Voltammetric Determination of Ivabradine Hydrochloride Using Multiwalled Carbon Nanotubes Modified Electrode in Presence of Sodium Dodecyl Sulfate

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Abstract

Purpose: A new sensitive sensor was fabricated for the determination of ivabradine hydrochloride (IH) based on modification with multiwalled carbon nanotubes using sodium dodecyl sulfate as micellar medium to increase the sensitivity.

Methods: The electrochemical behavior of IH was studied in Britton-Robinson buffer (pH: 2.0-11.0) using cyclic and differential pulse voltammetry.

Results: The voltammetric response was linear over the range of 3.984 x 10^{-6}-3.475 x 10^{-5} mol L^{-1}. The limits of detection and quantification were found to be 5.160 x 10^{-7} and 1.720 x 10^{-6} mol L^{-1}, respectively.

Conclusion: This method is suitable for determination of IH in tablets and plasma.

Introduction

Ivabradine HCl (IH) is used to reduce the heart rate through inhibition of the pacemaker current (If). IH is used in the treatment of heart failure, in sinus rhythm and angina pectoris when beta blockers are not responding.1-3 Several methods have been reported to determine IH such as spectrophotometric method,4 chromatographic methods,4,11 spectrofluorimetric method,12 and potentiometric method.13 The electroanalytical methods are simple, rapid, and in expensive techniques, they have great importance in environmental monitoring and pharmaceutical analysis.14-20 Carbon nanotubes (CNTs) have matchless geometrical, mechanical, electronic and chemical properties. Multiwalled carbon nanotubes (MWNTs) modified electrodes have plentiful characteristics compared with bare electrode according to their unrivalled properties. Nanoparticles increase the number of active sites and the rate of mass transport to the electrode surface.21-24 This study aims to determine IH at multiwalled carbon nanotubes modified carbon paste electrode (MWCNTCPE) utilizing voltammetric method based on the electrochemical oxidation of IH.

Materials and Methods

Apparatus

SP-150 (Biologic Science Instruments, France) was used for voltammetric experiments. The results were analyzed using EC-Lab software. Ag/AgCl (3.0 mol L^{-1} NaCl) reference electrode and a platinum wire counter electrode were purchased from BASi (USA), pH meter (JENWAY 3510, UK) was used to adjust buffer solutions. JSM-6700F scanning electron microscope (Japan Electro Company) was used to do scanning electron microscopy (SEM) experiments. FTIR-8400S spectrophotometer (Shimadzu, Japan) was used to obtain FTIR spectra of MWCNTCPE and MWCNTCPE/SDS. The charges of atoms of IH were calculated using Huckel's method (ChemBio 3D Ultra program).

Materials and reagents

IH (98.5%) and Procoralan® tablets (5.39 mg of IH per tablet) were provided by Servier Egypt Industries Limited. MWCNTs (6-13 nm in diameter and 2.5-20 μm in length; purity >98%), sodium dodecyl sulfate (SDS), Graphite and paraffin oil were supplied from Sigma-Aldrich. IH stock solution (1.0 x 10^{-3} mol L^{-1}) and SDS solution (1.0 x 10^{-2} mol L^{-1}) was prepared using deionized water. Britton-Robinson (BR) buffer solutions (pH: 2.0-11.0) were prepared as mentioned before.6 Plasma was purchased from blood bank of VACSERA (Egypt).

Working electrodes

MWCNTCPE was made by mixing and stirring 1.0% (w/w) MWCNTs and 99% (w/w) graphite powder in
ethyl ether to get good homogeneity, and then dry this mixture in air. The dried mixture was mixed with paraffin oil to obtain a uniformly wetted paste. The hole of the electrode was filled with paste and smoothed on a filter paper until a shiny appearance was obtained. A carbon paste electrode (CPE) was obtained using the same procedures without MWCNTs addition.

**Effect of SDS**
The cyclic voltammograms of IH (1.43 x 10^{-4} mol L^{-1}) in BR buffer (pH 3) were recorded at MWCNTCPE upon successive addition of different volumes of SDS (1.0 x 10^{-2} mol L^{-1}) to the voltammetric cell.

**Calibration curve of IH**
Different volumes of IH solution (1.0 x 10^{-3} mol L^{-1}) were added to 5 mL of BR buffer of pH 3.0. The solution was stirred for 5 s and the differential pulse voltammograms were done using scan rate of 10 mV s^{-1} at MWCNTCPE/SDS.

