Research Article

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Electrochemical determination of atenolol and propranolol using a carbon paste sensor modified with natural ilmenite

Abstract: In this study, a simple voltammetric method was reported for independent determination of propranolol (PROP) and atenolol (ATN) in pharmaceutical tablets using carbon paste electrode modified with natural Ilmenite (CPE-I). The analytical performance of the modified sensor was evaluated using the square wave voltammetry and cyclic voltammetry for determination of both β (beta) blockers in 0.1 mol L\(^{-1}\) of sulfuric acid solution (H\(_2\)SO\(_4\)). The signal obtained with modified carbon paste electrode in 0.1 mol L\(^{-1}\) of H\(_2\)SO\(_4\) showed a good electrocatalytic activity toward the oxidations of PROP and ATN compared with the bare one. The enhanced oxidation peak current response can be attributed to the catalytic effect of the ilmenite nanomaterial incorporated into the carbon paste electrode. Under optimal condition, good linear calibration curves were obtained ranging from 0.20 to 8.9 µmol L\(^{-1}\) for PROP and 2.0 to 9.9 µmol L\(^{-1}\) for ATN, with detection limits of 80 and 0.31 µmol L\(^{-1}\), respectively. The CPE-I sensor had good repeatability and reproducibility (RSD ≤ 3.2%) and high sensitivity for the detection of both ATN and PROP. The proposed sensor was applied for detection of these drugs in pharmaceutical tablets. The obtained results indicate that the voltammetric CPE-I sensor could be an alternative method for the routine quality control of the β blockers in complex matrices.

Keywords: β blockers, square wave voltammetry, ilmenite nanomaterial, cyclic voltammetry, pharmaceutical tablets

1 Introduction

The use of nanomaterials for the determination of variety of compounds is attracting attention in recent electroanalytical research [1]. In order to modify and improve the sensitivity and selectivity of working electrode, nanomaterials have been shown as suitable materials [2,3]. The presence of nanomaterials on the surface of the working electrode can improve the sensitivity and the rate of electron transfer to the surface electrode, according to some previous results. The development and application of modified carbon paste electrodes (CPE) have received considerable attention due to its low residual current, easy preparation, renewable surfaces, and low cost. Behpour et al. (2010) [8] have prepared a gold nanoparticle-modified carbon paste electrode (GN-CPE) for simultaneous determination of Acetaminophen (ACEP) and ATN. The results obtained demonstrated the potentiality of the GN-CPE for simultaneous determination of ACEP and ATN with high selectivity, good sensitivity, and low detection limits with the low cost of the sensor. Other authors like Ghapanvari et al. (2020) [9] have successfully modified the CPE with FeO\(_x\) at multi-walled carbon nanotubes at polyacrylonitrile for the detection of imatinib (IMA). Ilmenite (FeO-TiO\(_2\)) has been widely known as an excellent catalyst in antimicrobial activity, chemical oxygen demand sensing, photocatalysis, and photoelectrocatalysis. In recent studies, the catalytic effect of ilmenite and rutile on composite CPE was reported, where these modified sensors have shown an excellent performance for detection of phenol, pesticides, and drugs [4–7]. The modified process could improve the sensitivity, electrocatalytic behavior, and surface area. Several related studies reported that CPE modification is one of the most effective methods to improve electrode performance especially in electrode sensitivity for the determination of important compounds such as Epinephrine and Tyrosine, Amiodarone, Bisphenol A, and Losartan Potassium in trace level concentrations [3,4,10,11]. In clinical chemistry, doping and pharmaceutical investigations

