Egypt.J.Chem. **Vol. 63**, No. 6. pp. 2185 - 2199 (2020)

Egyptian Journal of Chemistry
http://ejchem.journals.ekb.eg/

Improvement of Adsorptive Voltammetric Methods for Determination of Midodrine by Carbon Paste Electrode Modified with Gold Nano Particles in Presence of B-Cyclodextrin

Waheed M. Salem*
Department of Chemistry, Faculty of Sciences, Damanhur University, Egypt.

AN effective novel electrochemical sensor constructed for the determination of Midodrine hydrochloride drug using differential pulse voltammetry. The sensor is based on a carbon paste electrode modified with gold nanoparticles and β-cyclodextrin in Britton-Robinson buffer of pH 3.0. The effect of various experimental parameters on the constructed electrodes properties including pH, β-cyclodextrin concentration and scan rate was investigated. At the optimum conditions, a linear range from 3.0 x 10^{-6} to 3.2 x 10^{-4} mol L^{-1} with correlation coefficient of 0.9997 and a detection limit of 5.14 x 10^{-7} mol L^{-1}were obtained. The modified electrodes were used for microdetermination of the drug in tablets and spiked human urine samples with appropriate an acceptable recovery, reproducibility, selectivity and robustness.

Keywords: Gold nanoparticles modified electrode, Midodrine hydrochloride, β-cyclodextrin, Differential Pulse Voltammetry, Urine analysis.

Introduction

Midodrine hydrochloride (MID) is a direct-acting sympathomimetic with selective alpha adrenergic agonist. It acts as a peripheral vasoconstrictor. So it is used in the treatment of hypotensive states particularly orthostatic hypotension [1-4]. To determine MID, some methods had been developed based such as; high liquid chromatography (HPLC) with fluorescence[5, 6]and ultraviolet (UV) detection[7, 8], capillary electrophoresis (CE)[9], potentiometry [10] and spectrophotometry[11-13]. Electroanalytical methods are rapid, accurate and cheap with very low detection limits for electroactive molecules. Applications of modified electrodes have great interest in various areas of research and development, such as electroanalysis, biosensors and electroanalysis [14-18]. Gold nanoparticles have been used in electroanalysis of pharmaceutical compounds studies, due to its large surface area, high conductivity and electroanalytical characteristics. They can act as tiny conduction centers and facilitate the transfer of electrons [19-22]. Cyclodextrin catchers(CDs) are talented of appealing various size of target molecules; due to its physically unique molecular configuration[23]. Since CDs are hydrophobic inside and hydrophilic outside, they can form complexes with hydrophobic compounds. The CD considers as a trap for certain molecules better due to its basket type physical[24-26]. Furthermore it is known as the host guest recognition [27-32].There is no attempts to determine MID using voltammetric methods. Therefore, gold nanoparticles carbon paste modified electrodes were fabricated in the presence of β-cyclodextrin solution for sensitive quantification of MID using differential pulse voltammetry (DPV) based the enhancement effect of gold nanoparticles and formation of inclusion complex with β-cyclodextrin (CD). The stereo-structure, numbering system; and IUPAC name of Midodrine hydrochloride (MID) are shown in Fig. 1.

*Corresponding author e-mail:waheedsalem1979@gmail.com, Tel.: 002 01006059535
Received 17/10/2019; Accepted 24/11/2019
DOI: 10.21608/ejchem.2019.17052.2131

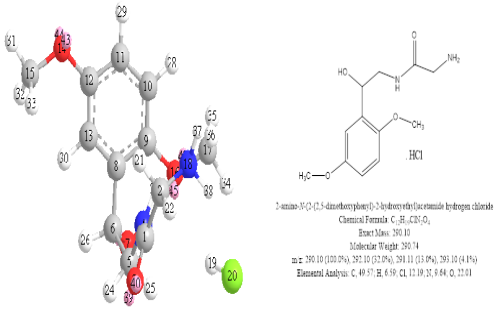


Fig. 1. Chemical and stereo structure of MID.

Experimental

Materials and solutions

Standard MID and its pharmaceutical dosage form, Midodrine 2.5 mg tablets, were provided by Nile Company for Pharmaceuticals and Chemical Industries, Egypt. MID stock solution was prepared by dissolving an appropriate amount of MID powder in deionized water to obtain 1.0 x 10^{-2}M solution. Standard working solutions were prepared by dilutions of the stock solution just before use. B-cyclodextrin (β-CD) was purchased from Fluka. Graphite powder, paraffin oil and hydrogen tetrachloroaurate were supplied from Sigma-Aldrich. Britton-Robinson (BR) buffer was prepared by mixing 0.04 M phosphoric acid, acetic acid and boric acid [33]. An appropriate amount of 0.2 M NaOH was added to BR buffer to obtain solutions of pH values varied from 2.0 to 11.0.

Preparation of gold nanoparticles modified carbon paste electrode

Carbon paste electrode (CPE): the carbon paste was prepared by mixing of 0.5 g graphite powder (particle dimension 20 µm, Sigma–Aldrich, Egypt) with 0.3 mL of paraffin oil in mortar with a pestle[34]. The carbon paste was packed into the hole of the electrode body and smoothed on a filter paper until its shiny appearance. CPE was immersed into a 6 mmol L^{-1} hydrogen tetrachloroaurate ($HAuCl_4$) solution containing 0.1 M KNO_3 prepared in doubly distilled water and deaerated by bubbling with nitrogen. A constant potential of -400 mV was applied for 400 sec [35]versus Ag/AgCl reference electrode. The obtained gold nanoparticles modified carbon paste electrode (GNCPE) was washed with doubly distilled water and dried carefully before being used.

Experimental and instrumental set up

All voltammetric measurements were performed using a pc-controlled AEW2 electrochemistry work station and data were analyzed with ECprog3 electrochemistry software, manufactured by Sycopel Scientific Limited (Tyne & Wear, UK). The one compartment glass cell with the three electrodes was connected to the electrochemical workstation through a C-3-stand from BAS (USA). A platinum wire from BAS (USA) was employed as auxiliary electrode. All the cell potentials were measured with respect to Ag/AgCl (3.0 mol L^{-1} NaCl) reference electrode from BAS (USA). Solutions were degassed using pure nitrogen prior and throughout the electrochemical measurements. A JENWAY 3510 pH meter (England) with glass combination electrode was used for pH measurements. Measurements of scanning electron microscopy (SEM) were investigated with a JSM-6700F scanning electron microscope (Japan ElectroCompany).

Effect of β-CD concentration

The cyclic voltammetry of 1.0 x 10^{-3}M MID (in BR buffer, pH 3.0) was studied on GNCPE upon successive additions from β-CD solution (1.0 x 10^{-2}M) to the electrolytic cell and the voltammograms were recorded using cyclic voltammetry.

Determination of MID in bulk powder

Aliquots of MID solution (1.0 x 10^{-3}M) were added to the electrolytic cell containing 5 mL of BR buffer of pH 3.0. The solution was stirred for 5 sec at open circuit conditions in presence of at GNCPE working electrode in the presence of β-CD solution (4.0 x 10^{-5}M) and the voltammograms were recorded at scan rate of 10 mV s^{-1}[34].

Analysis of MID in dosage form

Twenty tablets (Midodrine 2.5 mg tablets) were accurately weighed and finely powdered. A portion of the finely grounded powder needed to prepare 1.0 x 10^{-3}MMID solution was transferred into 100 mL calibrated flask containing 75 mL deionized water, then dissolved by sonication for 30 min and made up to the volume with deionized water. The solution was filtered to separate the insoluble excipients. 35 µL of the resulted solution and different aliquots of standard MID solution (1.0 x 10^{-3}M) were introduced into the electrolytic cell and the voltammograms were recorded[36].

Applications to human urine

Accurately measured aliquots of MID solutions were pipetted into centrifugation tubes containing 400 µL human urine in each tube, then vortex was done for 5 min. Into each tube, 0.5 ml of methanol, 0.1 mL NaOH (0.1 M) and 0.5 ml $ZnSO_4.7\ H_2O$ (5% w/v) [37] were added, then centrifuged for 10 min at 4000 rpm. The clear supernatant layer was filtered through 0.45 µm Milli-pore filter. The supernatant liquor (0.1 mL) was transferred into the voltammetric cell and completed to 5 mL with a pH 3.0 BR buffer. The drug MID was quantified by means of the proposed DPV procedure[38].

