ISSN 2078-5615. Вісник Львівського університету. Серія хімічна. 2025. Випуск 66. С. 122–136
Visnyk of the Lviv University. Series Chemistry. 2025. Issue 66. P. 112–136

Аналітична хімія

UDK 543.2 +543.5

VOLTAMMETRIC DETERMINATION OF QUININE AND ITS N-OXIDE USING SILVER SOLID AMALGAM ELECTRODES

V. Rybak[1], O. Dushna[1,2], T. Yakubova[1], L. Dubenska[1]*

[1]Ivan Franko National University of Lviv,
Kyryla i Mefodiya Str., 6, 79005 Lviv, Ukraine;

[2] Biological and Chemical Research Centre,
Faculty of Chemistry, University of Warsaw,
Żwirki i Wigury, 101, 02–089 Warsaw, Poland
**e-mail: liliya.dubenska@lnu.edu.ua*

For the first time, a voltammetric method for the determination of quinine using silver solid amalgam electrodes has been developed. The highest currents and a clear quinine reduction peak were achieved by a mercury meniscus-modified silver solid amalgam electrode (*m*-AgSAE). Quinine is reduced on *m*-AgSAE as a single irreversible peak in both slightly acidic and alkaline media. An optimal pH of 8 was selected and maintained using the Britton-Robinson buffer. The quinine reduction peak was adsorptive, promoting analyte accumulation on the electrode surface. Under optimal conditions, a calibration curve for the voltammetric determination of quinine was obtained, with a linear range from 2.0 10^{-6} to 2.0 10^{-5} M and a limit of detection of 1.7 10^{-6} M. The developed method was tested on tonic beverages. The results were statistically processed and confirmed by high-performance liquid chromatography with a diode-array detector as a reference method. The relative error of determination did not exceed 5 %. The proposed method is fast, portable, and suitable for routine analysis.

Keywords: voltammetry, alkaloids, quinine, N-oxide quinine, solid amalgam electrodes.

DOI: https://doi.org/10.30970/vch.6601.122

1. Introduction

Quinine (QN) is the main alkaloid from the bark of the cinchona tree, which belongs to quinoline derivatives [1]. Quinine is the most important among quinoline alkaloids. QN is an active substance with antipyretic, antimalarial, anti-inflammatory, analgesic, and muscle relaxant effects [2]. It inhibits thermoregulatory centres, which leads to a decrease in body temperature during febrile diseases. In addition, it reduces the excitability of the heart muscle, prolonging the refractory period and reducing the ability to contract. Quinine can stimulate uterine muscle contractions, and also can cause spleen contractions [3].

The main characteristic of QN is its ability to treat malaria [1]. Quinine is known as the first and, for several centuries, the only remedy for malaria [4]. Moreover, QN is a promising drug for the treatment of SARS-Cov-2 infection [6, 7].

© Rybak V., Dushna O., Yakubova T. et al., 2025

Nowadays, it is used as a bitter flavour in the production of soft drinks [8, 9]. However, excessive use of QN can cause headaches, dizziness, increased body temperature, insomnia, as well as tinnitus, impaired hearing, and visual impairment (blurry vision and impaired colour perception) [10]. This requires reliable, simple, and rapid methods of QN determination.

Currently, many different analytical methods, such as liquid chromatography [11], gas chromatography [12], capillary electrophoresis [13], isotachophoresis [14], fluorimetry [15], chemiluminescence [16], atomic [17], mass spectrometry [18] are known for the determination of QN in various matrices. Some electrochemical methods, which include potentiometry [18], polarography [19], and voltammetry, are also mentioned [2, 20–23].

Our work aims to develop a new voltammetric method for the determination of QN on silver solid amalgam electrodes. Solid amalgam electrodes are an alternative to traditional mercury electrodes. Silver amalgam-based electrodes (AgSAE) maintain most of the advantageous qualities of mercury electrodes, such as wide potential range, high hydrogen release potential and low background current. Furthermore, the surface of AgSAE can be quickly and easily regenerated (electrochemically or mechanically by polishing). Also, the simplicity of AgSAE construction and usage is quite beneficial. Besides, a work on the construction of screen-printed silver amalgam electrodes was published. It should be stressed that AgSAE is non-toxic and meets the requirements of "Green Analytical chemistry" [24, 25].

2. Experimental

2.1. Apparatus

In this work, we used digital voltammetric devices MTech POL-22 and MTech UVA-410 with a three-electrode cell (working dropping mercury electrode (DME) or silver amalgam-based electrodes with modified surfaces, namely polished one (*p*-AgSAE), covered by mercury meniscus (*m*-AgSAE), or by mercury film (*f*-AgSAE), a saturated calomel reference electrode, and a platinum wire auxiliary electrode).

Characteristics of DME: $m = 5{,}9 \cdot 10^{-4}$ g/s, $\tau = 10$ s in 0,2 M NH_4Cl in an open circuit. The surface of AgSAE was prepared and pre-treated for work, regenerated, and maintained accordingly to [24, 26–29].

Preparation of the surface of p-AgSAE. Before starting the work, the *p*-AgSAE was polished for 1 min with finely dispersed aluminium oxide. Before each measurement, the surface of the *p*-AgSAE was electrochemically regenerated directly in the working solution, which consisted of the analyte and background electrolyte ($E_{reg} = -1\ 500$ mV, $t_{reg} = 30$ s). With this procedure's help, the *p*-AgSAE's surface was cleaned from substances that can adsorb on the electrode's surface and passivate it.

Preparation of the surface of m-AgSAE and f-AgSAE. To obtain a mercury meniscus (*m*-AgSAE), a drop of mercury was attached to the surface of the polished AgSAE (the drop was obtained from a DME capillary). To obtain a mercury film (*f*-AgSAE), a polished AgSAE was immersed in metallic mercury for 30 seconds. The excess mercury was gently shaken off, and the electrode was rinsed with distilled water.

The *m*-AgSAE and *f*-AgSAE were activated electrochemically by immersion in a 0.2 M KCl solution, and application of –2.2 V potential for 5 min.

Before each measurement, the surface of the AgSAE was electrochemically regenerated directly in the working solution at a potential E_{reg}, which was 50–100 mV more positive than the hydrogen release potential in the particular electrolyte, with a regeneration time t_{reg} of 30 s. The pH value was controlled potentiometrically using a pH meter pH-150M with a combined glass electrode.