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the quantification and determination of drugs in pharmaceutical samples and biological fluids are essential [12]. ATN (4-(2-hydroxy-3-isopropylaminoproxy)phenylacetamide) and PROP (1-(isopropylamino)-3-(1-naphthoxy)-2-propranolol) are cardioselective-adrenergic receptor blocking agents. These blocker agents are widely used in the treatment of cardiovascular diseases, arterial hypertension, cardiac arrhythmias, angina pectoris cardiac arrhythmias, and myocardial infarction [13]. Therefore, the simpler and faster methods for analyses of different receptor blocking agents are interesting in the quality of pharmaceutical formulations that contain them and also for therapeutic drug monitoring purposes. Despite their high use and application, little work has been reported on the determination of cardiovascular drugs by the electrochemical and related sensing devices [14]. The determination of a wide range of drug compounds was conducted using electrochemical techniques. The redox properties of drugs can provide insight into their metabolic fate, their in vivo redox processes, and their pharmacological activities [15–17]. For that reason, it is important to develop more sensitive sensors for detection of these drugs.

In this work a simple, selective, and highly sensitive electrochemical sensor modified with ilmenite nanostructure CPE-I is being reported for the determination of ATN and PROP. The CPE-I is an effective sensor for determination of β(beta) blockers (ATN and PROP) because this natural material (containing TiO₂ and FeO) has the ability for fast electron transfer, a good biocompatibility, etc., [5,6,18,19]. The proposed method was also applied to the investigation of these analytes in pharmaceutical formulation.

2 Materials and methods

2.1 Experimental

2.1.1 Reagents and chemicals

A pure standard form of Propranolol hydrochloride (W00336) and ATN (series 00336) in powdered form was purchased from TCI Chemicals Pvt. Ltd., India. Chemicals and reagents used for all the experiments were of analytical grade (Sigma and Merck). All solutions were prepared using double distilled water. The H₂SO₄ used to prepare the supporting electrolyte was purchased from Merck. Acetic acid, dipotassium phosphate, and dihydrogen phosphate were purchased from Merck (99% Merck). The paraffin oil (Olio di Vaselina) used was from Zeta farmaceutici company and the graphite powder synthetic with particles size 90–71 µm was from Alfa Aesar (99.9% Alfa Aesar). Ilmenite natural nanomaterial was granulated with particle size of 90–70 µm and activated with 10% of H₂SO₄. Commercial pharmaceutical tablets including PROP 83 (40 mg) and ATN (Profarma Sh.a) (100 mg) were purchased from a local pharmacy. A stock solution of 100 mmol L⁻¹ of PROP and 10 mmol L⁻¹ of ATN was prepared in 0.1 mol L⁻¹ of H₂SO₄ solution and kept at 4°C in a refrigerator. These solutions were diluted to the desired concentration with 0.1 mol L⁻¹ of H₂SO₄.

2.2 Apparatus

All the electrochemical measurements were carried out using PalmSens4 (potentiostat–galvanostat) connected via Bluetooth with a personal computer and three-electrode system software. The working electrodes were a CPE-I sensor studied in this work, a platinum wire as counter electrode, silver-silver chloride Ag/AgCl/KCl (3M), and a reference electrode. The electrochemical determination of PROP and ATN was performed using cyclic voltammetry (CV) and square wave voltammetry (SWV). SW voltammograms were recorded at a potential from 0.6 to 1.5 V for PROP and 1.0 to 1.6 V (vs SCE) for ATN, with scan rate of 100 mV s⁻¹, amplitude of 0.03 V, and frequency of 25 Hz. All voltammetric measurements were done at 26 ± 0.5°C in an unstirred electrochemical cell containing 15 mL of 0.1 mol L⁻¹ of H₂SO₄ as supporting electrolyte. Scheme of the experiment and possible oxidation mechanism is shown in Figure 1.

2.3 Preparation of modified sensor CPE-I

The CPE-I was prepared by mixing 70% of graphite, 10% of ilmenite, and 20% of mineral oil for 30 min to give a homogeneous paste. Initially, the graphite powder (with particle size 90–72 µm) and paraffin were mixed together and after that, the inorganic modifier (ilmenite natural material with the same size activated with 10% of H₂SO₄) was added and mixed with a mortar and pestle until a uniform paste was obtained. The prepared composite material was kept in a refrigerator at 4°C for 24 h before measurement. The obtained paste was packed into the plastic syringe with internal diameter 8 mm and outer diameter of
9.5 mm containing a copper wire as the external electric contact. The unmodified CPE was also prepared in the same way by mixing 70% of graphite and 30% of mineral oil for 30 min, except that no modifier (ilmenite) was added. The electrode surface was smoothed on a glass surface before the measurements. The surface of the electrode was renewed by removing a part of the paste and polishing it again on the glass surface.