Conduct of stress studies

Hydrolytic-degradants of MID was prepared by refluxing in acidic medium according published method[39]. Substantially complete degradation was done under acidic condition by refluxing with 0.1MHCl for 13hrs; then the solution was neutralized. It was noted that the main degradant is similarly the main metabolite of the MID in the human body The UV-degradation was achieved by keeping the (30 µg mL^{-1}) MID solution in UV light lamp (254nm, 20watt) and after each 10 h interval the sample was withdrawn and requisite concentration was prepared for measuring.

Results and Discussion

SEM of surface electrodes

The sensitive response of a voltammetric sensor was according to its physical morphology of surface. The morphology of bare CPE (A) and GNCPE (B) were shown in Fig. 2. The SEM image displays that CPE surface was predominated by isolated and unevenly shaped graphite flakes and separated layers, but the SEM image of GNCPE displays that gold nanoparticles are sited at different sites of the elected surface[40], Nano-particles increased number of active nucleation sites and nucleation rate. Also, a spongy nanostructured of gold nanoparticles film was observed which particularly improved the active area of GNCPE surface. The active areas of bare CPE and GNCPE are calculated using chronoamperometry with equation: $\Gamma = Q/nFA$[41] where Q is the charge resulted by integration of the current against time, A is the working electrode surface area, and n means number of electrons involved. It was calculated to be 0.082 and 0.201 cm^2 for bare CPE, and GNCPE respectively, The Active surface areas of the compared CPE, and GNCPE were achieved by applying CV using 1.0 mM $K_4Fe\ (CN)_6$ as a probe with different scan rates. For a reversible process controlled by one electron system, using the Randles-Sevcik formula equation[34, 42]. In our experiment, electroactive areas of CPE and GNCPE were found to be 0.092 and 0.241 cm^2. Electro-active surface area of GNCPE was found to be higher than that of CPE, hence greater response of peak current was observed for GNCPE towards

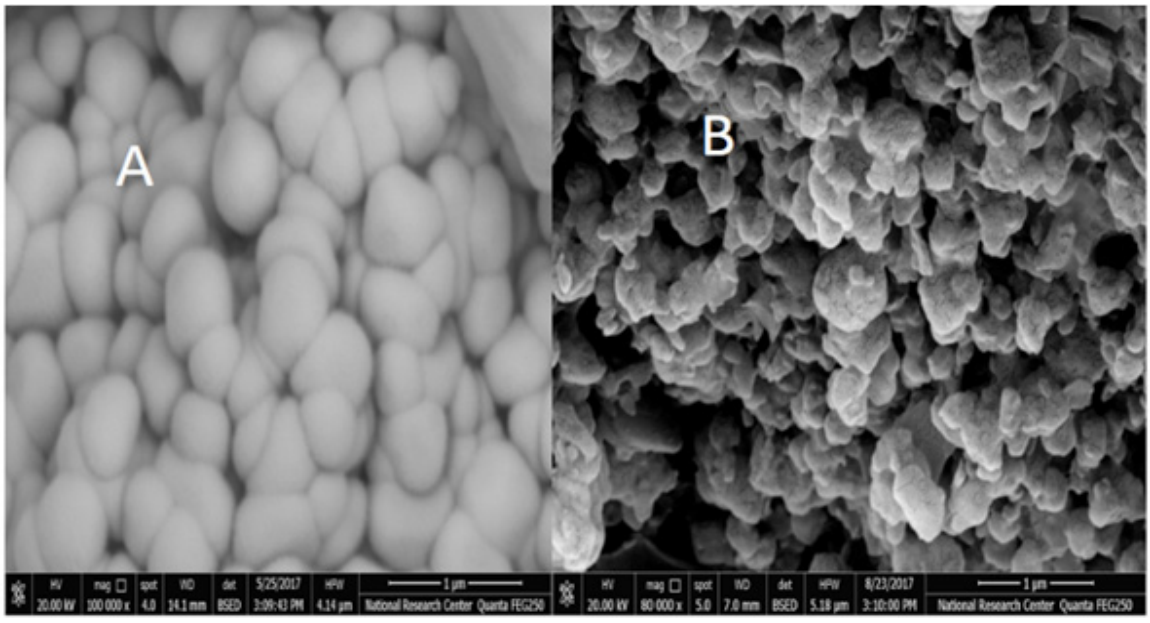


Fig. 2. Scanning electron microscope images of (A) bare CPE and (B) GNCPE.

MID oxidation.

Effect of pH and electrochemical behavior of MID

Preliminary cyclic voltammetry (CV) experiments for 1.0 x 10^{-3} mol L^{-1} MID were carried out at CPE in BR buffer background solutions over the pH range (2.0-11.0). Fig. 3 shows reversible oxidation process of MID within the pH range from 2.0 to 5.0 due to the oxidation of hydroxyl group and a second irreversible oxidation peak appears at more positive potentials from pH 6.0 to pH 11.0 due to the oxidation of primary amino group which is deactivated in acidic medium due to protonation.

Fig. 3A shows that the anodic peak potential increases by increasing the pH up to pH 3 reaching approximately steady state up to pH 5.0. The anodic peak potential decreases by increasing the pH up to 11.0. Fig. 3B shows that the anodic peak current (Ip) has three maximum values 23.23 µA, 29.05 µA and 29.07 µA at pH values 3.0, 7.0 and 11.0, respectively. Therefore, we study the effect of different modifiers such as gold nanoparticles and β-CD solution on the anodic peak current at these pH values.

Fig. 5A shows cyclic voltammograms of 1.0 x 10^{-3} mol L^{-1} MID at CPE and GNCPE, from the figure we note that the anodic peak currents of MID in case of GNCPE, 55.78 µA (pH 3), 95.92 µA (pH 7) and 123.22 µA (pH 11), have higher values than those at CPE. Fig 5B shows the cyclic voltammograms of MID at GNCPE in the presence of 4.0 x 10^{-5}mol L^{-1} β-CD, from the figure we note that the maximum anodic peak current value of 149.22 µA obtained at pH 3.0, while the peak current values at pH 7.0 (79.97 µA) and pH 11.0 (83.61 µA) are smaller than the corresponding values at GNCPE at pH 7.0 and pH 11.0 in absence of β-CD solution. Thus pH 3.0 is chosen as the optimum pH value for the determination of MID at GNCPE in the presence of β-CD solution indicating that acidic medium (pH 3.0) is suitable to form inclusion complex with β-CD rather than neutral (pH 7.0) and basic medium (pH 11.0).

Fig. 6 shows the suggested oxidation mechanism of MID at pH 3.0 which may be attributed to the oxidation of hydroxyl group to