Chromatographic measurements. The liquid chromatograph Waters equipped with Alliance 2 690 separation module combined with a PAD 996 diode array detector was used for the chromatographic analysis of soft drinks. The column utilized was Luna Omega Polar C18 (250 mm × 4.6 mm, 5 μm). Operating conditions were as follows: injection volume was 10 μL; mobile phase consisted of 60 % of component A (acetonitrile) and 40 % of component B (buffer (pH = 2.0), which contained 0.02 M KH_2PO_4 and 0.027 M tetrabutylammonium bromide; separation mode was isocratic; total flow rate was 1 mL/min; total run time was 10 min; column temperature was 25 °C, and the sample temperature was kept ambient. QN was detected at 250 nm. Chromatograms were recorded and data were processed using Empower 2 software [5].

Voltammetric measurements. In this work, we used cyclic voltammetry (CV) and linear sweep voltammetry (LSV) to study QN's electrochemical behaviour and to assess the analytical performance and the method's applicability on AgSAE. Differential pulse voltammetry (DPV) was used to study the simultaneous voltammetric determination of QN and QN N-oxide. The current I_p value was measured considering the baseline according to [30].

Origin 2018 (OriginLab, USA) statistically analysed the calibration curves, and the relevant results (slope and intercept) were evaluated with a 95 % confidence interval. The values of LOD and LOQ were calculated according to the IUPAC using the following approach: LOD = $3.3S_a/b$ and LOQ = $10S_a/b$, where S_a is the standard error of the intercept value and b is the slope of the calibration curve.

2.2. Reagents

QN stock solution was prepared by dissolving the QN hydrochloride substance (the purity 99,9 %, CAS No. 6119-47-7, Sigma-Aldrich). Stock standard solution with QN concentration $1.0 \cdot 10^{-3}$ M was prepared as follows: the exact amount of QN substance (0.0198 g) was dissolved in double-distilled water in a 50 mL volumetric flask, the volume was brought to the mark, then the solution was mixed thoroughly. The stock solution of QN was stored at the temperature of 4 ºC for not longer than a week.

Oxone ("extra pure" commercial triple potassium salt of Caro's acid) was purchased from Acros Organics and used in the present work as an oxidising agent. The active ingredient of Oxone is potassium peroxymonosulfate $KHSO_5$, which is present as a component of a triple salt potassium hydrogen peroxymonosulfate sulphate with the formula $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, (CAS 70693-62-8). The solution of $1.0 \cdot 10^{-2}$ M Oxone (KPMS) was prepared by diluting the exact amount of this substance in double-distilled water in a 100 mL volumetric flask, bringing the volume to the mark and mixing thoroughly [31, 32].

The Britton-Robinson (BRB) buffer was prepared using $Na_2B_4O_7 \cdot 10H_2O$, CH_3COOH, and H_3PO_4 of analytical grade. The pH of BRB (2.0–12.0) was reached by adding 2.5 M sodium hydroxide (controlled by a pH meter) [33–35].

The stock solution of quinine N-oxide was prepared as follows: 12.5 mL of the stock standard QN solution with $C_{QN} = 1.0 \cdot 10^{-3}$ M, 6.5 mL of KPMS, and 5 mL of BRB with pH 9.5 were added and mixed thoroughly.

After 15 min, by adding acid, the pH of the solution was changed to pH 6 (controlled with a pH meter), the reaction was stopped, the solution was brought to the 25 mL mark with double-distilled water in a 25 mL flask, and a QN N-oxide solution with $C_{\text{N-oxide QN}} = 5 \cdot 10^{-4}$ M was obtained.

2.3. Sample and Preparation

Samples of two tonic drinks containing QN were purchased from local stores. Before analysis, the samples of the beverages were degassed in an ultrasonic bath for 15 min.

Preparation of beverage for voltammetric analysis using working AgSAE. An aliquot of 2.00 mL of the beverage was transferred to a 25.0 mL volumetric flask, and 5 mL of BRB with pH 6.0 was added and filled up to the mark with double-distilled water and stirred. Then the prepared solution was transferred to an electrochemical cell for voltammetric analysis, dissolved oxygen was removed with purified argon for 10 min, and voltammograms were obtained in the potential range from –0.7 to –1.4 V.

Sample preparation of tonic drinks for chromatographic analysis. An aliquot of 5.00 mL of the beverage was poured into a 10.0 mL volumetric flask, brought to the mark with methanol, and mixed thoroughly. This solution was filtered through a 0.45 μm PTFE membrane filter and transferred to a vial for chromatography.

3. Results and Discussion

3.1. Influence of AgSAE surface modification on the current and potential of QN reduction

Fig. 1 *a* shows voltammograms of QN solutions on AgSAEs with different modifications (*m*-AgSAE, *f*-AgSAE, and *p*-AgSAE). QN is reduced on AgSAE, forming a single peak at a potential E = –0.98 V at pH 6.0. We did not observe any changes in the anode potential's region of the voltammograms, this indicates that the process is irreversible. The highest reduction current was achieved using *m*-AgSAE, since *f*-AgSAE and *p*-AgSAE show significantly lower reduction currents. Therefore, in this work, we used *m*-AgSAE to study quinine's electrochemical behaviour and to assess the analytical performance and the method's applicability.

On the surface of DME, QN is reduced, forming a single peak at the potential E = –1.03 V (Fig. 1, *b*). No changes were observed in the anode region of the voltammograms with the change of conditions, indicating the irreversibility of the process.

