Evaluation of Carbon Paste Electrode Modified with Heavy Metals for the Analysis of Paracetamol by Voltammetry and Impedance Spectroscopy

Hayat EL Ouafy[†], Tarik EL Ouafy[‡*], Mustapha Oubenali[†], Mohamed Mbarki[†], Malika Echajia[†]

[†] Laboratory of Organic and Analytical Chemistry, Sultan Moulay Slimane University, Faculty of Science and Technology, Beni Mellal, Morocco;
[‡] Laboratory of Organic and Analytical Chemistry, Sultan Moulay Slimane University, Polydisciplinary Faculty, Khouribga, Morocco; *e-mail: tarikelouafy@gmail.com

Recieved: August 15, 2020; Accepted: September 26, 2020
DOI: 10.17721/moca.2020.93-99

The present document reports on the electrocatalytic activity of heavy metals (Copper(II), Nickel(II), Manganese(II) and Lead(II)) modified carbon paste electrodes (HM/CPE) for the paracetamol (Pr) oxidation where its results are compared with carbon paste electrode. The voltammetric behavior of Pr is explored where a sensitive anodic peak has appeared at about 0.27 V (vs. Ag/AgCl/3 M KCl) in 0.1 M Na_2SO_4 (pH 12). This peak results from the irreversible oxidation of Pr at HM/CPE surface. The catalytic effect was evaluated using cyclic and square wave voltammetry. Electrochemical impedance spectroscopy also confirms our experimental results as the HM/CPE shows the least charge transfer resistance. Also, HM/CPE can be utilized successfully to ameliorate the electroanalysis of Pr at very weak concentration with excellent sensitivity. The calibration curves were linear from $6.0 \cdot 10^{-5}$ to $8.0 \cdot 10^{-4}$ mol L^{-1}. The detection limits were found approaching 10^{-9} mol L^{-1}. Then, the proposed method was applied to detect Pr in river water samples with satisfactory results.

Keywords: heavy metals, cyclic voltammetry, square wave voltammetry, electrodeposition, modified electrodes, paracetamol

Paracetamol (*Pr*) is a drug used for the first time in medicine by Von Mering in 1893. It is the most widely used analgesic and antipyretic in the world [1]. The anti-inflammatory activity of Pr is low and is not used in inflammatory infections. However, it is prescribed to diminish fever colds, cough and tension pains, migraine, muscular, chronic and tooth [2-4]. It is also effective in the cure of osteoarthritis [5] and cancer pain. New research suggests that Pr could help against cardiovascular diseases [6]. Pr is also an analgesic for people with asthma [7]. Other research suggests that Pr could protect women against ovarian cancer [8]. Pr is easily metabolized in the body [9]. Numerous methods of Pr analysis have been cited in the literature: titrimetry [10], spectrophotometry [11], spectrofluorometry [12], voltammetry [13], high-performance liquid chromatography [14], thin layer chromatography [15], colorimetry [16], fourier-transform infrared spectroscopy [17]. These methods are characterized by the disadvantages of high costs, long analysis time and pre-processing of samples. Pr is an electroactive compound and most electroanalytical methods can be considered effective for the analysis of Pr as a means of replacing the methods mentioned. The electrochemical techniques use cobalt hexacyanoferrate modified carbon electrode [18], glassy carbon electrode modified by carbon nanotube diacetyl phosphate film [19], carbon film resistors as electrode [20], C60-modified glassy carbon electrode [21], L-cysteine modified glassy carbon electrode [22,23], boron-doped diamond thin film electrode [24]. Polyaniline/multi-walled carbon nanotube composites modified electrodes [25] and Metalloporphyrin chemically modified glassy carbon electrodes. Yet other modified electrodes by carbon nanotubes have been applied for the determination of analytical samples [26-32]. In our work, we described the electroanalysis of Pr oxidation and their sensitive detection at the heavy metal modified carbon paste electrodes (HM/CPE) in 0.1 Na_2SO_4. Its oxidation performance is compared with CPE. The success of HM/CPE toward the electrochemical analysis of Pr is evaluated by cyclic voltammetry (CV), square wave voltammetry (SWV) and electrochemical impedance spectroscopy (EIS) methods. Therefore, theses electrodes were applied to the sensitive detection of concentrations of Pr in river water samples.

