Electrochemical Evaluation of the Catalytic Effect of Natural Phosphate on the Oxidation of Ascorbic Acid: Analytical Application in Human Blood

H. EL Ouafy[a], T. EL Ouafy[b,*], M. Oubenali[a], M. Mbarki[a] and M. Echajia[a]

[a]_Laboratory of Organic and Analytical Chemistry, Sultan Moulay Slimane University, Faculty of Science and Technology, Beni Mellal, Morocco_

[b]_Laboratory of Organic and Analytical Chemistry, Sultan Moulay Slimane University, Polydisciplinary Faculty, Khouribga, Morocco_

This work describes the electroanalytical activity of the natural phosphate modified carbon paste electrode (CPE-NP) for ascorbic acid (AA) oxidation, where its electrochemical response is compared to the carbon paste electrode (CPE). The voltammetric behavior of AA was studied when an anodic peak appeared at 0.35 V (_vs_. Ag/AgCl/3 M KCl) in the Britton-Robinson buffer solution (pH 6.0). This peak was obtained from the irreversible oxidation of AA at CPE-NP. The electro-catalytic influence was studied by cyclic voltammetry (CV) and differential pulse voltammetry (DPV). To give electroanalytical detection to oxidize AA on the CPE-NP, the differential pulse voltammograms were used in the potential range from -0.5 V to 1.5 V _vs_. Ag/AgCl/(sat. KCl). Besides, CPE-NP can be employed successfully to ameliorate the detection of AA at very feeble concentration with good sensitivity. The calibration range was from 1.0×10^{-6}-1.0×10^{-3} M. The calculated limit of detection (LD) was 1.44×10^{-9} M when the relative standard deviation (RSD) at 1.0×10^{-5} M AA concentration was 3.29% for nine repetitions. Afterward, the studied method was applied to detect AA in human blood with satisfactory results.

Keywords: Ascorbic acid, Nnatural phosphate, Human blood, Electrocatalysis

INTTRODUCTION

Graphene has shown excellent affection for scientific groups [1-16]. It is a 2-dimensional sp^2-hybridized carbon sheet with many good physicochemical behavior such as extremely high surface area, excellent electronic transport properties, high mechanical stiffness, and extraordinary thermal and electrical conductivity [1-6]. It has been also indicated to have outstanding commitment for numerous potential utilizations; for example, sensors, nanoelectronics, batteries, supercapacitors, hydrogen storage and nanocomposites [1,7-10]. These supreme properties make it good candidate for electrochemistry applications specially in sensing [10-12]. A Surfactant Enhanced Graphene Paste Electrode and anionic surfactant modified carbon nanocomposite material were used in the electroanalysis of the molecules thanks to its high sensitivity, fast response, excellent stability, and good reproducibility [13,14]. Carbon paste electrode modified by electropolymerization as well as immobilization technique was used for the resolution of antibacterial drug Ciprofloxacin (CFX) [15]. Sodium dodecyl sulfate surfactant modified graphene paste electrode, prepared by electrochemical immobilization of the sodium dodecyl sulfate surfactant on a graphene paste electrode, was applied for simultaneous determination of dopamine in the presence of ascorbic acid and uric acid [16]. Electropolymerization of aniline blue on the surface of carbon paste electrode was applied for individual and simultaneous determination of ascorbic acid, dopamine and uric acid [17]. Poly (maleic acid) Modified Carbon Paste Electrode was used for the electrochemical detection with stable and sensitive current responses [18]. Electrode based

---

*Corresponding author. E-mail: tarikelouafy@gmail.com

on modified carbon nanotube-graphite mixture paste electrode was determined in the electroanalysis of organic compounds [19]. Poly (Solid Red A) modified carbon nanotube paste electrode was used for simultaneous determination of epinephrine, uric acid and ascorbic acid [20]. Poly‑1‑leucine modified sensor for enhanced voltammetric determination of Riboflavin has been used [21]. A surfactant enhanced novel pencil graphite and carbon nanotube composite paste material as the effective electrochemical electrodes were used for determination of Riboflavin [22]. It has also been reported that graphene has the capacity to replace the other present materials used for the preparation of biosensors [23-26].

Vitamin C or AA, one of the important vitamins, generously exists in several plants and contributes to certain interesting biological reactions such as protection against cancer and elimination of free radicals; however, it cannot be synthesized by the human body. A recommended daily intake in AA is from 70 to 90 mg. Insufficient intake will lead to scurvy syndromes, gingival bleeding, *etc.* Excess AA will cause urinary stones, stomach convulsions, and diarrhea [27]. For the importance of AA in human life, its analysis in an aqueous medium is very important. Habitual techniques for AA analysis are often based on enzymatic techniques [28,29] and UV-Vis [30]. Recently, there has been significant interest in developing chemical sensors for electroanalysis of AA.

Advantages of electrochemical techniques include sensitive, low cost, simple, and excellent methods for the determination of drugs and related molecules in pharmaceutical products and biological fluids. There are many papers on characterization of the electrochemical properties of curcumin [14,15,23,31-33]. Electrochemical detection is a best substitute for the detection of many compounds in pharmaceutical and biological samples [20]. However, the main drawback for the voltammetric detection of AA in real samples is the interference of some concomitant compounds, leading in overlapped voltammetric responses due to their very similar oxidation peak potentials [34,35]. Recently, chemically modified electrode surface has been proved to be a successful method to solve this problem, and various materials and techniques have been used [36,37] the modified electrodes have many advantages like good biocompatibility, stability and easiness

of the preparation [38-40].

AA can be spontaneously oxidized electrochemically at classical electrodes which were employed to detect AA [41,42]. Nevertheless, the oxidation reaction of AA at the electrode necessitates high potential which results in electrode crass by its oxidation products with low reproducibility, feeble sensitivity, and selectivity. Also, some of the molecules, *e.g.* uric acid and dopamine, undergo oxidation in the same potential range as AA. To resolve this issue, chemically modified electrodes were developed and cited with different materials such as conducting polymers [43-47], ionic liquids [48,49], metal nanoparticles [44], carbon nanotubes [45,49,50] and macrocyclic compounds [51,52]. A lot of analytical methods including sensors and biosensors [53-55] have been suggested for determination of AA in various samples. Other techniques, based on the employed physicochemical methods, have been introduced for detection of AA such as HPLC [56-58] CE [59-62]. The research aimed at developing new analytical methods for AA detection is directed towards increasing their specificity, simplicity, sensitivity, and rapidity [63,64]. Electrochemical determination is a good method for electroanalysis of electroactive species. Similarly, some research groups also reported modified electrodes for selective detection and determination of AA. They are nano ZnO/poly (luminol) hybrid film modified electrode [65], poly (xanthurenic acid) and multi-walled carbon nanotubes [66], Pt disc working electrode [67], carbon paste electrode spiked with ferrocene carboxylic acid [68], anionic surfactant modified carbon nanocomposite material [69], modified multiwalled carbon nanotube paste electrode [70], carbon paste modified by 2,7-bis(ferrocenyl ethyl)fluoren-9-one [71], carbon paste modified by 2,2'-[1,2-ethanediylbis (nitriloethylidyne)]-bishydroquinone [72], carbon paste modified by bis(4'-(4-pyridyl)-2,2':6',2''-terpyridine) iron(II) thiocyanate [73].

In this work, we have described the electrochemical studies of AA oxidation and their electroanalysis sensitive at CPE-NP in Britton-Robinson solution buffer. Its oxidation performance is compared to that of CPE. The success of the CPE-NP surface toward the electrochemical analysis of AA is evaluated by CV and DPV techniques. The electrode is also applied for detection of AA concentrations in human blood using CV.