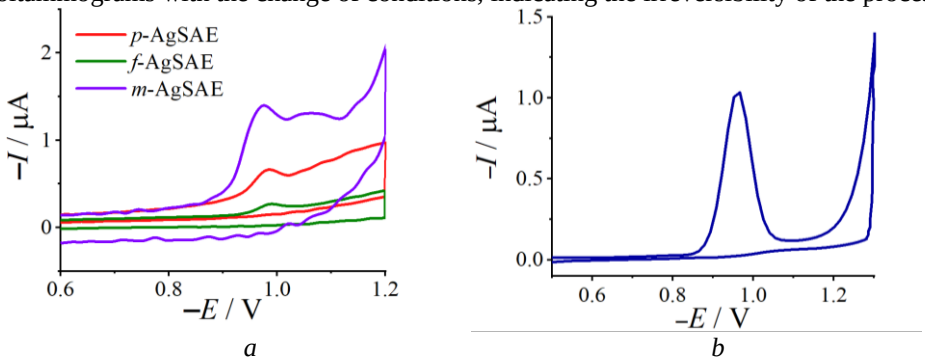


Fig. 1. Cyclic voltammograms obtained on modified AgSAEs (*m*-AgSAE, *f*-AgSAE and *p*-AgSAE) (*a*) and on DME (*b*) in QN solution in BRB with pH 6.0. $C = 4.0 \cdot 10^{-5}$ M, for *m*-AgSAE: V = 1.0 V/s; E_{acc} = –0.6 V; t_{acc} = 30 s; for DME: V = 0.5 V/s

3.2. Effect of pH on the reduction of QN on DME and m-AgSAE

The pH of the medium affects the current and the potential of QN reduction (Fig. 2). QN is reduced on *m*-AgSAE in the pH range from 6.0 to 11.0 and on DME – from 4.0 to 11.0. At pH < 6, QN is reduced at hydrogen release potentials, and the peak of QN reduction practically coincides with the peak of oxygen reduction. These factors make registering the QN signal in an acidic medium impossible. Therefore, pH 8.0 was chosen as the optimal pH value for further studies using *m*-AgSAE, and pH 6.0 using DME.

The potentials of QN reduction peaks shift to the more negative region with the increasing pH (Fig. 2, *b, d*). This suggests that there is a proton transfer stage in the electrochemical process. It was established that the dependence of $-E$, V from pH is linear. Table 1 shows the equation of dependence $-E$, V from pH for the reduction of QN on DME and *m*-AgSAE.

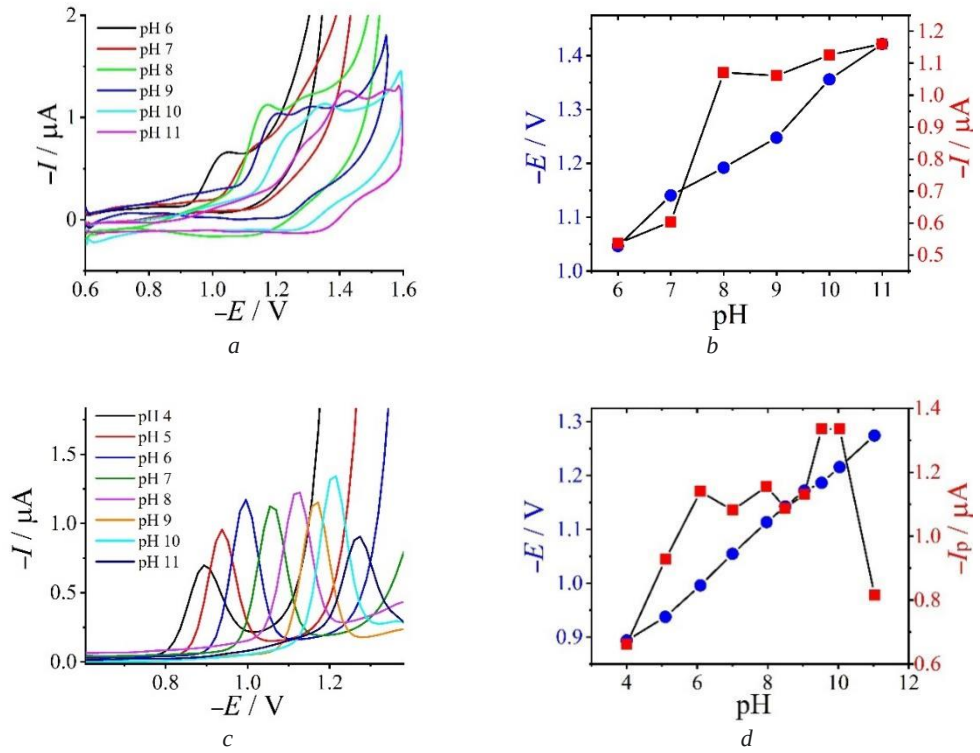


Fig. 2. Cyclic voltammograms of QN solutions on *m*-AgSAE (*a*) and on DME (*c*), the dependence of the current and potential of reduction on *m*-AgSAE (*b*) and on DME (*d*) of QN vs. pH of the medium. $C = 4.0 \cdot 10^{-5}$ M, for *m*-AgSAE: $V = 1.0$ V/s; $E_{acc} = -0.6$ V; $t_{acc} = 30$ s; for DME: $V = 0.5$ V/s

Table 1

Dependence equation –*E*, V vs. pH for QN on DME and *m*-AgSAE

Electrode	pH	Dependence equation –*E*, V vs. pH	Correlation coefficient, R
DME	4.0–11.0	$-E = (0.666 \pm 0.008) + (0.0552 \pm 0.0010)$ pH	0.9986
m-AgSAE	6.0–11.0	$-E = (0.61 \pm 0.03) + (0.074 \pm 0.004)$ pH	0.9947

3.3. Influence of the polarization voltage sweep rate on the current and potential of reduction of QN

To clarify the nature of the QN reduction current on *m*-AgSAE and DME, voltammograms were obtained under different conditions and scan rates (Table 2). As the scan rates increase, the peak height increases, and the potentials shift cathodically. No oxidation signals were detected. This indicates that the reduction process is irreversible.

All dependencies of the current logarithm from the scan rate's logarithm show one linear plot, the equations in Table 2. The tangent of the slope for all studied conditions ranges from 0.8 to 1.1, which is close to 1 and indicates the adsorptive nature of the current.

Table 2

Dependence equation log *I* – log *V* for QN on DME and *m*-AgSAE

Electrode	pH	Scan rate range, V/s	Dependence equation log *I* – log *V*	*R*
DME	5.0 (BRB)	0.1–5.0	$\log I = (0.261 \pm 0.005) + (0.984 \pm 0.014) \log V$	0.9979
	6.0 (BRB)		$\log I = (-0.080 \pm 0.006) + (0.892 \pm 0.022) \log V$	0.9969
	8.0 (BRB)		$\log I = (0.158 \pm 0.010) + (0.979 \pm 0.025) \log V$	0.9934
m-AgSAE	6.0 (BRB)	0.5–5.0	$\log I = (-0.492 \pm 0.012) + (0.80 \pm 0.03) \log V$	0.9924
	9.0 (PBS)	0.1–2.0	$\log I = (-0.425 \pm 0.009) + (1.13 \pm 0.04) \log V$	0.9968

3.4. Mechanism of QN reduction on mercury-based electrodes

The number of electrons that take part in an electrochemical reaction (n) according to the voltammograms, which were obtained under different conditions (different pH and concentrations of QN) according to equation [36]:

$$\alpha n = -47{,}7/(E_p - E_{p/2}),$$

n – number of electrons that take part in an electrochemical reaction; E_p – peak potential, mV; $E_{p/2}$ – the potential of half of the peak, mV.