Experimental part

Apparatus and reagents. The electrochemical results were obtained by the potentiostat voltalab (model PGSTAT 100) driven by the electrochemical data processing software (voltalab master 4) running under Windows 2007. The electrochemical system comprises three electrodes: working electrode (HM/CPE), reference electrode (saturated calomel electrode) and auxiliary electrode (platinum).

The pH-meter was utilized for adjusting pH values.

Pr, $CuSO_4$, $MnSO_4$, $NiSO_4$, $PbNO_3$ and Na_2SO_4 were bought from Sigma-Aldrich. The pH was adjusted by sulfuric acid or potassium hydroxide. All aqueous solutions used in the present work were prepared using distilled water. All experiments were realized at 25°C.

HM/CPE preparation and procedure. HM/CPE was prepared by depositing the heavy metals (Cu, Ni, Mn and Pb) at a fixed potential (0.1 V) for 1 hour onto the carbon paste electrode surface. The body of the HM/CPE for analysis experiments was a cylinder that was tightly packed with carbon paste. The area of this electrode was 0.1256 cm^2. Electrical contact is provided by a carbon rod.

Each electrode is valid for one test only, i.e. the study of the electrochemical behavior is done by an electrode, an electrode does the study of the scanning speed, the study of the effect of pH is done by one electrode and another does the study of the effect of concentration.

Several solutions have been tested such as K_2SO_4, Na_2SO_4, NaCl and KCl. The excellent electrochemical analysis response was recorded in Na_2SO_4. The electroanalysis consists of measuring the responses on the HM/CPE surface for a fixed concentration of Pr. The amount of Pr was added to the electrochemical cell containing 20 ml of the electrolytic medium. The CV and SWV were recorded in the potential range between -1.8 V and 1.8 V, at a scanning speed of 1 mV s^{-1}, step potential 50 mV, amplitude 2 mV and duration 0.1 s. Optimum conditions were found by measuring oxidation peak currents as a function of all parameters. Electrochemical experiments were performed at 25 °C.

Results and discussion

Characterization of HM/CPE. Fig. 1 and Fig. 2 represent a CVs in the potential range from -1.8 V to 1.8 V and the EIS recorded in 0.1 M Na_2SO_4 (pH 12) for CPE, Ni/CPE, Mn/CPE, Pb/CPE and Cu/CPE. It seems that the CVs and EIS have different forms, showing that the CPE surface was effectively modified by heavy metals.

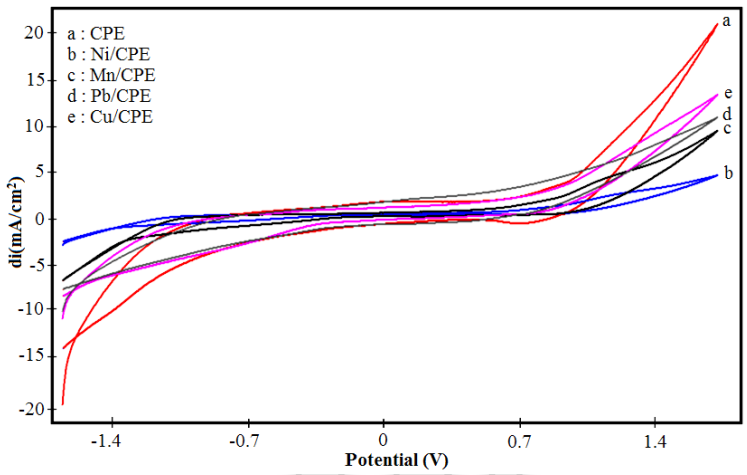


Fig. 1. CVs recorded on the HM/CPE surface in Na_2SO_4 (0.1M, pH 12), 100 mV s^{-1}.

