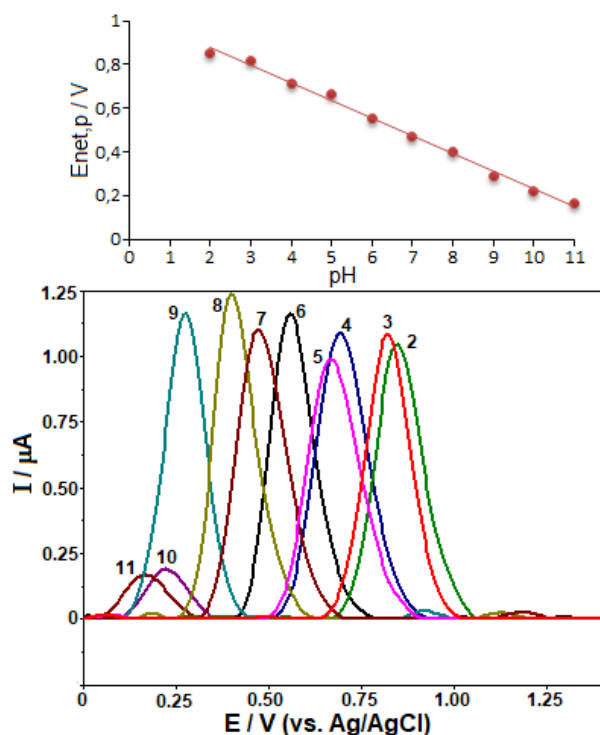
### 3.2. SW voltammetry in the presence and absence of a surfactant

The above CV voltammogram illustrated reversible peaks of ADQ on the BDD electrode in BR buffer at pH 8.0; this result motivated further work to assemble a methodology for ADQ determination by using SWV approach as a pulsed voltammetric technique, more sensitive than CV. Furthermore, the initial investigation was to study the effect of the solution pH and acidity on the electro-oxidation behavior of our analyte as well as its effect on the resultant peak currents using SWV analysis. Furthermore, SW voltammetric measurements were carried out on  $10 \mu\text{g ml}^{-1}$  ADQ in the potential range from 0.0 to  $+1.4$  V, and the pH effect was assessed over a pH range of 2.0 to 11.0 of the BR buffer solution in the absence of surfactants.

ADQ SW voltammograms displayed single anodic peak patterns throughout the BR buffer so-

lutions ranging from pH 2.0 to 11.0, as shown in Figure 2. Additionally, when increasing the pH of the solution, the peak potential shifted to the more negative direction. This suggests that the oxidation of ADQ on the surface of the BDD electrode is pH dependent. Moreover, a significant increase in the peak current was noticed when increasing the solution pH from 2.0 to 4.0. Then, the peak current slightly decreased using pH 5.0. Furthermore, after pH 5, the peak currents began to rise with increasing solution pH until it reached pH 8.0. The ADQ peak currents decreased at pH values from 9.0 to 11.0, and at pH 11.0 having the lowest peak current.

Hawley et al. explained the  $pK_a$  values of ADQ;  $pK_{a1} \sim 8.14$  and  $pK_{a2} \sim 7.08$ , which correspond to the side chain terminal diethylamine nitrogen and the first proton reaction involving the quinoline nucleus, respectively.<sup>50</sup> This confirms that ADQ is a diprotic weak base that works best in a neutral and alkaline pH solution.



**Fig. 2.** SW voltammograms for  $10 \mu\text{g ml}^{-1}$  amodiaquine in BR buffer pH 2.0–11.0 on the BDD electrode. Accumulation parameter 30 s at the open-circuit condition; SWV parameters: frequency, 50 Hz; step potential, 8 mV; pulse amplitude, 30 mV. A: Inset represents the plot of  $E_p$  vs. pH

The correlation between the anodic peak potential and the solution pH value (2.0–11.0) showed a linear relationship between the pH and the  $E_p$  (Fig. 2 inset). This could be understood by using the linear regression equation of  $E_p(\text{V}) = -0.080 \text{ pH} + 1.039$ , with a correlation coefficient of  $r = 0.998$ . The slope 80 mV/pH over the pH value range of 2.0 to 11.0 was found to be close to the Nernstian slope value (59 mV/pH), which, according to literature, suggests the participation of equal ratios of protons and electrons in the rate determining step of electronic transfer as well as electro-oxidation of ADQ at the BDD electrode.<sup>28–30</sup> Correspondingly, the proposed mechanism for the electrochemical oxidation of amodiaquine is presented in Scheme 1.<sup>49</sup>

Moreover, BR buffer at pH 8.0 was selected as the most suitable medium due to obtaining the highest peak current compared to the others. This pH was fixed for all subsequent electrochemical experiments.