The calculated values of n varied in the range from 1.8 to 2.2 on DME and *m*-AgSAE, indicates that two electrons are involved in the electrochemical reduction of QN on mercury-based electrodes.

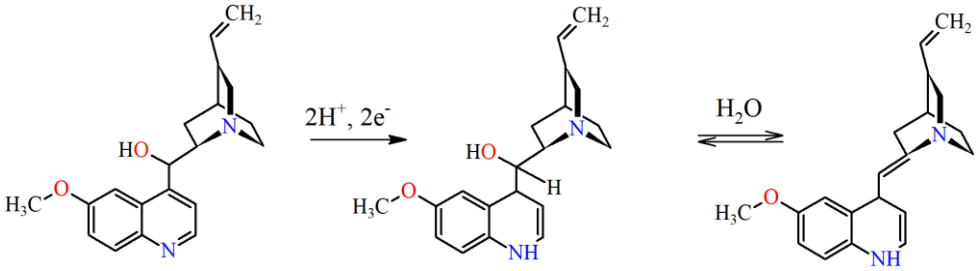
According to Table 1 using the tangent of the slope, the ratio of the number of protons to the number of electrons (xH^+/n) involved in the electrochemical process was calculated [37]:

$$dE/\text{pH} = (2{,}3RT \cdot xH^+)/\alpha n F,$$

F – Faraday constant; R – universal gas constant; T – temperature.

The values of protons calculated were respectively 2.13 for DME and 1.60 for *m*-AgSAE.

The literature source reports a mechanism for the reduction of QN on a mercury electrode at pH 11.0, which involves the addition of two electrons and two protons [4]. First, an unsaturated bond near the nitrogen atom is reduced to a saturated bond, and then a dehydration reaction occurs to form a stable product (Scheme).



Reduction mechanism of QN on mercury-based electrodes

3.5. Analytical characteristics for the determination of QN on DME and m-AgSAE

To obtain calibration curves on *m*-AgSAE and DME, voltammograms of QN reduction were obtained in the concentration range of 2–20 μM on *m*-AgSAE and 2–40 μM on DME (Fig. 3). In Figures 3, a, b, "0" shows the background line. The parameters of the calibration curves of the developed methods for determining QN are shown in Table 3.

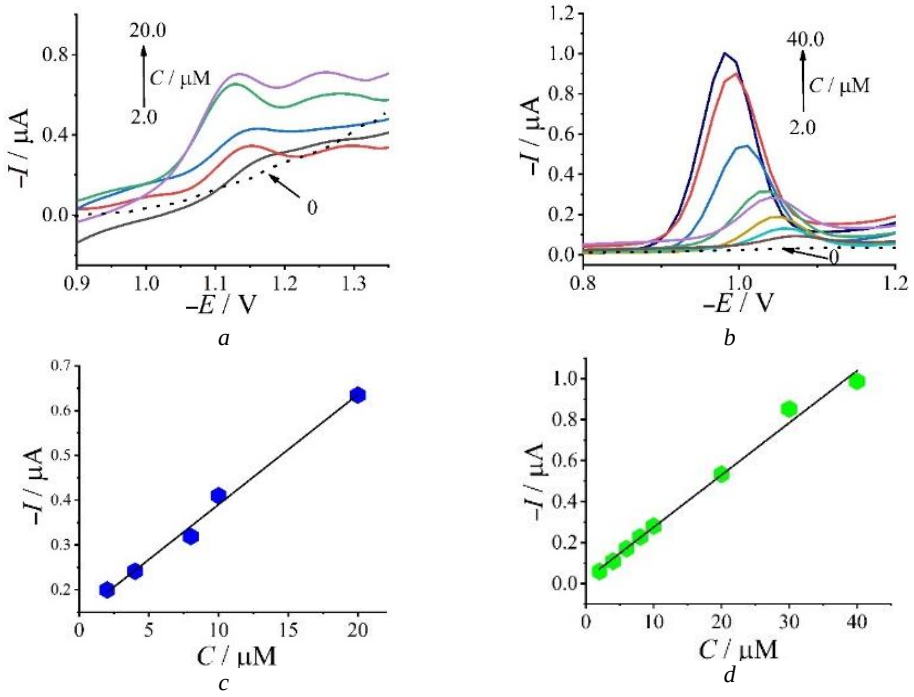


Fig. 3. Voltammograms (*a*, *b*) and calibration curves (*c*, *d*) for reduction peak of QN on *m*-AgSAE (*a*, *c*) and DME (*b*, *d*). For *m*-AgSAE: pH = 8.0; V = 1.0 V/s; t_{acc} = 60 s; E_{acc} = –0.6 V; for DME: pH = 6.0; V = 0.5 V/s

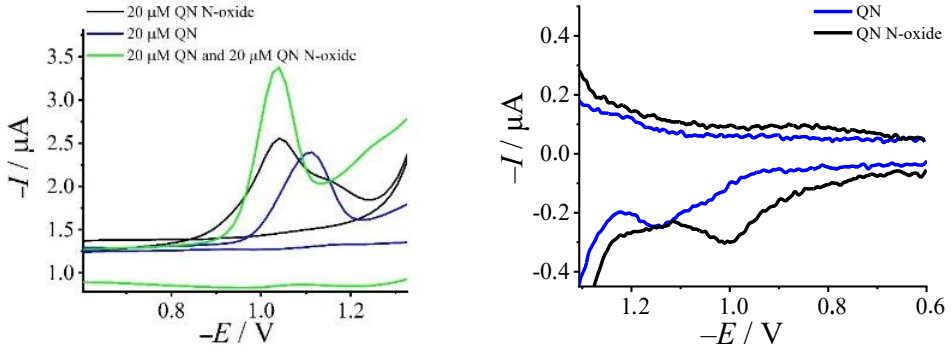
Table 3

Analytical characteristics of the voltammetric determination of QN on *m*-AgSAE and DME

