Journal of the Serbian Chemical Society
JSCS-info@shd.org.rs • www.shd.org.rs/JSCS
J. Serb. Chem. Soc. 83 (4) 449–462 (2018)
JSCS–5088
UDC 546.56+539.12+547.491.8: 544.6.076.32–033.5–039.26:543.552
Original scientific paper

Signal amplification for sumatriptan sensing based on polymeric surface decorated with Cu nanoparticles

GHASEM KARIM-NEZHAD*, SAMANE KHANALILOO, ZEYNAB KHORABLOU and PARISA SEYED DORRAJI

Department of Chemistry, Payame Noor University, P. O. Box 19395-3697 Tehran, Iran

(Received 27 July, revised 26 November, accepted 21 December 2017)

Abstract: A new nanocomposite, Cu NPs/poly-melamine, was deposited on a glassy carbon electrode by cyclic voltammetry. The uniform deposition of the nanocomposite was observed by the field emission scanning electron microscopy. The electron transfer characteristics of the drug sumatriptan (SUM), was greatly improved on the modified electrode. The prepared electrode was used for the sensitive determination of SUM by the differential pulse voltammetry. Linear calibration curve was obtained in the concentration ranges of 0.08–0.58 and 0.58–6.5 μM, and the detection limit of 0.025 μM. The proposed method was evaluated by the determination of SUM in human biological fluids such as urine and blood plasma with satisfactory results (recovery > 99 %).

Keywords: sumatriptan; melamine; glassy carbon electrode; copper nanoparticles; differential pulse voltammetry.

INTRODUCTION

Migraine is a multisymptom disorder that severely hampers daily activities of patients suffering from it, due to throbbing and intense headache in one half of the head. Sumatriptan succinate (SUM) is a serotonin (5-hydroxytryptamine) agonist, the most commonly prescribed medicine for migraine, and is available as oral tablets, nasal spray, and subcutaneous injection dosage formulations.[1,2] However, therapeutic efficacy of sumatriptan succinate is hampered in migraine patients due to gastric stasis, nausea and vomiting, resulting in erratic absorption from the gastrointestinal tract. Also, sumatriptan succinate is incompletely absorbed by oral administration and undergoes the first-pass metabolism, resulting in low bioavailability.[3,4]

A number of methods have been proposed for SUM analysis, including UV spectrophotometry,[5–7] liquid chromatography,[8–11] high performance liquid chromatography (HPLC),[12–17] capillary electrophoresis[18] and electrochemical

* Corresponding author. E-mail: g.knezhad@gmail.com
https://doi.org/10.2298/JSC170727006K

methods.[19–24] The advance in electrochemical techniques in the field of analysis of drugs and biological molecules is due to the simplicity, low cost and relatively short analysis time when compared to electrophoretic and chromatographic techniques. Moreover, the modification of electrodes by various compounds has greatly increased the sensitivity and selectivity of biological and pharmaceutical electroanalysis. Among various reagents used for electrode modification, metal nanoparticles (MNPs) have attracted the attention of electrochemists as the excellent electron transfer mediators.[25,26] However, the MNPs at the electrode surface can be fragile in the absence of stabilizing conductive material. To solve this problem, in the first step, the electrode surface can be modified with some conductive stabilizing materials such as ligands, carbon nanotubes and polymers.[27,28] Then, the MNPs are attached to the modified electrode surface. Moreover, the porous structure of a conducting polymer allows dispersing of the metal nanoparticles into the polymer matrix and generates additional electrocatalytic sites.[29–31]

Compared with noble metals, Cu nanoparticles are cheaper and easily available. Moreover, the Cu nanoparticles modified electrodes are favoured as electrochemical catalysts because of their high electrical conductivity and excellent catalytic properties. Also, melamine accelerates the electron transfer rate between SUM and electrode because there are three amine groups in its structure. Cu nanoparticles interact well with the poly-melamine (P-Mel) coupling and the remarkable peak current enhancement may be attributed to the enlarged specific surface area of the electrode after modification and the synergistic effect of the electrocatalytic properties of poly melamine and Cu nanoparticles.

In this work, melamine was polymerized on the surface of a glassy carbon electrode (GCE). The resulting film was decorated with Cu nanoparticles. The synergistic effect of the two components of the new electrode (Cu NPs/P-Mel/ /GCE) was observed in the electrochemical determination of SUM.

EXPERIMENTAL

Reagents and chemicals

All chemicals were of analytical reagent grade and used without further purification. Double distilled water was used in all experiments. Sumatriptan powder (pure) was purchased from Tehran Chemie pharmaceutical company (Tehran, Iran).

Apparatus

Cyclic voltammetric studies were conducted by Autolab with PGSTAT-12 (Eco Chemie B.V., Ultrecht, the Netherlands) connected to a personal computer for control and data storage. All electrochemical experiments were performed in a standard three electrode cell. The modified GCE was employed as the working electrode, the platinum wire as a counter electrode and the saturated Ag/AgCl electrode as a reference electrode. All potentials are reported *versus* the Ag/AgCl electrode.