2.4 Samples preparation (pharmaceutical tablets of ATN and PROP)

The PROP and ATN are taken from casual drugstore in tablet form. First, the tablets were accurately weighed (each tablet weighs; PROP 0.1708 g contains 40 mg and ATN 0.4196 g contains 100 mg). Five tablets of each were finely ground in the mortar pestle and a portion of respective powdered tablet (equivalent to the average weight of one tablet) was transferred into 50.0 mL volumetric flask using 50.0 mL of 0.1 mol L$^{-1}$ of H$_2$SO$_4$. From the prepared solution, 1 mL sample of PROP and 0.25 mL of ATN were taken and were analyzed by SWV technique in 15 mL of 0.1 mol L$^{-1}$ of H$_2$SO$_4$. The PROP and ATN contents were determined using the standard addition method.

**Ethical approval:** The conducted research is not related to either human or animal use.

3 Results and discussion

3.1 Electrochemical behavior of PROP and ATN at modified CPE-I sensor

The effect of nano-ilmenite material incorporated on CPE sensor was tested by comparing the voltammograms obtained with modified and unmodified sensor toward ATN and PROP. Figure 2a and b shows the typical SW voltammograms of 9.9 μmol L$^{-1}$ of ATN and 3.6 mmol L$^{-1}$ of PROP in 0.1 mol L$^{-1}$ of H$_2$SO$_4$ solution recorded with two different working electrodes (bare CPE and CPE-I).
As seen in Figure 2a and b, the SW voltammograms of ATN and PROP at CPE-I electrode appears with enhancement in response to peak current in both the cases compared with the bare one. The modified sensor showed a good improvement in oxidation peak currents for these β blockers. The results indicate that this behavior can be attributed to the catalytic nature of modified CPE-I for ATN and PROP oxidation. The possible oxidation mechanisms for ATN and PROP [21–25] at the surface of the modified electrode were considered as shown in Figure 1.

Regarding the role of Fe(II)/(III) species in the oxidation of organic substances, there are many evidences in the literature. [26–28]. It has been reported that these species that are generated at positive potentials have the role of a redox mediator in the oxidation of some compounds at Fe related electrodes. The electrode reaction may take place with a mechanism involving a rate limiting step where an intermediate reaction is formed upon a chemical reaction with Fe(n) and (m) species. [4,28]. Our results showed that the ilmenite natural material showed good improvement in oxidation peak currents for ATN and PROP. Therefore, it is suggested that the application of ilmenite leads to provide a current sensitivity in detection of these drugs.

3.2 Optimization of experimental parameters

The electrochemical performance of modified CPE-I sensor towards PROP and ATN was tested in optimal experimental condition. Different parameters were optimizing such as: (a) electrochemical technique, (b) scan rate, and (c) supporting electrolyte and pH. First, in order to choose the more selective and sensitive technique, the electrochemical behavior of ATN at the surface of the modified electrode using differential pulse voltammetry (DPV), SWV, and CV was investigated. Figure 3 shows the DPV, SWV, and CV voltammograms registered with CPE-I, at 320 µmol L⁻¹ of ATN, in 0.1 mol L⁻¹ of H₂SO₄.

As can be seen from the graph in Figure 3, SWV is more sensitive method for detection of ATN because the signal appears with a higher oxidation peak compared with the other two techniques. Regarding this aspect, in further experiments, SWV technique was used for determination of both the β blockers in lower concentration.