Analytical parameters	Electrode	
	m-AgSAE	DME
Scan rate *V*, V/s	1.0	0.5
Peak potential *E*, V	–1.12	–0.98
Linearity, M	$2.0\cdot10^{-6}$ – $2.0\cdot10^{-5}$	$2.0\cdot10^{-6}$ – $4.0\cdot10^{-5}$
Parameter $b\pm\Delta b$, μA/M	$(2.454\pm0.012)\cdot10^{4}$	$(2.548\pm0.010)\cdot10^{4}$
Parameter $a\pm\Delta a$, μA	0.145 ± 0.013	0.0200 ± 0.0019
Correlation coefficient, R	0.99615	0.99554
Limit of quantification (LOQ), M	$5.2\cdot10^{-6}$	$5.7\cdot10^{-6}$
Limit of detection (LOD), M	$1.7\cdot10^{-6}$	$1.9\cdot10^{-6}$

3.6. Simultaneous voltammetric determination of QN and its N-oxide using m-AgSAE

We reported on the preparation of quinine N-oxide using KPMS [38]. Quinine N-oxide is reduced as a single peak at a potential of –1.09 V on DME and –1.0 V on *m*-AgSAE. Therefore, whether it is possible to determine QN and its N-oxide together arose. Comparison of the voltammograms of the reduction of QN and its N-oxide (Fig. 4) gave reason to hope that the DPV method will be able to determine these two components simultaneously from one sample, at least if they are present in the sample in equimolar amounts.



a *b*

Fig. 4. Polarograms (a) and voltammograms (*b*) *m*-AgSAE in QN and QN N-oxide solutions. Conditions: $C_{QN} = 2.0\cdot10^{-5}$ M; $C_{QN\ N\text{-}oxide} = 2.0\cdot10^{-5}$ M; pH = 6.0; on DME, $V = 0.5$ V/s

The method of measuring by adding the standard solution to the electrochemical cell. During the exploration of the effect of QN on the voltammetric determination of QN N-oxide, an aliquot of 7.0 ml of the working solution of QN N-oxide was added to the electrochemical cell with a measuring pipette, dissolved oxygen was removed, and a voltammogram was obtained. Then, 0.14 ml of the original QN standard solution was added to the cell. The solution was mixed by purging argon for 3 min, and the oxygen, which was dissolved in an aliquot of the added solution, was removed. The procedure for introducing the QN additions was repeated three times, and the concentration of QN in the final volume of solution in the cell was calculated considering the dilution (Fig. 5).

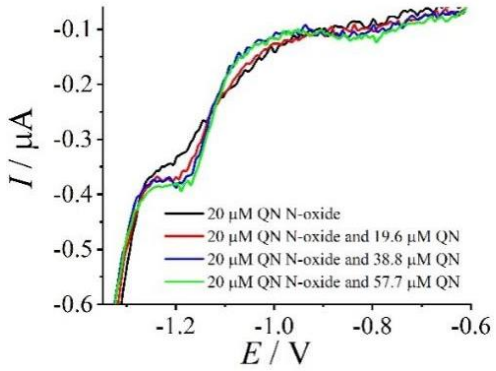


Fig. 5. DPV voltammograms of QN N-oxide with QN additions were obtained on *m*- AgSAE. Conditions: $C_{\text{QN N-oxide}} = 2.0 \cdot 10^{-5}$ M; pH 6.0; $C_{\text{add1}} = 1.96 \cdot 10^{-5}$ M, $C_{\text{add2}} = 3.88 \cdot 10^{-5}$ M; $C_{\text{add3}} = 5.77 \cdot 10^{-5}$ M; $E_{\text{start}} = -0.60$ V; $E_{\text{end}} = -1.50$ V; $dE = 5$ mV; $P = 50$ mV; $t_1 = 0.05$ s; $t_2 = 0.1$ s

The study of the effect of QN N-oxide on the voltammetric determination of QN was performed similarly. First, 7.0 mL of the working solution of QN was added to the electrochemical cell with a measuring pipette, dissolved oxygen was removed, and a voltammogram was obtained. Then, 0.60 mL of the original standard QN N-oxide of quinine was added to the cell. The solution was mixed and the oxygen dissolved in the additive aliquot was removed by purging with argon for 3 min. The procedure for introducing the QN N-oxide addition was repeated twice, 0.30 mL of the standard solution of QN N-oxide was added. The concentration of QN and its N-oxide in the final volume of solution in the cell was calculated considering the dilution (Fig. 6).

The voltammograms clearly show that when QN is added to its N-oxide or vice versa, the QN's reduction peaks increase each time, overlapping the indistinct peak of the reduction of N-oxide. Therefore, the simultaneous determination of QN and its metabolite, QN N-oxide, is impossible.

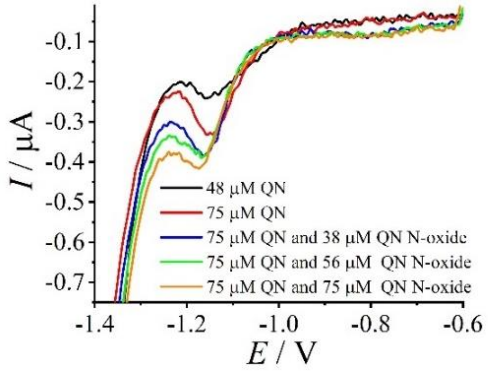


Fig. 6. DPV voltammograms of QN with additions of its N-oxide were obtained on AgSAE. Conditions: Solutions of QN: $C_{QN} = 2.0 \cdot 10^{-5}$ M; $C_{QN} = 1.0 \cdot 10^{-3}$ M, pH 6.0; $n_{add} = 2$; $V_{add} = 0.2$ mL; $C_{add1} = 4.8 \cdot 10^{-5}$ M; $C_{add2} = 7.5 \cdot 10^{-5}$ M; $C_{QN\ N\text{-}oxide} = 5.0 \cdot 10^{-4}$ M; $n_{add} = 3$; $V_{add1} = 0.6$ mL; $V_{add2,\ 3} = 0.3$ mL; $C_{add1} = 3.8 \cdot 10^{-5}$ M; $C_{add2} = 5.6 \cdot 10^{-5}$ M; $C_{add3} = 7.5 \cdot 10^{-5}$ M; $E_{start} = -0.60$ V; $E_{end} = -1.50$ V; $dE = 5$ mV; $P = 50$ mV; $t_1 = 0.05$ s; $t_2 = 0.1$ s

3.7. Voltammetric determination of QN in tonic drinks using m-AgSAE

We used the standard addition method to determine the concentration of QN in tonic drinks (Fig. 7). The analysis results are presented in Table 4. The results were statistically analysed. The determination results were compared with those obtained by high-performance chromatography with a diode array detector (HPLC-DAD).