Fabrication of the modified electrode

Prior to the modification, GCE was polished by the alumina powder (0.05 μm) and rinsed with HNO_3 (1:1 volume part of water), absolute ethanol and water, respectively. GCE was immersed in a melamine solution (1.0 mM) in 0.1 M H_2SO_4, and cyclic voltammetry was carried out in the potential range of 0.0 to 1.6 V at a scan rate of 100 mV s^{-1} (25 cycles).[32] In this step, poly-melamine (P-Mel) was deposited on the electrode. The obtained modified electrode (P-Mel/GCE) was washed with water and dried on air. Finally, the metallic Cu nanoparticles (Cu NPs) were electrochemically deposited in the electrolytic solution containing 0.025 M H_2SO_4, 5 mM $CuSO_4$ at –0.1 V, at room temperature. Cu nanoparticles were obtained on the surface of the poly melamine films after 8 min in the solution.[33] The obtained modified electrode (Cu NPs/P-Mel/ GCE) was washed with ultrapure water several times. Stepwise electrodes were also prepared with the same procedures described above, for comparison purposes. The schematic illustration for constructing the modified is shown in Fig. 1.

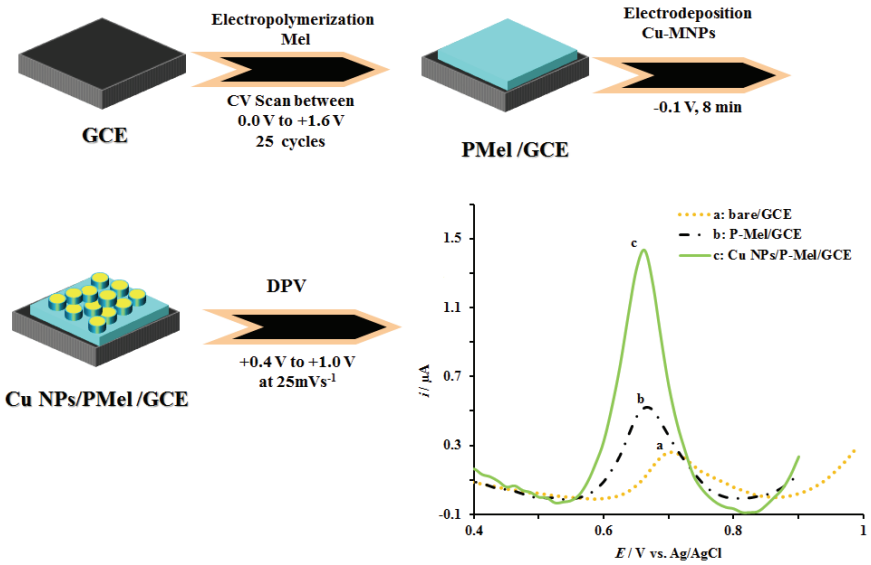

Fig. 1. Schematic illustration of the preparation steps of Cu NPs/P-Mel/GCE.

Sample preparation

Human plasma samples were obtained from the Pastor Laboratory (Khoy, Iran) and aliquots were transferred into microtubes and frozen at –4 °C until analysis was performed. Human plasma samples frozen at –4 °C were defrosted at room temperature daily and stirred to ensure homogeneity. After defrosting the samples, 2 mL of an aliquot volume of this sample was spiked with SUM. Then the mixture with the volume ratio of acetonitrile:plasma 2:1 was added to precipitate plasma proteins. The mixture was centrifuged for 5 min at 6000 rpm to separate the residues of plasma proteins. Approximately, 2 mL of supernatant was taken and added into supporting electrolytes to reach a total volume of 10 mL.

The human urine samples were spiked with 20 μM SUM and treated with 0.2 mL of methanol for the subsequent removal of the proteins. These samples were shaken and placed

in a micro-centrifuge during 3 min at 6000 rpm. The superior liquid was removed and transferred to a solution of 10 mL of PBS with pH 7.

RESULTS AND DISCUSSION

The surface morphology of the Cu NPs/P-Mel modified electrode

The surface morphologies of different modified films were analyzed by the field emission scanning electron microscopy (FESEM). Fig. 2 depicts the FESEM micrographs of P-Mel and Cu NPs/P-Mel films. As is shown in Fig. 2A, P-Mel was assembled on the bare GCE surface as grass-like branches. The whole assembly on the electrode surface (Cu NPs/P-Mel) is shown in image B, in which the Cu nanoparticles can be observed. Energy dispersive X-ray spectroscopy (EDS) spectrum of Cu NPs/P-Mel film confirmed the deposition of Cu particles on the modified electrode (Fig. 2C).

