



Electrochemical determination of mangiferin using glassy carbon electrodes modified with carbonaceous nanomaterials

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ABSTRACT

The mangiferin molecule (MG) is a *c*-glucosyl xanthone present in the mango tree. Its structure contains polyphenolic groups which are responsible for its antioxidant properties. These properties make this natural molecule, an attractive additive for pharmaceutical products and functional food. In this work, we report on an investigation of the electrochemical behavior of mangiferin upon bare and carbonaceous nanomaterials-modified glassy carbon electrodes (GCEs). The electrodes modification was made with graphene oxide (GO), multi-walled carbon nanotubes (MWCNT) or single-walled carbon nanotubes (SWCNT) suspended in water or in Nafion® ion exchanger. The data obtained show that the mangiferin's oxidation process is governed by a mixed mechanism of diffusion and adsorption. By implementing the electrodes modification, it was determined that, not only the sensitivity increases in the oxidation signal of MG, but also the adsorption of the oxidized product is lower, allowing the execution of several successive measurements without the need to polish the electrode. Calibration curves were performed for all three systems (GCE-GO, GCE-MWCNT, and GCE-SWCNT); the obtained correlation coefficients were higher than 0.9940 with detection limits of 0.063 μM, 0.189 μM, and 0.476 μM respectively. These results make the developed material a viable option for direct determination of mangiferin.

1. Introduction

Because of the known role of free radicals in diverse diseases, like cancer, diabetes, Parkinson and Alzheimer [1], antioxidant activity benefits from functional food receive great attention. Antioxidants counteract the action of radicals by reacting with them before they reach biological targets [2].

Vitamins, carotenoids, minerals, and polyphenols are the main components responsible for the antioxidant activity, and are present in fruits and vegetables like mango, apple, orange, broccoli and carrot [1,3–5]. In particular, mango trees (*Mangifera indica* L.) have been reported to contain large amounts of polyphenols in leaves, peel, stem, bark, and fruit [6–9]. For the mango fruit, approximately 70%–80% of the total mass is pulp, 10%–12% is seed and between 8%–15% is peel, depending on the particular species considered [11]. Regarding its physicochemical properties, the seed and the shell have carbohydrate percentages of 34%, as well as 5%–7% of proteins [12,13] and phenolic

compounds of around 90 mg/g–200 mg/g [14,15].

According to a study by Mejía et al. [12], a mass percentage fraction of 50%–55% of the constituent material of the fruit is wasted in the pulping of the mango at industrial level. This waste is composed mostly of shell, seed, pulp and fiber remains. For Colombia's 2014 production alone, it represents 135,216 of the total 270,432 tons produced. Mango residue materials have high contents of ascorbic acid and polyphenolic compounds in the seed and the shell which confer antioxidant activity [10,14–17] and therefore can be used in the food industry.

The mangiferin molecule (Fig. 1A) is a glycosylated xanthone present predominantly in leaves, bark, and the root of *Mangifera indica* L. and has been the subject of studies associated with cognitive deficit [18], antioxidant and anti-inflammatory activity [19], immunotherapeutic effects [20], cytoprotective activity [21,22], anti-tumor agent, and hepatoprotective effect [23], among others.

Because of the increasing importance of MG, it is necessary to develop methodologies that grant its determination in an easy, fast,

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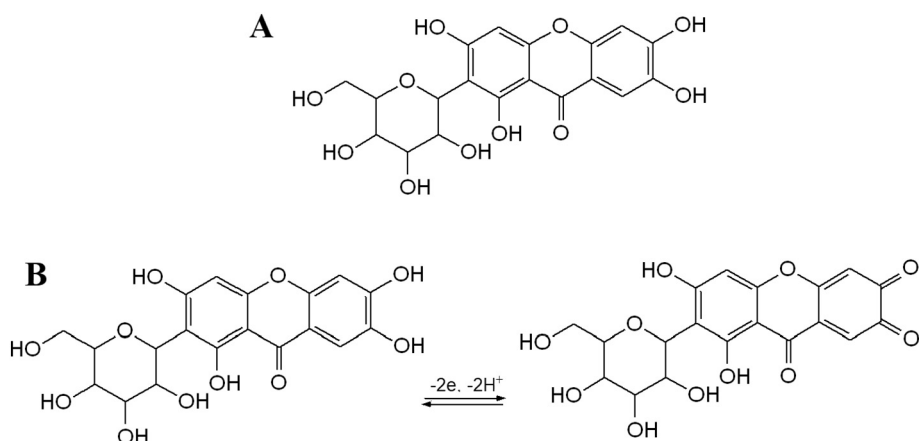


Fig. 1. A) Chemical structure of mangiferin, B) electrochemical oxidation of mangiferin.