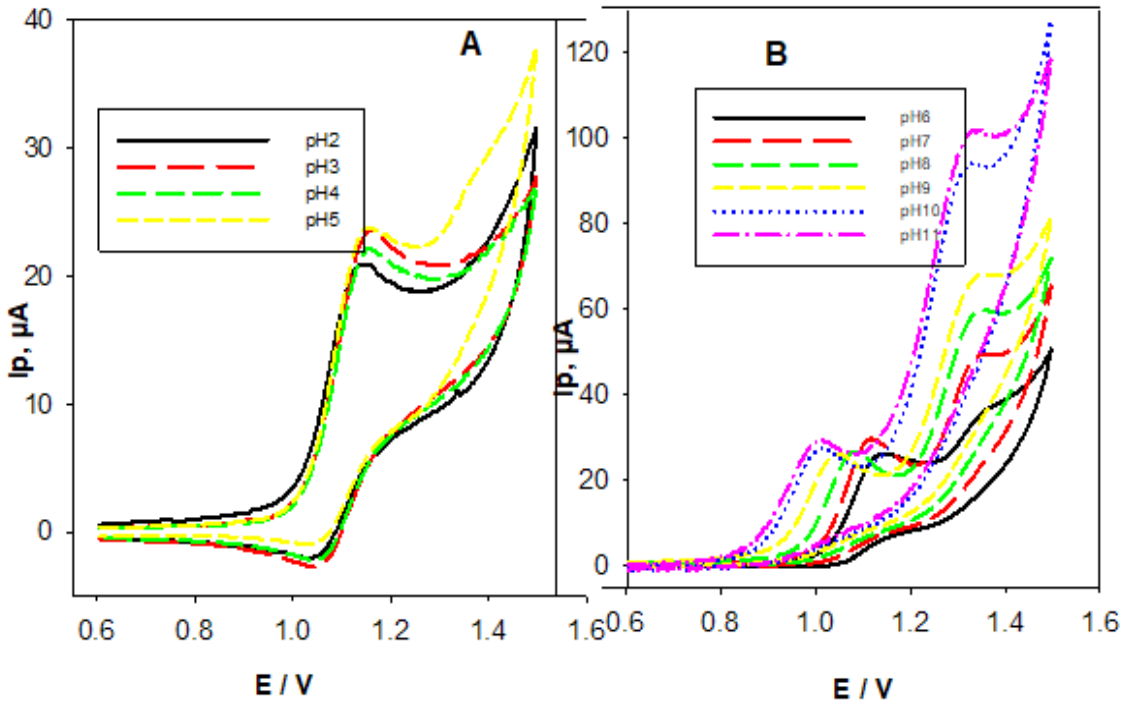


Fig. 3.Cyclic voltammograms of the effect of solution pH on the oxidation of MID (1.0 x 10-3 mol L-1) at CPE using BR buffer from (A)pH 2.0 to 5.0 and (B) pH6.0-11.0.

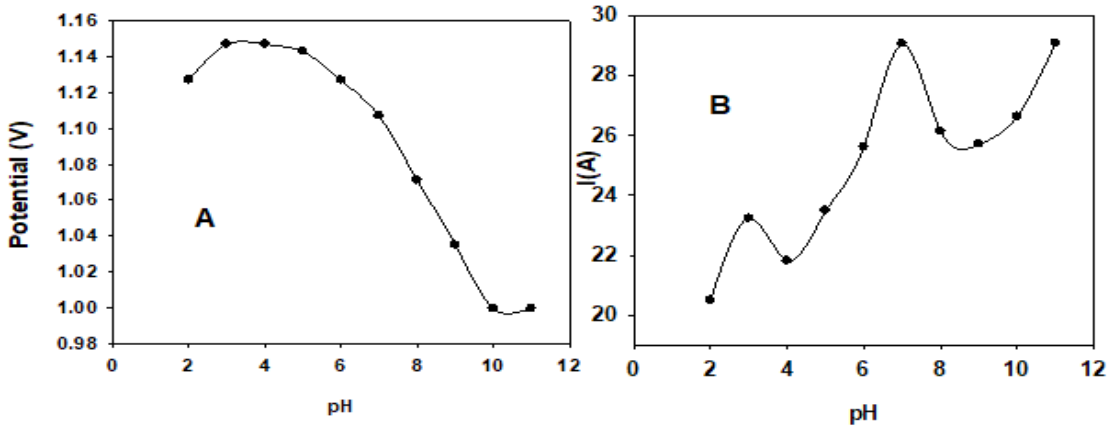


Fig. 4.The plot of anodic peak potential (A) anodic and peak current (B) of MID (1.0 x 10^{-3}M) as a function of pH at CPE.

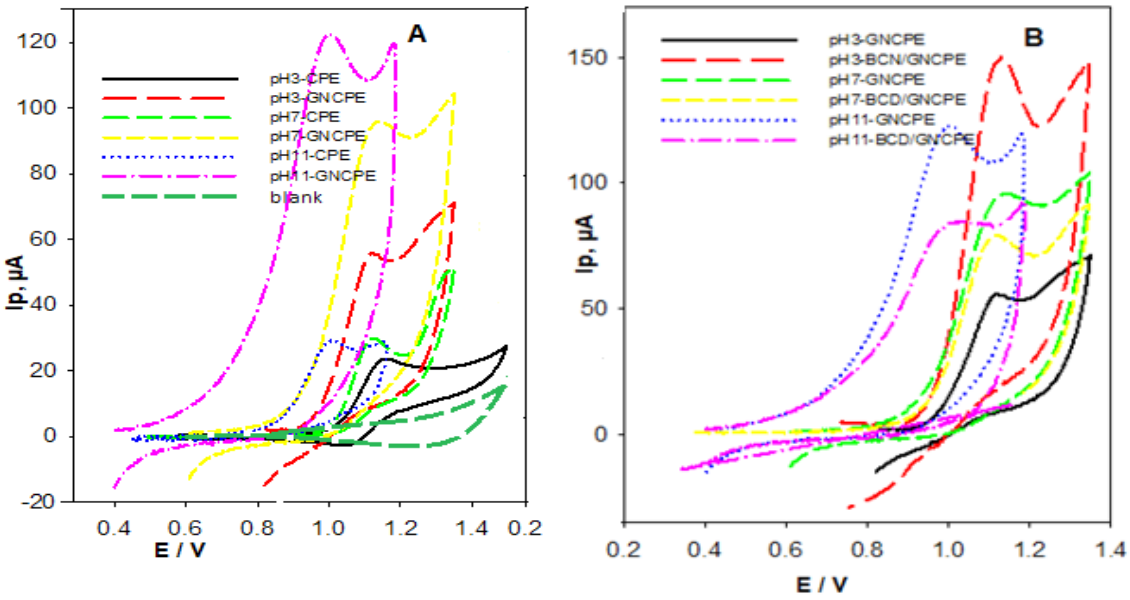


Fig. 5.Comparison of different modifiers on the anodic peak current of MID (1.0 x 10^{-3} M) at (A) CPE,GNCPE scan rate of 100 mV $s^{-1}$and (B) CPE,GNCPE, BCD/GNCPE at different pH values 3.0, 7.0 and 11.0.

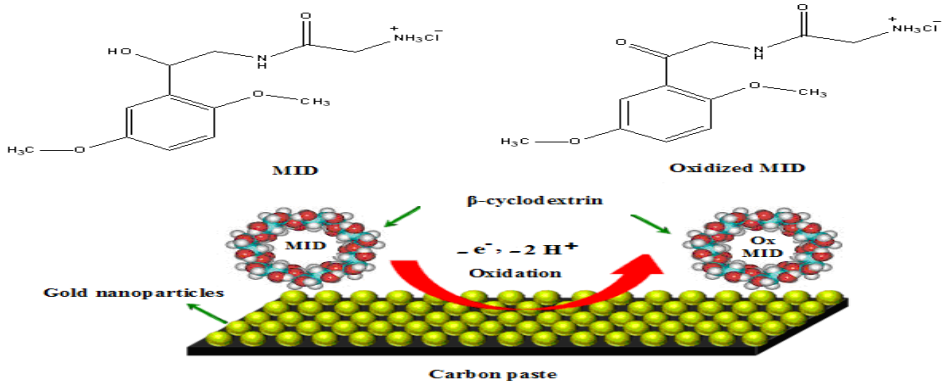


Fig. 6.The oxidation mechanism of MID at GNCPE in presence of 4.0 x 10^{-5}M β-CD, BR of pH 3.0

carbonyl group.

Effect of β-CD concentration

Fig. 7 shows anodic peak current of 1.0 x 10^{-3} mol L^{-1} MID at GNCPE (in BR buffer, pH 3.0) as a function of β-CD concentration through successive additions from β-CD solution (1.0 x 10^{-2} mol L^{-1}) to the electrolytic cell. From the figure we note that as the β-CD concentration increases, the peak current increases up to 4.0 x 10^{-5} mol L^{-1}β-CD and reaches steady state above this concentration. Therefore, 4.0 x 10^{-5} mol $L^{-1}$is chosen as the optimum concentration of β-CD.