The effect of scan rate on peak current response was studied at a concentration of 340 µmol L⁻¹ of ATN in 0.1 mol L⁻¹ of H₂SO₄. The cyclic voltammograms obtained with CPE-I sensor at different scan rates from 20 to
charge transfer, which is reported in the previous studies [29–31]. Cathodic peak current was proportional to the square root of the scan rate according to the previous study [32] indicating that electrooxidation is diffusion-controlled process. A linear relationship was observed between \( I_p \) and \( \sqrt{v} \) (Figure 4 insert) and \( R^2 = 0.9928 \). Plots of the logarithm of the peak current versus the logarithm of the scan rate for ATN is linear with slopes of 0.62, which are close to the theoretical expected value of 0.50 for an ideal reaction of species in solution [33].

In order to choose the best supporting electrolyte and pH for further electroanalytical measurements, the SW voltammograms were registered in 3.3 mmol L\(^{-1}\) for PROP and 3.3 µmol L\(^{-1}\) for ATN using different supporting electrolytes with pH from 2.0 to 7.0. The best well-defined oxidation peak for both analytes was obtained in H\(_2\)SO\(_4\) solution with adjusted pH of 2.0 at potential of 1.2 V (PROP) and 1.5 V (ATN) as shown in Figure 5.

It is clearly seen that the potential for PROP and ATN oxidation depends on the type of the supporting electrolyte and pH, so in acetate buffer solution, the intensity of oxidation current for PROP is lower and potential peak shifted to the positive value. Regarding the voltammograms obtained in phosphate buffer solution, no well-defined peak was observed. The same situation is observed with ATN in phosphate buffer solution, while in NaNO\(_3\) solution, no oxidation peak appeared. Therefore, the solution of 0.1 mol L\(^{-1}\) of H\(_2\)SO\(_4\) (pH = 2) was selected as a suitable supporting electrolyte for further experiments.

### 3.3 Analytical curves and validation parameters of the methods proposed for PROP and ATN determination

Analytical curves for ATN and PROP using modified CPE-I sensor were obtained using experimental parameters optimized previously. The analytical parameters obtained for ATN and PROP with two applied voltammetric techniques CV and SWV are shown in Table 1. The best analytical parameters like precision, sensitivity, and low detection limits were obtained by SWV, so this method was chosen for the determination of PROP and ATN in pharmaceutical tablets.

The SW voltammograms registered in 0.1 mol L\(^{-1}\) of H\(_2\)SO\(_4\) for different concentrations of each \( \beta \) blocker using CPE-I sensor are shown in Figure 6 for concentration ranges: 0.20–8.9 mmol L\(^{-1}\) of PROP (Figure 6a) and 2.0–9.9 µmol L\(^{-1}\) of ATN (Figure 6b).

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**Figure 3:** Voltammograms of 320 µmol L\(^{-1}\) of ATN in 0.1 mol L\(^{-1}\) of H\(_2\)SO\(_4\) at CPE-I composite electrode using the CV, SWV, and DPV techniques. Conditions: CV, scan rate = 100 mV s\(^{-1}\); DPV, scan rate = 20 mV s\(^{-1}\) and pulse amplitude = 30 mV; SWV, pulse amplitude = 30 mV, frequency = 25 Hz, and step potential = 5 mV.

**Figure 4:** Cyclic voltammograms for 340 µmol L\(^{-1}\) of ATN in 0.1 mol L\(^{-1}\) of H\(_2\)SO\(_4\) solution obtained using CPE-I at different scan rates from 20 to 200 mV s\(^{-1}\). Insert: linear dependence of the peak current with \( v^{1/2} \).
The respective analytical curves obtained for PROP ($R^2 = 0.9969$) and ATN ($R^2 = 0.9979$) with corresponding regression equations $I_{ap} (\mu A) = 0.0084 + 0.05019 [c (\text{mmol L}^{-1})]$ and $I_{ap} (\mu A) = 0.0039 + 0.0195 [c (\text{µmol L}^{-1})]$ are shown in the insert of Figure 6a and b (where $I_{ap}$ is the anodic peak current and $c$ is the concentration of respective analyte. The detection limit ($3\sigma$) values calculated are 80 $\mu$mol L$^{-1}$ for PROP and 0.31 µmol L$^{-1}$ for ATN. The repeatabilities of sensor determined by successive measurements at modified CPE-I electrode using 3.7 mmol L$^{-1}$ of PROP and 3.3 µmol L$^{-1}$ of ATN ($n = 5$), resulted with relative standard deviation (RSD) of 3.2 and 2.5%, respectively. The reproducibility of modified sensor estimated using the working electrodes CPE-I prepared ($n = 3$ electrodes) independently for the same concentration of PROP and ATN were obtained with RSDs of 0.57 and 1.2%, respectively.