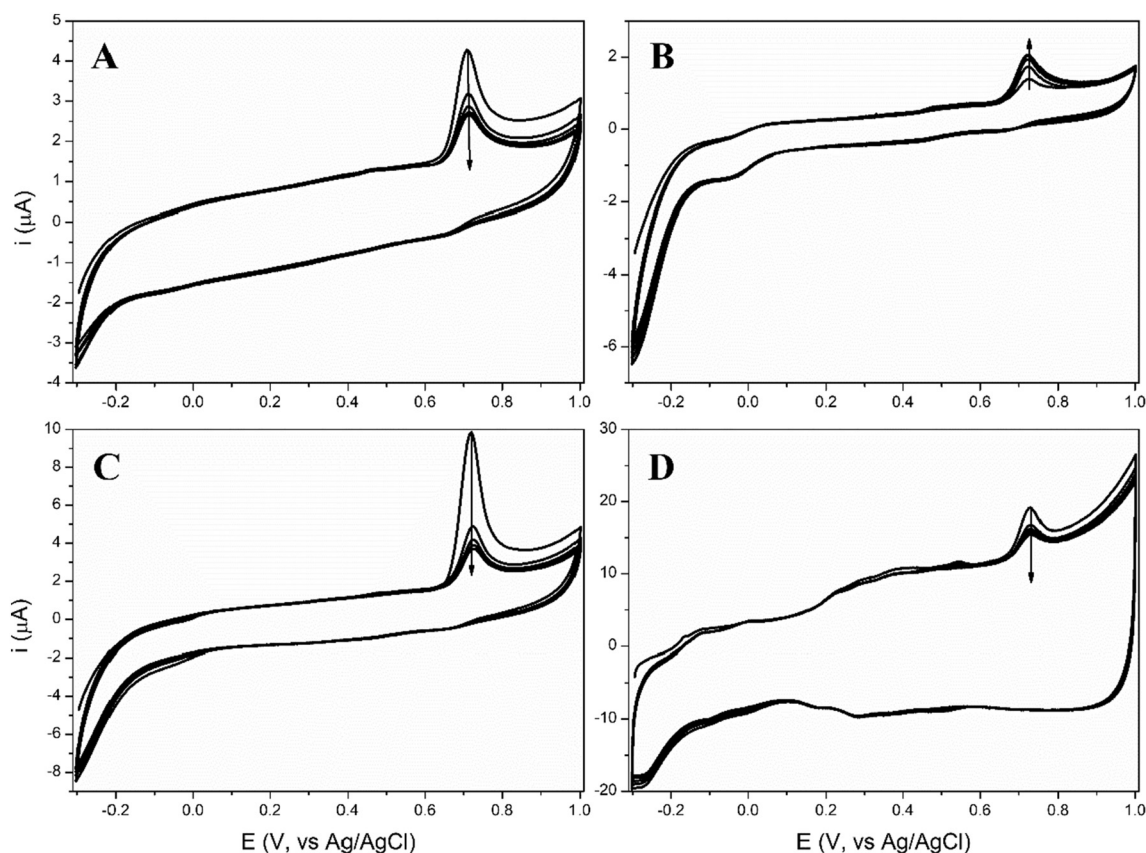


Fig. 2. Successive cyclic voltammetry for mangiferin detection by GCE electrodes modified with nanocarbon materials suspended in H_2O . A) Bare GCE, B) GCE-GO, C) GCE-MWCNT, D) GCE-SWCNT at $v = 50 \text{ mV}\cdot\text{s}^{-1}$, $HClO_4$ 0.1 M as supporting electrolyte.

sensitive, and cheap way. The determination of molecules that present antioxidant activity is usually carried out by spectrophotometric techniques that use radical scavenging molecules [3,24]. Nevertheless, the electrochemical approach could offer a faster, cleaner, more sensitive and economical alternative for the detection of this kind of molecules [25].

Electrochemical techniques have impacted the field of pharmaceutical, biological and food analysis because of their simplicity, reasonable accuracy and precision, in addition to their low cost, high sensitivity, selectivity, and rapidity. Furthermore, electrochemical techniques have allowed the simultaneous detection and quantification of substances such as uric acid, folic acid, ascorbic acid, epinephrine, norepinephrine, acetaminophen, tryptophan, and many other

pharmaceutically relevant molecules, allowing significant recovery percentages for these metabolites in real samples, and facilitating the analysis of samples [27–33].

Studies about antioxidant activity of complex MG-Fe using cyclic voltammetry (CV) with GCEs have been reported [21,22]. However, there is little information regarding the use of electrochemical techniques for quantification purposes of this particular polyphenol. The main difficulty reported for this kind of sensors is the adsorption of the oxidation products of polyphenols at the electrode surface [21,22,26], which leads to a progressive electrode passivation.

The use of electrodes modified with ion exchange resins and carbonaceous materials, has allowed the development of sensors that are specific and selective to different types of target molecules, such as

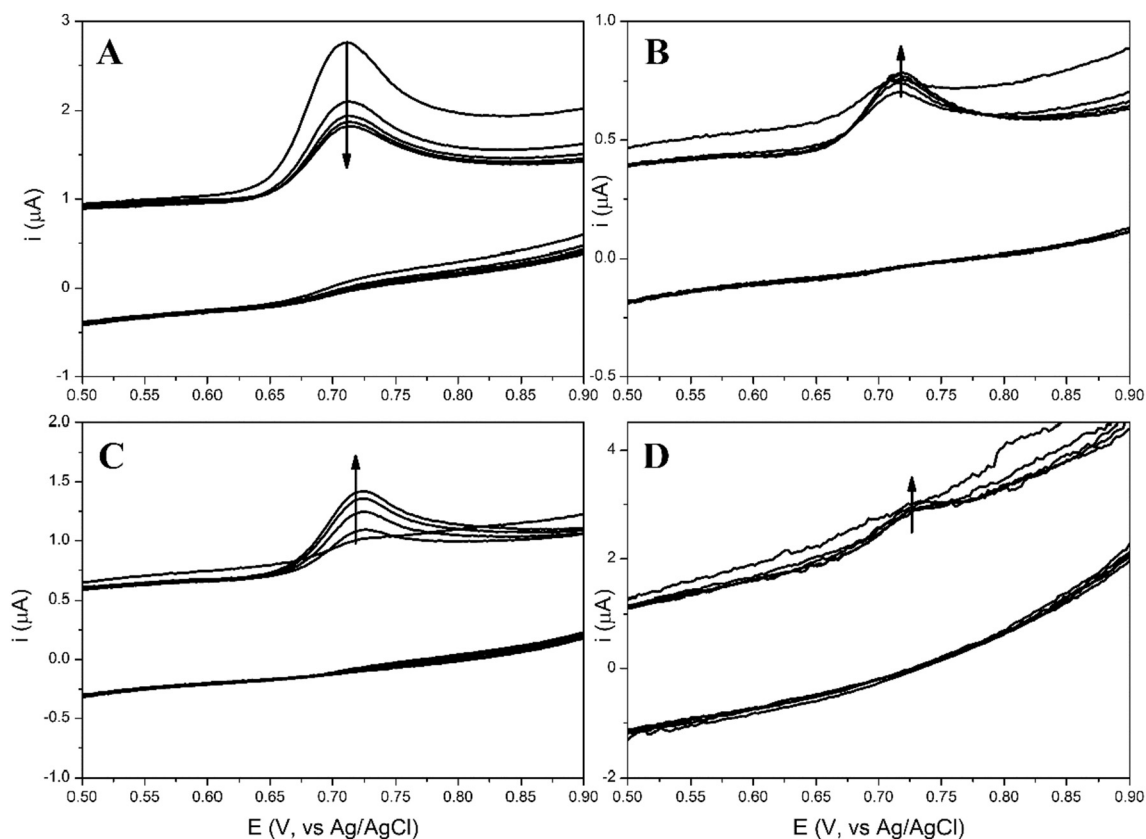


Fig. 3. Successive cyclic voltammetry for mangiferin detection by GCE electrodes modified with nanocarbon materials in a Nafion matrix. A) GCE, B) GCE-GO/Naf, C) GCE-MWCNT/Naf, D) GCE-SWCNT/Naf at $v = 50 \text{ mV}\cdot\text{s}^{-1}$, HClO_4 0.1 M as supporting electrolyte.