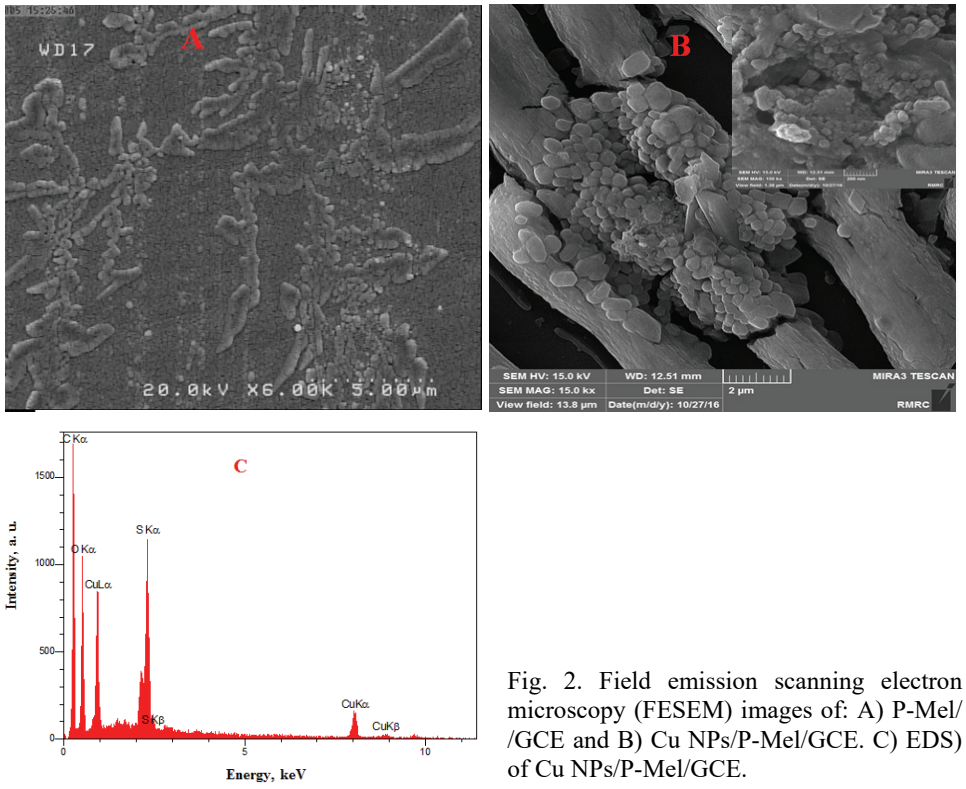

Fig. 2. Field emission scanning electron microscopy (FESEM) images of: A) P-Mel/ /GCE and B) Cu NPs/P-Mel/GCE. C) EDS) of Cu NPs/P-Mel/GCE.

Electrochemical impedance spectroscopic study

Electrochemical impedance spectroscopy (EIS) was employed to characterize the interface properties of modified electrodes. The impedance spectra include a semicircle part and a linear part. The semicircle diameter at higher fre-

quencies corresponds to the electron-transfer resistance (Ret), and the linear part, at lower frequencies, corresponds to the diffusion process. The typical results of ac impedance spectra of the bare GCE, P-Mel/GCE and Cu NPs/P-Mel/GCE obtained in 0.1 mol L^{-1} KCl, containing 1.0 mmol L^{-1} Fe $(CN)_6^{3-}$/Fe $(CN)_6^{4-}$, with the frequency ranging from 0.01 kHz to 100 kHz are shown in Fig. 3. As displayed in Fig. 3, a big well-defined semicircle at higher frequencies, obtained for the bare GCE (curve a), indicated a huge interface electron transfer resistance (R_{ct} = 725 Ω). When Mel polymer film was deposited on GC electrode surface, a very large semicircle domains in the high-frequency region appeared at the P-Mel/GCE (curve b, R_{ct} = 312 Ω). However, only very small semicircle domains in the high-frequency region appeared at the Cu NPs/P-Mel/GCE (curve c, R_{ct} = 31 Ω), demonstrating the low charger transfer resistance. This was mainly attributed to the synergistic effect of Cu NPs and polymer of melamine. This is the evidence that the support of charge transfer kinetics was at a huge extent in the case of Cu NPs/P-Mel/GCE due to a poor charge transfer resistance at this nanocomposite sensor.

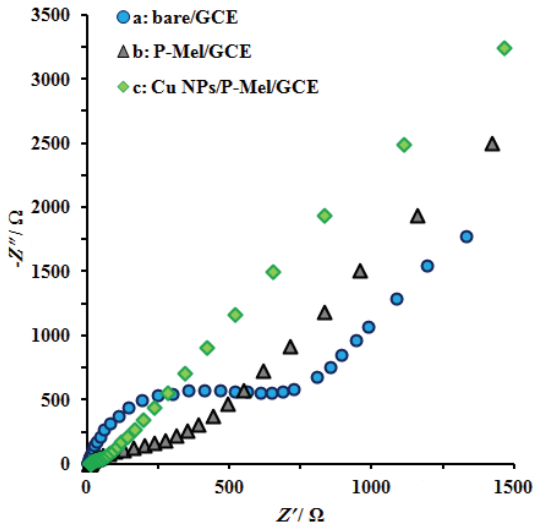

Fig. 3. Nyquist plots of the different electrodes in 1.0 mmol L^{-1} Fe $(CN)_6^{3-}$ /Fe $(CN)_6^{4-}$ and 0.10 M KCl for: a) ●, GCE, b) ▲, P-Mel/GCE and c) ♦, Cu NPs/P-Mel/GCE. The frequency range was 100 kHz to 0.01 Hz.