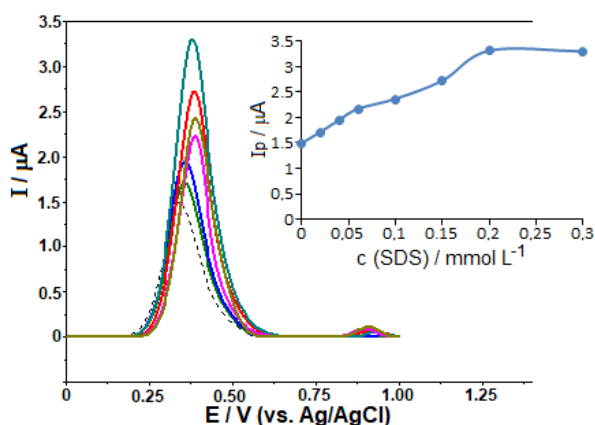
For the next step in assembling a methodology for ADQ determination, we focused on three types of surfactants; SDS (anionic), CTAB (cationic), and Tween 20 (non-ionic) to obtain the highest peak current for the ADQ oxidation process. Therefore, a fixed ADQ concentration of  $15.0 \mu\text{g}$

$\text{ml}^{-1}$ , BR buffer solution at pH 8.0, and  $2 \cdot 10^{-4} \text{ mol l}^{-1}$  of each surfactant was used separately for the purpose of testing the effect of different types of the surfactants (data not shown). First of all, the effect of the surfactants was tested with (accumulation time of 30 s at the open-circuit condition) and without accumulation, and it was determined that under the accumulation parameters, the highest peak current of ADQ was obtained. Thus, subsequent experiments were performed under accumulation. SW-AdS voltammograms of Tween 20 and CTAB containing solutions showed no alteration in the peak current of the ADQ signal. This might be due to electrode fouling that happens in the unfavorable interaction between the fouling agent and the electrode surface.<sup>51</sup> Moreover, the addition of SDS to the solution contributed to the enhancement of the oxidation peak current of ADQ with a slight potential value shift toward a more positive direction.

To increase the sensitivity of the voltammetric method, the effect of the SDS concentration in the electrolyte solution BR buffer (pH 8.0) on the peak current of ADQ was studied using the SW-AdSV technique in the open-circuit condition (30 s). It should be mentioned that in the potential range mentioned, there was no SDS oxidation process involved. For this purpose, the ADQ concentration was fixed at  $15.0 \mu\text{g ml}^{-1}$ , and SDS was added to the BR buffer solution at pH 8.0 within the range of  $2 \cdot 10^{-5} \text{ mol l}^{-1}$  to  $3 \cdot 10^{-4} \text{ mol l}^{-1}$ . As seen in Figure 3, when increasing the SDS concentration in the electrolyte solution, the intensity of the ADQ peak current increased gradually to the highest point up to the SDS concentration of  $2 \cdot 10^{-4} \text{ mol l}^{-1}$ . Furthermore, at higher concentrations of SDS, no significant change occurred towards the peak current (Fig. 3 inset). Concerning the peak potentials, they shifted slightly to the more positive direction with SDS containing solutions. Another observation is the background current signals, which were lower with the addition of SDS in the electrolyte solution.

As known, the critical micelle concentration (CMC) of SDS is approximately  $8.2 \cdot 10^{-3} \text{ mol l}^{-1}$  at 25 °C in the absence of any other additives.<sup>52</sup> This states that SDS does not form micelles at lower concentrations, as it is the case in our study. Nevertheless, in cases where the concentration is lower than the CMC of the surfactant, bilayers or hemimicelles (surface micelles) are formed on the electrode surface that supports one (adsorption at the interface) of its properties.<sup>32,33</sup> To summarize, the SDS concentration that was utilized for further analytical investigation was  $2.0 \cdot 10^{-4} \text{ mol l}^{-1}$ , which

provided the highest peak current intensity and a high-resolution oxidation peak at + 0.38 V. Furthermore, we establish that the BDD electrode in the presence of  $2.0 \cdot 10^{-4}$  mol l<sup>-1</sup> SDS surfactant provided a minimum background current signal as well as sharper and well-defined oxidation peaks for ADQ. In this condition, the ADQ oxidation signals were at about 3.0 times higher compared to the surfactant free solution.



**Fig. 3.** SW stripping voltammograms for 15 µg ml<sup>-1</sup> amodiaquine in BR buffer at pH 8.0 in the presence of different SDS concentrations ( $2.0 \cdot 10^{-5}$ – $3 \cdot 10^{-4}$  mol l<sup>-1</sup>) on the BDD electrode. The signal peak without SDS is represented using dashed lines. Inset: plot of  $i_p$  against the concentration of SDS. The other operating conditions are as indicated in Figure 2

It should be noted that the SDS-containing solutions enhance the adsorption process as well as improve the sensitivity of this compound. The effect of the preconcentration/stripping conditions, such as the preconcentration time ( $t_{acc}$ ) and accumulation potential ( $E_{acc}$ ) for 10 mg ml<sup>-1</sup> ADQ, was assessed under the chosen optimal experimental conditions (data not presented). The effect of the preconcentration time was evaluated against the resultant peak current signal in the range of 0 – 180 s at the open-circuit condition. It was noticed that the peak currents increased until up to 30 s. After reaching this value, it remained constant. Therefore,  $t_{acc}$  of 30 s was selected for all the SW-AdSV experiments. The effect of the accumulation potential ( $E_{acc}$ ) on the oxidation signal of ADQ was examined under open-circuit and different accumulation potentials over the potential range from +0.1 to +0.3 V. It was found that the anodic peak current remained almost unchanged in the whole range, revealing that this parameter had no effect on the detection of ADQ; thus, the open-circuit accumulation was used.