EXPERIMENTAL

Reagents and Chemicals

All chemicals used in the present work were of analytical grade or of the highest purity available. Sulfuric acid and potassium hydroxide, acetic acid, boric acid, and phosphoric acid were obtained from Merck (Darmstadt, Germany), Fluka (St. Gallen, Switzerland), and Riedel de Haen (Seelze, Germany) and used as received. Ascorbic acid, hydroquinone, dopamine, resorcinol, salicylic acid, ibuprofen purchased from Sigma-Aldrich were dissolved in 0.1 M Britton-Robinson Buffer (BR; pH 6) to prepare a stock solution of 1.0×10^{-3} M. By diluting the stock solutions, the working standard solutions were prepared. Paraffin was used as the pasting liquid for the carbon-paste electrode (CPE). Carbon paste was supplied from Carbone Lorraine (Lorraine, France; ref. 9900). The pH was adjusted by sulfuric acid or potassium hydroxide. The natural phosphate utilized in the present work was obtained from the Khouribga region (Morocco). All these experiments were performed using distilled water, at room temperature.

Switchgear

The electroanalysis activity of the CPE-NP toward oxidation of AA has been studied by the CV and DPV connected to a computer for control, data acquisition, and storage. The software employed was VoltaLab Master 4. The oxidation of AA was carried out in a three-electrode cell. Ag/AgCl/KCl (3 M) was utilized as a reference electrode and a platinum wire as a counter electrode. The CPE-NP (0.2 cm^2) is the working electrode utilized in the present work.

Electrodes Preparation

The CPE-NP was elaborated by mixing graphite carbon powder and natural phosphate using paraffin oil as a binder. The working electrode was a cylinder that was tightly filled with a mixture of graphite carbon and natural phosphate. The electrical contact was established using a carbon rod.

Procedure

Different supporting electrolytes were tested such as acetate buffer, phosphate buffer, and Britton-Robinson buffer. The excellent electrochemical response was obtained by Britton-Robinson buffer (pH 6.0). In working procedure the electrochemical responses of the CPE-NP surface is measured at a concentration of AA. A known concentration of AA solution was prepared in 0.1 M Britton-Robinson buffer solution (pH 6.0) and 20 ml of the prepared solution was transferred to an electrochemical cell. The cyclic and differential voltammograms were obtained between -0.5 and 1.5 V at 100 mV s^{-1}. The optimal conditions were determined by measuring the currents as a function of all parameters.

RESULTS AND DISCUSSION

Electrochemical Behavior of AA

Figures 1A and 1B show respectively the cyclic voltammograms (CVs) and the differential pulse voltammograms (DPVs) recorded in the potential range between -0.5 V and 1.5 V on the surfaces of CPE and CPE-NP in 0.1 M BR buffer (pH 6). It seems that the CVs and DPVs have different forms, showing that the CPE surface has been effectively modified by the natural phosphate.

The electroanalysis activity of the CPE-NP toward AA oxidation was studied by CV and DPV at CPE and CPE-NP in BR buffer (pH 6) containing 1.0×10^{-3} M of AA (Figs. 1C and 1D). The anodic peak for AA on CPE and CPE-NP surface appeared at about 0.35 V. The CPE-NP exhibited efficient electrocatalytic oxidation of AA compared to the CPE. Besides, the CPE-NP can promote AA detection. Scheme 1 shows the reaction of oxidation of L-ascorbate to dehydro-L-ascorbic.

Optimization of Experimental Variables

In addition to electrochemical properties, the CPE-NP shows a big capacity for the electroanalysis of AA. This electroanalytical was carried out by the DPV method. Firstly, all electroanalysis parameters were optimized in BR solution (pH 6.0) containing 1.0×10^{-3} M of AA. The effect of the accumulation time on the voltammetric responses was investigated (Fig. 2A). Figure 2B represents an increase in the current intensity as a function of preconcentration time during the first 4 min. After 4 min, the peak intensity decreases with a net increase in the accumulation time. Hence, 4 min was used in all experiments.

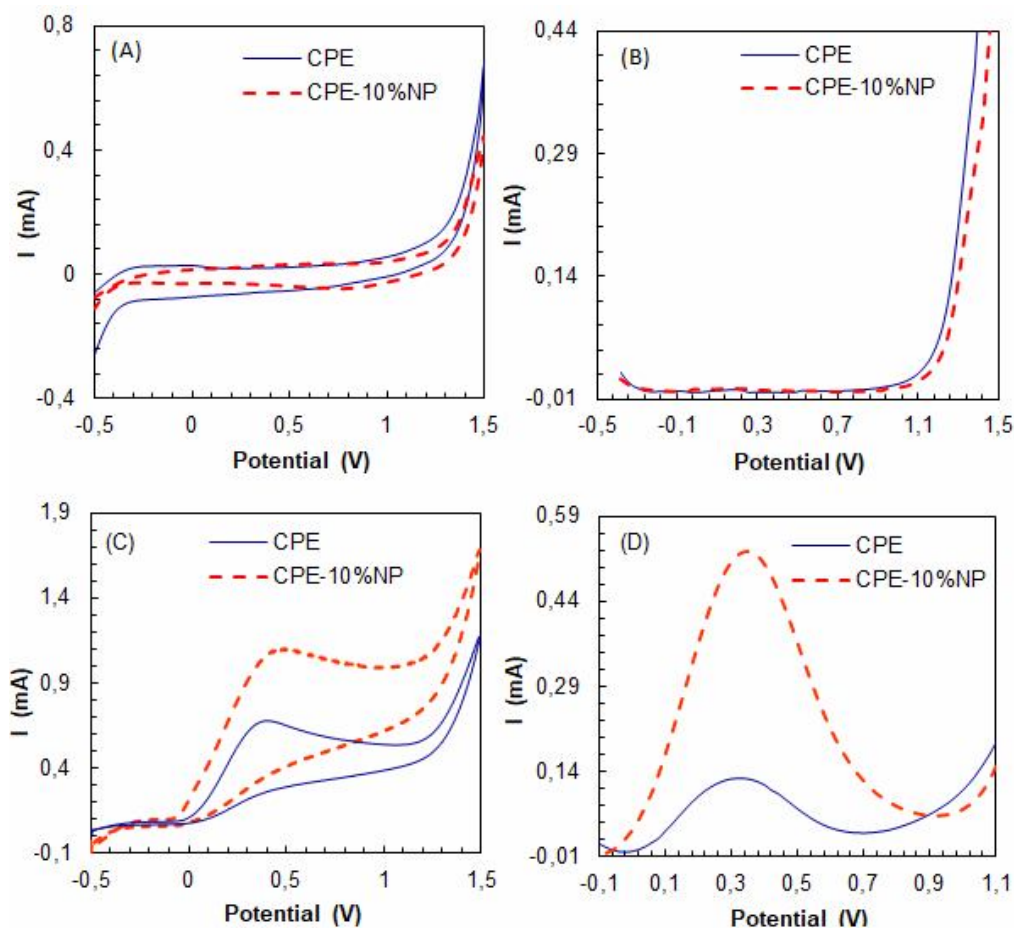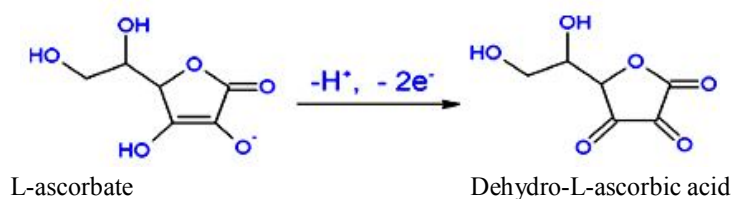The increase of the modifier loading (from 2 to 30% by

Fig. 1. (A) CVs (100 mV s^{-1}), and (B) DPVs obtained for CPE and CPE-NP in the absence of AA. (C) CVs (100 mV s^{-1}) and (D) DPVs of 1.0×10^{-3} M AA for CPE and CPE-NP in 1.0×10^{-1} M BR buffer (pH 6).