Electrochemical response of SUM

The cyclic voltammograms of SUM in phosphate buffer solution (0.1 M, pH 7) showed that SUM's response at bare GCE is rather poor and only a weak oxidation peak is observed at 0.76 V. Modification of GCE with melamine increased the anodic peak current of SUM. Further increasing in the peak current of the drug was observed when the Cu NPs/P-Mel/GCE was used as working electrode. These results indicate that the Cu NPs/P-Mel as modifier not only facilitates the electron transfer kinetic, but also increases the sensitivity of the

electrode for SUM monitoring, which may be due to the presence of nanoparticles and polymer in the composition of the modified electrode and probably reflects the larger surface area of the modified electrode. The accumulation drug on the surface of electrode increases the peak current and sensitivity of the proposed electrode for the monitoring of SUM. On the other hand, during these experiments no cathodic peak was observed for SUM in the reverse scan, suggesting a totally irreversible behaviour for the electrode process at the surface of all tested electrodes.

Fig. 4 shows the differential pulse voltammetry (DPV) curves obtained on different electrodes. Bare GCE (curve a) shows low current intensity for SUM, revealing poor selectivity and sensitivity of the unmodified electrode. The oxidation current of SUM on P-Mel/GCE (curve b) was higher than bare GCE, indicating the improvement of the catalytic activity toward the SUM oxidation obviously. Contrary to that, the highest improvement of the anodic peak current was obtained at the Cu NPs/P-Mel/GCE. The remarkable peak current enhancement may be attributed to the enlarged specific surface area of the electrode after modification and the synergistic effect of the electrocatalytic properties of polymelamine and Cu nanoparticles.

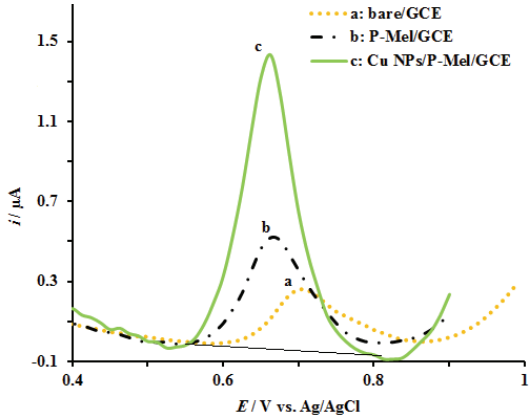

Fig. 4. Differential pulse voltammograms of 3.9 µM sumatriptan (SUM) at three different electrodes: a) GCE, b) P-Mel/GCE and c) Cu NPs/P-Mel/GCE. Conditions: pulse amplitude 0.05 V, scan rate 0.025 V/s and pulse time 0.04 s.

The higher peak current and the negative oxidation potential suggested that Cu NPs/P-Mel had good electrocatalytic ability for the electrochemical reaction of SUM, which may be ascribed to a faster electron transfer rate, higher electrochemical activity, larger specific surface area and higher conductivity.

Optimization of parameters for SUM detection

Effect of pH. Influences of solution pH on the oxidation of SUM at the Cu NPs/P-Mel film modified electrode were also investigated. Cyclic voltammetry was carried out in pH range from 2.0 to 10 to examine the effect of the pH value

on the electrochemical behaviour of SUM. Fig. 5 shows the influence of pH on the i_{pa} and E_{pa} at the Cu NPs/P-Mel/GCE.

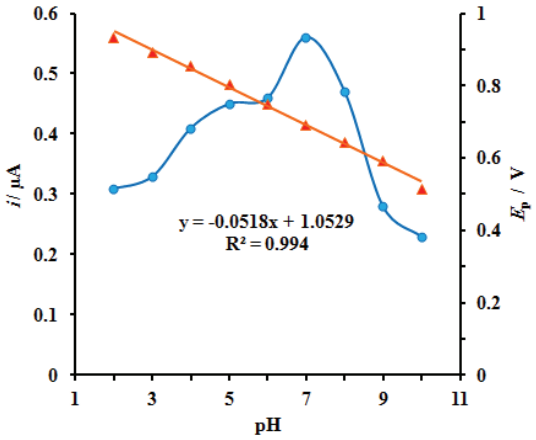

Fig. 5. Plots of peak potential (▲) and peak current (●) of 3.9 μM sumatriptan (SUM) in 0.1 M phosphate buffer solutions of different pH at Cu NPs/P--Mel/GCE electrode in scan rate 100 mV s^{-1}.

When pH increases from 2.0 to 7.0, the i_{pa} gradually increases. As further increasing of pH value from 7.0 to 10, i_{pa} decline. So, 0.1 M phosphate buffer solution (PBS) with pH 7.0 solution was employed for the determination of SUM to achieve higher sensitivity. Unlike i_{pa}, with the solution pH increasing, the E_{pa} shifts negatively and linearly in the range of pH 2.0–10. The linear regression equation: E_{pa} / V = 1.0529 – 0.0518pH, R^2 = 0.994. This result was close to the expected Nernstian theoretical value of 59 mV per pH at 25 °C, suggesting that the electron uptake was accompanied by an equal number of protons.

Effect of multiple cycles on the preparation of P-Mel/GCE

The number of electro-polymerization cycles for the electrochemical oxidation of SUM was investigated (Fig. 6). The oxidation current increased dramatically as the polymerization cycles were raised from 10 to 25 and then decreased after 25 cycles. The phenomenon could be associated with the increasing thickness of the composite film, which hindered the transfer of electrons on the electrode surface. Therefore, 25 electro-polymerization cycles were selected as optimum.