In SWV, the parameters frequency ( $f$ ), pulse amplitude ( $\Delta E_{sw}$ ), and step potential ( $\Delta E_s$ ) were

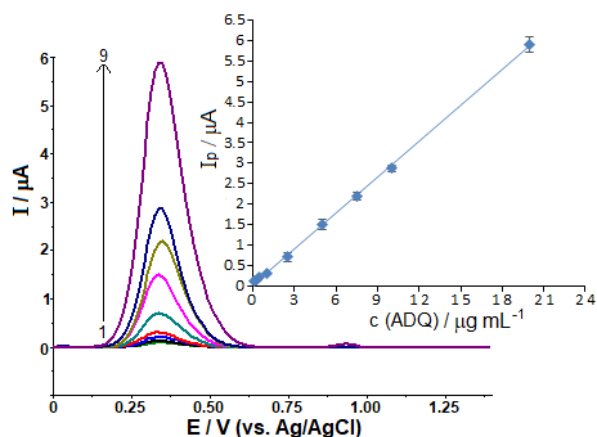
each explored on their own to achieve the highest possible oxidation peak current value and the best possible sensitivity. When one parameter was altered, the other parameters remained stable. The value of  $f$  was calculated across a frequency range from 25 to 125 Hz (assuming  $\Delta E_s$  and  $\Delta E_{sw}$  were held constant at 8 mV and 30 mV, respectively). The measured anodic peak current increased when the  $f$  value was increased. Nevertheless, for  $f$  higher than 50 Hz, a considerable broadening of the peak width was found. When applied to SW voltammetric responses, it has been found that this effect reflects an increase in the analytical selectivity. As an outcome,  $f = 50$  Hz was used for the rest of the study. The impact of  $\Delta E_{sw}$  (remaining parameters:  $\Delta E_s = 8$  mV,  $f = 50$  Hz) on the oxidation peak current intensity was also investigated in the range from 20 to 60 mV. The oxidation peak current values enhanced linearly with respect to  $\Delta E_{sw}$  in the test area. While  $\Delta E_{sw}$  improved to values greater than 50 mV, the SW voltammograms broadened significantly. While  $\Delta E_s$  was also examined from 6 to 14 mV, all the other variables were stable ( $f = 50$  Hz,  $\Delta E_{sw} = 50$  mV), and the observed voltammetric signal increased to 12 mV and then increased slowly from 12 to 14 mV. Nevertheless, the SW curves broadened at  $\Delta E_s$  values greater than 12 mV. Thus,  $\Delta E_s = 12$  mV was selected. Consequently, the best SWV parameters on the BDD electrode were  $f = 50$  Hz;  $\Delta E_s = 12$  mV; and  $\Delta E_{sw} = 50$  mV.

### 3.3. Analytical application of amodiaquine using the BDD electrode in the presence of SDS

With regard to the obtained results mentioned above, the SW-AdSV technique was evaluated for ADQ determination in the surfactant media. Therefore, the calibration was performed on the BDD electrode by plotting the peak current against ADQ concentration using the previously mentioned optimized operating conditions in BR buffer pH 8.0 containing  $2.0 \cdot 10^{-4}$  mol l<sup>-1</sup> SDS solution. Figure 4 displays the SW stripping voltammogram and the obtained calibration curve by subsequent additions of ADQ in the range of 0.1 – 20.0 µg ml<sup>-1</sup> ( $2.2 \cdot 10^{-7}$  –  $4.3 \cdot 10^{-5}$  mol l<sup>-1</sup>). It can be observed that the peak current at a potential of + 0.34 V increased proportionally with increasing ADQ concentration to achieve a linear calibration plot expressed according to the following equation:

$$i_p (\mu\text{A}) = 0.292 C (\mu\text{g ml}^{-1}) + 0.027 \quad (r = 0.999, n = 9),$$

where  $i_p$  is the adsorptive stripping peak current,  $r$  is the correlation coefficient, and  $n$  is the number of experiments.



**Fig. 4.** SW stripping voltammograms for amodiaquine concentrations of (1–9) 0.1, 0.25, 0.5, 1.0, 2.5, 5.0, 7.5, 10.0, and 20.0  $\mu\text{g ml}^{-1}$  in BR buffer at pH 8.0 containing  $2 \cdot 10^{-4} \text{ mol l}^{-1}$  SDS. Accumulation parameter 30 s at the open circuit condition; SWV parameters: frequency, 50 Hz; step potential, 12 mV; pulse amplitude, 50 mV. Inset shows the corresponding calibration plot of current vs. concentration of amodiaquine

The sensitivity of the proposed methodology was evaluated using the limits of detection (LOD) and quantitation (LOQ) values. These two factors were calculated using the following equations:

**Table 1**

*Comparison of the analytical performance of the proposed approach with the other previously reported electrochemical ADQ sensors in literature*