### 3.4 Analytical determination of PROP and ATN in pharmaceutical formulation

The development method was applied for determination of both β blockers in pharmaceutical tablets using SWV, since SWV possesses high sensitivity and good resolution. To determine the content of these drugs in real samples, the standard addition method was used. Solutions obtained by dissolving ATN and PROP tablets in 0.1 mol L$^{-1}$ of

Table 1: Quantitative analytical results of the investigated β blockers by SWV and CV techniques

|                      | Propranolol (in 0.1 mol L$^{-1}$ of H$_2$SO$_4$) | Atenolol (in 0.1 mol L$^{-1}$ of H$_2$SO$_4$) |
|----------------------|-----------------------------------------------|-----------------------------------------------|
|                      | Cyclic voltammetry | Square wave voltammetry                     | Square wave voltammetry | Cyclic voltammetry |
| Linear range (µmol L$^{-1}$) | 500–6600          | 200–8900                                     | 2.0–9.9                 | 33–566              |
| Correlation coefficient | 0.9920            | 0.9969                                       | 0.9979                  | 0.9943              |
| Slope $\mu$A (µmol L$^{-1}$)$^{-1}$ | 43                | 50                                           | 19.5                    | 3.2                 |
| RSD (%)               | 4.1               | 3.2                                          | 2.5                     | 3.9                 |
| Detection limit (µmol L$^{-1}$) | 100               | 80                                           | 0.31                    | 1.9                 |
| Peak potential (V)    | 1.2               | 1.2                                          | 1.5                     | 1.6                 |
H$_2$SO$_4$ were subsequently diluted, in order that ATN and PROP concentrations fall in the range of the calibration plot. The SW voltammograms were obtained at CPE by spiking appropriate samples in H$_2$SO$_4$ solution, at optimum conditions for ATN and PROP (as described in Section 2.4).

Table 2 shows the amount ATN and PROP determined with CPE-I sensor using SWV technique. It was found that ATN and PROP content determined in pharmaceutical tablets using this method are in good agreement with the reported label value. Recovery test of PROP and ATN was carried out by spiking each analyte in highly diluted tablet samples and results obtained are also shown in Table 2. The tablet samples were spiked with two different amounts of ATN and PROP. The recoveries were found to be in the range of 97.7–101%.

### Table 2: Determination of ATN and PROP in real samples with CPE-I using square wave voltammetry (n = 3)

| Analyte/Sample Method | Spiked$^b$ | Found$^c$ | Recovery$^e$ |
|-----------------------|-----------|-----------|--------------|
| Propranolol (mg/tablet) | 1.8 | 1.82 ± 0.2 | 101 |
| Label | 3.6 | 3.54 ± 0.4 | 98.0 |
| value 40 mg | 0 | 98.0 ± 5.2 | 99.0 |
| Atenolol (mg/tablet) | 6.6 | 6.45 ± 0.15 | 97.7 |
| Label | 13 | 12.88 ± 0.25 | 99.0 |

$^a$Mean value ± SD. $^b$The unit of spiked concentration for PROP is mmol L$^{-1}$ and for ATN is µmol L$^{-1}$. $^c$The measured unit is mmol L$^{-1}$ for PROP and µmol L$^{-1}$ for ATN. $^d$The measured unit is mg/tablet. $^e$The measured unit is %.