**Analysis of IH in tablets**
Fifteen Procoralan tablets were grounded. Suitable amount needed to get IH solution of 1.0 x 10^{-3} mol L^{-1} was added to flask containing 60 mL deionized water, then dissolved by sonication for 15 min and the volume was completed to 100 mL with deionized water. The solution was filtered to remove the insoluble excipients. Standard addition method was performed to determine IH in dosage form.

**Analysis of IH in plasma**
One mL of human plasma and 2 mL of acetonitrile were added to a series of 10 mL centrifuge tubes containing different volumes of IH (1.0 x 10^{-3} mol L^{-1}), the mixture was centrifuged at 5000 rpm for 10 min to get rid of protein residues. 0.5 mL from the supernatant was transferred into voltammetric cell containing 4.5 mL of BR buffer (pH 3.0) and SDS solution (3.58 x 10^{-4} mol L^{-1}). The procedures mentioned in calibration curve were done. The institutional board (NODCAR, Egypt) have agreed for testing with human subjects. Agreement was acquired from all contributors.

**Results and Discussion**

**Voltammetric behavior of IH**
Figure 1A displays the cyclic voltammograms of IH (1.43 x 10^{-4} mol L^{-1}) at CPE in BR buffer of different pH values. The forward scan shows anodic peak due to the oxidation process, while the reverse scan shows no peaks, indicating the irreversibility of the electrochemical process.

**Influence of pH**
The electrochemical action of IH (1.43 x 10^{-4} mol L^{-1}) was studied in different pH solutions (2.0-11.0) at CPE using cyclic voltammetry (CV) and scan rate of 100 mV s^{-1} as shown in Figure 1. Figure 1A shows that well defined and sharp anodic peaks in acidic medium (pH: 2.0-6.0) and broad peaks in neutral and basic medium (pH: 7.0-11.0). Figure 1 (A, B) shows that the anodic peak currents increases as pH increases up to pH 6.0, and decreases as pH increases up to pH 11.0.

![Figure 1](image-url)
IH. Electronic Supplementary Information 1 (ESI 1) shows the difference in the surface shape between CPE and MWCNTCPE according to their SEM. ESI 2 shows the FTIR spectra of MWCNTCPE and MWCNTCPE/SDS. MWCNTCPE does not show clear absorption peaks in its FTIR spectrum.27,28 MWCNTCPE/SDS shows S-O-C vibration peaks at 850 cm\(^{-1}\) and 980 cm\(^{-1}\), C-O stretching vibration peak at 1040 cm\(^{-1}\), SO\(_2\) symmetric vibration peak at 1100 cm\(^{-1}\), CH\(_2\) scissoring at 1460 cm\(^{-1}\), CH\(_2\) stretching at 2890 (asymmetric) and 2830 cm\(^{-1}\) (symmetric), and a broad band between 3000 and 3650 cm\(^{-1}\) due to O-H stretching vibration.29

**Figure 2.** Cyclic voltammograms of IH (1.43 x 10\(^{-4}\) mol L\(^{-1}\)) at CPE, MWCNTCPE and MWCNTCPE/SDS in BR buffer of pH 3.0 at scan rate of 100 mV s\(^{-1}\) (A), effect of SDS concentration on the anodic peak current of IH (B), the oxidation mechanism of IH at MWCNTCPE/SDS (C).

**Influence of SDS**
Since IH is positively charged in acidic medium, SDS (as anionic surfactant) was used to enhance the peak current giving better sensitivity in the analysis of IH. Different volumes of SDS solution of concentrations varied from 2.85 x 10\(^{-5}\) to 5.91 x 10\(^{-4}\) mol L\(^{-1}\) were added to the electrolytic cell containing IH (1.43 x 10\(^{-4}\) mol L\(^{-1}\)) in BR buffer (pH 3.0). Figure 2B shows that the peak current increases as the concentration of SDS increases up to 3.58 x 10\(^{-4}\) mol L\(^{-1}\) then after this concentration the peak current decreases as the concentration of SDS increases. Hence, the optimum SDS concentration was 3.58 x 10\(^{-4}\) mol L\(^{-1}\).