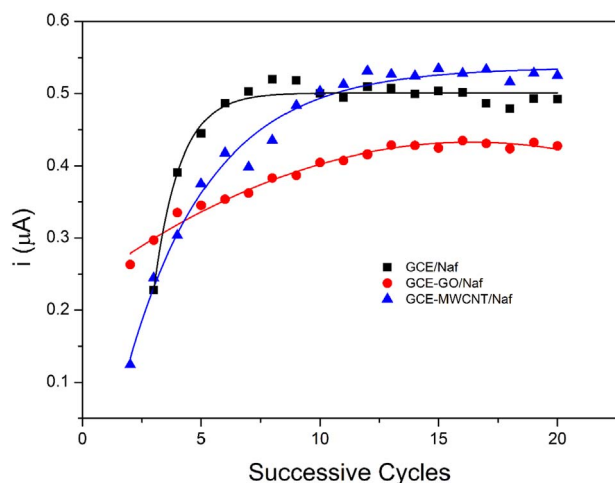


Fig. 4. Successive measurement effects in mangiferin oxidation current by GCE-nanocarbon/Nafion modified electrodes using CV ($v = 50 \text{ mV}\cdot\text{s}^{-1}$). HClO_4 0.1 M was used as supporting electrolyte for all the experiments. Results for the system GCE-SWCNT/Naf not shown due to the high interference of capacitive current.

caffeine, dopamine, morphine, ondansetron, urea, and *Escherichia coli* [34–39]. Electrodes modified with Nafion–CNT eliminate interfering signals and possess enhanced storage time and performance; they also present an improvement in surface area with high selectivity to charged molecules [36,38].

In order to find the best composite to electrochemically quantify MG at low concentrations, we compare various glassy carbon electrodes modified with different carbonaceous nanomaterials (GO, MWCNT, or SWCNT) suspended in water or in an ion exchange resin.

2. Experimental method

2.1. Materials

MG was purchased from Indofine Chemicals and MWCNT from Smart Materials. GO, Nafion® and SWCNT were provided by Sigma-Aldrich. Sodium hydroxide, ethanol, and perchloric acid were purchased from Merck and were analytical grade.

2.2. Equipment

The electrochemical experiments were carried out using an Autolab PGSTAT 101 potentiostat controlled by Nova 1.11 software (Metrohm, The Netherlands). A conventional three-electrode configuration cell was used, which includes a GCE as the working electrode, an $\text{Ag}|\text{AgCl}|\text{KCl}_{\text{sat}}$ as a reference electrode, and a Pt wire as counter electrode.

2.3. Electrode modification

The GCEs were mechanically polished for 1 min using alumina powder (Buehler, $0.05 \mu\text{m}$) and then rinsed with abundant deionized water to eliminate any alumina residue. The GCEs were next polished with diamond paste (Buehler, $0.25 \mu\text{m}$) for 1 min. The electrodes were then rinsed with deionized water and sonicated for 10 s at low frequencies. This procedure was done for each experiment before the electrode modification. Finally, the electrodes were subjected to an electrochemical activation process by chronoamperometry at 1.2 V (vs Ag/AgCl) for 300 s in NaOH 0.1 M [40].

The carbonaceous nanomaterials (GO, MWCNT, SWCNT) were suspended as received, in deionized water or Nafion® solutions. The final concentration of the GO, MWCNT or SWCNT dispersions was

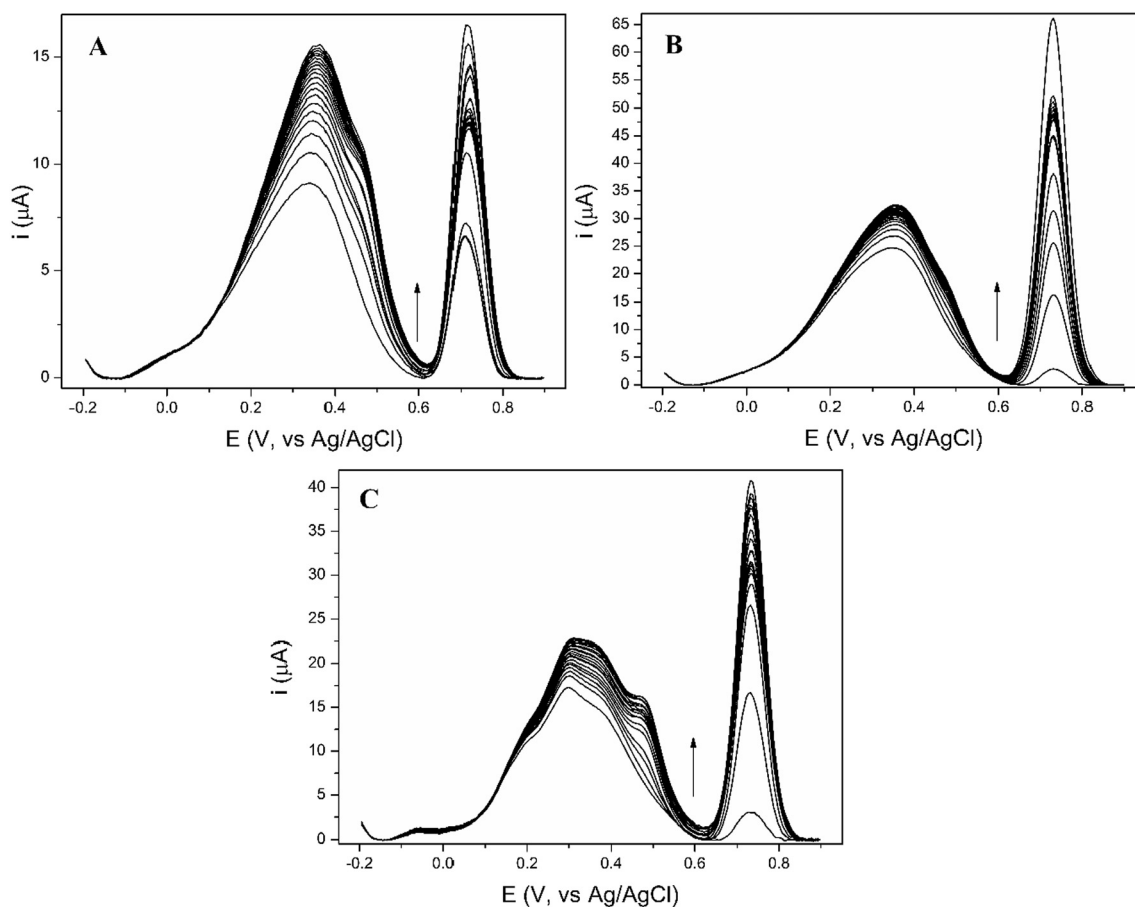


Fig. 5. Square wave voltammetry responses of CGE-nanocarbon/Nafion modified electrodes in a 5×10^{-5} mol/L mangiferin solution after successive measurements. A) GCE-GO/Naf, B) GCE-MWCNT/Naf, C) GCE-SWCNT/Naf. At conditions $f = 80$ Hz, $\Delta E_{sw} = 35$ mV, $\Delta E_s = 5$ mV, HClO_4 0.1 M as supporting electrolyte.