L-ascorbate   Dehydro-L-ascorbic acid

Scheme 1. Electrochemical oxidation of AA at CPE-NP [74,75]

weight of carbon paste) affects the AA detection at the CPE-NP surface, represented in Fig. 2C using the DPVs. The oxidation current of AA increases with the increase of the natural phosphate until 10%, beyond this value the oxidation current intensity decreases (Fig. 2D). This is possibly due to the decrease in the CPE-NP conductivity. Hence, 10% of the ratio by weight was used in this work. In other experimental studies, the optimal electroanalysis parameters to make the AA detection were 14 mV s^{-1}, 120 ms, 100 mV, 400 ms for the step, pulse, width, and
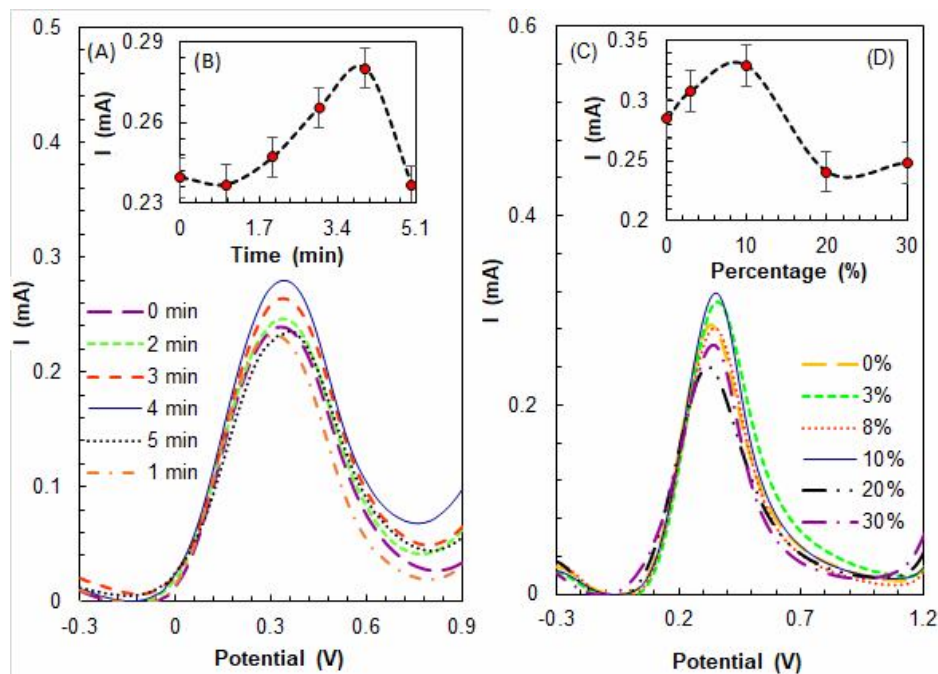
Fig. 2. Influence of the experimental variables ((A) and (B) accumulation time, (C) and (D)% of natural phosphate) involved in the DPV method, 1.0×10^{-3} M AA in BR solution (pH 6.0) at CPE-NP.
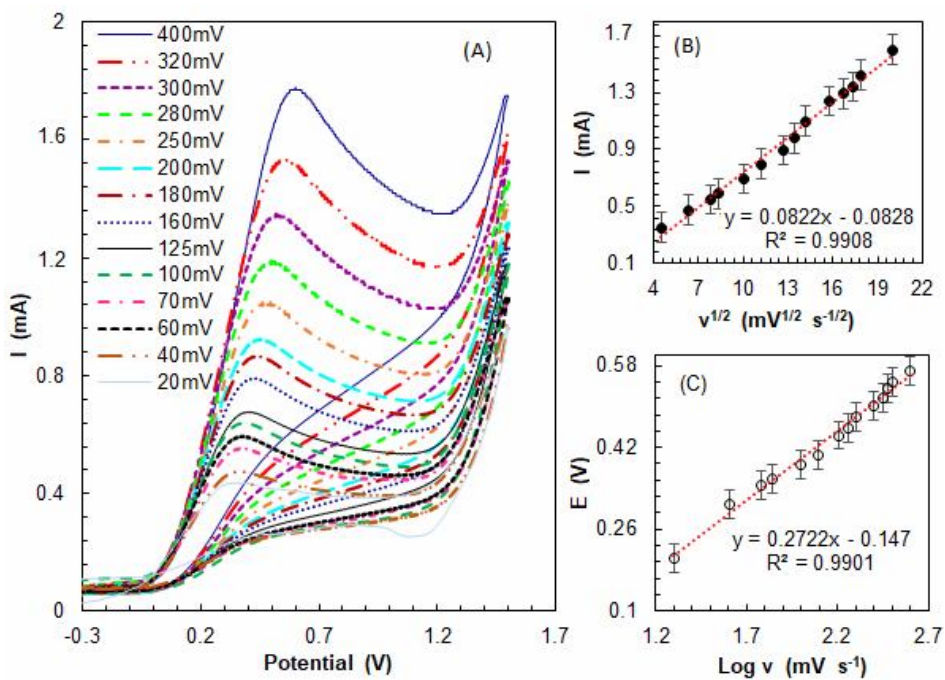

Fig. 3. CVs of 1.0×10^{-3} M AA in 0.1 M BR buffer (pH 6). (A) CVs at different scanning rates, (B) variations of Ip with the $V^{1/2}$, and (C) variations of Ep with $\log V$.
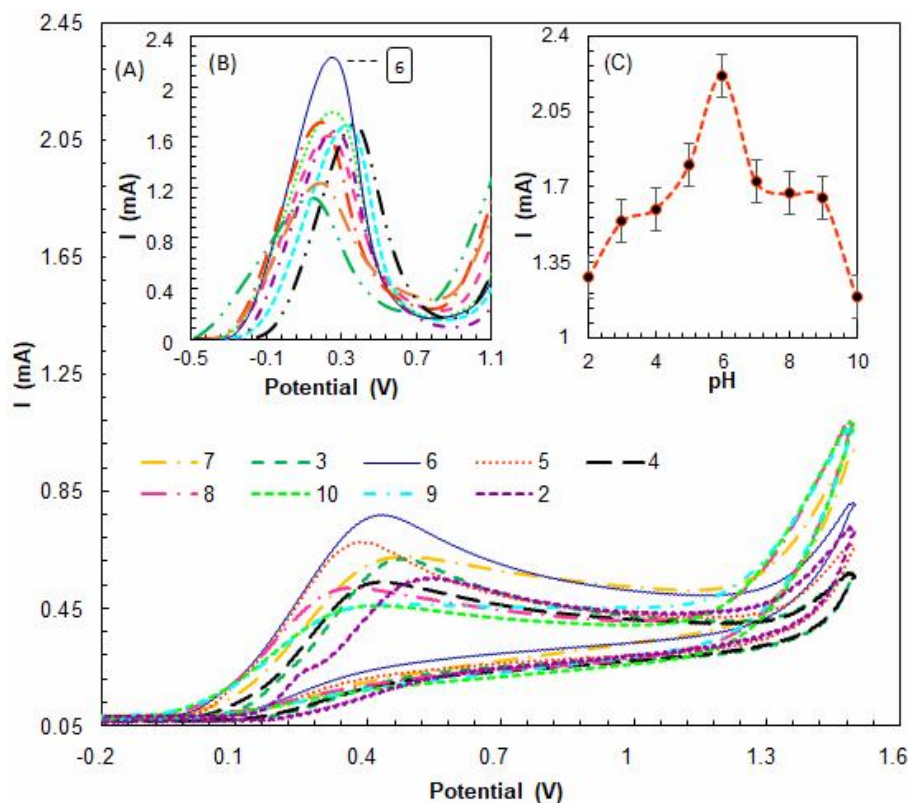
Fig. 4. (A) CVs (at 100 mV s^{-1}) and (B) DPVs of 1×10^{-3} M AA at different pHs. Inset: plot of *Ip vs.* pH.

period, respectively.