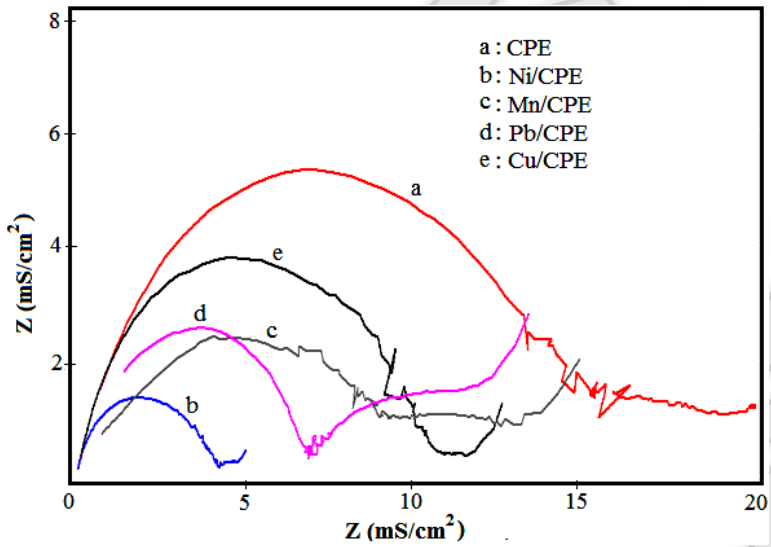
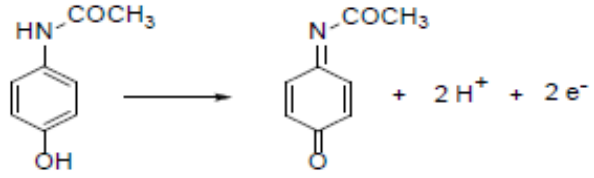


Fig. 2. EIS recorded on the HM/CPE surface in Na_2SO_4 (0.1 M, pH 12).

Electrochemical behavior of Pr. The catalytic activity of the CPE and HM/CPE toward Pr oxidation was evaluated by the SWV in Na_2SO_4 (0.1M, pH 12) containing 3.5 × 10^{-5} mol L^{-1} of Pr in the range from -1.8 V to 1.8 V (Fig. 3). No peak is observed in the case of CPE. The anodic peak of Pr on the surface of the modified electrodes appeared at about 0.27 V. No reduction peak of the Pr was observed in the SWVs at all electrodes, suggesting that the electrochemical reaction is completely irreversible. Therefore, the Mn/CPE exhibited effectual electro-catalytic oxidation of Pr compared to other electrodes. Moreover, the Mn/CPE can too promote Pr detection. Fig. 4 shows the behavior of impedance diagrams recorded for HM/CPE in the presence of Pr. We conclude that the modified electrode reacts with the studied compound. The oxidation peak of Pr on the HM/CPE surface is obtained according to the reaction in scheme 1.



Paracetamol N-acetyl-p-quinone imine

Schema 1. The electro-oxidation of Pr.

Effect of Scan rate and pH. To further investigate the Pr characteristics at the HM/CPE surface, the influence of scan rates and pH on the Pr (3.5 × 10^{-5} mol L^{-1}) voltammetric behavior was evaluated in Na_2SO_4 (0.1M, pH 12). The oxidation peak currents increased linearly with increasing the scan rate from 40 to 120 mV s^{-1} (Fig. 5) suggesting that the electron transfer for Pr at the HM/CPE is an adsorption-controlled reaction.

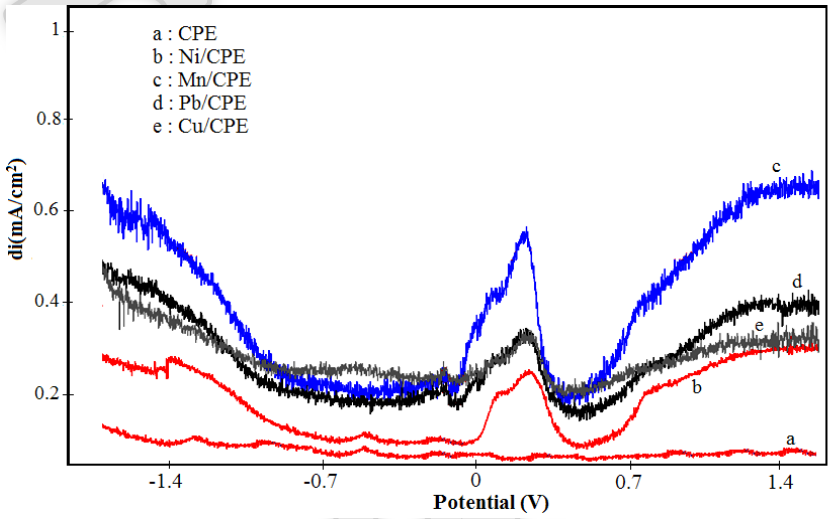


Fig. 3. SWVs recorded in 0.1M Na_2SO_4 (pH 12) containing 3.5 × 10^{-5} mol L^{-1} Pr at the surfaces of the electrodes.