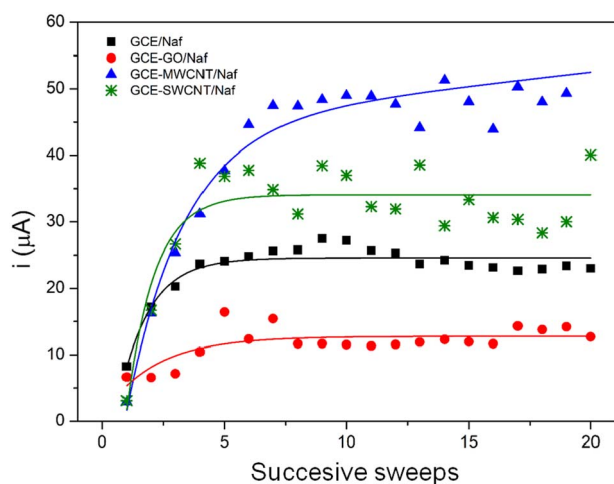


Fig. 6. Successive measurement effects in mangiferin oxidation current by CGE-nanocarbon/Nafion modified electrodes in SWV experiments ($f = 80$ Hz, $\Delta E_{sw} = 35$ mV, $\Delta E_s = 5$). HClO_4 0.1 M was used as supporting electrolyte for all the experiments.

1 mg/mL. The mixtures were vortexed for 30 s and then sonicated for 10 min more. The immobilization of the materials was made by adding a 5 μL drop of the suspension on the electrode surface that was previously activated. The solvent was evaporated during 1 h at room temperature and the modified GCE was activated by immersing it in 0.1 M HClO_4 , and applying a cathodic swipe between -0.3 V and 1.0 V at $50 \text{ mV}\cdot\text{s}^{-1}$ by CV.

2.4. Electrochemical procedures

Electrochemical measurements were carried out using CV and square wave voltammetry (SWV) techniques. The CV experiments were made using HClO_4 0.1 M as the supporting electrolyte. The cyclic voltammograms were performed scanning the potential from -0.3 V to 1.0 V (vs Ag/AgCl) at an optimized scan rate of $50 \text{ mV}\cdot\text{s}^{-1}$. In the SWV experiments, the stripping process was made prior to the scanning, using -0.2 V (vs Ag/AgCl) as stripping potential and 80 s as stripping time (frequency $f = 80$ Hz, the amplitude of square wave $\Delta E_{sw} = 35$ mV, and step potential $\Delta E_s = 5$ mV).

3. Results and discussion

3.1. MG detection over GCEs modified with carbonaceous nanomaterials

Fig. 2 shows the successive cyclic voltammograms for MG detection using unmodified and modified glassy carbon electrodes with GO, MWCNT, and SWCNT suspended in water. It can be observed from the Figure that the electrodes modified with both SWCNT and MWCNT present, after the first voltammetric cycle, current values at 710 mV that are higher than that of the unmodified electrode. This is attributed to the oxidation of the catechol group present in the MG structure (Fig. 1B). Both, the unmodified GC electrode and the electrodes modified with nanotubes present a decrease in current values after successive sweeps. This behavior has been previously observed during the analysis of various polyphenols, including MG, and it is explained by the formation of a non-electroactive polymeric film through an electrochemical-chemical coupled mechanism [41,42].