Electrode	Linearity range ( $\text{mol l}^{-1}$ )	LOD ( $\text{mol l}^{-1}$ )	Ref.
PVC membrane sensors	$3.2 \times 10^{-6} - 2.0 \times 10^{-2}$	–	20
Hemin-based electrode	$1.9 \times 10^{-5} - 1.0 \times 10^{-4}$	$7.04 \times 10^{-6}$	27
MWCNT/PMO/GCE	$1.0 \times 10^{-7} - 3.5 \times 10^{-6}$	$8.90 \times 10^{-8}$	28
PGE	$1.0 \times 10^{-9} - 2.0 \times 10^{-7}$	$3.0 \times 10^{-4}$	29
Poly(CCN)/PGE	$5.0 \times 10^{-7} - 2.5 \times 10^{-5}$	$1.6 \times 10^{-7}$	30
BDD (in the presence of SDS)	$2.2 \times 10^{-7} - 4.3 \times 10^{-5}$	$6.5 \times 10^{-8}$	This work

PVC: poly (vinyl chloride); MWCNT: multi-walled carbon nanotube; PMO: polymethyl orange; GCE: glassy carbon electrode; PGE: pencil graphite electrode; Poly (CCN)/PGE: poly(calcein)-modified pencil graphite electrode; BDD, boron-doped diamond; SDS, sodium dodecyl sulfate

To determine the precision of the developed method, the intra-day (ten replicates) as well as inter-day (three days) evaluation by repetitive measurements of  $0.1 \mu\text{g ml}^{-1}$  ADQ in BR buffer pH 8.0 containing SDS was examined under similar conditions. The relative standard deviation (RSD) values were found to be 5.39 % and 6.26 %, respectively. These data suggested that the BDD is a suitable electrode material for the determination of the ADQ drug. It showed repeatable results, indicating the electrode's stability and sensitivity for ADQ analysis in real samples.

$$\text{LOD} = 3.3 s/m; \quad \text{LOQ} = 10 s/m,$$

where  $s$  is the standard deviation of the peak current (10 measurements) of the lowest level of concentration of the calibration curve and  $m$  is the slope of the related calibration equation. LOD and LOQ were found to be  $0.03 \mu\text{g ml}^{-1}$  ( $6.5 \cdot 10^{-8} \text{ mol l}^{-1}$ ) and  $0.1 \mu\text{g ml}^{-1}$  ( $2.2 \cdot 10^{-7} \text{ mol l}^{-1}$ ), respectively.

A comparison of the related analytical performance and parameters of the present method and methods reported in literature for voltammetric determination of ADQ using various electrodes is presented in Table 1. As a result, we can conclude from the obtained data that the present voltammetric method displays the highest sensitivity (obtained from LOD result) compared to the previous electrochemical analysis methods for ADQ determination, although different techniques and modified electrodes were used. Also, the use of the BDD electrode in the presence of the surfactant provides us with a wide linearity concentration range for ADQ analysis showing advantageous analytical parameters.

It should be mentioned that the presence of electroactive species may interfere with the signal of the tested drug in the environmental samples. The selectivity of ADQ determination on the BDD electrode was evaluated based on the presence of several ions mostly present in water samples by monitoring the change in the peak current of ADQ when these interfering compounds were added to  $1 \mu\text{g ml}^{-1}$  ( $2.2 \cdot 10^{-6} \text{ mol l}^{-1}$ ) ADQ at the concentration ratios of 1:1, 1:10, and 1:100 (ADQ: interfering compound) under the same optimized experimental conditions. The tolerance limit was set to a concentration that

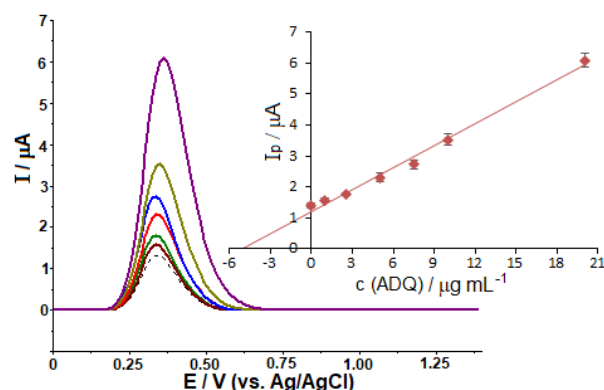


produced an average error of  $\pm 5\%$  in the oxidation peak current of ADQ. The results revealed that the effect of 100-fold excess the cations and anions ( $K^+$ ,  $Na^+$ ,  $Mg^{2+}$ ,  $Ca^{2+}$ ,  $Cu^{2+}$ ,  $Fe^{3+}$ ,  $Al^{3+}$ ,  $Cl^-$ ,  $SO_4^{2-}$ ,  $NO_3^-$ ,  $PO_4^{3-}$ ) concentrations had no meaningful influence on the oxidation peak current of ADQ. The results show that the proposed method presents good selectivity and offers the possibility for its applicability to the water samples.

Lastly, the practical applicability of the developed approach was tested by measuring ADQ in tap water samples. The same previous optimization conditions with the selected pH and surfactant were used. For tap water application, 0.5 ml of tap water was added to 10 ml of the sample solution in the voltammetric cell with the addition of ADQ using the standard addition method of concentrations ranging from 1 to 20  $\mu\text{g mL}^{-1}$ .