The mechanism of oxidation of IH is through the loss of one electron and one proton to form cation radical and cation in acidic and basic medium, respectively as shown in Figure 2C. The charges of atoms of IH were shown in ESI 3; N (amine) has the smallest negative value of -0.0586 (highest positive value) than those of the other atoms. Thus, it is the center of oxidation which loss one electron and its attached proton to form cation radical in acidic medium, while in basic medium this nitrogen atom loss one electron and the carbon atom C (18) which has
the highest positive charge (0.0243) than those of the other carbon atoms loss one proton to form cation.

**Influence of scan rate**

Figure 3 represents the oxidation of IH (1.43 x 10^{-4} mol L^{-1}) in BR buffer (pH 3.0) as a function of scan rate (ʋ) (10-400 mV s^{-1}) at MWCNTCPE/SDS. As ʋ increases, the peak current increases, and the peak potentials increases (Figure 3A). Figure 3B, 3C show linear relationships were found between the peak current and ʋ^{1/2} and between the logarithms of the peak current and ʋ (log I = 0.80 + 0.48 log ʋ, R (Correlation coefficient) = 0.9997), the slope 0.48 is near to 0.50 (theoretical value) suggesting diffusion controlled process of the oxidation of IH.

**Chronoamperometry study**

The diffusion coefficient of IH was determined in BR buffer (pH 3.0) at MWCNTCPE/SDS; the potential was set at 1.167 V. The diffusion coefficient of IH was determined using Cottrell equation: \( I = nFAC(D/πt)^{1/2} \) where I, n, F, C, D, and A are the current, the number of electrons (n = 1 for IH), Faraday constant (96480 C mol^{-1}), analyte concentration (mol cm^{-3}), the diffusion coefficient (cm^2 s^{-1}), and electroactive area of the working electrode, respectively. A was obtained using the diffusion coefficient of K3[Fe (CN)6] which is equal to 7.6 x 10^{-6} cm^2 s^{-1}^{27} and thus A was calculated to be 0.115 cm^2.

Figure 4A represents the chronoamperograms of IH at MWCNTCPE/SDS in BR buffer of pH 3.0. It was shown that the chronoamperometric signal increases as the concentration of IH increases. It was found that 16 s is a sufficient electrolysis time to reach steady state. Figure 4B shows the linear relationships between I and t^{1/2}. The plot of the slopes of straight lines obtained in Figure 4B against the concentration of IH gives a straight line as shown in Figure 4C; the slope of this relation is used to calculate D based on Cottrell equation. D of IH was found to be 3.175 x 10^{-5} cm^2 s^{-1}.

The reaction rate constant (K) was determined using the following equation: \( Ic/I_L = (πKc)^{1/2} \) where \( Ic \) and \( I_L \) are the catalytic and limited currents in the presence and in the absence of IH, respectively. The value of K above equation was calculated from the slope of the plot of \( Ic/I_L \) vs. t^{1/2} for 3.0 x 10^{-6} mol L^{-1} IH (Figure 4D), K was determined as 1.92 x 10^{4} mol^{-1} L s^{-1}.

**Determination of IH**

Linear range, limits of detection (LOD) and quantification (LOQ) of IH were obtained using differential pulse voltammetry (DPV) at the
MWCNTCPE/SDS. Figure 5 depicts the calibration curve of IH (3.984 x 10⁻⁶ - 3.475 x 10⁻⁵ mol L⁻¹), I (µA) = 3.51 + 0.52 C (µmol L⁻¹), R = 0.9994. LOD and LOQ were found to be 5.160 x 10⁻⁷ and 1.720 x 10⁻⁶ mol L⁻¹, respectively.

Figure 5. Calibration curves of IH in bulk and plasma using DPV at MWCNTCPE/SDS in BR buffer solution of pH 3.0, ʋ = 10 mV s⁻¹.