Effect of deposition potential and deposition time on the preparation of Cu NPs/P-Mel/GCE

To obtain a good microenvironment for the electrochemical oxidation of SUM, Cu NPs deposition potential and time was investigated by using DPV in 0.1 M PBS solution containing 3.9 μM SUM. The oxidation peak currents of SUM increased gradually and then decreased with the potentials shifting positively from –0.4 to 0.2 V. When the deposition potential was –0.1 V, the peak current of SUM reached the maximum value. Therefore, −0.1 V was selected as

the optimal deposition potential. In addition, the effect of deposition time on the peak current of SUM, at deposition potential of –0.1 V, was also investigated. The response current increased as deposition time increased from 2 to 8 min and reached the maximum at 8 min, then decreased, as deposition time was increased to 10 min. Therefore, 8 min was selected as the optimized value for the deposition time.

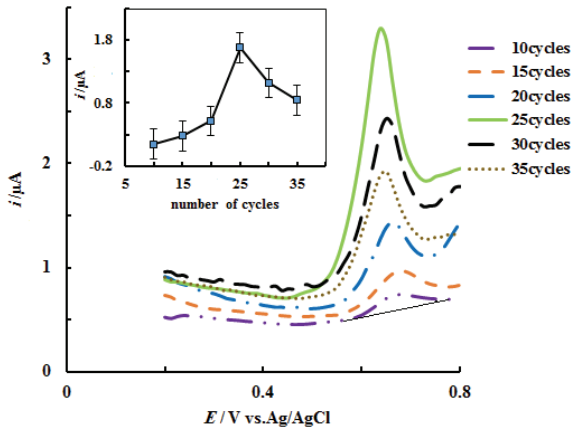

Fig. 6. Differential pulse voltammograms of the Cu NPs/P-Mel/GCE electrode with various numbers of polymerization cycles; inset: corresponding curve of peak current *versus* number of polymerization cycles.

Effect of DPV parameters (pulse amplitude and scan rate) for SUM determination

The effect of differential pulse amplitude and the scan rate on the peak current of 2.99 μM SUM in pH 7.0 PBS solutions was studied in the range of 20 to 65 mV and 10–50 mV/s, respectively. As shown in Fig. 7, upon increasing both amplitude and scan rate, a linear increase in the peak current was observed accompanied by the peak broadening after 50 mV decreases. Thus, 50 mV of amplitude and 25 mV/s of scan rate were chosen as optimum values.

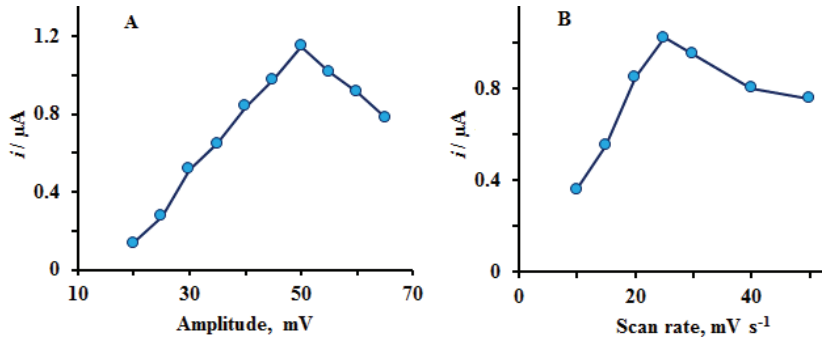

Fig. 7. Plot of differential pulse voltammetric peak current response of Cu NPs/P-Mel/GCE electrode for 2.99 μM SUM: A) *versus* differential pulse amplitude and B) *versus* scan rate at 50 mV of amplitude.

Effect of scan rate on the peak current of SUM

The effect of the scan rate on the electrochemical response of 3.9 μM SUM in 0.1 M PBS (pH 7.0) was studied, by recording cyclic voltammograms in the range of 10–130 mV s^{-1} utilizing modified electrode: as illustrated in Fig. 8A. The results show that the oxidation peak current increases gradually with an increase in the scan rate. A linear relationship was observed between i_p and the square root of the scan rate ($v^{1/2}$) over the whole scan rate range with correlation coefficients greater than 0.99 (Fig. 8B). These results indicate that the electrode reaction of SUM at the surface of tested electrodes is the diffusion-controlled process.