Figure 5 displays the representative stripping voltammograms for the analysis of tap water (with spiked concentrations of 5.0  $\mu\text{g/mL}$  in the voltammetric cell). As the result shows, an oxidation peak was observed at +0.35 V. Also, the intensity of the peak increased proportionally with increasing concentration of ADQ by using the standard addition method of six measurements (as shown in the inset of Fig. 5), resulting in a linear calibration plot:  $i_p$  ( $\mu\text{A}$ ) = 0.236 C ( $\mu\text{g mL}^{-1}$ ) + 1.215 ( $r = 0.990$ ). This

electrochemical analysis using the developed approach for ADQ determination suggests satisfactory results in terms of the recovery percentage in tap water and relative standard deviation (RSD) value. As shown in Table 2, good recovery as well as RSD values demonstrate the potential application of this proposed method for routine and/or environmental analyses for direct determination of ADQ in complex real environmental samples.



**Figure 5.** SW stripping voltammograms for ADQ in tap water (dashed line) and after standard additions of 1.0, 2.5, 5.0, 7.5, 10.0, and 20.0  $\mu\text{g mL}^{-1}$  amodiaquine in BR buffer at pH 8.0 containing  $2 \cdot 10^{-4} \text{ mol l}^{-1}$  SDS on the BDD electrode.

The other operating conditions are as indicated in Figure 4

**Table 2**

*Analysis of tap water samples spiked with ADQ standard solutions using the proposed voltammetric method*

Added <sup>a</sup> ( $\mu\text{g mL}^{-1}$ )	Expected <sup>a</sup> ( $\mu\text{g mL}^{-1}$ )	Found <sup>a,b</sup> ( $\mu\text{g mL}^{-1}$ )	Recovery (%) $\pm$ RSD (%)
0	5.00	5.14	102.8 $\pm$ 3.48
1.0	6.00	6.48	108.0 $\pm$ 4.22
2.5	7.50	6.93	92.4 $\pm$ 3.87
5.0	10.00	9.48	94.8 $\pm$ 3.64

<sup>a</sup> Concentration in the measured solution.

<sup>b</sup> Average of three replicate measurements.

#### 4. CONCLUSION

The electrochemical analysis of ADQ in the existing literature is based on the application of the modified or non-modified form of carbonaceous electrodes. In this study, electrochemical determination of ADQ was evaluated by using a non-modified BDD electrode with the use of the SW-AdSV technique for the development of a simple electroanalytical method for ADQ determination in tap water samples. The results showed one quasi-

reversible and diffusion-controlled anodic peak of ADQ using CV at a positive potential of about +0.48 V and a cathodic peak at +0.05 V in BR pH 8.0 as the supporting electrolyte. Also, analytical parameters evaluated showed high sensitivity with a LOD of  $6.5 \cdot 10^{-8} \text{ mol l}^{-1}$  and good reproducibility (RSD of 5.39 %). The results obtained from this study can provide vital information about the behavior and electroanalytical application method of ADQ in the presence of a surfactant using a BDD electrode.

**Conflict of interest:** On behalf of all authors, the corresponding author states that there is no conflict of interest.