Table 1. Comparison between the proposed DPV method and the reported HPLC method for determination of IH. Statistical analysis of the proposed method and the reported HPLC method for determination of IH.¹

| Method                      | Linear range          | Reference |
|-----------------------------|-----------------------|-----------|
| DPV (mol L⁻¹) (µg mL⁻¹)     | 3.984 x 10⁻⁶ - 3.475 x 10⁻⁵ (2.012 - 17.550) | This work |
| Spectrophotometry (µg mL⁻¹) | 4.2 - 31.6            | [4]       |
| Chromatography (µg mL⁻¹)    | 4.2 - 31.6            | [4]       |
| Potentiometry (mol L⁻¹)     | 70.69 - 131.29        | [11]      |
| Potentiometry (mol L⁻¹)     | 1.0 x 10⁻⁵ - 1.0 x 10⁻² | [13]      |

| Statistical term       | Proposed method | Reported method¹¹ |
|-------------------------|-----------------|------------------|
| %Mean recovery          | 100.316         | 100.852          |
| SD                      | 1.593           | 1.450            |
| Variance                | 2.537           | 2.163            |
| n                       | 5               | 5                |
| t-test (2.306)          | 0.553           |                  |
| F-ratio (6.39)¹         | 1.173           |                  |

¹Figures in parenthesis are the theoretical values of t and F at confidence limit 95%.

Interference study
Lactose, microcrystalline cellulose, titanium dioxide and magnesium stearate are used as excipients in pharmaceutical industry. Interference studies were performed prior to analysis of IH in dosage forms using 1.0 x 10⁻⁵ mol L⁻¹ and 1.0 x 10⁻⁴ mol L⁻¹ of IH and all excipients, respectively. The presence of excipient not affect drug estimate.

Analysis of IH in tablets
Standard addition method was applied for analysis of IH in Procoralan tablets without any extraction steps prior to the analysis. The results showed that interference from the matrix was negligible (Table 2). IH can be determined in pharmaceutical formulation within the linear range (3.984 x 10⁻⁶ - 3.475 x 10⁻⁵ mol L⁻¹).

Analysis of IH in plasma
DPV method was successfully used to determine IH in spiked human plasma over the range of 5.964 x 10⁻⁶ - 2.723 x 10⁻⁵ mol L⁻¹ (Figure 5) obeying analytical equation: I (µA) = 3.29 + 0.43 C (µmol L⁻¹), R = 0.9991. LOD and LOQ were 1.15 x 10⁻⁶ and 3.82 x 10⁻⁶ mol L⁻¹, respectively. The recovery values were in the range of 99.16-102.32%. The relative standard deviation was 0.996%.
Table 2. Precision data for the proposed method. Determination of IH in Procoralan tablets by applying standard addition method.

| Concentration (mol L⁻¹) | Intra-day precision | Inter-day precision | Recovery (%) |
|-------------------------|---------------------|---------------------|--------------|
|                         | Amount found (a)    | %Recovery (a)       | %Mean Recovery ± SD | %RSD |
| 7.936 x 10⁻⁵            | 7.938 x 10⁻⁵        | 100.025             | 99.854±0.372   | 0.372 |
| 1.574 x 10⁻⁵            | 1.565 x 10⁻⁵        | 99.428              | 99.630±0.403   | 0.404 |
| 2.723 x 10⁻⁵            | 2.726 x 10⁻⁵        | 100.110             | 99.780        |        |

| Concentration (mol L⁻¹) | Amount Found (a) | %Recovery (a) | %Mean Recovery ± SD | %RSD |
|-------------------------|-----------------|--------------|---------------------|------|
| 7.936 x 10⁻⁵            | 7.931 x 10⁻⁵    | 99.937       | 99.634±0.553        |      |
| 1.574 x 10⁻⁵            | 1.561 x 10⁻⁵    | 99.174       |                     |      |
| 2.723 x 10⁻⁵            | 2.717 x 10⁻⁵    | 99.780       |                     |      |

| Dosage form | IH (mol L⁻¹) Taken | IH (mol L⁻¹) Added | IH (mol L⁻¹) Found | Recovery (%) |
|-------------|--------------------|--------------------|-------------------|--------------|
| Procoralan  | 5.964 x 10⁻⁶       | 1.984 x 10⁻⁵       | 7.880 x 10⁻⁵      | 99.144       |
|             | 3.964 x 10⁻⁵       | 9.898 x 10⁻⁵       | 99.698            |              |
|             | 5.940 x 10⁻⁵       | 11.95 x 10⁻⁵       | 100.386           |              |
|             | 7.912 x 10⁻⁵       | 13.78 x 10⁻⁵       | 99.308            |              |

*Mean of three different samples for each concentration. SD: Standard deviation of three different determinations. RSD: Relative standard deviation.