Distinctive behavior in the cyclic voltammograms of the GCE

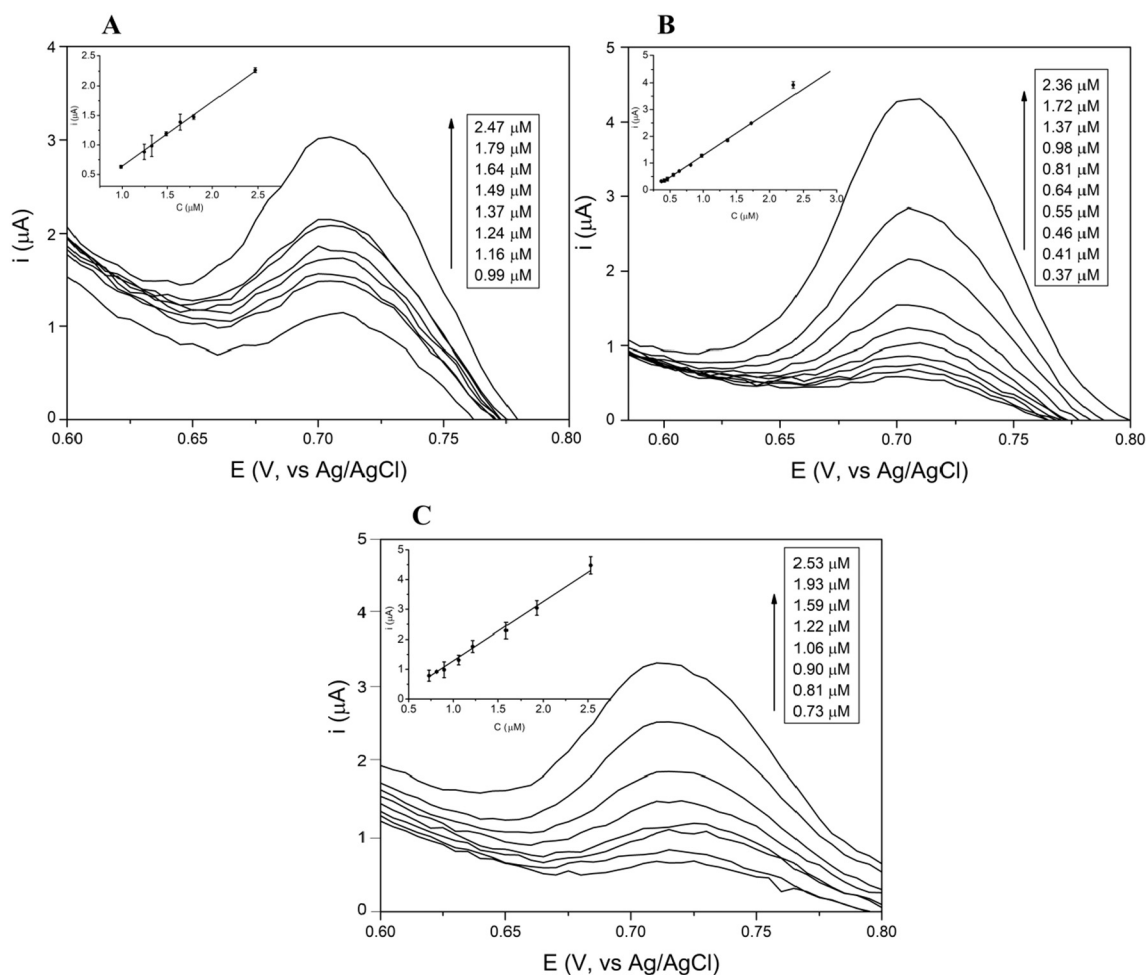


Fig. 7. Amperometric responses of nanocarbon/Nafion modified electrodes after successive additions of mangiferin as obtained by SWSV. A) GCE-GO/Naf, B) GCE-MWCNT/Naf, C) GCE-SWCNT/Naf. At conditions $f = 80$ Hz, $\Delta E_{sw} = 35$ mV, $\Delta E_s = 5$ mV, HClO_4 0.1 M as supporting electrolyte. Inset figures: each point is the average of three replicated measurements.

Table 1

Summary of calibration parameters obtained for mangiferin detection by GCE-nanocarbon/Nafion sensors.

Electrode configuration	Limit of detection (M)	Limit of quantification (M)	Regression equation	R^2
GCE-GO/Naf	6.3×10^{-8}	2.1×10^{-7}	$i = 1.0946C_{MG} - 0.4512$	0.9987
GCE-MWCNT/Naf	1.9×10^{-7}	6.3×10^{-7}	$i = 1.6470C_{MG} - 0.3495$	0.9965
GCE-SWCNT/Naf	4.8×10^{-7}	1.6×10^{-6}	$i = 1.9717C_{MG} - 0.6859$	0.9942

i : observed current, C_{MG} : concentration of MG.

modified with GO was also observed; initially the current increases, but after 5 or 6 successive cycles, it decreases progressively. Such a behavior may be due to the fact that the surface groups present in the GO structure are reduced partially until an equilibrium is reached [43–45]. It is possible that the oxidation reaction of the MG, and the modification of the GO surface groups occur simultaneously during cycling. Compared to the other systems, for the SWCNT, a larger capacitive current is observed. This may be due to the presence of a single layer of folded graphene, forming a nanotube-like structure, which has greater resistance to charge transfer than other materials that are composed of several layers [46–48].

Even if the redox signals for mangiferin oxidation were detected using all the presented electrode configurations, we have shown that the signal decreases after successive voltammetry cycles. Further modifications were thus developed in order to avoid that problem and also to give repeatability to the measurements realized using the same electrode. The results are shown below.

In order to give stability to the sensor and to avoid the influence of

negatively charged interferences in real samples, we implement Nafion® as a part of the composite. This polymer is considered a proton conductor for membrane applications because of its excellent thermal and mechanical stability [37]. Fig. 3 shows the successive cyclic voltammograms for the detection of MG using modified GCEs with carbonaceous nanomaterials in a matrix of Nafion®. An increase in the current at 710 mV is observed as successive sweeps are carried out. The rise in the electrochemical signal can be due to three leading factors: i) the increase of the electroactive area after the modification, ii) the resin used is cationic exchange and the oxidation process of the catechol group involves the transfer of 2 electrons and 2 protons [42], and iii) a possible tunnel effect increases the connectivity at the electrode surface [38].

Fig. 4 shows the current values that correspond to the MG oxidation signal in successive cycles for the cyclic voltammograms presented in Fig. 3. In these experiments, the GCE-SWCNT/Naf system presented a high capacitive current that overlaps the signal associated with MG oxidation; therefore, the corresponding current values are not

indicated. It is observed that for the first successive cycles, the current increases but eventually reaches a steady value. The determination of the number of cycles needed to reach a steady value in the current is very important when the quantification of MG is intended.

CV is widely used for systems characterization but not so much for quantification purposes, while the SWV technique, which implements the pulse to avoid the interference associated with the capacitive current, provides greater sensitivity, since the obtained current is higher than that in the CV technique [25,49,50]. For this reason, we use the SWV for quantification of our analyte.

3.2. MG determination by means of SWV

In order to evaluate the stability and efficiency of each composite electrode system, the SWV technique was used. Using a 5×10^{-5} M MG solution, 20 successive sweeps were performed for each modified electrode. Fig. 5 shows the obtained voltammograms. Increases in the current at 710 mV are observed as the sweeps increase until it reaches a constant value. This signal is attributed to the MG oxidation. The signal centered at 300 mV corresponds to the presence of oxygenated groups, such as quinones and hydroquinones, in carbonaceous nanomaterials [51].

Fig. 6 shows the current values observed for the MG oxidation signal in successive sweeps using the SWV technique, for systems modified with carbonaceous nanomaterials suspended in the Nafion® resin. As expected, when these results are compared with the corresponding ones obtained by the CV experiments (Fig. 4); the current values are significantly higher in magnitude when using SWV due to the theoretical basis of both electrochemical techniques. As in CV experiments, it is observed that during the first successive sweeps, the current increases, eventually reaching a steady value. It has been reported that electrodes containing carbon nanotubes (CNT) dispersed in Nafion® present an improvement in peak currents compared to bare electrodes, possibly due to a phenomenon of tunneling effect of CNT and/or a conduction model based on electrons passing, one by one, between two neighboring CNT [38]. Regarding the non-adsorptive behavior of the system in presence of Nafion®, Hoyer et al. report that this resin offers minimal obstruction to the diffusion of the analyte to the electrode surface, and at the same time, prevents the adsorption processes of organic compounds [52].

Fig. 7 shows the voltamperometric responses of the GCEs modified with carbonaceous nanomaterials suspended in Nafion® (GO, MWCNT, SWCNT) obtained through SWV. The signals correspond to MG oxidation as a result of the analyte concentration. For all the systems under evaluation, a line was fitted to the experimental points applying the minimum square technique (inset figures).