## REFERENCES

- (1) Kwiatkowski, D. P., How malaria has affected the human genome and what human genetics can teach us about malaria. *Am. J. Hum. Genet.* **2005**, *77*, 171–192. <https://doi.org/10.1086/432519>.
- (2) Al-Awadhi, M.; Ahmad, S.; Iqbal, J., Current status and the epidemiology of malaria in the Middle East Region and beyond. *Microorganisms* **2021**, *9*, 338. <https://doi.org/10.3390/microorganisms9020338>.
- (3) Cibulskis, R. E.; Alonso, P.; Aponte, J.; Aregawi, M.; Barrette, A.; Bergeron, L.; Fergus, C. A.; Knox, T.; Lynch, M.; Patouillard, E.; Schwarte, S., Malaria: global progress 2000–2015 and future challenges. *Infect. Dis. Poverty* **2016**, *5*, 1–8. <https://doi.org/10.1186/s40249-016-0151-8>.
- (4) World Health Organization, *World health statistics 2018: monitoring health for the SDGs, sustainable development goals*, WHO, 2018.
- (5) Baton, L. A.; Ranford-Cartwright, L. C., Spreading the seeds of million-murdering death: metamorphoses of malaria in the mosquito. *Trends Parasitol.* **2005**, *21*, 573–580. <https://doi.org/10.1016/j.pt.2005.09.012>
- (6) Ashley, E. A.; Phyto, A. P., Drugs in development for malaria. *Drugs* **2018**, *78*, 861–879. <https://doi.org/10.1007/s40265-018-0911-9>.
- (7) Turkson, B. K.; Agyemang, A. O.; Nkrumah, D.; Nketia, R. I.; Baidoo, M. F.; Mensah, M. L., Treatment of malaria infection and drug resistance. In: *Plasmodium Species and Drug Resistance. IntechOpen*, **2021**. <http://dx.doi.org/10.5772/intechopen.98373>.
- (8) Scholar, E., Amodiaquine. *xPharm: The Comprehensive Pharmacology Reference* **2007**, 1–4. <https://doi.org/10.1016/b978-008055232-3.61219-x>
- (9) Fitoussi, S.; Thang, C.; Lesauvage, E.; Barré, J.; Charon, B.; Filali-Ansary, A.; Lameyre, V., Bioavailability of a co-formulated combination of Amodiaquine and Artesunate under fed and fasted conditions. *Arzneimittelforschung* **2009**, *59*, 370–376. <https://doi.org/10.1055/s-0031-1296410>
- (10) Yeiby, W. G., *Green Chemical Synthesis of Amodiaquine*. Purification and Cocrystal Formation Studies of Piperine with HIV-1 Integrase Inhibitor: Dolutegravir, PhD diss., Howard University (2020).
- (11) Lai, C. S.; Nair, N. K.; Muniandy, A.; Mansor, S. M.; Olliaro, P. L.; Navaratnam, V., Validation of high-performance liquid chromatography-electrochemical detection methods with simultaneous extraction procedure for the determination of artesunate, dihydroartemisinin, amodiaquine and desethylamodiaquine in human plasma for application in clinical pharmacological studies of artesunate–amodiaquine drug combination. *J. Chromatogr. B* **2009**, *877*, 558–562. <https://doi.org/10.1016/j.jchromb.2008.12.037>
- (12) Mount, D. L.; Patchen, L. C.; Nguyen-Dinh, P.; Barber, A. M.; Schwartz, F. C. Churchill, Sensitive analysis of blood for amodiaquine and three metabolites by high-performance liquid chromatography with electrochemical detection. *J. Chromatogr. B. Biomed. Sci. Appl.* **1986**, *383*, 375–386. [https://doi.org/10.1016/S0378-4347\(00\)83483-0](https://doi.org/10.1016/S0378-4347(00)83483-0)
- (13) Le Vaillant, Y.; Brenier, C.; Grange, Y.; Nicolas, A.; Bonnet, P. A.; Massing-Bias, L. R.; Rakotomanga, P.; Koumaré, B.; Mahly, A.; Absi, M.; Ciss, M., Simultaneous determination of artesunate and amodiaquine in fixed-dose combination by a RP-HPLC method with double UV detection: implementation in interlaboratory study involving seven African National Quality Control Laboratories. *Chromatographia* **2012**, *75*, 617–628. <https://doi.org/10.1007/s10337-012-2241-5>
- (14) Sanghi, S. K.; Verma, A.; Verma, K. K., Determination of amodiaquine in pharmaceuticals by reaction with periodate and spectrophotometry or by high-performance liquid chromatography. *Anal.* **1990**, *115*, 333–335. <https://doi.org/10.1039/AN9901500333>
- (15) Lohmann, W.; Karst, U., Generation and identification of reactive metabolites by electrochemistry and immobilized enzymes coupled on-line to liquid chromatography/mass spectrometry. *Anal. Chem.* **2007**, *79*, 6831–6839. <https://doi.org/10.1021/ac071100r>
- (16) Johansson, T.; Jurva, U.; Grönberg, G.; Weidolf, L.; Masimirembwa, C., Novel metabolites of amodiaquine formed by CYP1A1 and CYP1B1: structure elucidation using electrochemistry, mass spectrometry, and NMR. *Drug Metab. Dispos.* **2009**, *37*, 571–579. <https://doi.org/10.1124/dmd.108.025171>
- (17) Ibrahim, F. A.; Belal, F.; El-Brashy, A., Fluorometric determination of some aminoquinoline antimalarials using eosin. *Microchem. J.* **1989**, *39*, 65–70. [https://doi.org/10.1016/0026-265X\(89\)90010-6](https://doi.org/10.1016/0026-265X(89)90010-6)
- (18) Amin, A. S.; Issa, Y. M., Conductometric and indirect AAS determination of antimalarials. *J. Pharm. Biomed. Anal.* **2003**, *31*, 785–794. [https://doi.org/10.1016/S0731-7085\(02\)00334-5](https://doi.org/10.1016/S0731-7085(02)00334-5).
- (19) Ansari, M. T.; Ansari, T. M.; Raza, A.; Ashraf, M.; Yar, Y., Spectrophotometric determination of amodiaquine and sulfadoxine in pharmaceutical preparations. *Chem. Anal.* **2008**, *53*, 305.
- (20) Malongo, T. K.; Blankert, B.; Kambu, O.; Amighi, K.; Nsangu, J.; Kauffmann, J. M., Amodiaquine polymeric membrane electrode. *J. Pharm. Biomed. Anal.* **2006**, *41*, 70–76. <https://doi.org/10.1016/j.jpba.2005.10.014>
- (21) Mufusama, J. P.; Hoellein, L.; Feineis, D.; Holzgrabe, U.; Bringmann, G., Capillary zone electrophoresis for the determination of amodiaquine and three of its synthetic impurities in pharmaceutical formulations. *Electrophor.* **2018**, *39*, 2530–2539. <https://doi.org/10.1002/elps.201800170>
- (22) Amin, N.; Blanchin, M. D.; Aké, M.; Montels, J.; Fabre, H., Capillary electrophoresis for the assay of fixed-dose combination tablets of artesunate and amodiaquine. *Mal. J.* **2012**, *11*, 1–7. <https://doi.org/10.1186/1475-2875-11-149>.
- (23) Müller, D.; Blaschke, G., Enantioselective assay of chloroquine and its main metabolite desethylchloroquine in human plasma by capillary electrophoresis. *J. Chromatogr. Sci.* **2000**, *38*, 435–440. <https://doi.org/10.1093/chromsci/38.10.435>.