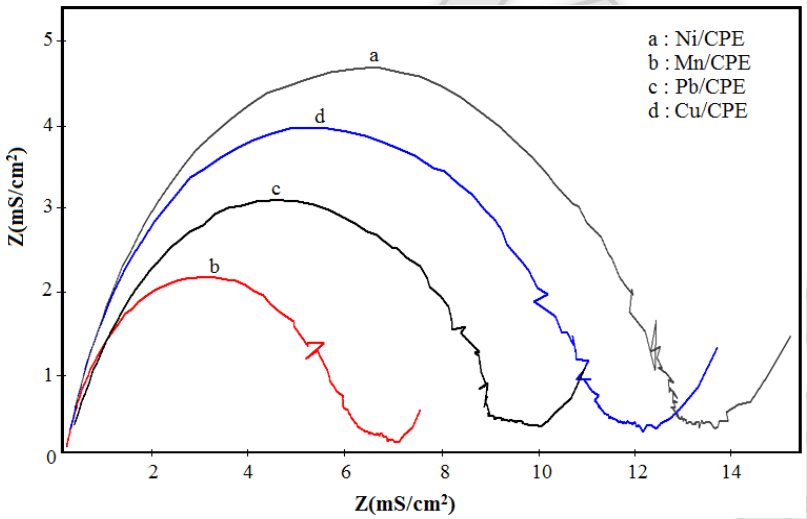


Fig. 4. EIS in 0.1M Na_2SO_4 (pH 12) containing 3.5 × 10^{-5} mol L^{-1} Pr at the modified electrodes.

The effect of pH on the electrochemical responses of the HM/CPE was investigated in the range from 2 to 12. The pH of the solution affects the current and potential peak of the catalytic oxidation of Pr. Fig. 6 and 7 show the effect of pH on the current density and the peak potential for Pr oxidation, respectively. The excellent intensity is obtained with pH 12.

Concentration effect of Pr. Calibration curves have been obtained for Pr under optimum experimental conditions. Fig. 8 shows the linear relationship between the anodic peak currents and the Pr concentration on the HM/CPE surface in the range from 6.0×10^{-5} to 8.0×10^{-4} mol L^{-1} of Pr. The anodic peak currents increase with the increase of Pr concentration. The reactivity of the HM/CPE surface towards the Pr determination is well-improved thanks to the heavy metals. Detection limits (LOD) were calculated on the oxidation peak current by the following equation: LOD = 3 S/m, (S - standard deviation of the peak currents nine runs; m - slope of the calibration curve). The detection limits obtained in the present work and in [33-38] are shown in table 1.

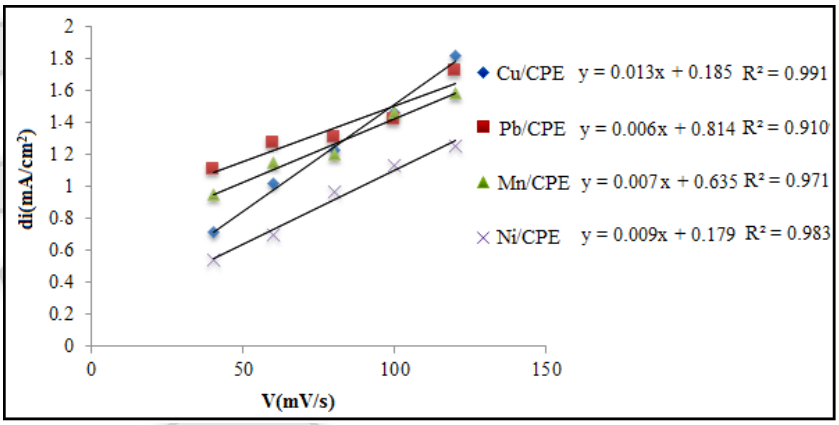


Fig. 5. The linearity between the anodic peak intensity and the scanning rates at the HM/CPE.