Electrochemical calculation of hermodynamic constant of the claimed inclusion complex

At electrode surface of GNCPE in HCLO4, the response of complexation between β –CD and midodrine (2mM) for 20 min is recorded. Adhesion of MID at the GNCPE-(β -CD) s surface through complex formation is well at 1070mV as applied potential. Langmuir equation Eq. (1)[29] is used to calculate formation constant as following

([MID])/Ip=1/KImax+([MID][MID])/(Imax ×Ip)=1/KImax+([MID])/Imax (1)

Ip is the peak current obtained at each concentration of MID

I_{max} is the maximum peak current when the current is kept constant

In Figure (a) is plotted between [MID]/Ip versus [MID] with linearly relation, I_{max} and k is conclude from slope and intercept. The formation constant for the GNCPE - (β -CD) s complex calculated from Figure (a) was found to be 2930 M^{-1} at room temperature.

Thermodynamic parameters of the formation of the GNCPE -(β -CD)s inclusion complex can be calculated as change in Gibbs energy , ΔG° using Eq. (2) ,and enthalpy, ΔH°, and entropy, ΔS° by using Van't Hoff's law, Eq. (3),which are listed in table (1)

ΔG°= - RT ln K (2).

lnK=(-ΔH°)/RT+□ΔS□^°/R (3)

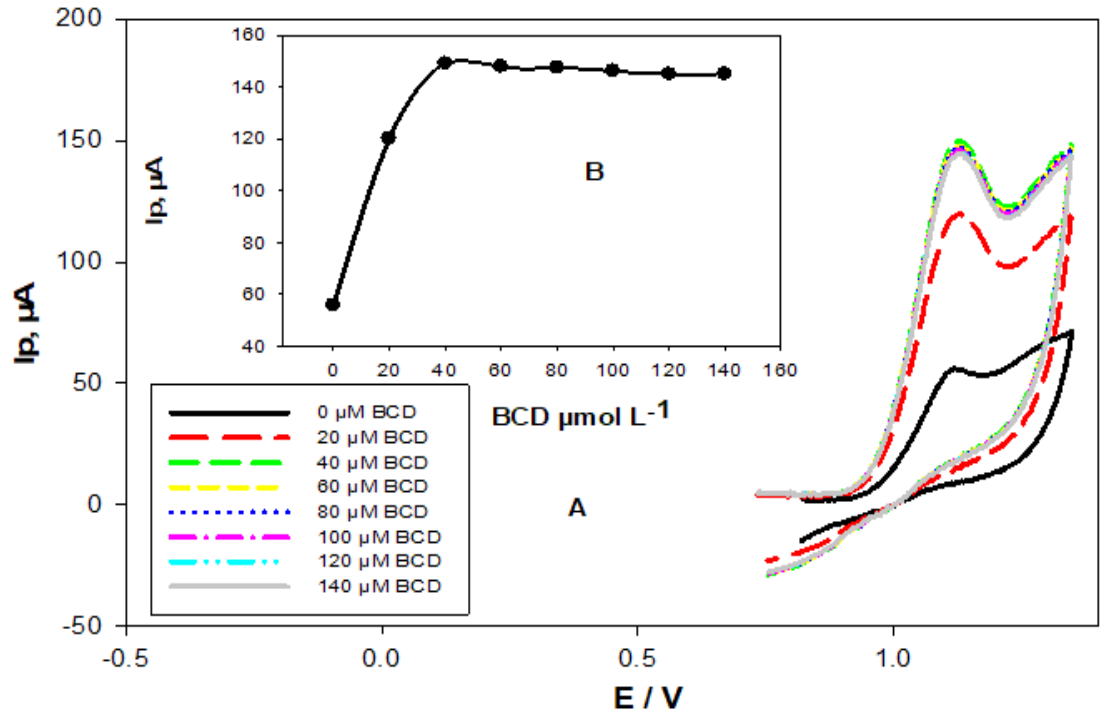
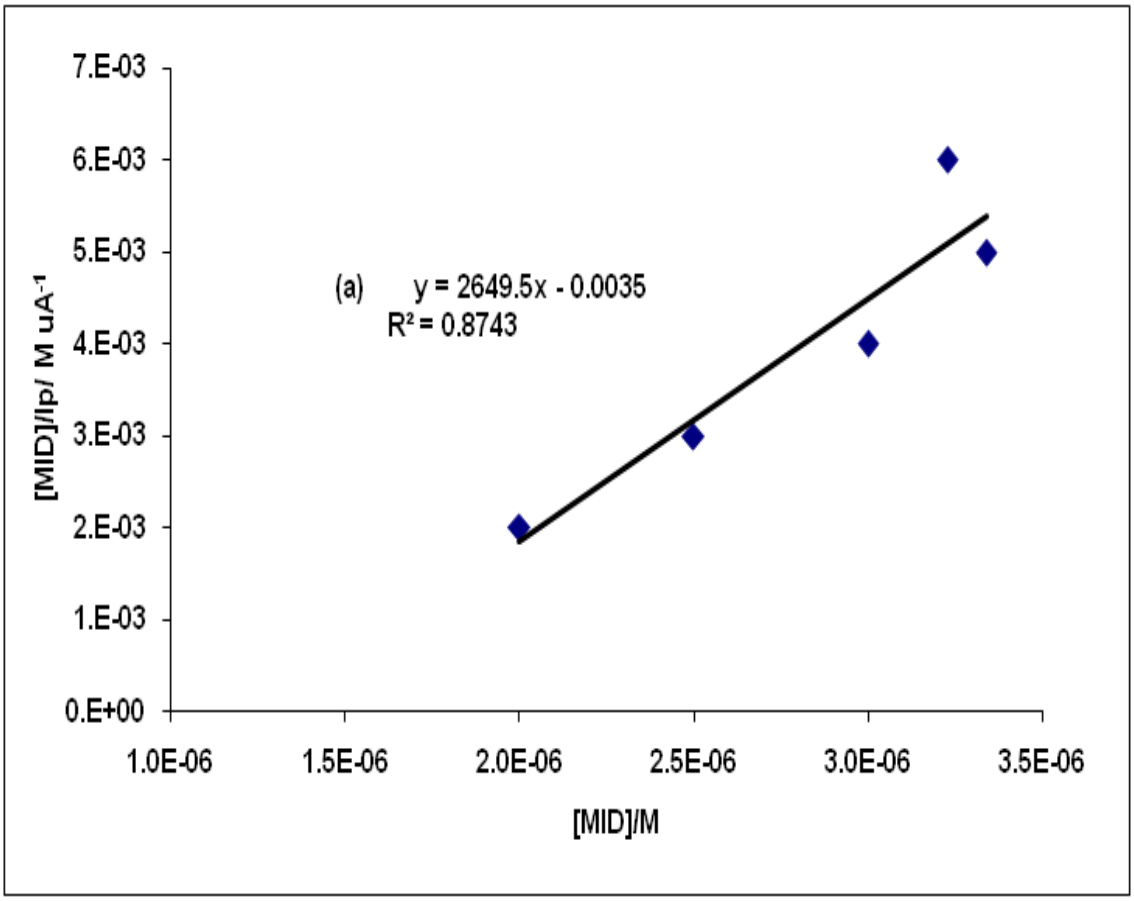


Fig. 7. (A) Cyclic voltammograms of MID (1.0 x 10-3 mol L-1) in BR buffer of pH 3.0 at scan rate of 100 mV s-1 as a function of β-CD concentration at GNCPE. The inset (B): plot of the anodic peak current as a function of β-CD concentration.