The Catalytic Effect of CPE-NP

Influence of scanning rate and pH. To further study the AA characteristics at the CPE-NP, the influence of the scanning rates on the voltammetric behavior of AA was studied. Figure 3A illustrates the cyclic voltammograms of AA (1.0×10^{-3} M) in Britton-Robinson buffer at the CPE-NP surface with increasing scanning rates between 20 and 400 mV s^{-1}. The density of the peak current is proportional to the square root of the scanning rate ($V^{1/2}$) at the CPE-NP surface (Fig. 3B). This phenomenon proposed a diffusion-controlled mechanism at the CPE-NP [76]. The oxidation of AA at the CPE-NP was constantly irreversible, which can be appeared by the potential of AA varied with the logarithm of scan rates. The oxidation peak potentials shifted regularly toward the positive direction with the scan rate varied from 20 to 400 mV s^{-1} (Fig. 3C).

The electrochemical behavior of CPE was carefully studied in BR buffer by CV and DPV. The influence of on CV and DPV responses of the CPE-NP was studied in the pH range between 1 and 10 and well-defined CVs (Fig. 4A) and DPVs (Fig. 4B) curves were observed. With the increase of buffer pH from 2 to 6, the oxidation peak current increased up to 2.4 mA. When the pH of the electrolytic medium exceeds to 6, the current of the AA oxidation peak decreased. Therefore, pH = 6 is best for the catalytic activity of CPE-NP toward the oxidation of AA (Fig. 4C).

Concentration Effect of AA

The influence of AA concentration has been studied under the optimized conditions by DPV at CPE-NP (Fig. 5A). Figure 5B shows the calibration curve for the oxidation of AA. The current density of the oxidation peak of AA increases with its concentration from 1.0×10^{-6} to 1.0×10^{-3} M of AA. The limit of detection calculated by the CPE-NP is 1.44×10^{-9} M. The LD calculated by CPE-NP

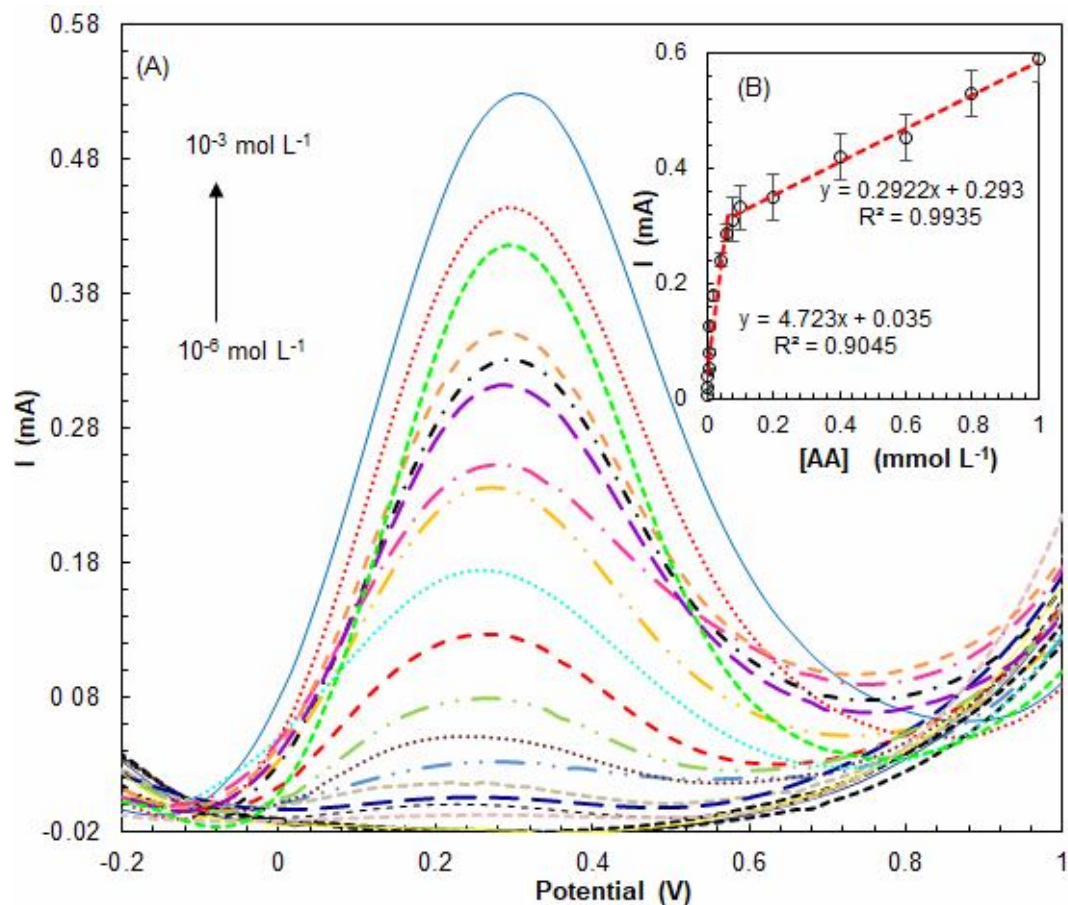**Fig. 5.** (A) DPVs of AA in 0.1 M B-R (pH 6) 1.0×10^{-3}, 8.0×10^{-4}, 6.0×10^{-4}, 4.0×10^{-4}, 2.0×10^{-4}, 1.0×10^{-4}, 8.0×10^{-5}, 6.0×10^{-5}, 4.0×10^{-5}, 2.0×10^{-5}, 1.0×10^{-5}, 8.0×10^{-6}, 6.0×10^{-6}, 4.0×10^{-6}, 2.0×10^{-6} and 1.0×10^{-6} M. (B) plots of electrocatalytic peak current *versus* AA concentration.

was compared with those obtained by other electrodes (Table 1) [65-73]. The repeatability of our analysis method was also investigated as a relative standard deviation (RSD). Therefore, the RSD calculated is 3.29% after nine measurements in solutions of 1.0×10^{-5} M AA.

Electroanalysis of AA in Human Blood

In order to verify the applicability and validity of the analytical method, the rock phosphate modified carbon paste electrode was used for the detection of AA in human blood samples. The human blood solutions were utilized without any pretreatment. The electroanalytical curves were

recorded by the method of differential pulse voltammetry (Fig. 6A). Preliminary analysis indicates that this sample does not contain AA. For this reason, we proceeded by contaminating this sample with ibuprofen at well-defined concentration levels. The AA oxidation peak was well displayed. The calibration curve of the human blood samples using the optimum conditions was linear with a good correlation coefficient ($R^2 = 0.9921$) (Fig. 6B). Consequently, the limit of detection obtained was 8.81×10^{-8} M. The RSD calculated was 4.08% after nine measurements in solutions of 1.0×10^{-5} M AA. This shows the possibility to determine AA in human blood samples.