The calibration parameters obtained using the modified-GCE are grouped in Table 1. Limits of detection (LOD) and limits of quantification (LOQ) were calculated using the equations: $LOD = (3SD_B/m_{cc})$ and $LOQ = (10SD_B/m_{cc})$ respectively; where SD_B is the standard deviation of the blank, and m_{cc} is the slope of the linear calibration curve obtained for both equations [53]. A good linear response, and very good LOD and LOQ were achieved, suggesting that all 3 systems are appropriate for their application in the electrochemical quantification of MG under the studied conditions.

The obtained detection limits are comparable and, in the case of the sensor composed of GCE-GO/Naf, better than those reported in recent work using fluorescence (L.O.D. = 2.1×10^{-7} M) [54], or voltammetric techniques (L.O.D. = 3.9×10^{-7} M and L.O.D. = 2.0×10^{-8} M) [55,33]. In addition, the stability of oxidation currents through time was analyzed, observing not significant variations during the first 6 h after sensor preparation.

4. Conclusions

GCEs were successfully modified using Nafion®-suspended

carbonaceous nanomaterials to determine MG through electrochemical techniques. The composite Nafion/carbonaceous nanomaterials improved the diffusion of the analyte to the electrode surface and avoided the adsorption of the MG oxidation product, which would lead to the passivation of the electrode. In addition, the Nafion® gave mechanical stability to the composite, allowing the analysis of several samples without the necessity of further treatment. The obtained results suggest the suitability of the studied GCE/carbonaceous nanomaterials/Nafion as a fast, simple, and practical analytical method for MG determination. The GCE/GO/Nafion configuration seems to be the optimum option for MG quantification because it gives the best straight line correlation and the lowest limit of detection (63 nM).

Conflict of interest

The authors declare no conflicts of interest.

Acknowledgments

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References

- [1] D.V. Ratnam, D.D. Ankola, V. Bhardwaj, D.K. Sahana, M.N.V.R. Kumar, Role of antioxidants in prophylaxis and therapy: a pharmaceutical perspective, *J. Control. Release* 113 (2006) 189–207, <http://dx.doi.org/10.1016/j.jconrel.2006.04.015>.
- [2] R.L. Prior, G. Cao, In vivo total antioxidant capacity: comparison of different analytical methods 1, *Free Radic. Biol. Med.* 27 (1999) 1173–1181.
- [3] M. Oroian, I. Escriche, Antioxidants: characterization, natural sources, extraction and analysis, *Food Res. Int.* 74 (2015) 10–36, <http://dx.doi.org/10.1016/j.foodres.2015.04.018>.
- [4] C.A. Rice-Evans, N.J. Miller, G. Paganga, Structure-antioxidant activity relationships of flavonoids and phenolic acids, *Free Radic. Biol. Med.* 20 (1996) 933–956, [http://dx.doi.org/10.1016/0891-5849\(95\)02227-9](http://dx.doi.org/10.1016/0891-5849(95)02227-9).
- [5] C. André, I. Castanheira, J.M. Cruz, P. Paseiro, a. Sanches-Silva, Analytical strategies to evaluate antioxidants in food: a review, *Trends Food Sci. Technol.* 21 (2010) 229–246, <http://dx.doi.org/10.1016/j.tifs.2009.12.003>.
- [6] S.M.R. Ribeiro, A. Schieber, Bioactive Compounds in Mango (*Mangifera indica* L.), (2010), <http://dx.doi.org/10.1016/B978-0-12-374628-3.00034-7>.
- [7] C.M. Ajila, K.a. Naidu, S.G. Bhat, U.J.S.P. Rao, Bioactive compounds and antioxidant potential of mango peel extract, *Food Chem.* 105 (2007) 982–988, <http://dx.doi.org/10.1016/j.foodchem.2007.04.052>.
- [8] C.M. Ajila, U.J.S. Prasada Rao, Mango peel dietary fibre: composition and associated bound phenolics, *J. Funct. Foods* 5 (2013) 444–450, <http://dx.doi.org/10.1016/j.jff.2012.11.017>.
- [9] A. Asif, U. Farooq, K. Akram, Z. Hayat, A. Shafi, F. Sarfaraz, et al., Therapeutic potentials of bioactive compounds from mango fruit wastes, *Trends Food Sci. Technol.* 53 (2016) 102–112, <http://dx.doi.org/10.1016/j.tifs.2016.05.004>.
- [10] M. Agronet, Producción nacional por producto - Mango (n.d.), http://www.agronet.gov.co/www/hm3b/ReportesAjax/parametros/reporte16_2011.aspx?cod=16, Accessed date: 25 August 2017.
- [11] M.S. Abourayya, N.E. Kassim, M.H. El-Sheikh, A.M. Rakha, Fruit physical and chemical characteristics at maturity stage of Tommy Atkins, Keitt and Kent mango cultivars grown under Nubirya conditions, *J. Am. Sci.* 7 (2008) 2005–2007.
- [12] L.F. Mejía Giraldo, H.A. Martínez Correa, J.E. Betancourt Gutiérrez, C.E. Castrillón Castaño, Usage of the common mango agroindustrial waste (*Mangifera indica* L.) in the distraction of fermentable sugars, *Ing. Cienc.* 3 (2007) 41–62 <http://search.ebscohost.com/login.aspx?direct=true&db=zhh&AN=32518410&lang=es&site=ehost-live>.
- [13] A.E.M. Abdalla, S.M. Darwish, E.H.E. Ayad, R.M. El-Hamahy, Egyptian mango by-product 1. Compositional quality of mango seed kernel, *Food Chem.* 103 (2007) 1134–1140.
- [14] H. Kim, J.Y. Moon, H. Kim, D.S. Lee, M. Cho, H.K. Choi, et al., Antioxidant and antiproliferative activities of mango (*Mangifera indica* L.) flesh and peel, *Food Chem.* 121 (2010) 429–436, <http://dx.doi.org/10.1016/j.foodchem.2009.12.060>.
- [15] M. Pitchaon, Antioxidant capacity of extracts and fractions from mango (*Mangifera indica* Linn.) seed kernels, *Int. Food Res. J.* 18 (2011) 523–528.
- [16] S.O. Jekayinfa, A.O. Adebayo, S.O. Afolayan, E. Daramola, On-farm energetics of mango production in Nigeria, *Renew. Energy* 51 (2013) 60–63, <http://dx.doi.org/>