Table 4

Results of QN determination in tonic drinks ($n = 3$)

Sample	Determined using *m*-AgSAE, mg/L	Standard deviation, %	Determined using HPLC-DAD, mg/L	Relative error, %
Sample 1	34.39±0.06	0.25	33.4812±0.0015	2.71
Sample 2	38.930±0.013	0.16	37.237±0.003	4.54

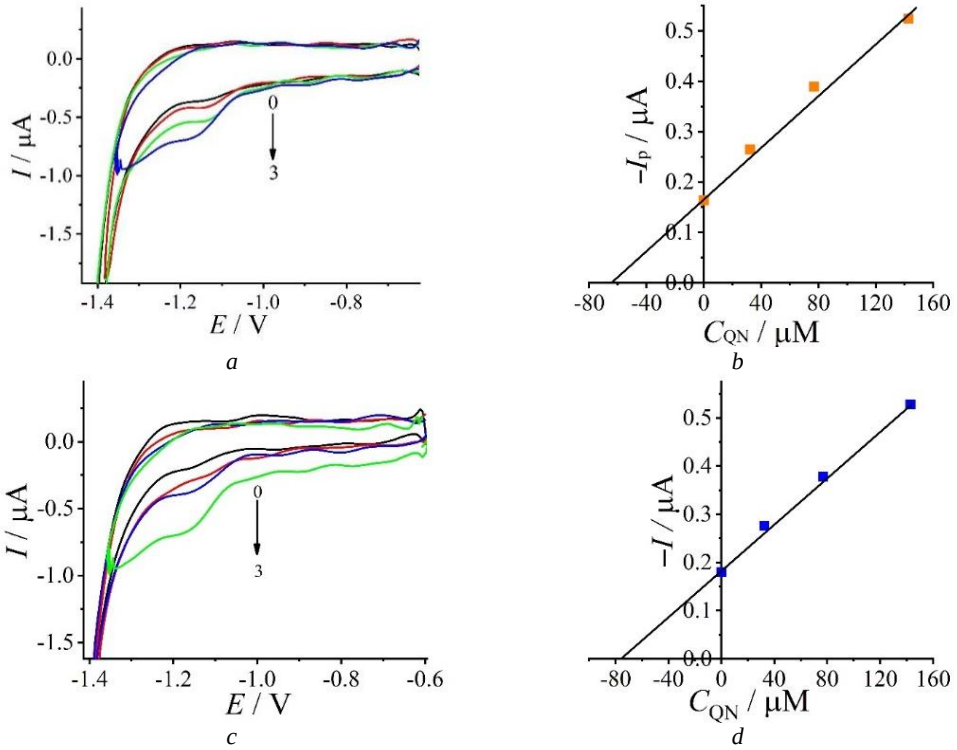


Fig. 7. Cyclic voltammograms QN on *m*-AgSAE, during the determination of QN in tonic beverage samples 1 (*a*) and 2 (*c*) and the corresponding graphs obtained by the standard additions method for determining the concentration of QN in tonic beverages – samples 1 (*b*) and 2 (*d*). The mark 0 corresponds to the solution without additions of the standard solution of QN, 1–3 – the corresponding additions of 32.00; 77.00, and 142.00 μM QN. Conditions: pH 6.0, V = 1.0 V/s

4. Conclusions

For the first time, silver solid amalgam electrodes (AgSAE) were used for the voltammetric determination of QN, and for comparison, a mercury drop electrode was used. Quinine is reduced on mercury-based electrodes as a single peak. The highest reduction currents were obtained on AgSAE modified with mercury meniscus (*m*-AgSAE) and DME. The pH affects the appearance of *m*-AgSAE voltammograms in QN solutions. With an increase of pH, the potential of the QN reduction peak shifts cathodically, which indicates the participation of protons in the electrochemical reaction. At pH<6, QN is reduced on *m*-AgSAE at the potentials of hydrogen reduction. As optimal pH values for measuring the analytical signal of QN, pH = 8.0 was chosen for *m*-AgSAE and pH = 6.0 for DME.

Based on the study of the effect of scan rate on the process of QN reduction, it was proven that the nature of the current is absorptive. This allows the use of adsorptive accumulation and helps to reduce the limit of detection of the analyte. The accumulation time t_{aac} = 60 s and the accumulation potential E_{acc} = –0.6 V were chosen after conducting experiments.

Under optimal conditions for the reduction of QN, calibration curves were obtained. The limit of determination reaches 10^{-6} mol/L, which is sufficient for analysing medicines, beverages enriched with QN, and extracts from plant materials.

Simultaneous voltammetric determination of QN and its N-oxide in their mixture is impossible since adding QN to its N-oxide or vice versa causes their reduction peaks to overlap and quinine's reduction peak to increase.

The new voltammetric method for determining quinine was tested on real objects, which were tonic drinks. The proposed method is rapid, portable, suitable for routine analysis and well aligned with recent applications in medical, toxicological and forensic chemistry. The accuracy of the voltammetric analysis results has been confirmed by HPLC-DAD method. The relative error of determination did not exceed 5 %. However, voltammetric methods are more rapid and significantly more economical than HPLC methods.

5. Acknowledgment

This work was financed by the Ministry of Education and Science of Ukraine (Grant Number 0116U001541) and was partly supported by the Simons Foundation (SFI-PD-Ukraine-00014574).