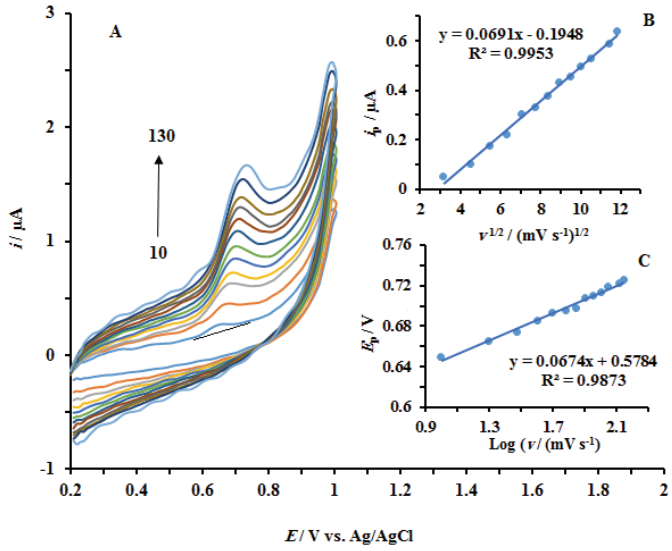

Fig 8. A) Cyclic voltammograms of SUM (3.9 μM) at Cu NPs/P-Mel/GCE electrode at different scan rates of 10 to 130 mV s^{-1} in 0.1 M phosphate buffer at pH 3.0. B) Plot of I_{pa} *versus* $v^{1/2}$ for the oxidation of SUM at Cu NPs/P-Mel/GCE electrode. C) variation of peak potential (E_{pa}) with log v.

There is a linear correlation between the peak potential and the logarithm of scan rate, log v (Fig. 8C). The equation is found to be: E_{pa} / V = 0.5807 + 0.0674 log (v / mV s^{-1}) with R^2 = 0.9873. Based on Laviron's model,[34] the slopes of the line for E_{pa} can be expressed as $2.303RT/2(1-\alpha)nF$. Therefore, the values of the electron-transfer coefficient (α) and the electron-transfer number (n) can be calculated as 0.44 and 0.87 (approximately equal to 1), respectively.

On the basis of foregoing research results in the Section *Effect of pH*, which represents the numbers of electron and proton involved in the oxidations of SUM was both equal, the electrooxidations of SUM on the the Cu NPs/P-Mel/GCE was one-electron, one-proton-transfer process, which is associated with the rem-

oval of one electron and one proton from the nitrogen atom of the indole ring present in the molecule.[19]

Analytical performances

Under the optimum conditions, the oxidation peak currents of various concentrations of SUM at the Cu NPs/P-Mel/GCE were recorded by DPV. As shown in Fig. 9, the peak current was proportional to the concentration of SUM in the range 0.08–0.58 and 0.58–6.5 μM. The linear regression equation (for the first linear segment) was i_{pa} / μA =1.1404c_{SUM} / μM + 0.1198 (R^2 = 0.9942) and for the second linear segment i_{pa} / μA =0.2487c_{SUM} / μM + 0.6494 (R^2 = 0.9939). Such a good sensitivity can be attributed to the efficiency of the electron-transfer between the modified electrode and SUM due to the catalytic effect and the low charge transfer resistance of the modified electrode. The limit of detection defined as $LOD = 3S_b/m$, where LOD, S_b and m are the limit of detection, standard deviation of the blank and the slope of the calibration graph, respectively, was found to be 0.025 μM. S_b was estimated by the five replicate determinations of the blank signals. Comparison of the detection limit and linear dynamic range of SUM by the proposed method with other voltammetric sensors from the literature is illustrated in Table I.

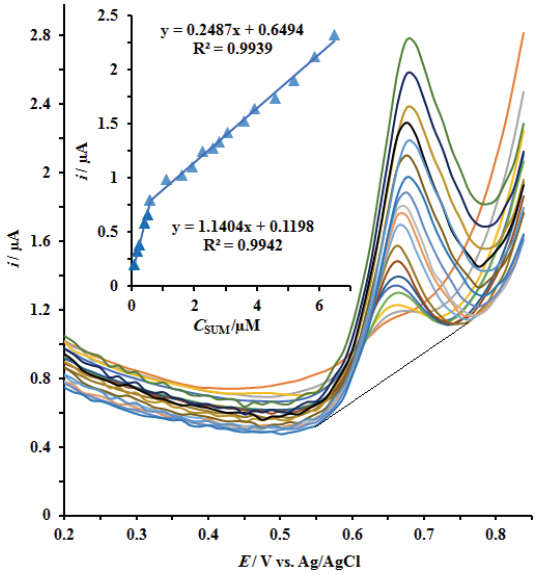

Fig. 9. Differential pulse voltammograms of the Cu NPs/P-Mel/GCE electrode at the different sumatriptan (SUM) concentrations (0.12–0.87 μM and 0.87–9.2 μM). Inset: calibration plot of the dependence of the measured current on SUM concentrations. Supporting electrolyte: phosphate buffer (pH 7.0); pulse amplitude 0.05 V, scan rate 0.025 V/s and pulse time 0.04 s.

Reproducibility, repeatability and stability

The operational stability of the Cu NPs/P-Mel/GC electrode has been assessed by the consecutive measurements of a 2.99 μM SUM sample. The relative standard deviation of 2.9 % was obtained for 10 measurements. In addi-

tion, five Cu NPs/P-Mel/GC electrodes prepared independently but following the same fabrication protocol were used to determine 2.99 μM SUM. All five electrodes exhibit similar DPV responses and a relative standard deviation of 4.3% was obtained. These experimental results indicate the the proposed electrochemical sensor possesses a good reproducibility. The long-term stability of the Cu NPs/P-Mel/GC electrode has also been studied. The Cu NPs/P-Mel/GC electrode retains 95 % of its initial activity after 1 month, demonstrating high stability. The above results showed that the present Cu NPs/P-Mel/GC electrode sensor was very stable and reproducible towards the detection of SUM.