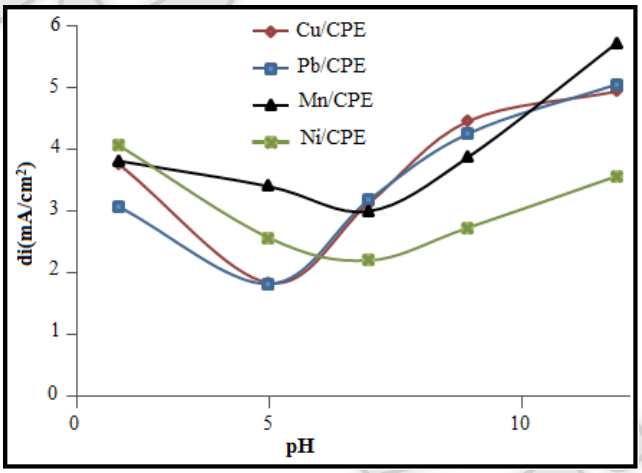


Fig. 6. Curves of the evolution of the oxidation peak current according to pH.

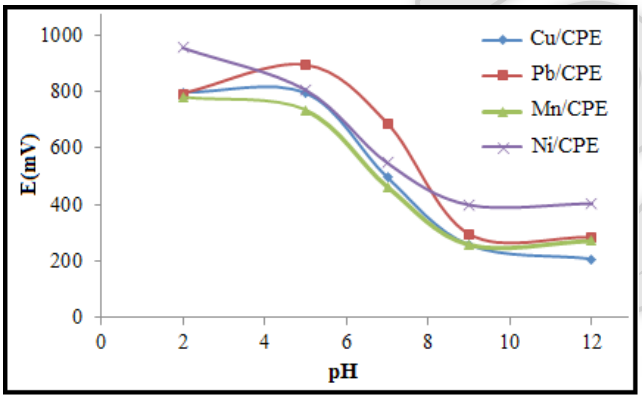


Fig. 7. The evolution of the oxidation peak potential according to pH.

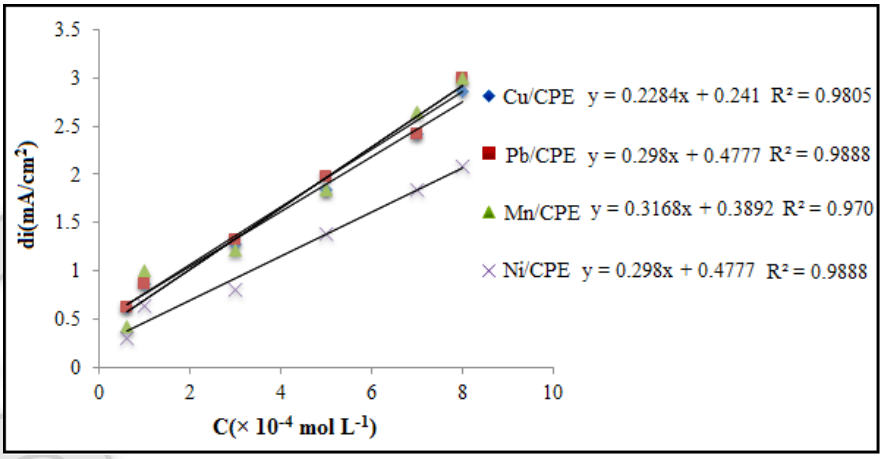


Fig. 8. Linearity between oxidation peaks versus the added Pr concentration.

Table 1. Comparison of the various electrodes using for Pr detection.

Modified electrode	Analytical technique	LOD, mol L^{-1}	Epa (V)	pH	References
A nanogold modified indium tin oxide electrode	Differential pulse voltammetry	1.8×10^{-7}	0.11	7.2	[33]
MgB_2 microparticles modified glassy carbon electrode	Cyclic voltammetry	3×10^{-7}	0.6	6	[34]
Nafion/TiO_2-graphene modified glassy carbon electrode	Cyclic volammetry	2.1×10^{-7}	0.575	7	[35]
Glassy carbon electrode	Differential pulse voltammetry	3.69×10^{-7}	0.6	4.51	[36]
Boron-doped diamond electrode	Differential pulse voltammetry	4.9×10^{-7}	0.8	4.5	[37]
Aluminum electrode modified by thin layer of palladium	Cyclic voltammetry	5×10^{-5}	0.6	6	[38]
Mn/CPE Pb/CPE Cu/CPE Ni/CPE	Square wave voltammetry	5.27×10^{-9} 6.77×10^{-9} 8.02×10^{-9} 8.45×10^{-9}	0.27	12	Present work