- (24) Mirceski, V.; Gulaboski, R., Recent achievements in square-wave voltammetry (a review). *Maced. J. Chem. Chem. Eng.* **2014**, *33*, 1–12. <http://dx.doi.org/10.20450/mjccce.2014.515>
- (25) Gulaboski, R.; Mirceski, V., Application of voltammetry in biomedicine – Recent achievements in enzymatic voltammetry. *Maced. J. Chem. Chem. Eng.* **2020**, *39*, 1–14. <http://dx.doi.org/10.20450/mjccce.2020.2152>
- (26) Molina, A.; Gonzalez, J., *Pulse Voltammetry in Physical Electrochemistry and Electroanalysis*, Springer, 2016. <https://doi.org/10.1007/978-3-319-21251-7>
- (27) Valente, C. O.; Garcia, C. A.; Alves, J. P.; Zanoni, M. V.; Stradiotto, N. R.; Arguelho, M. L., Electrochemical determination of antimalarial drug amodiaquine in maternal milk using a hemin-based electrode. *ECS Trans.* **2012**, *43*, 297. <https://doi.org/10.1149/1.4704970>
- (28) Chiwunze, T. E.; Palakollu, V. N.; Gill, A. A.; Kayamba, F.; Thapliyal, N. B.; Karpoomath, R., A highly dispersed multi-walled carbon nanotubes and poly(methyl orange) based electrochemical sensor for the determination of an anti-malarial drug: Amodiaquine. *Mater. Sci. Eng. C* **2019**, *97*, 285–292. <https://doi.org/10.1016/j.msec.2018.12.018>
- (29) Karakaya, S.; Kartal, B.; Dilgin, Y., Ultrasensitive voltammetric detection of an antimalarial drug (amodiaquine) at a disposable and low-cost electrode. *Monatsh. Chem.-Chem. Mont.* **2020**, *151*, 1019–1026. <https://doi.org/10.1007/s00706-020-02637-y>
- (30) Karakaya, S.; Kartal, B.; Dilgin, Y., Development and application of a sensitive, disposable and low-cost electrochemical sensing platform for an antimalarial drug: Amodiaquine based on poly(calcein)-modified pencil graphite electrode. *Int. J. Environ. Anal. Chem.* **2020**, *1–14*. <https://doi.org/10.1080/03067319.2020.1791332>
- (31) Unal, D. N.; Yıldırım, S.; Kurbanoglu, S.; Uslu, B., Current trends and roles of surfactants for chromatographic and electrochemical sensing. *Trends Analyt. Chem.* **2021**, *144*, 116418. <https://doi.org/10.1016/j.trac.2021.116418>
- (32) Vittal, R.; Gomathi, H.; Kim, K. J., Beneficial role of surfactants in electrochemistry and in the modification of electrodes. *Adv. Colloid Interface Sci.* **2006**, *119*, 55–68. <https://doi.org/10.1016/j.cis.2005.09.004>
- (33) Ali, H. S.; Barzani, H. A.; Yardım, Y.; Şentürk, Z., First electrochemical study of a potent antifungal drug caspofungin: Application to its enhanced voltammetric sensing based on the performance of boron-doped diamond electrode in CTAB-mediated measurements. *Diam. Relat. Mater.* **2022**, *125*, 109031. <https://doi.org/10.1016/j.diamond.2022.109031>
- (34) Shrivastav, R.; Satsangee, S. P.; Jain, R., Effect of surfactants on the voltammetric response and determination of an antihypertensive drug phentolamine at boron doped diamond electrode. *ECS Trans.* **2013**, *50*, 23. <https://doi.org/10.1149/05054.0023ecst>
- (35) Barzani, H. A.; Ali, H. S.; Özok, H. İ.; Yardım, Y., Developing an electroanalytical procedure for the determination of caffeic acid phenethyl ester at a boron-doped diamond electrode by the use of cationic surfactant media. *Diam. Relat. Mater.* **2022**, *124*, 108934. <https://doi.org/10.1016/j.diamond.2022.108934>
- (36) Pinar, P. T.; Şentürk, Z., Electrochemical and analytical performance of cathodically pretreated boron-doped diamond electrode for the determination of oxazolidinone antibiotic linezolid in cationic surfactant media. *J. Electroanal. Chem.* **2020**, *878*, 114681. <https://doi.org/10.1016/j.jelechem.2020.114681>
- (37) Allahverdiyeva, S.; Yardım, Y.; Şentürk, Z., Electrooxidation of tetracycline antibiotic demeclocycline at unmodified boron-doped diamond electrode and its enhancement determination in surfactant-containing media. *Talanta* **2021**, *223*, 121695. <https://doi.org/10.1016/j.talanta.2020.121695>
- (38) Rocha, L. R.; De Cássica Mendonça, J.; Capelari, T. B.; Medeiros, R. A.; Tarley, C. R., Development of a reliable and selective voltammetric method for determination of designer drug 1-(3-chlorophenyl) piperazine (mCPP) using boron-doped diamond electrode and exploiting surfactant-mediated measurements. *Sens. Actuators B Chem.* **2020**, *310*, 127812 (2020). <https://doi.org/10.1016/j.snb.2020.127812>
- (39) Keskin, E.; Allahverdiyeva, S.; Alali, A.; Yardım, Y., Voltammetric quantification of a nonsteroidal anti-inflammatory agent diflunisal based on the enhancement effect of cationic surfactant on boron-doped diamond electrode. *Maced. J. Chem. Chem. Eng.* **2021**, *40*, 11–20. <https://doi.org/10.20450/MJCCCE.2021.2172>
- (40) Levent, A.; Yardım, Y.; Şentürk, Z., Electrochemical performance of boron-doped diamond electrode in surfactant-containing media for ambroxol determination. *Sens. Actuators B Chem.* **2014**, *203*, 517–526. <https://doi.org/10.1016/j.snb.2014.07.035>
- (41) Pinar, P. T.; Yardım, Y.; Şentürk, Z., Square-wave voltammetric sensing of lawsone (2-hydroxy-1,4-naphthoquinone) based on the enhancement effect of cationic surfactant on anodically pretreated boron-doped diamond electrode. *Acta Chim. Slov.* **2021**, *68*, 1027–1032. <http://dx.doi.org/10.17344/acsi.2020.6617>
- (42) Mielech-Łukasiewicz, K.; Leoniuk, M., Voltammetric determination of natamycin using a cathodically pretreated boron-doped diamond electrode in the presence of sodium dodecyl sulfate. *Microchem. J.* **2020**, *159*, 105570. <https://doi.org/10.1016/j.microc.2020.105570>
- (43) Aşlışen, B.; Koçak, Ç. C.; Koçak, S., Electrochemical determination of sesamol in foods by square wave voltammetry at a boron-doped diamond electrode. *Anal. Lett.* **2020**, *53*, 343–354. <https://doi.org/10.1080/00032719.2019.1650752>
- (44) Muzyka, K.; Sun, J.; Fereja, T. H.; Lan, Y.; Zhang, W.; Xu, G., Boron-doped diamond: Current progress and challenges in view of electroanalytical applications. *Anal. Met.* **2019**, *11*, 397–414. <https://doi.org/10.1039/C8AY02197J>
- (45) Luong, J. H.; Male, K. B.; Glennon, J. D., Boron-doped diamond electrode: synthesis, characterization, functionalization and analytical applications. *Analyst* **2009**, *134*, 1965–1979. <https://doi.org/10.1039/B910206J>
- (46) Petković, B. B.; Ognjanović, M.; Krstić, M.; Stanković, V.; Babincev, L.; Pergal, M.; Stanković, D. M., Boron-doped diamond electrode as efficient sensing platform for simultaneous quantification of mefenamic acid and indomethacin. *Diam. Relat. Mater.* **2020**, *105*, 107785. <https://doi.org/10.1016/j.diamond.2020.107785>