TABLE I. Comparison of major characteristics of different electrochemical sensors for determination of sumatriptan

Electrode	Linear dynamic range, μM	Detection limit, μM	Ref.
Pt-ZONPs/ CPE	0.01–55	0.003	19
CMK-3/GCE	1.50–120	0.8	20
Gr/AuNP/NAF/GCE	0.002–41.2	0.0007	24
AgNPs-MWCNT/(PGE)	0.08–100	0.04	23
PPY/CNT/GCE	0.02–10	0.006	22
MWCNT/cobalt- schiff base/CPE	1–1000	0.3	21
Cu NPs/P-Mel/GCE	0.08–0.58 and 0.58–6.5	0.025	This work

Interference study

In some cases, the interference of foreign compounds can be overcome by using the oxidation peak for determination. Under the optimum experimental conditions, the effects of some organic and inorganic compounds which commonly existed in pharmaceuticals and biological samples were evaluated by the analysis of solutions containing SUM spiked with an excess of different compounds. The interference study was carried out by recording DPV in the presence of 0.99 μM of SUM with the potential interfering substances at pH 7. It was found that, at Cu NPs/P-Mel/GCE, five well separated peaks at –0.16, 0.1, 0.32, 0.51 and 0.65 V were observed corresponding to the oxidation of ascorbic acid (AA), epinephrine (EP), acetaminophen (AC), piroxicam (PXM) and SUM, respectively (Fig. 10). Moreover, the results showed that 1000-fold of Ca^{2+}, Mg^{2+}, Na^{+}, Al^{3+}, NH_4^{+}, SO_4^{2-} and NO_3^{-}, and 500-fold of glucose did not affect the selectivity. These results showed that the selectivity of the method was acceptable and this method was suitable for analysis of SUM in biological fluids.

Real samples analysis

In order to assess the applicability of the proposed method in physiological sample and its background interference, human blood serum and human urine was selected as sample. There was no distinct signal of SUM observed in healthy human blood serum and urine samples. For evaluating the accuracy, some SUM

standard solution was added into blood serum or urine (diluted to a certain concentration) before analysis and the recovery was determined by the standard addition method. The results of determination were listed in Table II. The mean recovery of SUM was 99.6 % (healthy human serum) and 99 % (healthy human urine), respectively.

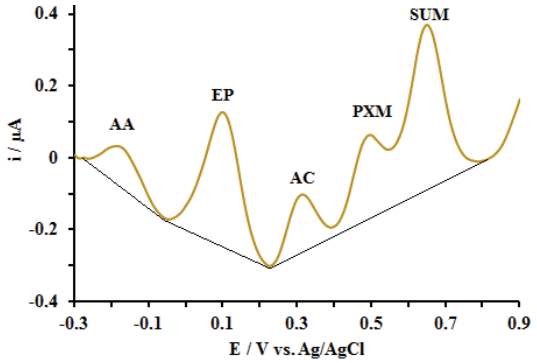

Fig 10. DPV of SUM (0.99 μM) in the presence of 50 μM ascorbic acid (AA), 2.2 μM epinephrine (EP), 4.9 μM acetaminophen (AC) and 5.2 μM piroxicam (PXM).

TABLE II. Determination of sumatriptan in human blood serum and urine sample

No.	Amount of sumatriptan added, μM	Amount of sumatriptan found, μM	Recovery, %
		Human blood serum	
1	0	Not detected	–
2	1	1.03	103
3	2	1.95	97.5
4	3	2.95	98.3
		Urine sample	
1	0	Not detected	–
2	2	1.93	96
3	4	4.07	101.7
4	6	5.96	99.3

CONCLUSIONS

The result of this investigation shows that the glassy carbon electrode modified with Cu NPs/P-Mel is a high sensitive and selective sensing element in the voltammetric determination of SUM. The proposed modified electrode showed an effective novel electro catalytic activity towards the anodic oxidation of SUM leading to the significant enlargement in the peak currents. All the above investigations as well as other properties of proposed electrode showed the excellent reproducibility, the good selectivity and stability and the low detection limit. The modified electrode was very useful for the electrochemical determination of SUM in biological fluid.

Acknowledgment. The authors gratefully acknowledge the Research Council of Payame Noor University, Iran, for its financial support.

ИЗВОД

УВЕЋАЊЕ СИГНАЛА ЗА ДЕТЕКЦИЈУ СУМАТРИПАНА НА ПОВРШИНИ ПОЛИМЕРА СА НАНОЧЕСТИЦАМА БАКРА

GHASEM KARIM-NEZHAD, SAMANE KHANALILOO, ZEYNAB KHORABLOU и PARISA SEYED DORRAJI

Department of Chemistry, Payame Noor University, P. O. Box 19395-3697 Tehran, Iran

Нови нанокомпозит Cu-наночестице/полимеламин таложен је електрохемијски у условима циклизирања потенцијала на електроду од стакластог угљеника. Скенирајућом електронском микроскопијом са емисијом поља утврђено је да је добијен униформан талог нанокомпозита. Показано је да су карактеристике преноса наелектрисања сумат-риптана значајно боље на модификованој електроди. Оваква електрода је коришћена за прецизно одређивање суматрипана методом диференцијалне пулсне волтамтерије. Линеарни калибрациони дијаграм је добијен у опсегу концентрација 0,08–0,58 μM и 0,58–6,5 μM са границом детекције 0,025 μM. Предложена метода је тестирана одре-ђивањем суматриптана у хуманим биолошким флуидима као што су урин и крвна плазма. Добијени резултати су били задовољавајући (аналитички принос > 99 %).