Detection of Pr in river water samples. To confirm the repeatability of the sensitivity of the HM/CPE, the detection of Pr was done in samples of river water of Oum Erbie (Morocco) without any pretreatment. The proposed method was used to analyze river water samples contaminated with Pr at different concentrations. The linear calibration curve of Pr was obtained by varying the concentration from 6.0×10^{-5} to 8.0×10^{-4} mol L^{-1} of Pr for river water samples (Fig. 9). The limit quantifications (LOQ) was calculated by following equation: LOQ = 10S/m. The LOD and LOQ are shown in table 2.

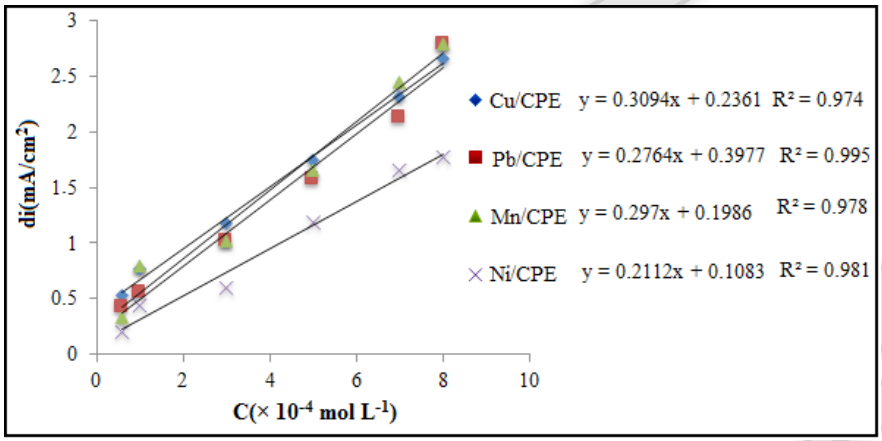


Fig. 9. Plot of peaks current versus Pr concentration in the optimum conditions.

Table 2. LOD and LOQ for the electroanalysis of Pr in river water samples at the surface of HM/CPE.

Modified electrode	Analytical technique	LOD (mol L^{-1})	LOQ (mol L^{-1})
Mn/CPE	Square wave voltammetry	8.40×10^{-9}	2.8×10^{-8}
Pb/CPE		3.24×10^{-9}	1.08×10^{-8}
Cu/CPE		1.33×10^{-9}	0.44×10^{-8}
Ni/CPE		9.88×10^{-8}	3.29×10^{-7}