- 10.1016/j.renene.2012.09.004.
- [17] L. Serna-Cock, E. García-Gonzales, C. Torres-León, Agro-industrial potential of the mango peel based on its nutritional and functional properties, *Food Rev. Int.* 9129 (2015) 1–13, <http://dx.doi.org/10.1080/87559129.2015.1094815>.
- [18] Y. Fu, H. Liu, C. Song, F. Zhang, Y. Liu, J. Wu, et al., Mangiferin regulates cognitive deficits and heme oxygenase-1 induced by lipopolysaccharide in mice, *Int. Immunopharmacol.* 29 (2015) 950–956, <http://dx.doi.org/10.1016/j.intimp.2015.10.035>.
- [19] C.G. Mohan, M. Deepak, G.L. Viswanatha, G. Savinay, V. Hanumantharaju, C.E. Rajendra, et al., Anti-oxidant and anti-inflammatory activity of leaf extracts and fractions of *Mangifera indica*, *Asian Pac J Trop Med* 6 (2013) 311–314, [http://dx.doi.org/10.1016/S1995-7645\(13\)60062-0](http://dx.doi.org/10.1016/S1995-7645(13)60062-0).
- [20] S. Muruganandan, J. Lal, P.K. Gupta, Immunotherapeutic effects of mangiferin mediated by the inhibition of oxidative stress to activated lymphocytes, neutrophils and macrophages, *Toxicology* 215 (2005) 57–68, <http://dx.doi.org/10.1016/j.tox.2005.06.008>.
- [21] G.L. Pardo-Andreu, C. Sánchez-Baldoquín, R. Ávila-González, E.T.S. Yamamoto, A. Revilla, S.A. Uyemura, et al., Interaction of Vimang (*Mangifera indica* L. extract) with Fe(III) improves its antioxidant and cytoprotecting activity, *Pharmacol. Res.* 54 (2006) 389–395, <http://dx.doi.org/10.1016/j.phrs.2006.08.001>.
- [22] G.L. Pardo-Andreu, C. Sánchez-Baldoquín, R. Avila-González, R. Delgado, Z. Naal, C. Curti, Fe(III) improves antioxidant and cytoprotecting activities of mangiferin, *Eur. J. Pharmacol.* 547 (2006) 31–36, <http://dx.doi.org/10.1016/j.ejphar.2006.07.040>.
- [23] M.M. Pinto, M.E. Sousa, M.S. Nascimento, Xanthone derivatives: new insights in biological activities, *Curr. Med. Chem.* 12 (2005) 2517–2538, <http://dx.doi.org/10.2174/092986705774370691>.
- [24] M.N. Alam, N.J. Bristi, M. Rafiqzaman, Review on in vivo and in vitro methods evaluation of antioxidant activity, *Saudi Pharm. J.* 21 (2013) 143–152, <http://dx.doi.org/10.1016/j.jsps.2012.05.002>.
- [25] J. Hoyos-Arbeláez, M. Vázquez, J. Contreras-Calderón, Electrochemical methods as a tool for determining the antioxidant capacity of food and beverages: a review, *Food Chem.* 221 (2017) 1371–1381, <http://dx.doi.org/10.1016/j.foodchem.2016.11.017>.
- [26] H. Nady, M.M. El-Rabie, G.M.A. El-Hafez, Electrochemical oxidation behavior of some hazardous phenolic compounds in acidic solution, *Egypt. J. Pet.* (2016), <http://dx.doi.org/10.1016/j.ejpe.2016.10.009>.
- [27] H. Beitollahi, A. Gholami, M.R. Ganjali, Preparation, characterization and electrochemical application of Ag-ZnO nanoplates for voltammetric determination of glutathione and tryptophan using modified carbon paste electrode, *Mater. Sci. Eng. C* 57 (2015) 107–112, <http://dx.doi.org/10.1016/j.msec.2015.07.034>.
- [28] M.R. Akhgar, H. Beitollahi, M. Salari, H. Karimi-Maleh, H. Zamani, Fabrication of a sensor for simultaneous determination of norepinephrine, acetaminophen and tryptophan using a modified carbon nanotube paste electrode, *Anal. Methods* 4 (2012) 259–264, <http://dx.doi.org/10.1039/C1AY05503H>.
- [29] S.E. Baghbamidi, H. Beitollahi, S.Z. Mohammadi, S. Tajik, S. Soltani-Nejad, V. Soltani-Nejad, Nanostructure-based electrochemical sensor for the voltammetric determination of benzerazide, uric acid, and folic acid, *Cuihua Xuebao/Chin. J. Catal.* 34 (2013) 1869–1875, [http://dx.doi.org/10.1016/S1872-2067\(12\)60655-X](http://dx.doi.org/10.1016/S1872-2067(12)60655-X).
- [30] Z. Taleat, M.M. Ardakani, H. Naeimi, H. Beitollahi, M. Nejati, H.R. Zare, Electrochemical behavior of ascorbic acid at a 2,2'-[3,6-dioxo-1,8-octanediybis (nitriloethylidene)]-bis-hydroquinone carbon paste electrode, *Anal. Sci.* 24 (2008) 1039–1044, <http://dx.doi.org/10.2116/analsci.24.1039>.
- [31] H. Beitollahi, S. Tajik, H. Parvan, H. Soltani, A. Akbari, M.H. Asadi, Nanostructured based electrochemical sensor for voltammetric determination of ascorbic acid in pharmaceutical and biological samples, *Anal. Bioanal. Electrochem.* 6 (2014) 54–66.
- [32] H. Beitollahi, H. Karimi-Maleh, H. Khabazzadeh, Nanomolar and selective determination of epinephrine in the presence of norepinephrine using carbon paste electrode modified with carbon nanotubes and novel 2-(4-oxo-3-phenyl-3,4-dihydro-quinazoliny)-N'-phenyl-hydrazinecarbothioamide, *Anal. Chem.* 80 (2008) 9848–9851, <http://dx.doi.org/10.1021/ac801854j>.
- [33] S. Tajik, M.A. Taher, H. Beitollahi, The first electrochemical sensor for determination of mangiferin based on an ionic liquid-graphene nanosheets paste electrode, *Ionics (Kiel)* 20 (2014) 1155–1161, <http://dx.doi.org/10.1007/s11581-013-1063-2>.
- [34] L.V. Tarditto, F.J. Arévalo, M.A. Zon, H.G. Ovando, N.R. Vettorazzi, H. Fernández, Electrochemical sensor for the determination of enterotoxigenic *Escherichia coli* in swine feces using glassy carbon electrodes modified with multi-walled carbon nanotubes, *Microchem. J.* 127 (2016) 220–225, <http://dx.doi.org/10.1016/j.microc.2016.03.011>.