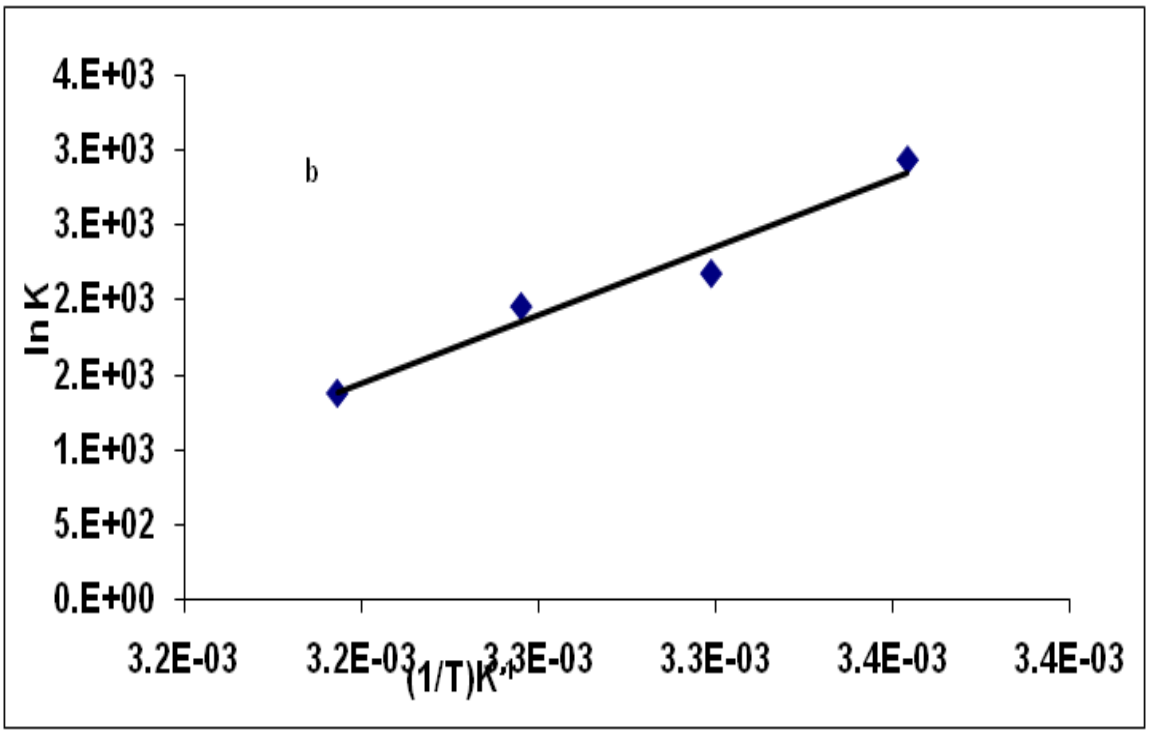


Fig (8). (a) Graph of [MID]/Ip versus [MID]. (b) ln K versus 1/T graph for estimation of the thermodynamic parameters of the formation of the GNCPE -(β -CD)s inclusion complex.

TABLE. 1. Thermodynamic parameters calculated for the formation of the inclusion complex GNCPE - (β -CD)s.

T (8C)	K(M^{-1})	ΔG° ($kJmol^{-1}$)	ΔH°($kJmol^{-1}$)	ΔS°($Jmol^{-1}K^{-1}$)
25	2930	-19.79	19.4	31.54
30	2170	-19.36		
35	1950	-19.41		
40	1370	-18.80		

Effect of scan rate

Fig. 9 shows the effect of scan rate (υ) on the anodic peak current of MID at CPE and GNCPE (in absence and in the presence of β-CD solution) in BR buffer (pH 3.0)in the range from 10-150 mV s^{-1}. It is found that the logarithm of oxidation peak current (log Ip) is linear to the logarithm of scan rate (log υ) as shown in Fig. 8A, with the linear regression equations: log Ip = 0.54log υ + 1.16, r (correlation coefficient) = 0.9997 (CPE), log Ip= 0.48log υ + 0.74, r (correlation coefficient) = 0.9993 (GNCPE) and log Ip = 0.32log υ + 0.69, r (correlation coefficient) = 0.9991 (GNCPE in the presence of β-CD solution). From the slope values, it can be deduced that the oxidation process of MID is an adsorption contribution process at CPE and GNCPE in the presence of β-CD solution[43].

The relation between the anodic peak current of MID and the square root of scan rate (Fig. 9B) can be used to determine diffusion coefficient of MID using Randles-Sevcik equation: Ip = (2·99 x 10^5) $n^{3/2}$ A C_o^* $D_o^{1/2}$ $\upsilon^{1/2}$[43]where Ip is the anodic peak current (A), D_o is the diffusion coefficient of the electroactive species (cm^2 s^{-1}), υ is the scan rate (V s^{-1}), n is the number of electrons exchanged during oxidation, A is the electrode area of (0.0706 cm^2) and C_o^* is the concentration of the analyte. Values of diffusion coefficient for MID at CPE , GNCPE and GNCPE /β-CD are 1.083 x 10^{-6},1.142 x 10^{-5} and 8.019 x $10^{-5}$$cm^2$ s^{-1} respectively, indicating a quick mass transfer of the analyte molecules towards the surface of GNCPE from bulk solution in the presence of β-CD solution.

Effect of accumulation time

Fig. 10 shows the influence of accumulation time (T_{acc}) on the anodic peak current of 1.0 x 10^{-3}M MID solution along with accumulation time between 0 and 30 sec at open circuit condition at GNCPE in presence of 4.0 x 10^{-5} M of β-CD. The peak current increases as the adsorption time increases up to 10 sec, then the peak current reaches a plateau with the increase of T_{acc}, this is because the active sites of electrode surface were fully saturated by the analyte, so 10 sec is chosen as the optimum T_{acc}.

Analytical application

In order to develop an analytical method for the determination of MID, quantitative measurements were performed using DPV at GNCPE in the presence of β-CD solution (4.0 x 10^{-5}M). Calibration curve was constructed through consecutive additions of MID solution (1.0 x 10^{-3}M) to the electrolytic cell containing 5 mL BR buffer of pH 3.0 by plotting the peak currents against MID concentrations. The anodic peak current increases linearly with increasing concentration of MID from 3.0 x 10^{-6} to 3.2 x 10^{-4} M with correlation coefficient of 0.9997 (Fig. 11).

The limits of quantification(LOQ) and detection (LOD) [44, 45] were found to be 1.71 x 10^{-6} M and 5.14 x 10^{-7} M, respectively as listed in Tab. 2. To check the validity [46] of the method, the relative standard deviations and the percentage recoveries were calculated for different concentrations in the linear range from 3.0 x 10^{-6} to 3.2 x 10^{-4} The relative standard deviation (RSD) and the percentage recovery values were found in the following ranges: 0.255-1.515% and 99.18-101.43%, respectively.

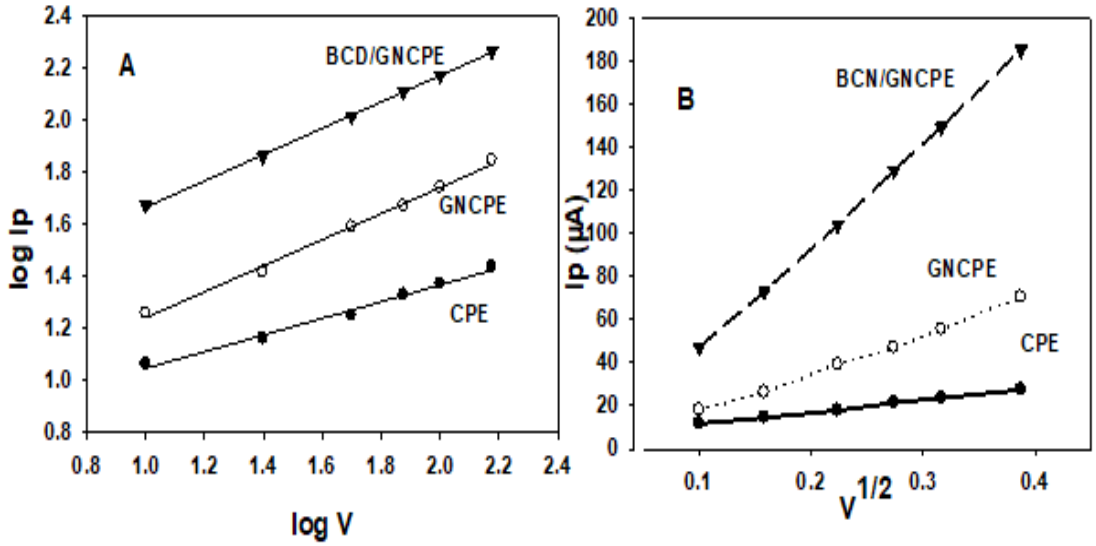


Fig. 9.Plot of anodic peak current as a function of scan rate, (A) log I versus log ν and (B) logI versus ν1/2.