Conclusions

At the surface of HM/CPE, Pr can produce an irreversible anodic peak at about 0.27 V in 0.1 M Na_2SO_4 solutions. The HM/CPE exhibits an excellent electrocatalytic performance toward the oxidation of Pr. The catalytic study was carried out using a CV, SWV and EIS. The results showed that the oxidation peak current of Pr at the Mn/CPE surface increased significantly compared with the user working electrodes. The linearity between the oxidation peak current and the concentration of Pr was studied in the range from 6×10^{-5} to 8×10^{-4} mol L^{-1}. The limits of detection were found to 10^{-9} mol L^{-1}.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Goyal, R.N.; Gupta, V.K.; Oyama, M.; et al. Differential pulse voltammetric determination of paracetamol at nanogold modified indium tin oxide electrode. *Electrochem. Commun.* **2003**, 7 (8), 803-807.
2. Tjølsen, A.; Lund, A.; Hole, K. Antinociceptive effect of paracetamol in rats is partly dependent on spinal serotonergic systems. *Eur. J. Pharmacol*. **1991**, 193 (2), 193-201.
3. Bianchi, M.; Panerai, A.E. The dose-related effects of paracetamol on hyperalgesia and nociception in the rat. *Brit. J. Pharmacol*. **1996**, 117 (1), 130-132.
4. Yin, H.; Shang, K.; Meng, X.; et al. Voltammetric sensing of paracetamol, dopamine and 4-aminophenol at a glassy carbon electrode coated with gold nanoparticles and an organophillic layered double hydroxide. *Microchim. Acta*. **2011**, 175 (1-2), 39-46.
5. Björkman, R.; Hallman, K.M.; Hedner, J.; et al. Acetaminophen blocks spinal hyperalgesia induced by NMDA and substance P. *Pain*. **1994**, 57 (3), 259-264.
6. Hunskaar, S.; Fasmer, O.B.; Hole, K. Acetylsalicylic acid, paracetamol and morphine inhibit behavioral responses to intrathecally administered substance P or capsaicin. *Life Sci*.**1985**, 37 (19), 1835-1841.
7. Carlsson, K.H.; Jurna, I. Central analgesic effect of paracetamol manifested by depression of nociceptive activity in thalamic neurones of the rat. *Neurosci. let*. **1987**, 77 (3), 339-343.
8. Ross, R.K.; McCurtis, J.W.; Henderson, B.E.; et al. Descriptive epidemiology of testicular and prostatic cancer in Los Angeles. *Brit. J. Canc*. **1979**, 39 (3), 284-292.
9. Goyal, R.N.; Gupta, V.K.; Chatterjee, S. Voltammetric biosensors for the determination of paracetamol at carbon nanotube modified pyrolytic graphite electrode. *Sens. Actuators. B Chem*. **2010**, 149 (1), 252-258.
10. Srivastava, M.K.; Ahmad, S.; Singh, D. et al. Titrimetric determination of dipyrone and paracetamol with potassium hexacyanoferrate (III) in an acidic medium. *Analyst*. **1985**, 110 (6), 735-737.
11. Cañada, M.A.; Reguera, M.P.; Medina, A.R.; et al. Fast determination of paracetamol by using a very simple photometric flow-through sensing device. *J. Pharm. Biomed. Anal.* **2000**, 22 (1), 59-66.
12. Vilchez, J.; Blanc, R.; Avidad, R.; et al. Spectrofluorimetric determination of paracetamol in pharmaceuticals and biological fluids. *J. Pharm. Biomed. Anal*. **1995**, 13 (9), 1119-1125.
13. Lau, O.W.; Luk, S.F.; Cheung, Y.M. Simultaneous determination of ascorbic acid, caffeine and paracetamol in drug formulations by differential-pulse voltammetry using a glassy carbon electrode. *Analyst*. **1989**, 114 (9), 1047-1051.
14. Ravisankar, S.; Vasudevan, M.; Gandhimathi, M.; et al. Reversed-phase HPLC method for the estimation of acetaminophen, ibuprofen and chlorzoxazone in formulations. *Talanta*. **1989**, 46 (6), 1577-1581.
15. Collier, J.; Dickinson, D.; McKechnie, S. EMEA and consumer representation. *Lancet*. **1997**, 350 (9084), 1107.
16. Felix, F.S.; Brett, C.M.; Angnes, L. Carbon film resistor electrode for amperometric determination of acetaminophen in pharmaceutical formulations. *J. Pharm. Biomed. Anal*. **2007**, 43 (5), 1622-1627.
17. Ramos, M.L.; Tyson, J.F.; Curran, D.J. Determination of acetaminophen by flow injection with on-line chemical derivatization: Investigations using visible and FTIR spectrophotometry. *Anal. Chim. Acta*. **1998**, 364 (1-3), 107-116.
18. Sun, D.; Zhang, H. Electrochemical determination of acetaminophen using a glassy carbon electrode coated with a single-wall carbon nanotube-dicetyl phosphate film. *Microchim. Acta*. **2007**, 158 (1-2), 131-136.
19. Li, M.; Jing, L. Electrochemical behavior

of acetaminophen and its detection on the PANI–MWCNTs composite modified electrode. *Electrochim. Acta.* **2007**, 52 (9), 3250-3257.

20. Felix, F.S.; Angnes, L. Fast and accurate analysis of drugs using amperometry associated with flow injection analysis. *J. pharm. Sci*. **2010**, 99 (12), 4784-4804.

21. Wang, C.; Li, C.; Wang, F.; et al. Covalent modification of glassy carbon electrode with L-cysteine for the determination of acetaminophen. *Microchim. Acta*. **2006**, 155 (3-4), 365-371.

22. Lin, Y.T.; Yantasee, W.; Ren, Z. Carbon Nanotubes based nanoelectrode arrays. *Electroanalysis*. **2005**, 17 (1), 79-84.