Table 1. Detection Limit Obtained by Several Electrodes for the Electroanalysis of AA

Modified electrode	Analytical technique	Detection limit (M)	Ep (V)	pH	Ref.
Nano-ZnO/poly(luminol) hybrid film modified electrode	CV	1.0×10^{-6}	0.4	7	[65]
Poly (xanthurenic acid) and multi-walled carbon nanotubes	CV	0.1×10^{-7}	0.3	7	[66]
Pt disc working electrode	CV	9×10^{-5}	0.49	7	[67]
Carbon paste electrode Spiked with ferrocene carboxylic acid	CV	1.08×10^{-5}	0.248	5	[68]
Anionic surfactant modified carbon nanocomposite material	DPV	2.7×10^{-8}	0.3	7	[69]
Modified Multiwalled Carbon Nanotube Paste Electrode	CV	8.9×10^{-8}	0.235	7	[70]
Carbon paste modified by 2,7-bis(ferrocenyl ethyl)fluoren-9-one	CV	9×10^{-6}	0.3	7	[71]
Carbon paste modified by 2,2'-[1,2-ethanediylbis (nitriloethylidyne)]-bishydroquinone	CV	7.5×10^{-8}	0.38	7	[72]
Carbon paste modified by bis(4'-(4-pyridyl)-2,2':6',2''-terpyridine) iron(II) thiocyanate	CV	2×10^{-6}	0.2	5	[73]
CPE-NP	DPV	1.44×10^{-9}	0.35	6	Present work

Influence of Interferences

The effect of interferents was also studied to determine the selectivity of CPE-NP. These interferents were hydroquinone (HQ), dopamine (DA), ascorbic acid (AA), resorcinol (RSC), salicylic acid (As), ibuprofen (IBU) into the solution containing 1.0×10^{-4} M of AA. Electrochemical measurements were studied to determine the influence of interferents on the intensity of the oxidation currents of the compound examined (Fig. 7). The results obtained illustrate that the presence of interfering agents in a solution containing AA does not influence the density of the current of the AA oxidation peak.

CONCLUSIONS

At the surface of CPE-NP, AA can produce an irreversible anodic peak at 0.35 V in pH 6 BR buffer solutions. The CPE-NP exhibits good electrocatalytic performance toward the oxidation of AA. A large positive shift in the peak potentials of AA was observed. The catalytic evaluation was carried out using the CV and DPV. So, to obtain the detection limit of AA, the DPV method was utilized to determine AA in aqueous media. The results illustrated that the oxidation current for AA at the CPE-NP increased significantly compared with CPE. The relationship between the oxidation current and the concentration of AA was linear from 1.0×10^{-6} to 1.0×10^{-3} M. The detection limit found was 1.44×10^{-9} M. In addition, the results showed the feasibility of determining AA in real samples of human blood.
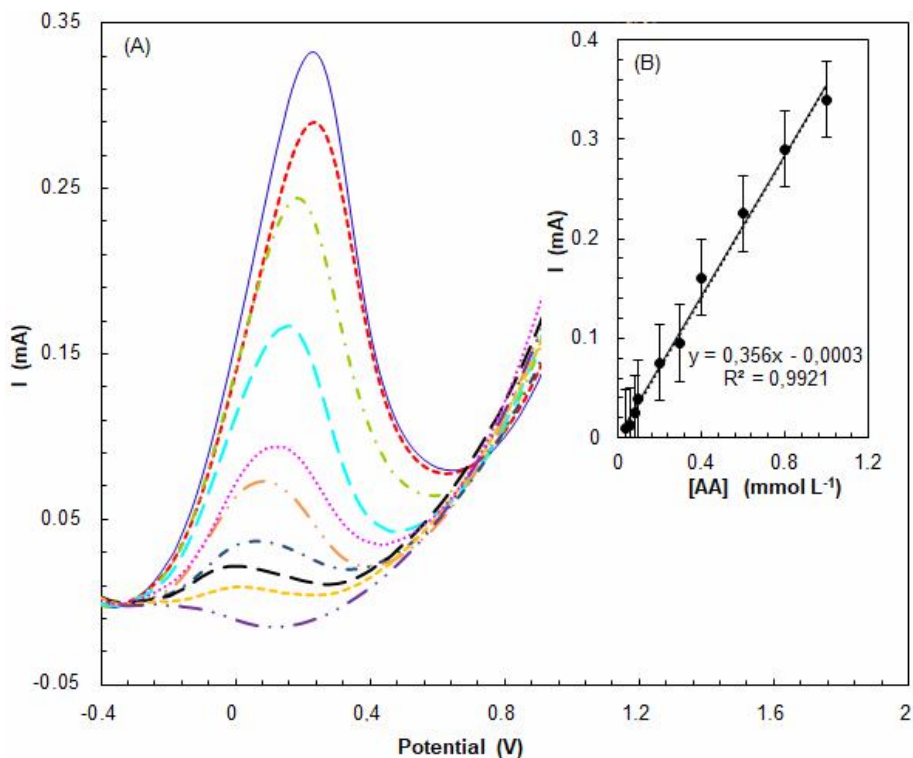
Fig. 6. (A) DPVs of AA from 10^{-5} to 10^{-3} M in 20 ml of human blood samples under optimized conditions, (B) plots of peak current *versus* AA concentration.
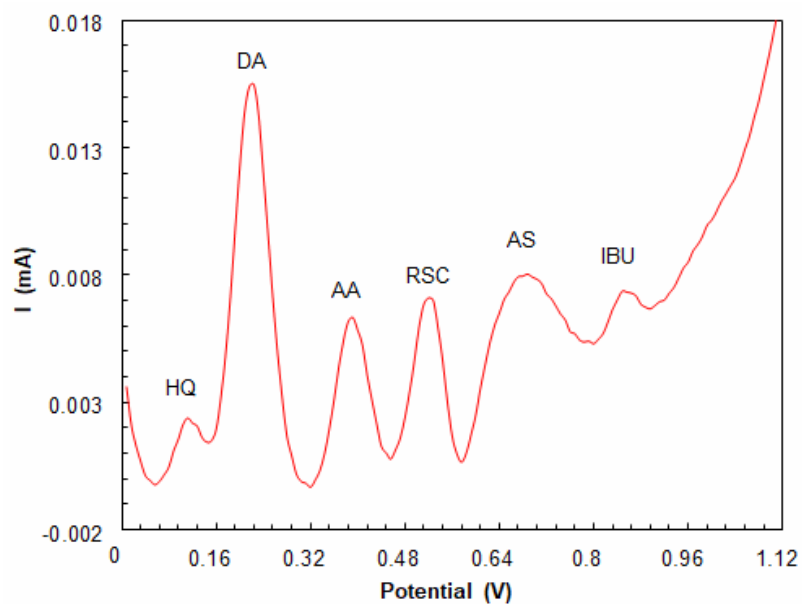

Fig. 7. DPV of a mixture of molecules containing 1.0×10^{-4} M of hydroquinone (HQ), dopamine (DA), ascorbic acid (AA), resorcinol (RSC), salicylic acid (As) and ibuprofen (IBU).

REFERENCES

[1] Ke, Q.; Wang, J., Graphene-based materials for supercapacitor electrodes: A review. *J. Materiomics.* **2016**, *2*, 37-54. DOI: 10.1016/j.jmat.2016.01.001.

[2] Bhuyan, S. A.; Uddin, N.; Islam, M.; Bipasha, F. A.; Hossain, S. S., Synthesis of graphene. *Int. Nano Lett.* **2016**, *6*, 65-83. DOI: 10.1007/s40089-015-0176-1.

[3] Lee, H. C.; Liu, W. W.; Chai, S. P.; Mohamed, A. R.; Lai, C. W.; Seong Khe, C.; Voon, C. H.; ashim, U. H.; Hidayah, N. M. S., Synthesis of single-layer graphene: A review of recent development. *Proced. Chem.* **2016**, *19*, 916. DOI: 10.1016/j.proche.2016.03.135.

[4] Saqib Shams, S. S.; Zhang, R.; Zhu, J., Graphene synthesis: A review. *Mater. Sci. Poland.* **2015**, *33*, 566-578. DOI: 10.1515/msp-2015-0079.

[5] Jacobberger, R. M.; Machhi, R.; Wroblewski, J.; Taylor, B.; Gillian-Daniel, A. L.; Arnold, M. S., Simple graphene synthesis *via* chemical vapor deposition. *J. Chem. Edu.* **2015**, *92*, 1903-1907. DOI: 10.1021/acs.jchemed.5b00126.