- (47) Yunusoğlu, O.; Allahverdiyeva, S.; Yardım, Y.; Şentürk, Z., A simple approach to simultaneous electroanalytical quantification of acetaminophen and tramadol using a boron-doped diamond electrode in the existence of sodium dodecyl sulfate. *Electroanal.* **2020**, *32*, 429–436. <https://doi.org/10.1002/elan.201900452>
- (48) Allahverdiyeva, S.; Keskin, E.; Pınar, P. T.; Yunusoğlu, O.; Yardım, Y.; Şentürk, Z., Electroanalytical investigation and determination of hepatitis C antiviral drug ledipasvir at a non-modified boron-doped diamond electrode. *Diam. Relat. Mater.* **2020**, *108*, 107962. <https://doi.org/10.1016/j.diamond.2020.107962>
- (49) Plattner, S.; Erb, R.; Chervet, J. P.; Oberacher, H., Studying the reducing potencies of antioxidants with the electrochemistry inherently present in electrospray ionization-mass spectrometry. *Anal. Bioanal. Chem.* **2014**, *406*, 213–224. <https://doi.org/10.1007/s00216-013-7445-5>
- (50) Hawley, S. R.; Bray, P. G.; Park, B. K.; Ward, S. A., Amodiaquine accumulation in *Plasmodium falciparum* as a possible explanation for its superior antimalarial activity over chloroquine. *Mol. Biochem. Parasitol.* **1996**, *80*, 15–25. [https://doi.org/10.1016/0166-6851\(96\)02655-2](https://doi.org/10.1016/0166-6851(96)02655-2)
- (51) Hanssen, B. L.; Siraj, S.; Wong, D. K., Recent strategies to minimize fouling in electrochemical detection systems, *Rev. Anal. Chem.*, **2016**, *35*, 1–28. <https://doi.org/10.1515/revac-2015-0008>
- (52) Markarian, S. A.; Harutyunyan, L. R.; Harutyunyan, R. S., The properties of mixtures of sodium dodecyl sulfate and diethylsulfoxide in water. *J. Solution Chem.* **2005**, *34*, 361–368. <https://doi.org/10.1007/s10953-005-3056-x>