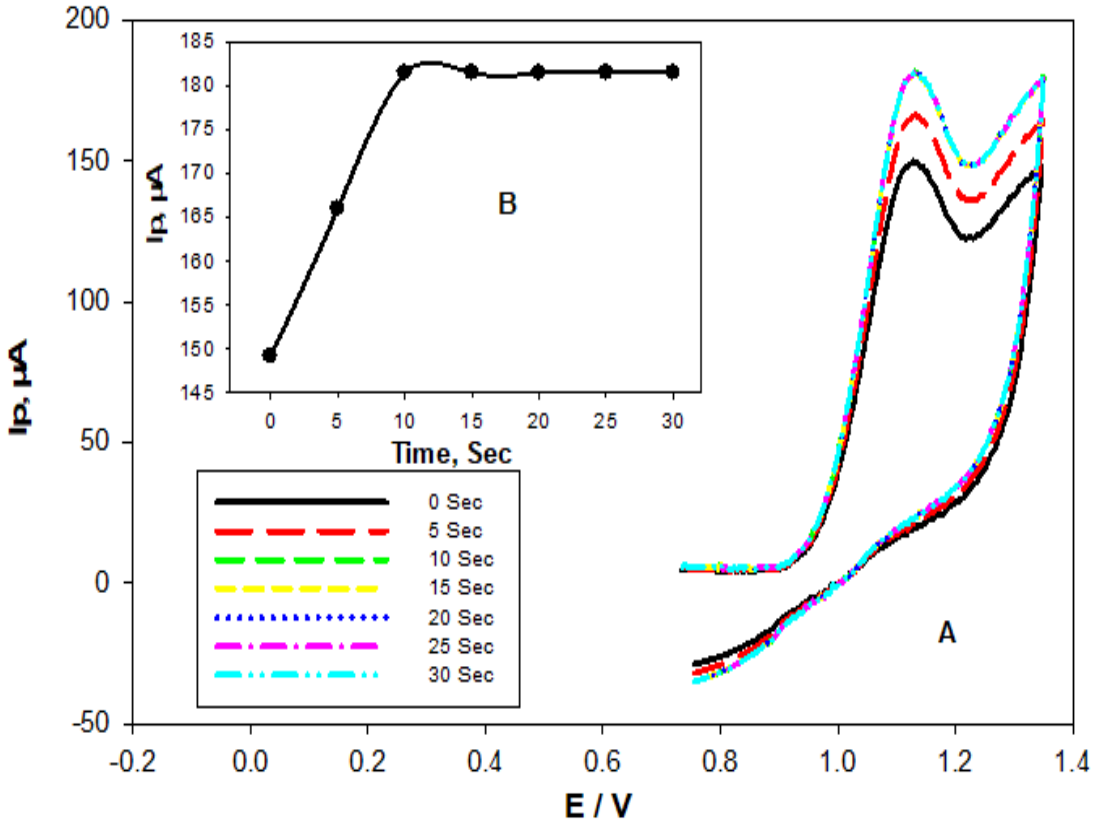


Fig. 10. (A) Cyclic voltammograms of 1.0 x 10^{-3} M MID at GNCPE in BR buffer of pH 3.0 as a function of accumulation time from 0.0 to 30 sec at in presence of 4.0 x 10^{-5} M β-CD, scan rate of 100 mV s^{-1}. The inset (B): plot of the anodic peak current values versus accumulation time.

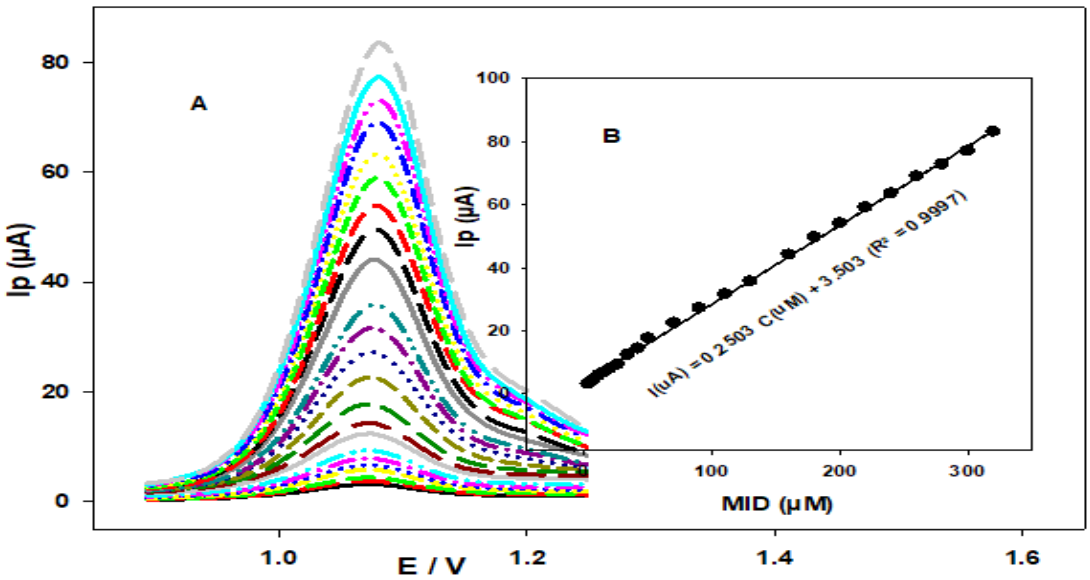


Fig. 11. (A) Calibration voltammograms curve of MID, using DPV mode at GNCPE in BR buffer pH 3.0 and scan rate of 10 mV s^{-1} in presence of 4.0 x 10^{-5}M β-CD. The inset (B): The calibration plot of the oxidation peak current versus the concentration range of MID.

TABLE 2. Analytical parameters of MID at GNCPE in the presence of β-CD by using DPV technique.

Parameters	
pH	3.0
Concentration (M)	3.0 x 10^{-6} - 3.2 x 10^{-4}
SD	0.898
RSD %	2.3
Slope of regression line (a)	0.25
$S_{y/x}$ (µA cm^{-2} nM)	0.019
Intercept of regression line (b)	3.62
S_b (µA cm−2 nM)	0.298
Correlation coefficient (r^2)	0.9997
LOD (nmol L^{-1})	(5.14 ± 0.075) 10^{-7}
LOQ (nmol L^{-1})	(1.71 ± 0.004)10^{-6}

a = intercept; b = slope; s_a = standard deviation of intercept; s_b = standard deviation of slope; $s_{y/x}$ = error standard deviation; LOD = limit of detection; LOQ = limit of quantification.

Analysis of real samples

Initially, the standard addition method was used for the analysis of Midodrine 2.5 mg tablets, and aliquots of MID standard solution (1.0 x 10^{-3}M) were added in order to evaluate the accuracy of the proposed method. The calculated recoveries, ranging from 99.14% to 101.35% with RSD values within the range of 0.493 - 1.338% in six replicate experiments, are in good agreement with the labelled content (Table 3). As can be seen, other ingredients present in tablets did not cause the appearance of any additional signals in the examined potential window, so it can be concluded that there are no interferences from the matrix.

The proposed DPV method is more sensitive than potentiometric methods: 1.0 x 10^{-4} - 1.0 x 10^{-1}M and 5.0 x 10^{-5} - 1.0 x 10^{-1}M [10] and spectrophotometric methods: 10.32 x 10^{-3} - 68.8 x 10^{-3}M [11] and 17.20 x 10^{-3} - 120.40 x 10^{-3} mM [12] for the determination of MID in bulk and pharmaceutical formulations.

The results obtained were compared statistically with those from the reference method[47] by using Student's t-test and the variance ratio F-test. The results in Table 4 show that the t and F values were smaller than the critical values, indicating that there is no significant difference between the proposed voltammetric method and the published method

TABLE 3. Determination of MID in tablets.

Midodrine tablets	MID (μM) Taken	MID (μ M) added	%RSD*	%Recovery
2.5 mg MID/ tab	7.0	13.00	1.061	100.25
		35.00	0.493	99.140
		50.00	0.745	101.23
		83.00	0.691	101.28
		123.0	0.725	101.35
		173.0	1.338	99.730
		233.0	0.526	99.280
		293.0	0.960	100.13

*Number of replicates (n) = 6.