[6] Li, X.; Colombo, L.; Ruoff, R. S., Synthesis of graphene films on copper foils by chemical vapor deposition. *Adv. Mater.* **2016**, *28*, 6247-6252. DOI: 10.1002/adma.201504760.

[7] Li, D.; Muller, M. B.; Gilje, S.; Kaner, R. B.; Wallace, G. G., Processable aqueous dispersions of graphene nanosheets. *Nature Nanotechnol.* **2008**, *3*, 101-105. DOI: 10.1038/nnano.2007.451.

[8] Stankovich, S.; Dikin, D. A.; Dommett, G. H. B.; Kohlhaas, K. M.; Zimney, E. J.; Stach, E. A.; Piner, R. D.; Nguyen, S. T.; Ruoff, R. S., Graphene-based composite materials. *Nature.* **2006**, *442*, 282-286. DOI: 10.1038/nature04969.

[9] Xu, Y. X.; Bai, H.; Lu, G. W.; Li, C.; Shi, G. Q., Flexible Graphene Films *via* the Filtration of Water-Soluble Noncovalent Functionalized Graphene Sheets. *J. Am. Chem. Soc.* **2008**, *130*, 5856-5857. DOI: 10.1021/ja800745y.

[10] Muszynski, R.; Seger, B.; Kamat, P. V. J., Decorating graphene sheets with gold nanoparticles. *J. Phys. Chem. C.* **2008**, *112*, 5263-5266. DOI: 10.1021/jp800977b.

[11] Novoselov, K. S.; Fal'ko, V. I.; Colombo, L.; Gellert, P. R.; Schwab, M. G.; Kim, K., A roadmap for graphene. *Nature.* **2012**, *490*, 192-200. DOI: 10.1038/nature11458.

[12] Shan, C.; Yang, H.; Song, J., Han, D.; Ivaska, A.; Niu, L., Direct electrochemistry of glucose oxidase and biosensing for glucose based on graphene. *Anal. Chem.* **2009**, *81*, 2378-2382. DOI: 10.1021/ac802193c.

[13] Manjunatha, J. G., A surfactant enhanced graphene paste electrode as an effective electrochemical Sensor for the sensitive and simultaneous determination of catechol and resorcinol. *Chem. Data Coll.,* **2019**, *25*, 100331, DOI: 10.1016/j.cdc.2019.100331.

[14] Chenthattil, R.; Jamballi, G.; Manjunatha, Girish T., Low-cost voltammetric sensor based on an anionic surfactant modified carbon nanocomposite material for the rapid determination of curcumin in natural food supplement. *Instrum. Exp. Tech.,* 2020, *63*, 750-757, DOI: 10.1080/10739149.2020.1756317.

[15] Pemmatte, A. P.; Jamballi, G. M.; Mellekatte T. S., The electrochemical resolution of ciprofloxacin, riboflavin and estriol using anionic surfactant and polymer-modified carbon paste electrode. *Chem. Select,* **2019**, *4*, 13427-13433, DOI: 10.1002/slct.201903897.

[16] Jamballi G. M.; Mohamad D., Graphene paste electrode modified with sodium dodecyl sulfate surfactant for the determination of dopamine, ascorbic acid and uric acid. *Anal. Bioanal. Electrochem.* **2017**, *9*, 198-213, DOI: 10.1002/slct.201903897.

[17] Manjunatha, J. G.; Kumara Swamy, B. E.; Deraman, M.; Mamatha, G. P., Simultaneous determination of ascorbic, dopamine and uric acid at poly (inline blue) modified carbon paste electrode: a cyclic voltammetric study. *Int. J. Pharm. Pharm. Sci.,* **2013**, *5*, 355-361. DOI: 10.20964/2013.01.5.

[18] Jamballi, G. M.; Bahaddurghatta, E. K. S; Ganjeenahalli, P. M.; Ongera, G.; Bailure, S. S., Poly(maleic acid) modified carbon paste electrode for simultaneous detection of dopamine in the presence of uric acid: A cyclic voltammetric study. *Anal. Bioanal. Electrochem.* **2011**, *3*, 146-15. DOI: 11.20081/2011.04.3.

[19] Manjunatha, J. G., A new electrochemical sensor based on modified carbon nanotube-graphite mixture paste electrode for voltammetric determination of resorcinol. *Asian J. Pharm. Clin. Res.,* **2017**, *10*, 295-300, DOI: 10.22159/ajpcr.2017.v10i12.21028.

[20] Manjunatha, J. G.; Deraman, M.; Basri, N. H.; Talib, I. A., Fabrication of poly (Solid Red A) modified carbon nano tube paste electrode and its application for simultaneous determination of epinephrine, uric acid and ascorbic acid. *Arab. J. Chem.,* **2018**, *11*, 149-158, DOI: 10.1016/j.arabjc.2014.10.009.

[21] Amrutha, B. M.; Jamballi, G. G. M.; Aarti, S. B.; Pushpanjali, P. A., Fabrication of a sensitive and selective electrochemical sensing platform based on poly□l□leucine modified sensor for enhanced voltammetric determination of Riboflavin. *J. Food Meas. Charact.,* **2020**, *14*, 3633-3643, DOI: 10.1007/s11694-020-00608-9.

[22] Girish, T.; Manjunatha, J. G., A surfactant enhanced novel pencil graphite and carbon nanotube composite paste material as an effective electrochemical sensor for the determination of riboflavin. *J. Sci. Adv. Mat. Dei.,* **2020**, *5*, 56-64, DOI: 10.1016/j.jsamd.2019.11.001.

[23] Kuila, T.; Bose, S.; Khanra, P.; Mishra, A. K.; Kim, N. H.; Lee, J. H., Recent advances in graphene-based biosensors. *Biosens. Bioelectron.* **2011**, *26*, 4637-4648. DOI: 10.1016/j.bios.2011.05.039.

[24] Liu, Y.; Dong, X.; Chen, P., Biological and chemical sensors based on graphene materials. *Chem. Soc. Rev.* **2012**, *41*, 2283-2307. DOI: 10.1039/C1CS15270J.

[25] Allen, M. J.; Tung, V. C.; Kaner, R. B., Honeycomb Carbon: A Review of Graphene. *Chem. Rev.* **2010**, 110, 132-145. DOI: 10.1021/cr900070d.

[26] Shao, Y.; Wang, J.; Wu, H.; Liu, J.; Aksay, I. A.; Lin, Y., Graphene based electrochemical sensors and biosensors: A review. *Electroanalysis.* **2010**, *22*, 1027-1036. DOI: 10.1002/elan.200900571.

[27] Lin, K. C.; Yeh, P. C.; Chen, S. M., Electrochemical determination of ascorbic acid using poly (xanthurenic acid) and multi-walled carbon nanotubes. *Int. J. Electrochem. Sci.* **2012**, *7*, 12752-12763. DOI: 10.20964/2020.01.49.

[28] Saari, N. B.; Osman, A.; Selamat, J.; Fujita, S., Ascorbate oxidase from starfruit (Averrhoa carambola): preparation and its application in the determination of ascorbic acid from fruit juices. Food Chem. **2005**, *66*, 57-61, DOI: 10.1016/S0308-8146(98)00170-8.

[29] Liu, Z. H.; Wang, Q. L.; Mao, L. Y.; Cai, R. X.; Liu, Z.; Wang, Q.; Mao, L.; Cai, R., Highly sensitive spectrofluorimetric determination of ascorbic acid based on its enhancement effect on a mimetic enzyme-catalyzed reaction. *Anal. Chim. Acta.* **2000**, *413*, 167-173, DOI: 10.1016/S0003-2670(00)00774-1.

[30] Ruiz, T. P.; Lozano, C. M.; Tomas, V., Fluorimetric determination of total ascorbic acid by a stopped-flow mixing technique. *Analyst.* **2001**, *126*, 1436-1439, DOI: 10.1039/B102458M.