23. Kachoosangi, R.T.; Wildgoose, G.G.; Compton, R.G. Sensitive adsorptive stripping voltammetric determination of paracetamol at multiwalled carbon nanotube modified basal plane pyrolytic graphite electrode. *Anal. Chim. Acta*. **2008**, 618 (1), 54-60.

24. Kang, X.; Wang, J.; Wu, H.; et al. A graphene-based electrochemical sensor for sensitive detection of paracetamol. *Talanta*, **2010**, 81 (3), 754-759.

25. Bosch, M.E.; Sánchez, A.R.; Rojas, F.S.; et al. Determination of paracetamol: Historical evolution. *J. Pharm. biomed. Anal*. **2006**, 42 (3), 291-321.

26. Christie, I.; Leeds, S.; Baker, M.; et al. Direct electrochemical determination of paracetamol in plasma. *Anal. Chim. Act*. **1993**, 272 (1), 145-150.

27. Vieira, I.C.; Lupetti, K.O.; Fatibello, O. Determination of paracetamol in pharmaceutical products using a carbon paste biosensor modified with crude extract of zucchini (Cucurbita pepo). *Quím. Nova*. **2003**, 26 (1), 39-43.

28. Săndulescu, R.; Mirel, S.; Oprean, R. The development of spectrophotometric and electroanalytical methods for ascorbic acid and acetaminophen and their applications in the analysis of effervescent dosage forms. *J. Pharm. biomed. Anal*. **2000**, 23 (1), 77-87.

29. Gilmartin, M.A.; Hart, J.P. Novel, reagent-less, amperometric biosensor for uric acid based on a chemically modified screen-printed carbon electrode coated with cellulose acetate and uricase. *Analyst*. **1994**, 119 (5), 833-840.

30. Lahav, M.; Shipway, A.N.; Willner, I. Au-nanoparticle–bis-bipyridinium cyclophane superstructures: assembly, characterization and sensoric applications. *J. Chem. Soci*. Perkin transaction. **1999**, 2 (9), 1925-1931.

31. El Mhammedi, M.A.; Achak, M.; Bakasse, M. Physico-chemical characterization of electrochemical deposit of $Ca_{10}(PO_4)_6(OH)_2$ on copper surfaces. *App. Sur. Sci*. **2007**, 253 (14), 5925-5930.

32. El Qouatli, S.; Najih, R.; Hambate, V. Electrochemical Studies and Square Wave Voltammetry of Paracetamol at Managanese Modified Carbon Paste Electrode. *Pharm. Anal. Acta*. **2013**, 4 (412), 1-5.

33. Rajendra, N.G.; Vinod, K.G.; Munetaka, O.; et al. Differential pulse voltammetric determination of paracetamol at nanogold modified indium tin oxide electrode. *Electrochem. Commun*. **2005**, 7 (8), 803-809.

34. Zidan, M.; Tee, T.W.; Abdullah, A.H.; et al. Electrochemical oxidation of paracetamol mediated by MgB_2 microparticles modified glassy carbon electrode. *J. Chem*. **2011**, 8 (11), 553-560.

35. Fan, Y.; Liu, J.H.; Lu, H.T.; et al. Electrochemical behavior and voltammetric determination of paracetamol on Nafion/TiO_2–graphene modified glassy carbon electrode. *Colloids. Surf. B.* **2011**, 85 (2), 289-292.

36. Engin, C.; Yilmaz, S.; Saglikoglu, G.; et al. Electroanalytical investigation of paracetamol on glassy carbon electrode by voltammetry. *Int. J. Electrochem. Sci*. **2015**, 10 (4), 1916-1925.

37. Lourencao, B.C.; Medeiros, R.A.; Rocha-Filho, R.C.; et al. Simultaneous voltammetric determination of paracetamol and caffeine in pharmaceutical formulations using a boron-doped diamond electrode. *Talanta*. **2009**, 78 (3), 748-752.

38. Pournaghi-Azar, M.H.; Saadatirad, A. Simultaneous determination of paracetamol, ascorbic acid and codeine by differential pulse voltammetry on the aluminum electrode modified by thin layer of palladium. *Electroanalysis*. **2010**, 22 (14), 1592-1598.