(Примљено 27. јула, ревидирано 26. новембра, прихваћено 21. децембра 2017)

REFERENCES

1. C. M. Villalon, D. Centurion, L. F. Valdivia, P. de Vries, P. R. Saxena, *Curr. Vasc. Pharmacol.* **1** (2003) 71
2. K. Ahonen, M. L. Hamalainen, H. Rantala, K. Hoppu, *Neurology* **62** (2004) 883
3. E. Fuseau, O. Petricoul, K. H. Moore, A. Barrow, T. Ibbotson, *Clin. Pharmacokin.* **41** (2002) 801
4. M. W. Pierce, *Neurotherapeutics* **7** (2010) 159
5. B. K. Ramu, K. Raghubabu, *Int. J. Pharm. Biomed. Sci.* **1** (2010) 49
6. A. Avadhanulu, J. Srinivas, Y. Anjaneyulu, *Indian Drugs* **33** (1996) 334
7. D. Tipre, P. Vavia, *Indian Drugs* **36** (1999) 501
8. J. Oxford, M. Lant, *J. Chromatogr., B* **496** (1989) 137
9. K. Vishwanathan, MG. Bartlett, JT. Stewart, *Rapid Commun. Mass Spectrom.* **14** (2000) 168
10. A. Tan, P. Hang, J. Couture, S. Hussain, F. Vallée, *J. Chromatogr., B* **856** (2007) 9
11. J. J. Seo, J. Park, M. H. Bae, M.-S. Lim, S. J. Seong, J. Lee, S. M. Park, H. W. Lee, Y.-R. Yoon, *J. Chromatogr., B* **919** (2013) 38
12. M. Dunne, P. Andrew, *J. Pharm. Biomed. Anal.* **14** (1996) 721
13. C. Saka, Ö. Şahin, *Crit. Rev. Anal. Chem.* **43** (2013) 2
14. C. Saka, *Crit. Rev. Anal. Chem.* **39** (2009) 32
15. A. Femenía-Font, V. Merino, V. Rodilla, A. López-Castellano, *J. Pharm. Biomed. Anal.* **37** (2005) 621
16. Z. Ge, E. Tessier, L. Neirinck, Z. Zhu, *J. Chromatogr., B* **806** (2004) 299
17. M. Franklin, J. Odontiadis, E. Clement, *J. Chromatogr., B* **681** (1996) 416
18. K. Altria, *J. Chromatogr., A* **735** (1996) 43
19. M. B. Gholivand, L. Mohammadi-Behzad, *J. Electroanal. Chem.* **712** (2014) 33
20. L. Torkian, N. Mohammadi, E. Amereh, *Middle East J. Sci. Res.* **14** (2013) 754
21. M. Amiri, Z. Pakdel, A. Bezaatpour, S. Shahrokhian, *Bioelectrochemistry* **81** (2011) 81
22. S. Shahrokhian, Z. Kamalzadeh, R-S. Saberi, *Electrochim. Acta* **56** (2011) 10032
23. M. Ghalkhani, S. Shahrokhian, F. Ghorbani-Bidkorbeh, *Talanta* **80** (2009) 31
24. B. J. Sanghavi, P. K. Kalambate, S. P. Karna, A. K. Srivastava, *Talanta* **120** (2014) 1

25. A. Safavi, N. Maleki, F. Tajabadi, E. Farjami, *Electrochem. Commun.* **9** (2007) 1963
26. A. N. Shipway, M. Lahav, I. Willner, *Adv. Mater.* **12** (2000) 993
27. D. N. Muraviev, *Contrib. Sci.* **3** (2005) 19
28. Y. Ohnuki, H. Matsuda, T. Ohsaka, N. Oyama, *J. Electroanal. Chem.* **158** (1983) 55
29. S. Tian, J. Liu, T. Zhu, W. Knoll, *Chem. Mater.* **16** (2004) 4103
30. R. Davies, G. A. Schurr, P. Meenan, R. D. Nelson, H. E. Bergna, C. A. Brevett, R. H. Goldbaum, *Adv. Mater.* **10** (1998) 1264
31. L. Zhang, M. Wan, *J. Phys. Chem., B* **107** (2003) 6748
32. X. Liu, L. Luo, Y. Ding, Q. Wu, Y. Wei, D. Ye, *J. Electroanal. Chem.* **675** (2012) 47
33. D. Hai-Yun, Z. Ye, S-J. Zhang, Y. Xue-Bo, L. Yi-Jun, H. Xi-Wen, *Chin. J. Anal. Chem.* **36** (2008) 839
34. E. Laviron, *J. Electroanal. Chem.* **10** (1979) 19.