TABLE 4.Determination of MID in tablets compared with the reference method[47].

Claimed (mg/tab)	reference method [47] Recovery (%) ± SD[a]	DPV method Recovery (%) ± SD[a]
2.5	99.15 ± 1.82	99،88 ± 0.857
	F-test[b]	2.38
	t-test[b]	0.78

[a]Averaged from five determinations. [b] Tabulated F and t values at 95% confidence level = 6.39 and 2.776, respectively [31].

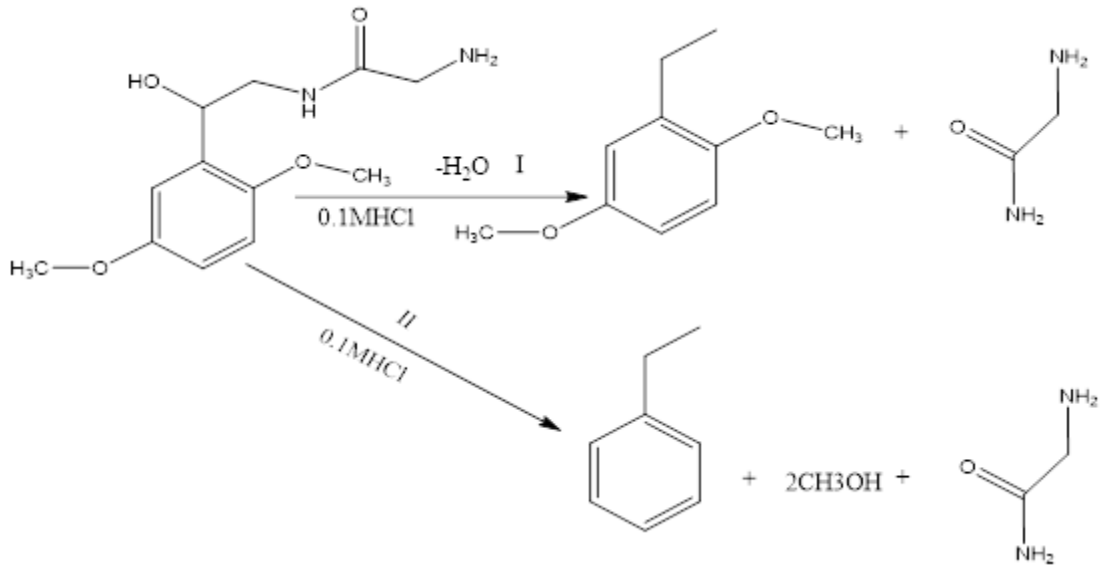
with respect to accuracy and precision.

Applications to human urine

To check the applicability of the proposed method to determine MID in biological fluids, spiked human urine samples were analyzed. Urine samples were collected from healthy volunteer and the samples were prepared as described in experimental section. The calibration curve shows a straight line in the range of 1.0×10^{-5} - 3.0×10^{-4} mol L^{-1} with correlation coefficient of 0.9995, the LOQ and LOD were found to be 2.57×10^{-6} mol L^{-1} and 7.70×10^{-7} mol L^{-1}, respectively. The relative standard deviations and the percentage recoveries were found in the following ranges: 0.621 - 1.420% and 99.30-101.65%, respectively. Therefore, the proposed procedure can be successfully and easily used to determine MID in human urine..

Specificity and Interference Study

DPV technique was studied for MID in electrolyte of research laboratory preparedmixes having different concentrations (1–50%) oftheir hydrolytic drug degradants. Peak is ourmain group of interest due to its complete specificity for MID in presence of oxidative hydrolytic -degradants at GNCPE. The RSD% and mean recovery verified the high specificity of the established method. The achieved high specificity of the established methodof MID at GNCPE was concerning to the mechanismof oxidation of drug in relation to the pathways of the hydrolytic and oxidative degradation as presented in (schemes 1). The effect of interfering complexes regularly existing in pharmaceutical tablets such as excipients was moreover examined. The interfering study was appreciated by adding of every constituent with changing concentration to the electrolyte solution containing definite amount of 30.0 mM of each drug separately at pH 3.0. It was found that glucose monohydrate, uric acid, ascorbic acid; sodium carbonate and sodium bicarbonate did not significantly different interfere with oxidation of MID at GNCPE. The obtained RSD% and mean percentage recoveries values constructed on an average of three reproduces, 99.75 ±0.62, displayed no considerable interference from excipients. These results proposed that quantitative determination of MID in their pharmaceutical form was not influenced with the most communal interfering mixes; therefore, the



Scheme 1. General suggested pathways of hydrolytic (I) and oxidative (II)-degradation forMID.

suggested method is satisfactorily selective.

Reproducibility and stability

The reproducibility of the fabricated sensor was examined at in 0.04 M BR buffer (pH 3) for electrode constructed independently under similar conditions and for a set of five different DPV measurements for the same electrode. The average values from five experiments showed a RSD was found to be 3.22 %, signifying the good reproducibility of GNCPE. Stability study was an essential requirement in the fabrication of modified GNCPE, The stability of the sensor was explored by storing the GNCPE at refrigerator condition for two weeks and the test was done using DPV at optimum conditions of experimental and was periodically checked every 5th day. The electrode retained 98% of the current activity towards drug on the 5th day, 96% on 10th day and could retain 93% of its initial value after 15 days, demonstrating the long-term stability of the GNCPE

Conclusion

In the present work, a new, cheap, simple and precise differential pulse voltammetric method was optimized for the quantitative determination of MID concentrations in bulk, pharmaceutical formulations and urine at gold nanoparticles modified carbon paste electrode in the presence of β-CD solution based the enhancement effect of gold nanoparticles and formation of inclusion complex with β-cyclodextrin. The experimental conditions such as pH, β-CD concentration, and scan rate and accumulation time were optimized for the determination of MID with good precision, accuracy and low detection limit. The developed method can be used in routine analysis of MID in quality control laboratories in the pharmaceutical industry.

Acknowledgment

The author would like to express his gratitude to Department of Chemistry, Faculty of Sciences, Damanhur University, Egypt for providing instruments and the means necessary to accomplish this work.

References

1. Neil M.J., The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals. Whitehouse Station, New Jersey: Merck Research Laboratories, Division of Merck and Co. Inc. (2006).
2. McTavish D. and Goa K.L., Midodrine. Drugs, 38, 757–777 (1989).
3. Pittner H., Vasoconstrictor effects of midodrine, ST 1059, noradrenaline, etilefrine and norfenefrine on isolated dog femoral arteries and veins. Gen Pharmacol, 14, 107–109 (1983).
4. Sweetman S.C., Martindale: the complete drug reference. Pharmaceutical Press (2009).
5. Posch W. and Lindner W., Quantification of midodrine and its active metabolite in plasma using a high performance liquid chromatography column switching technique. Biomed Chromatogr, 3, 153–156 (1989).

6. Yoshida H., Ohno Y., Yoshikuni K., Todoroki K., Nohta H. and Yamaguchi M., Determination of midodrine in human plasma by high-performance liquid chromatography with fluorescence detection. Anal Sci, 19, 317–319 (2003).

7. Quaglia M., Farina A., Bossù E. and Cotichini V., Human α 1-glycoprotein acid as chiral selector in the enantioseparation of midodrine and deglymidodrine racemates by HPLC. J Pharm Biomed Anal, 18, 171–177 (1998).

8. Barth T., Aleu J., Pupo M.T., Bonato P.S. and Collado I.G., HPLC analysis of midodrine and desglymidodrine in culture medium: evaluation of static and shaken conditions on the biotransformation by fungi. J Chromatogr Sci, 51, 460–467 (2013).

9. Barth T., Pupo M.T., Borges K.B., Okano L.T. and Bonato P.S., Stereoselective determination of midodrine and desglymidodrine in culture medium: application to a biotransformation study employing endophytic fungi. Electrophoresis, 31, 1521–1528 (2010).

10. Elzanfaly E.S., Zaazaa H.E. and Merey H.A., Ion selective phosphotungestate and β-cyclodextrin based membrane electrodes for stability-indicating determination of midodrine hydrochloride (2013).