[31] Hadi, B.; Mohammad, A. T.; Malihe, A.; Rahman, H., Electrocatalytic determination of captopril using a modified carbon nanotube paste electrode: application to determination of captopril in pharmaceutical and biological samples. *Measurement.* **2014**, *47*, 770-776. DOI: 10.1016/j.measurement.2013.10.001.

[32] Hadi, B.; Jahan-Bakhsh, R.; Rahman, H., Electroanalysis and simultaneous determination of 6-thioguanine in the presence of uric acid and folic acid using a modified carbon nanotube paste electrode. *Anal. Sci.* **2011**, *27*, 991-997. DOI: 10.2116/analsci.27.991.

[33] Jahan-Bakhsh, R.; Reza, O.; Hadi, B.; Rahman, H., Electrocatalytic oxidation and highly selective voltammetric determination of L-cysteine at the surface of a 1-[4-(ferrocenyl ethynyl)phenyl]-1-ethanone modified carbon paste electrode. *Anal. Sci.* **2006**, *22*, 1213-1220. DOI: 10.2116/analsci.22.1213.

[34] Zahra, T.; Mohammad, M. A.; Hossein, N.; Hadi, B.; Maryam, N.; Hamid, R. Z., Electrochemical behavior of ascorbic acid at a 2,2′-[3,6-dioxa-1,8-octanediylbis (nitriloethylidyne)]-bis-hydroquinone carbon paste electrode. *Anal. Sci.* **2008**, *24*, 1039-1044. DOI: 10.2116/analsci.24.1039.

[35] Somayeh, M.; Hadi, B.; Alireza, M., Electrochemical behaviour of a modified carbon nanotube paste electrode and its application for simultaneous determination of epinephrine, uric acid and folic acid. *Sensor Lett.* **2013**, *11*, 388-394. DOI: 10.1166/

sl.2013.2723.

[36] Ali, M.; Hassan, K. M.; Ali, A. E.; Hadi, B., Application of modified multiwall carbon nanotubes paste electrode for simultaneous voltammetric determination of morphine and diclofenac in biological and pharmaceutical samples. *Sens. Actuators. B*. **2012**, *169*, 96-105. DOI: 10.1016/ j.snb.2012.03.059.

[37] Somayeh, T.; Mohammad, A. T.; Hadi, B., Simultaneous determination of droxidopa and carbidopa using a carbon nanotubes paste electrode. *Sens. Actuators B*. **2013**, *188*, 923-930. DOI: 10.1016/ j.snb.2013.07.085.

[38] Jahan-Bakhsh, R.; Reza, O.; Hadi, B., L-cysteine voltammetry at a carbon paste electrode bulk-modified with ferrocenedicarboxylic acid. *Electroanalysis*. **2007**, *19*, 1822-1830. DOI: 10.1002/ elan.200703932.

[39] Jahan-Bakhsh, R.; Ojani, R.; Hadi, B.; Hossienzadeh, R., Electrocatalytic determination of ascorbic acid at the surface of 2,7-bis(ferrocenyl ethyl)fluoren-9-one modified carbon paste electrode. *Electroanalysis*. **2005**, *18*, 1193-1201. DOI: 0.1002/elan.200503516.

[40] Mohammad, M. A.; Hadi, B.; Mohammad, K. A.; Fakhradin, M.; Mohammad, A. A., New strategy for simultaneous and selective voltammetric determination of norepinephrine, acetaminophen and folic acid using ZrO_2 nanoparticles-modified carbon paste electrode. *Sens. Actuators. B*. **2010**, *151*, 243-249. DOI: 10.1016/j.snb.2010.09.011.

[41] Raoof, J. B.; Ojani, R.; Kiani, A., Carbon paste electrode spiked with ferrocene carboxylic acid and its application to the electrocatalytic determination of ascorbic acid. *J. Electroanal. Chem*. **2001**, *515*, 45-51, DOI: 10.1016/S0022-0728(01)00642-8.

[42] Zen, J. M.; Tsai, D. M.; Kumar, A. S.; Dharuman, V., Amperometric determination of ascorbic acid at a ferricyanide-doped Tosflex-modified electrode. *Electrochem. Commun*. **2000**, *2*, 782-785, DOI: 10.1016/S1388-2481(00)00121-1.

[43] Kalimuthu, P.; Jone, S. A., Selective determination of 3,4-dihydroxyphenylacetic acid in the presence of ascorbic and uric acids using polymer film modified electrode. *J. Chem. Sci*. **2011**, *123*, 349-355, DOI:

10.1007/s12039-011-0086-3.

[44] Manoj, D.; Satheesh, D., Reactive template method for the synthesis of Pd nanoparticles supported PoPd hollow spheres for electrochemical oxidation of ascorbic acid. *Trans. Indian Inst. Met.* **2011**, *64*, 195-198, DOI: 10.1007/s12666-011-0038-0.

[45] Ragupathy, D.; Park, J.J.; Lee, S. C.; Kim, J. C.; Gomathi, P., Electrochemical grafting of poly (2,5-dimethoxy aniline) onto multiwalled carbon nanotubes nanocomposite modified electrode and electrocatalytic oxidation of ascorbic acid. *Macromol. Res.* **2011**, *19*, 764-769, DOI: 10.1007/s13233-011-0802-3.

[46] Roy, P. R.; Okajima, T.; Ohsaka, T., Simultaneous electrochemical detection of uric acid and ascorbic acid at a poly (N,N-dimethylaniline) film-coated GC electrode. *J. Electroanal. Chem.* **2004**, *561*, 75-82, DOI: 10.1016/j.jelechem.2003.07.003

[47] Lin, L.; Chen, J. H.; Yao, H., Chen, Y. Z.; Zheng, Y. J.; Lin, X. H., Simultaneous determination of dopamine, ascorbic acid and uric acid at poly (evans blue) modified glassy carbon electrode. *Bioelectrochem.* **2008**, *73*, 11-17, DOI: 10.1016/ j.bioelechem.2008.01.009.

[48] Zhao, Y.; Gao, Y.; Zhan, D.; Liu, H.; Zhao, Q.; Kou, Y.; Zhu, Z., Selective detection of dopamine in the presence of ascorbic acid and uric acid by a carbon nanotubes-ionic liquid gel modified electrode. *Talanta,* **2005**, *66*, 51-57, DOI: 10.1016/ j.talanta.2004.09.019.

[49] Chen, Y.; Chen, X.; Lin, Z.; Dai, H.; Qiu, B.; Sun, J.; Chen, G., An electrically heated ionic-liquid/multi-wall carbon nanotube composite electrode and its application to electrochemiluminescent detection of ascorbic acid. *Electrochem. Commun*. **2009**, *11*, 1142-1145, DOI: 10.1016/j.elecom.2009.03.033.

[50] Hu, C. G.; Wang, W. L.; Feng, B.; Wang, H., Simultaneous measurement of dopamine and ascorbic acid at CNT electrode. *Inter. J. Mod. Phys. B,* **2005**, *19*, 607-610, DOI: 10.1142/S0217979205029146.

[51] Ijeri, V. S.; Jaiswal, P. V.; Srivastava, A. K., Chemically modified electrodes based on macrocyclic compounds for determination of Vitamin C by electrocatalytic oxidation. *Anal. Chim. Acta*. **2001**,

439, 291-297, DOI: 10.1016/S0003-2670(01)00989-8.

[52] Agboola, B. O.; Vilakazi, S. L.; Ozoemena, K. I., Electrochemistry at cobalt(II) tetrasulfophthalo-cyanine-multi-walled carbon nanotubes modified glassy carbon electrode: a sensing platform for efficient suppression of ascorbic acid in the presence of epinephrine. *J. Solid State Electrochem.* **2009**, *13*, 1367-1379, DOI: 10.1007/s10008-008-0691-3.