Conclusion
The proposed method used MWCNTs and SDS based on their properties for the quantitative determination of IH in bulk, tablets and plasma. The sensor sensitivity and selectivity were enhanced using MWCNTs and SDS in comparison with CPE. The proposed DPV method is not time consuming method, there is no extraction stage. It can be used for quality control of IH.

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Ethical Issues
Not applicable.

Conflict of Interest
Authors declare no conflict of interest in this study.

References
1. Sweetman SC. Martindale: The Complete Drug Reference. 36th ed. London, UK: Pharmaceutical Press; 2009.
2. Vilaine JP. The discovery of the selective I1 current inhibitor ivabradine. A new therapeutic approach to ischemic heart disease. Pharmacol Res 2006;53(5):424-34. doi: 10.1016/j.phrs.2006.03.016
3. Tubati VP, Murthy TEGK, Rao ASS.Comparison of different techniques involved in the development of ivabradine HCl floating pulsatile multiparticulate systems for chronotherapeutic delivery. Br J Pharm Res 2016;9(4):1-12. doi: 10.9734/BJPR/2016/22566
4. Maheshwari S, Khandhar AP, Jain A. Quantitative determination and validation of ivabradine HCl by stability indicating RP-HPLC method and spectrophotometric method in solid dosage form. Eurasian J Anal Chem 2010;5(1):53-62.
5. Klippert P, Jeanniot JP, Polve S, Lefevre C, Merdjan H. Determination of ivabradine and its N-demethylated metabolite in human plasma and urine, and in rat and dog plasma by a validated high-performance liquid chromatographic method with fluorescence detection. J Chromatogr B Biomed Sci Appl 1998;719(1-2):125-33. doi: 10.1016/S0378-4347(98)00406-X
6. Francois-Bouchard M, Simonin G, Bossant, Boursier-Neyret C. Simultaneous determination of ivabradine and its metabolites in human plasma by liquid chromatography--tandem mass spectrometry. J Chromatogr B Biomed Sci Appl 2000;745(2):261-9. doi: 10.1016/S0378-4347(99)00275-9
7. Lu C, Jia Y, Yang J, Jin X, Song Y, Liu W, et al. Simultaneous determination of ivabradine and N-desmethylivabradine in human plasma and urine using a LC-MS/MS method: application to a pharmacokinetic study. Acta Pharm Sin B 2012;2(2):205-12. doi: 10.1016/j.apsb.2012.01.004
8. Pikul P, Nowakowska J, Ciura K. Chromatographic analysis of ivabradine on polar, nonpolar and chemically modified adsorbents by HPTLC. J Food Drug Anal 2013;21(2):165-8. doi: 10.1016/j.jfda.2013.05.006
9. Damle MC, Bagwe RA. Development and validation of stability-indicating HPTLC method for ivabradine HCl. Pharm Sci Monitor 2015;6(1):141-52.
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10. Motisariya MH, Patel KG, Shah PA. Validated stability-indicating high performance thin layer chromatographic method for determination of Ivabradine hydrochloride in bulk and marketed formulation: an application to kinetic study. Bull Fac Pharm Cairo Univ 2013;51(2):233-41. doi: 10.1016/j.bfpcu.2013.07.001

11. Kumar PS, Pandiyani K, Rajagopal K. Development and validation of stability indicating rapid HPLC method for estimation of ivabradine hydrochloride in solid oral dosage form. Int J Pharm Pharm Sci 2014;6(4):378-82.

12. Patel KG, Motisariya MH, Patel KR, Shah PA, Gandhi TR. Development and validation of spectrofluorimetric method for estimation of ivabradine hydrochloride in marketed formulation and its applicability in plasma. Pharm Lett 2014;6(5):8-13.

13. Abo-Talib NF, Tammam MH, Attia AK. Electrochemical study of ivabradine hydrochloride ion selective electrodes using different ionophores. RSC Adv 2015;5(116):95592-7. doi: 10.1039/c5ra21033j

14. Majidi MR, Pournaghi-Azar MH, Azar P, Fadakar Bajeh Baj R, Naseri A. Fabrication of ferrocene functionalised ionic liquid/carbon nanotube nanocomposite modified carbon-ceramic electrode: application to the determination of hydrazine. Int J Environ Anal Chem 2016;96(1):50-67. doi: 10.1080/03067319.2015.1114106