1. *Kovalenko S. I., Kryvoshey O. V., Vos-Koboinik O. Y., Berest G. G., Bilyi A. K.* Antimalarial drugs: quinine and its analogues by pharmacological action: Study guide. Zaporizhzhia: ZSMU Publishing House, 2014. 322 p. (in Ukrainian).
2. *Dar R. A., Brahman P. K., Tiwari S., Pitre K. S.* Electrochemical studies of quinine in surfactant media using hanging mercury drop electrode: A cyclic voltametric study // Colloids Surf. B. 2012. Vol. 98. P. 72–79. DOI: https://doi.org//10.1016/j.colsurfb.2012.04.035
3. *Kovalenko S. I., Kryvoshey O. V., Vos-Koboinik O. Y., Berest G. G., Bilyi A. K.* Antimalarial drugs: quinine and its analogues by pharmacological action: Study guide. Zaporizhzhia: ZSMU Publishing House, 2014. P. 58–59 (in Ukrainian).
4. *Dondorp A., Nosten F., Stepniewska K., Day N., White N.* Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial // The Lancet. 2005. Iss. 366 (9487). P. 717–725. DOI: https://doi.org/10.1016/S0140-6736(05)67176-0
5. *Dushna O., Dubenska L., Marton M., Hatala M., Vojs M.* Sensitive and selective voltammetric method for determination of quinoline alkaloid, quinine in soft drinks and urine by applying a boron-doped diamond electrode // Microchem. J. 2023. Vol. 191. P. 108839. DOI: https://doi.org/10.1016/j.microc.2023.108839
6. *Latarissa I. R., Barliana M. I., Meiliana A., Lestari K.* Potential of quinine sulfate for COVID-19 treatment and its safety profile: Review // Clin Pharmacol. 2021. Vol. 13. P. 225–234. DOI: https://doi.org/10.2147/CPAA.S331660
7. *Große M., Ruetalo N., Layer M., Hu D., Businger R.* et al. Quinine inhibits infection of human cell lines with SARS-CoV-2 // Viruses 2021. Iss. 13 (4). P. 647. DOI: https://doi.org/10.3390/v13040647
8. *Sowunmi A., Salako L. A.* Effect of dose size on the pharmacokinetics of orally administered quinine // Eur J. Clin Pharmacol. 1996. Vol. 49. P. 383–386. DOI: 10.1007/BF00203782
9. REGULATION (EU). 2012. No. 872. https://www.fao.org/faolex/results/details/en/c/LEX-FAOC1

10. *Liles N. W., Page E. E., Liles A. L., Vesely S. K., Raskob G. E., George J. N.* Diversity and severity of adverse reactions to quinine: A systematic review // Am. J. Hematol. 2016. Vol. 91. P. 461–466. DOI: https://doi.org/10.1002/ajh.24314
11. *Ohira A., Yamaguchi S., Miyagi T., Yamamoto Y., Yamada S., Shiohira H., Takahashi K.* Fixed eruption due to quinine in tonic water: A case report with high-performance liquid chromatography and ultraviolet A analyses // J. Dermatol. 2013. Iss. 40 (8). P. 629–631. DOI: 10.1111/1346-8138.12195
12. *Damien R., Daval S., Souweine B., Deteix P., Eschalier A., Coudoré F.* Rapid gas chromatography/mass spectrometry quinine determination in plasma after automated solid-phase extraction // Rapid Commun. Mass Spectrom. 2006. Iss. 20 (17). P. 2528–2532. DOI: 10.1002/rcm.2625
13. *Zaugg S., Thormann W.* Capillary electrophoretic separation, immunochemical recognition and analysis of the diastereomers quinine and quinidine and two quinidine metabolites in body fluids // JPBA. 2001. Vol. 24. P. 785–799. DOI: 10.1016/s0731-7085(00)00546-x
14. *Reijenga J. C., Aben G. V., Lemmens A. A., Verheggen T. P., De Bruijn C. H., Everaerts F. M.* Determination of quinine in beverages, pharmaceutical preparations and urine by isotachophoresis // J. Chromatogr. B. 1985. Vol. 320. P. 245–252. DOI: 10.1016/s0021-9673(01)90502-3
15. *Ortega-Algar S., Ramos-Martos N., Molina-Diaz A.* Fluorimetric Flow-Through Sensing of Quinine and Quinidine // Microchim. Acta. 2004. Iss. 147 (4). P. 211–217. DOI: https://doi.org/10.1007/s00604-004-0233-3
16. *Li B., Zhang Z., Wu M.* Flow-injection chemiluminescence determination of quinine using on-line electrogenerated cobalt (III) as oxidant // Talanta. 2000. Vol. 51. P. 515–521. DOI: 10.1016/s0039-9140(99)00310-0
17. *Yebra M. C., Cespon R. M.* Automatic determination of quinine by atomic absorption spectrometry // Microchem. J. 2000. Vol. 65. P. 81–86. DOI: https://doi.org/10.1016/S0026-265X(00)00034-5
18. *Kamel A. H., Sayour H. E. M.* Flow-through assay of quinine using solid contact potentiometric sensors based on molecularly imprinted polymers // Electroanalysis. 2009. Vol. 21. P. 2701–2708. DOI: https://doi.org/10.1002/elan.200904699
19. *Thomas F. G., Gierst L.* On the electrochemical behaviour of quinine at the mercury electrode in aqueous solutions // J. Electroanal. Chem. Interf. Electrochem. 1983. Vol. 154. P. 239–260. DOI: https://doi.org/10.1016/S0022-0728(83)80545-2
20. *Awasthi S., Srivastava A., Singla M. L.* Voltammetric determination of citric acid and quinine hydrochloride using polypyrrole–pentacyanonitrosylferrate/platinum electrode // Synth. Met. 2011. Vol. 161. P. 1707–1712. DOI: https://doi.org/10.1016/j.synthmet.2011.06.009
21. *Zhan X. M., Liu L. H., Gao Z. N.* Electrocatalytic oxidation of quinine sulfate at a multiwall carbon nanotubes-ionic liquid modified glassy carbon electrode and its electrochemical determination // J. Solid State Electrochem. 2011. Vol. 15. P. 1185–1192. DOI: https://doi.org/10.1007/s10008-010-1184-8
22. *Buleandra M., Rabinca A. A., Cheregi M. C., Ciucu A. A.* Rapid voltammetric method for quinine determination in soft drinks // Food Chemistry. 2018. Vol. 253. P. 1–4. DOI: https://doi.org/10.1016/j.foodchem.2018.01.130