[53] Noctor, G.; Foyer, C. H., Ascorbate and glutathione: keeping active oxygen under control. *Rev. Plant Physiol. Plant Molec. Biol.* **1998**, *49*, 249-279, DOI: 10.1146/annurev.arplant.49.1.249.

[54] Wang, Y.; Xu, H.; Zhang, J.; Li, G., Electrochemical sensors for clinic analysis. *Sensors,* **2008**, *8*, 2043-2081, DOI: 10.3390/s8042043.

[55] Yogeswaran, U.; Chen, S. M., A review on the electrochemical sensors and biosensors composed of nanowires as sensing material. *Sensors,* **2008**, *8*, 290-313, DOI: 10.3390/s8010290.

[56] Behrens, W. A.; Madère, R., A highly sensitive high-performance liquid chromatography method for the estimation of ascorbic and dehydroascorbic acid in tissues, biological fluids and foods. *Anal. Biochem.* **1987**, *165*, 102-107, DOI: 10.1016/0003-2697(87)90206-5.

[57] Shakya, R.; Navarre, D. A., Rapid screening of ascorbic acid, glycoalkaloids, and phenolics in potato using high-performance liquid chromatography. *J. Agric. Food Chem.* **2006**, *54*, 5253-5260, DOI: 10.1021/jf0605300.

[58] Meléndez-Martínez, A. J.; Vicario, I. M.; Heredia, F. J., Provitamin A carotenoids and ascorbic acid contents of the different types of orange juices marketed in Spain. *Food Chem.* **2007**, *101*, 177-184, DOI: 10.1016/j.foodchem.2006.01.023.

[59] Wang, J.; Chatrathi, M. P.; Tian, B.; Polsky, R., Microfabricated electrophoresis chips for simultaneous bioassays of glucose, uric acid, ascorbic acid, and acetaminophen. *Anal. Chem.* **2000**, *72*, 2514-2518, DOI: 10.1021/ac991489l.

[60] Davey, M. W.; Bauw, G.; Van Montagu, M., Simultaneous high-performance capillary electrophoresis analysis of the reduced and oxidised

forms of ascorbate and glutathione. *J. Chromatogr. B.* **1997**, *697*, 269-276, DOI: 10.1016/S0378-4347(96)00536-1.

[61] Klejdus, B.; Petrlová, J.; Potěšil, D.; Adam, V.; Mikelová, R.; Vacek, J.; Kubáň, V., Simultaneous determination of water-and fat-soluble vitamins in pharmaceutical preparations by high-performance liquid chromatography coupled with diode array detection. *Anal. Chim. Acta.* **2004**, *520*, 57-67, DOI: 10.1016/j.aca.2004.02.027.

[62] Wu, T.; Guan, Y.; Ye, J., Determination of flavonoids and ascorbic acid in grapefruit peel and juice by capillary electrophoresis with electrochemical detection. *Food Chem.* **2007**, *100*, 1573-1579, DOI: 10.1016/j.foodchem.2005.12.042.

[63] Hansen, P. D., Usedom, A. V., New biosensors for environmental analysis. In Frontiers in Biosensorics II. *Birkhäuser Basel,* **1997**, *4*, 109-120. DOI: org/10.1007/978-3-0348-9045-8_8.

[64] Lamari, A. S.; El Fattouh, A., Electrochemical detection of ascorbic acid using a polymer modified carbon paste electrode. *Acta Tech. Corv. Bull. Engin.* **2013**, *6*, 39-42. DOI: 10.20964/2018.01.41.

[65] Kumar, S. A.; Cheng, H. W.; Chen, S. M., Electroanalysis of ascorbic acid (vitamin C) using nano-ZnO/poly (luminol) hybrid film modified electrode. *React. Funct. Polym.* **2009**, *69*, 364-370, DOI: 10.1016/j.reactfunctpolym.2009.03.001.

[66] Lin, K. C.; Yeh, P. C.; Chen, S. M., Electrochemical determination of ascorbic acid using poly (xanthurenic acid) and multi-walled carbon nanotubes. *Int. J. Electrochem. Sci.* **2012**, *7*, 12752-12763. DOI: 10.20964 / 2020.01.49.

[67] Bartolome, J. P.; Fragoso, A., Electrochemical detection of nitrite and ascorbic acid at glassy carbon electrodes modified with carbon nano-onions bearing electroactive moieties. *Inorganica Chimica Acta,* **2008**, *468*, 223-231, DOI: 10.1016/j.ica.2017.06.024.

[68] Raoof, J. B.; Ojani, R.; Kiani, A., Carbon paste electrode spiked with ferrocene carboxylic acid and its application to the electrocatalytic determination of ascorbic acid. *J. Electro. Chem.* **2001**, *515*, 45-51, DOI: 10.1016/S0022-0728(01)00642-8.

[69] Chenthattil, R.; Jamballi, G. M.; Girish, T., Low-cost

voltammetric sensor based on an anionic surfactant modified carbon nanocomposite material for the rapid determination of curcumin in natural food supplement. *J. Inst. Sci. Tech.* **2020**, *5*, 561-582. DOI: 10.1080/10739149.2020.1756317.

[70] Hadi, B.; Hassan, K. M.; Iran, S., Simultaneous voltammetric determination of ascorbic acid and uric acid using a modified multiwalled carbon nanotube paste electrode. *Caspian. J. Chem.* **2012**, *1*, 17-29. DOI: 10.1002/elan.200703974.

[71] Raoof, J. B.; Ojani, R.; Beitollahi, H.; Hossienzadeh, R., Electrocatalytic determination of ascorbic acid at the surface of 2,7-bis(ferrocenyl ethyl)fluoren-9-one modified carbon paste electrode. *Electroanalysis.* **2006**, *18*, 1193-1201. DOI: 10.1002/elan.200503516.

[72] Beitollahi, H.; Mazloum Ardakani, M.; Naeimi, H.; Ganjipour, B., Electrochemical characterization of 2,2′-[1,2-ethanediylbis (nitriloethylidyne)]-bis-hydroquinone-carbon nanotube paste electrode and its application to simultaneous voltammetric determination of ascorbic acid and uric acid. *J. Solid State Electrochem.* **2009**, *13*, 353-363. DOI: 10.1007/s10008-008-0553-z.

[73] Kamyabi, M. A.; Asgari, Z.; Monfared, H. H.; Morsali, A., Electrocatalytic oxidation of ascorbic acid and simultaneous determination of ascorbic acid and dopamine at a bis(4′-(4-pyridyl)-2,2′:6′,2″-terpyridine) iron(II) thiocyanate carbon past modified electrode. *J. Electroanal. Chem.* **2009**, *632*, 170-176. DOI: 10.1016/j.jelechem.2009.04.015.

[74] Malinauskas, A.; Garjonyt, R.; Mažeikien, R.; Jurevičiūt, I., Electrochemical response of ascorbic acid at conducting and electrogenerated polymer modified electrodes for electroanalytical applications: a review. *Talanta,* **2004**, *64*, 121-192, DOI: 10.1016/j.talanta.2004.02.010.

[75] Li, Y.; Lin, X., Simultaneous electroanalysis of dopamine, ascorbic acid and uric acid by poly (vinyl alcohol) covalently modified glassy carbon electrode. *Sensors Actua. B Chem.* **2006**, *115*, 134-139, DOI: 10.1016/j.snb.2005.08.022.

[76] Antoniadou, S.; Jannakoudakis, A. D.; Theodoridou, E., Electrocatalytic reactions on carbon fibre electrodes modified by hemine II. Electro-oxidation of hydrazine. *Synth. Met.* **1989**, *30*, 295-304, DOI: 10.1016/0379-6779(89)90652-8.