11. El-Gindy S.S.a.R.A.A.-S. A., Spectrophotometric method for determination of midodrine hydrochloride using ninhydrin in pharmaceutical formulations. Anal Chem Indian J, 7, 1–16 (2008).

12. Ghada M., Hadad S.E. and Abdel-Salam R.A., Optimized and validated flow injection spectrophtometric analysis of midodrine hydrochloride in bulk and pharmaceutical formulations. Az J Pharm, 38, 11 (2008).

13. Sattar O., Rezk M., Badawy A. and Khattab O., Selective determination of midodrine hydrochloride in the presence of its acidic degradation product. Anal Chem Indian J, 12, 182–187 (2013).

14. Narang J., Malhotra N., Singh G. and Pundir C., Electrochemical impediometric detection of anti-HIV drug taking gold nanorods as a sensing interface. Biosens Bioelectron, 66, 332–337 (2015).

15. Mirceski V., Aleksovska A., Pejova B., Ivanovski V., Mitrova B., Mitreska N. and Gulaboski R., Thiol anchoring and catalysis of gold nanoparticles at the liquid interface of thin-organic film-modified electrodes. Electrochem Commun, 39, 5–8 (2014).

16. Tajik S., Taher M.A., Beitollahi H. and Torkzadeh-Mahani M., Electrochemical determination of the anticancer drug taxol at a ds-DNA modified pencil-graphite electrode and its application as a label-free electrochemical biosensor. Talanta, 134, 60–64 (2015).

17. Attia A.K., Determination of antihypertensive drug moexipril hydrochloride based on the enhancement effect of sodium dodecyl sulfate at carbon paste electrode. Talanta, 81, 25–29 (2010).

18. Gupta P. and Goyal R.N., Sensitive determination of domperidone in biological fluids using a conductive polymer modified glassy carbon electrode. Electrochim Acta, 151, 1–7 (2015).

19. Segura R., Pizarro J., Diaz K., Placencio A., Godoy F., Pino E. and Recio F., Development of electrochemical sensors for the determination of selenium using gold nanoparticles modified electrodes. Sensor Actuat B Chem, 220, 263–269 (2015).

20. Afkhami A., Soltani-Felehgari F. and Madrakian T., A sensitive electrochemical sensor for rapid determination of methadone in biological fluids using carbon paste electrode modified with gold nanofilm. Talanta, 128, 203–210 (2014).

21. Esteva A., Blanco E., Pina J., Balbin A., Quintana C. and Hernández P., Determination of nevirapine in the presence of cucurbit (7) uril with a gold electrode. J Electrochem Sci Eng, 4, 37–44 (2014).

22. Ahmed H.M., Mohamed M.A. and Salem W.M., New voltammetric analysis of olanzapine in tablets and human urine samples using a modified carbon paste sensor electrode incorporating gold nanoparticles and glutamine in a micellar medium. Anal Methods, 7, 581–589 (2015).

23. Hromadova M., Pospíšil L., Giannarelli S., Fuoco R. and Colombini M., Electrochemical evidence of host–guest interactions. Changes in the redox mechanism of fungicides iprodione and procymidone in the nano-cavity of cyclodextrins. Microchem J, 73, 213–219 (2002).

24. Wu Y.L. and Li J., Synthesis of supramolecular nanocapsules based on threading of multiple cyclodextrins over polymers on gold nanoparticles. Angew Chem Int Ed, 48, 3842–3845 (2009).

25. Gontero D., Lessard-Viger M., Brouard D., Bracamonte A.G., Boudreau D. and Veglia A.V.,

Smart multifunctional nanoparticles design as sensors and drug delivery systems based on supramolecular chemistry. Microchem J, 130, 316–328 (2017).

26. Yogeswaran U., Thiagarajan S. and Chen S.-M., Pinecone shape hydroxypropyl-β-cyclodextrin on a film of multi-walled carbon nanotubes coated with gold particles for the simultaneous determination of tyrosine, guanine, adenine and thymine. Carbon, 45, 2783–2796 (2007).

27. Bouchta D., Izaoumen N., Zejli H., El Kaoutit M. and Temsamani K.R., A novel electrochemical synthesis of poly-3-methylthiophene-γ-cyclodextrin film: application for the analysis of chlorpromazine and some neurotransmitters. Biosensor Bioelectron, 20, 2228–2235 (2005).

28. Alarcón-Angeles G., Pérez-López B., Palomar-Pardave M., Ramírez-Silva M., Alegret S. and Merkoci A., Enhanced host–guest electrochemical recognition of dopamine using cyclodextrin in the presence of carbon nanotubes. Carbon, 46, 898–906 (2008).

29. Ferancova A., Korgova E., Labuda J., Zima J. and Barek J., Cyclodextrin modified carbon paste based electrodes as sensors for the determination of carcinogenic polycyclic aromatic amines. Electroanalysis, 14, 1668–1673 (2002).

30. Li W., Jin G., Chen H. and Kong J., Highly sensitive and reproducible cyclodextrin-modified gold electrodes for probing trace lead in blood. Talanta, 78, 717–722 (2009).

31. Tredici I., Merli D., Zavarise F. and Profumo A., α-Cyclodextrins chemically modified gold electrode for the determination of nitroaromatic compounds. J Electroanal Chem, 645, 22–27 (2010).

32. Favero G., Campanella L., D'Annibale A. and Ferri T., Preparation and characterization of a chemically modified electrode based on ferrocene-tethered β-cyclodextrin self assembled monolayers. Microchem J, 76, 77–84 (2004).

33. Britton H.T.S. and Robinson R.A., CXCVIII.—Universal buffer solutions and the dissociation constant of veronal. J Chem Soc (Resumed), ■, 1456–1462 (1931).

34. Shalaby A., Hassan W.S., Hendawy H.A. and Ibrahim A., Electrochemical oxidation behavior of itraconazole at different electrodes and its anodic stripping determination in pharmaceuticals and biological fluids. J Electroanal Chem, 763, 51–62 (2016).

35. Atta N.F., Galal A. and Azab S.M., Electrochemical determination of paracetamol using gold nanoparticles–application in tablets and human fluids. Int J Electrochem Sci, 6, 5082–5096 (2011).

36. Hendawy H.A., Youssif R.M., Salama N.N., Fayed A.S. and Salem M.Y., Challenge approach of an inexpensive electrochemical sensor for rapid selective determination of two non-classical β-lactams in presence of different degradants and interference substances, electroanalysis.

37. Al-Ghamdi A.H., Al-Ghamdi A.F. and Al-Omar M.A., Electrochemical studies and square-wave adsorptive stripping voltammetry of spironolactone drug. Anal Lett, 41, 90–103 (2008).

38. Rizk M., Hendawy H.A., El-Alamin M.M.A. and Moawad M.I., Sensitive anodic voltammetric determination of methylergometrine maleate in bulk and pharmaceutical dosage forms using differential pulse voltammetry. J Electroanal Chem, 749, 53–61 (2015).

39. Afkhami A., Soltani-Felehgari F. and Madrakian T., Gold nanoparticles modified carbon paste electrode as an efficient electrochemical sensor for rapid and sensitive determination of cefixime in urine and pharmaceutical samples. Electrochim Acta, 103, 125–133 (2013).

40. Hendawy H.A., Manal A. and Azab S.M., A competitive nano-iron oxide sensor for the electrochemical detection of the anti-diabetic drug linagliptin in the presence of glucose and metformin.

41. Kissinger P.T. and Heineman W.R., Cyclic voltammetry. J Chem Educ, 60, 702 (1983).

42. Gosser D.K., Cyclic Voltammetry: Simulation and Analysis of Reaction Mechanisms. VCH; New York, NY: 1993.

43. I.H.T. Guideline. Validation of analytical procedures: text and methodology, Q2 (R1), 1 (2005).

44. Swartz M.E. and Krull I.S., Analytical method development and validation, CRC Press (1997).

45. Miller J.N. and Miller J.C., Statistics and chemometrics for analytical chemistry, Pearson Education (2005).

46. United States Pharmacopoeia and National Formulary (USP 30-NF25). Rockville, pp. 2612–2513 (2007).

47. United States Pharmacopoeia and National Formulary (USP 30-NF25). Rockville, 2007, pp. 2612–2513).