- [35] D.P. Quan, D.P. Tuyen, T.D. Lam, P.T.N. Tram, N.H. Binh, P.H. Viet, Electrochemically selective determination of dopamine in the presence of ascorbic and uric acids on the surface of the modified Nafion/single wall carbon nanotube/poly(3-methylthiophene) glassy carbon electrodes, *Colloids Surf. B: Biointerfaces* 88 (2011) 764–770, <http://dx.doi.org/10.1016/j.colsurfb.2011.08.012>.
- [36] B. Nigović, M. Sadiković, M. Sertić, Multi-walled carbon nanotubes/Nafion composite film modified electrode as a sensor for simultaneous determination of ondansetron and morphine, *Talanta* 122 (2014) 187–194, <http://dx.doi.org/10.1016/j.talanta.2014.01.026>.
- [37] A. Carolina Torres, M.M. Barsan, C.M.A. Brett, Simple electrochemical sensor for caffeine based on carbon and Nafion-modified carbon electrodes, *Food Chem.* 149 (2014) 215–220, <http://dx.doi.org/10.1016/j.foodchem.2013.10.114>.
- [38] R. García-González, M.T. Fernández-Abedul, A. Costa-García, Nafion modified-screen printed gold electrodes and their carbon nanostructuring for electrochemical sensors applications, *Talanta* 107 (2013) 376–381, <http://dx.doi.org/10.1016/j.talanta.2013.01.034>.
- [39] X. Zhang, Y. Shen, G. Shen, S. Wang, The fabrication of a label-free electrochemical immunosensor using Nafion/carbon nanotubes/charged pyridinecarboxaldehyde composite film, *Anal. Biochem.* 504 (2016) 14–19, <http://dx.doi.org/10.1016/j.ab.2016.03.022>.
- [40] D.M. Anjo, M. Kahr, M.M. Khodabakhsh, S. Nowinski, M. Wanger, Electrochemical activation of carbon electrodes in base: minimization of dopamine adsorption and electrode capacitance, *Anal. Chem.* 61 (1989) 2603–2608, <http://dx.doi.org/10.1021/ac00198a004>.
- [41] A.M.O. Brett, M.-E. Ghica, Electrochemical oxidation of quercetin, *Electroanalysis* 15 (2003) 1745–1750, <http://dx.doi.org/10.1002/elan.200302800>.
- [42] A.K. Timbola, C.D. De Souza, C. Giacomelli, A. Spinelli, Electrochemical oxidation of quercetin in hydro-alcoholic solution, *J. Braz. Chem. Soc.* 17 (2006) 139–148, <http://dx.doi.org/10.1590/S0103-50532006000100020>.
- [43] Y. Yang, J. Zhou, H. Zhang, P. Gai, X. Zhang, J. Chen, Electrochemical evaluation of total antioxidant capacities in fruit juice based on the guanine/graphene nanoribbon/glassy carbon electrode, *Talanta* 106 (2013) 206–211, <http://dx.doi.org/10.1016/j.talanta.2012.12.030>.
- [44] F. Gao, D. Zheng, H. Tanaka, F. Zhan, X. Yuan, F. Gao, et al., An electrochemical sensor for gallic acid based on Fe₂O₃/electro-reduced graphene oxide composite: estimation for the antioxidant capacity index of wines, *Mater. Sci. Eng. C* 57 (2015) 279–287, <http://dx.doi.org/10.1016/j.msec.2015.07.025>.
- [45] B. Liu, L. Luo, Y. Ding, X. Si, Y. Wei, X. Ouyang, et al., Differential pulse voltammetric determination of ascorbic acid in the presence of folic acid at electro-deposited NiO/graphene composite film modified electrode, *Electrochim. Acta* 142 (2014) 336–342, <http://dx.doi.org/10.1016/j.electacta.2014.07.126>.
- [46] M.S. Dresselhaus, Carbon nanotubes - preface, *Carbon N Y* 33 (1995) 871–872.
- [47] J.P. Issi, L. Langer, J. Heremans, C.H. Olk, Electronic properties of carbon nanotubes: experimental results, *Carbon N Y* 33 (1995) 941–948, [http://dx.doi.org/10.1016/0008-6223\(95\)00023-7](http://dx.doi.org/10.1016/0008-6223(95)00023-7).
- [48] R. Seshadri, H.N. Aiyer, A. Govindaraj, C.N.R. Rao, Electron transport properties of carbon nanotubes, *Solid State Commun.* 91 (1994) 195–199.
- [49] A.J. Bard, L.R. Faulkner, *Electrochemical Methods. Fundamentals and Applications*, 2nd ed., Wiley-VCH, New York, 2001, <http://dx.doi.org/10.1016/B978-0-12-381373-2.00056-9>.
- [50] V.S. Bagotsky, *Fundamentals of Electrochemistry*, 2nd edition, John Wiley & Sons, Inc., 2006, <http://dx.doi.org/10.1385/1-59259-877-3:003>.
- [51] C. Barbero, J.J. Silber, L. Sereno, Studies of surface-modified glassy carbon electrodes obtained by electrochemical treatment its effect on Ru (bpy) 2 + 3 adsorption and the electron transfer rates of the Fe²⁺ / Fe³⁺ couple, *J. Electroanal. Chem.* 248 (1988) 321–340, [http://dx.doi.org/10.1016/0022-0728\(88\)85093-9](http://dx.doi.org/10.1016/0022-0728(88)85093-9).
- [52] B. Hoyer, T.M. Florence, G.E. Batley, Application of polymer-coated glassy carbon electrodes in anodic stripping voltammetry, *Anal. Chem.* 59 (1987) 1608–1614, <http://dx.doi.org/10.1021/ac00140a007>.
- [53] D.C. Harris, *Quantitative Chemical Analysis*, 7th ed., W. H. Freeman and Company, New York, 2007.
- [54] C. Muñoz-Bustos, A. Tirado-Guázar, F. Paraguay-Delgado, G. Pina-Luis, Copper nanoclusters-coated BSA as a novel fluorescence sensor for sensitive and selective detection of mangiferin, *Sensors Actuators B Chem.* 244 (2017) 922–927, <http://dx.doi.org/10.1016/j.snb.2017.01.071>.
- [55] S. Tajik, M.A. Taher, H. Beitollahi, Mangiferin DNA biosensor using double-stranded DNA modified pencil graphite electrode based on guanine and adenine signals, *J. Electroanal. Chem.* 720–721 (2014) 134–138, <http://dx.doi.org/10.1016/j.jelechem.2014.03.039>.