15. Shishebore MR, Zare HR, Nematollahi D. Electrocatalytic determination of morphine at the surface of a carbon paste electrode spiked with a hydroquinone derivative and carbon nanotubes. J Electroanal Chem 2012;665:45-51. doi: 10.1016/j.jelechem.2011.11.018

16. Rizk M, Attia AK, Elshahed MS, Farag AS. Validated voltammetric method for the determination of antiparkinsonism drug entacapone in bulk, pharmaceutical formulation and human plasma. J Electroanal Chem 2015;743:112-9. doi: 10.1016/j.jelechem.2015.02.022

17. Babaei A, Afrasiabi M, Azim G. Nanomolar simultaneous determination of epinephrine and acetaminophen on a glassy carbon electrode coated with a novel Mg-Al layered double hydroxide-nickel hydroxide nanoparticles-multi-walled carbon nanotubes composite. Anal Methods 2015;7(6):2469-78. doi: 10.1039/C4AY02406K

18. Attia AK. Determination of antihypertensive drug moexipril hydrochloride based on the enhancement effect of sodium dodecyl sulfate at carbon paste electrode. Talanta 2010;81(1-2):25-9. doi: 10.1016/j.talanta.2009.11.031

19. Attia AK, Badawy AM, Abd-Elhamid SG. Determination of sparfloxacins and besifloxacin hydrochlorides using gold nanoparticles modified carbon paste electrode in micellar medium. RSC Adv 2016;6(46):39605-17. doi: 10.1039/C6RA04851J

20. Attia AK, Salem WM, Mona AM. Voltammetric assay of metformin hydrochloride using pyrrgal modified carbon paste electrode. Acta Chim Solv 2015;62(3):588-94. doi: 10.17344/asi.2014.950

21. Rao CN, Satishkumar BC, Govindaraj A, Nath M. Nanotubes. ChemPhysChem 2001;2(2):78-105. doi: 10.1002/1439-7641(20010216)

22. Baughman RH, Zakhidov AA, de Heer WA. Carbon nanotubes: the route toward applications. Science 2002;297(5582):787-92. doi: 10.1126/science.1060928

23. Xiong H, Zhao Y, Liu P, Zhang X, Wang S. Electrochemical properties and the determination of nicotine at a multi-walled carbon nanotubes modified glassy carbon electrode. Mikrochim Acta 2010;168(1):31-6. doi: 10.1007/s00604-009-0258-8

24. Kasumov AY, Bouchiat H, Reulet B, Stephan O, Khodos II, Gorbatov YB, et al. Conductivity and atomic structure of isolated multiwalled carbon nanotubes. Europhys Lett 1998;43(1):89-94. doi: 10.1209/epl/i1998-00324-1

25. Shi G, Shen Y, Liu J, Wang C, Wang Y, Song B, et al. Molecular-scale hydrophilicity induced by solute: molecular-charge thickened pancakes of aqueous salt solution on hydrophobic carbon-based surfaces. Sci Rep 2014;4:6793. doi: 10.1038/srep06793

26. Rusling JF. Molecular aspects of electron transfer at electrodes in micellar solutions. Colloids Surf Physicochem Eng Aspects 1997;123-124:81-8. doi: 10.1016/S0927-7577(96)03789-2

27. Muraliganth T, Murugan AV, Manthiram A. Nanoscale networking of LiFePO4nanorods synthesized by a microwave-solvothermal route with carbon nanotubes for lithium ion batteries. J Mater Chem 2008;18(46):5661-8. doi: 10.1039/B812165F

28. Morávková Z, Trchová M, Tomšík E, Čechvala J, Stejskal J. Enhanced thermal stability of multiwalled carbon nanotubes after coating with polyaniline salt. Physicochem Eng Aspects 2015;77(1):157.

29. Coates J. Interpretation of infrared spectra, a practical approach. Encyclopedia of analytical chemistry. USA: John Wiley & Sons; 2000.

30. Gossler DK. Cyclic voltammetry: Simulation and analysis of reaction Mechanism. New York: VCH; 1993.

31. Bard AJ, Faulkner LR. Electrochemical methods: Fundamentals and applications. 2nd ed. New York: Wiley; 2001.

32. Galus Z. Fundamentals of electrochemical analysis. New York: Ellis Horwood; 1994.

33. Miller JR, Miller JC. Statistics and chemometrics for analytical chemistry. 4th ed. Harlow, England: Prentice Hall; 2000.