23. *Rudnicki K., Sobczak K., Borgul P., Skrzypek S., Poltorak, L.* Determination of quinine in tonic water at the miniaturized and polarized liquid-liquid interface // Food Chem. 2021. Vol. 364. P. 130417. DOI: https://doi.org/10.1016/j.foodchem.2021.130417
24. *Dmukhailo A., Tvorynska S., Dubenska L.* Rapid and straightforward electrochemical approach for the determination of the toxic food azo dye tartrazine using sensors based on silver solid amalgam // J. Electroanal. Chem. 2023. Vol. 932. 117250. DOI: https://doi.org/10.1016/j.jelechem.2023.117250
25. *Barek J.* Voltammetric and amperometric applications of silver amalgam electrodes for monitoring of reducible organic compounds // TrAC. 2024. Vol. 170. 117416. DOI: https://doi.org/10.1016/j.trac.2023.117416
26. *Yosypchuk B., Barek J.* Analytical applications of solid and paste amalgam electrodes // Crit. Rev. Anal. Chem. 2009. Vol. 39. P.189–203. DOI: https://doi.org/10.1080/10408340903011838
27. *Yosypchuk B., Novotny L.* Electrodes of nontoxic solid amalgams for electrochemical measurements // Electroanalysis. 2002. Vol. 14. P. 1733–1738. DOI: https://doi.org/10.1002/elan.200290018
28. *Yosypchuk B., Novotny L.* Nontoxic electrodes of solid amalgams // Crit. Rev. Anal. Chem. 2002. Vol. 32. P. 141–151. DOI: https://doi.org/10.1080/10408340290765498
29. *Yosypchuk B., Barek J., Yosypchuk O.* Preparation and properties of reference electrodes based on silver paste amalgam // Electroanalysis. 2011. Vol. 23. P. 2226–2231. DOI: https://doi.org/10.1002/elan.201100143
30. *Inczedy J., Lengyel T., Ure A. M.* IUPAC Compendium on Analytical Nomenclature: Definitive Rules, 3rd Edition. Blackwell Science, 1998.
31. *Dubenska L., Dushna O., Pysarevska S.* et al. A new approach for voltammetric determination of nefopam and its metabolite // Electroanalysis. 2020. Vol. 32, No. 3. P. 626–634. DOI: https://doi.org/10.1002/elan.201900595
32. *Dubenska L., Dushna O., Plyska M.* et al. Method of polarographic determination of platyphylline in a form of N-oxide and its validation in solution for injection // Methods Objects Chem. Anal. 2020. Vol. 15, No. 2. P. 83–92. DOI: https://doi.org/10.17721/moca.2020.83-92
33. *Dushna O., Dubenska L., Plotycya S.* et al. The alternative voltammetric method for the determination of nicotine and its metabolite nicotine N-oxide // J. Electrochem. Soc. 2022. Vol. 169 (1), No. 016513. DOI: https://doi.org/10.1149/1945-7111/ac4b26
34. *Dubenska L., Dushna O., Blazheyevskiy M.* et al. Kinetic and polarographic study on atropine N-oxide: its obtaining and polarographic reduction // Chem. Pap. 2021. Vol. 75. P. 4147–4155. DOI: https://doi.org/10.1007/s11696-021-01638-3
35. *Dushna O., Dubenska L., Blazheyevskiy M.* Polarographic determination of anabasine in a form of its N-oxide in urine // Visnyk Lviv Univ. Ser. Chem. 2024. Iss. 65. P. 142–154 DOI: https://doi.org/10.30970/vch.6501.142
36. *Gosser D. K.* Cyclic Voltammetry: Simulation and Analysis of Reaction Mechanisms // Synth. React. Inorg. Met.-Org. Chem. 1994. Vol. 24. P. 1237–1238. DOI: https://doi.org/10.1080/00945719408001398
37. *Brett C. B. A.* Electrochemistry Principles, Methods, and Applications (first ed.). Oxford Science Publications. 1993.
38. *Dushna O., Dubenska L., Gawor A., Karasiński J.* et al. Structural Characterization and Electrochemical Studies of Selected Alkaloid N-Oxides // Molecules. 2024. Vol. 29. P. 2721. DOI: https://doi.org/10.3390/molecules29122721

ВОЛЬТАМПЕРОМЕТРИЧНЕ ВИЗНАЧЕННЯ ХІНІНУ ТА ЙОГО N-ОКСИДУ З ВИКОРИСТАННЯМ ЕЛЕКТРОДІВ НА ОСНОВІ ТВЕРДОЇ АМАЛЬГАМИ СРІБЛА

В. Рибак[1], О. Душна[1,2], Т. Якубова[1], Л. Дубенська[1]*

[1]Львівський національний університет імені Івана Франка,
вул. Кирила і Мефодія, 6, 79005 Львів, Україна;

[2]Центр біологічних та хімічних досліджень, хімічний факультет,
Варшавський університет,
вул. Жвірки і Вігури, 101, 02–089 Варшава, Польща
**e-mail: liliya.dubenska@lnu.edu.ua*

Уперше розроблено вольтамперометричну методику визначення хініну з використанням електродів на основі твердої амальгами срібла (АЕ). Найбільшого струму та чіткого піку відновлення хініну можна досягнути з використанням АЕ, який модифіковано ртутним меніском (м-АЕ). Хінін відновлюється на м-АЕ з утворенням одного необоротного піку в слабо кислому та в лужному середовищах. Як оптимальне pH обрали pH 8, яке забезпечували універсальною буферною сумішшю. Пік відновлення хініну має адсорбційну природу струму, що сприяє накопиченню аналіту на поверхні електрода. За оптимальних умов отримали градуювальний графік для вольтамперометричного визначення хініну, для якого лінійна залежність струму від концентрації зберігається в межах від $2{,}0\cdot10^{-6}$ до $2{,}0\cdot10^{-5}$ М, а межа виявлення становить $1{,}7\cdot10^{-6}$ М.

Розроблену методику апробували під час аналізу тонізуючих напоїв. Отримані результати статистично опрацювали та підтвердили референтною методикою (методом високоефективної рідинної хроматографії з діодоматричним детектором). Відносна похибка визначення не перевищувала 5 %. Запропонована методика є швидкою, портативною, придатною для рутинного аналізу.

Ключові слова: вольтамперометрія, алкалоїд, хінін, N-оксид хініну, тверді амальгамні електроди.

Стаття надійшла до редколегії 01.11.2024
Прийнята до друку 21.01.2025