**Figure 6:** Square wave voltammograms obtained using a nano-ilmenite modified CPE as working electrode for: (a) (1) 0; (2) 0.2 mmol L$^{-1}$; (3) 0.5 mmol L$^{-1}$; (4) 1.2 mmol L$^{-1}$; (5) 1.8 mmol L$^{-1}$; (6) 2.4 mmol L$^{-1}$; (7) 3.1 mmol L$^{-1}$; (8) 3.7 mmol L$^{-1}$; (9) 4.3 mmol L$^{-1}$; (10) 4.9 mmol L$^{-1}$; (11) 5.5 mmol L$^{-1}$; (12) 6.1 mmol L$^{-1}$; (13) 6.7 mmol L$^{-1}$; (14) 7.8 mmol L$^{-1}$; (15) 8.9 mmol L$^{-1}$ of PROP in 0.1 mol L$^{-1}$ of H$_2$SO$_4$ and (b) (1) 2.0 µmol L$^{-1}$; (2) 3.3 µmol L$^{-1}$; (3) 6.6 µmol L$^{-1}$; (4) 9.9 µmol L$^{-1}$ of ATN in 0.1 mol L$^{-1}$ of H$_2$SO$_4$ (pH 2.0). Inserts: Respective analytical curves for the oxidation processes of PROP (a) and ATN (b).
with a relative SD of 5.2%. These results demonstrated that the proposed methods could be used for the determination of these drugs in pharmaceutical preparations.

4 Conclusion

This work describes the preparation of CPE electrode modified with natural nano-ilmenite for the independent voltammetric determination of ATN and PROP using adequate supporting electrolyte solution of 0.1 mol L\(^{-1}\) of H\(_2\)SO\(_4\). The presence of modifier ilmenite could improve and facilitate the electron transfer in the electrooxidation of both \(\beta\) blockers through the diffusion mechanism process. The modified CPE-I sensor resulted in a higher analytical performance toward PROP and ATN compared with the bare CPE. The proposed method can be used to determine both \(\beta\) blockers ATN and PROP in real sample (commercial drugs) with good reproducibility and with reliable accuracy.

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Reference

[1] Goyal RN, Singh SP. Voltammetric determination of atenolol at C60-modified glassy carbon electrodes. Talanta. 2006;69:932–7. doi: 10.1016/j.talanta.2005.11.041.

[2] Canevari TC, Rossi MV, Alexiou ADP. Development of an electrochemical sensor of endocrine disruptor bisphenol A by reduced graphene oxide for incorporation of spherical carbon nanoparticles. J Electroanal Chem. 2019;832:24–30. doi: 10.1016/j.jelechem.2018.10.044.

[3] Fadillah G, Triana S, Chasanah U, Saleh TA. Titania-nanorods modified carbon paste electrode for the sensitive voltammetric determination of BPA in exposed bottled water. Sens Bio-Sens Res. 2020;30:1003912020. doi: 10.1016/j.sbsr.2020.100391.

[4] Hasanzadeh M, Pournaghi-Azar MH, Shadjouc N, Jouyban A. Magnetic nanoparticles incorporated on functionalized mesoporous silica: an advanced electrochemical sensor for simultaneous determination of amiodarone and atenolol. RSC Adv. 2014;4:4710–7. doi: 10.1039/c3ra45433a.

[5] Nurdina M, Agusub L, Putraa AAM, Maulidiyahaha M, Arhmac Z, Wibowo D, et al. Synthesis and electrochemical performance of graphene-\(\text{TiO}_2\)-carbon paste nanocomposites electrode in phenol detection. J Phys Chem Solids. 2019;131:104–10. doi: 10.1016/j.jpcs.2019.03.014.

[6] Nurdina M, Prabowoa OA, Arhamb Z, Wibowoc D, Maulidiyah M, Saadd SKM, et al. Highly sensitive fipronil pesticide detection on ilmenite (\(\text{FeO-\TiO}_2\))-carbon paste composite electrode. Surf Interfaces. 2019;16:108–13. doi: 10.1016/j.surfin.2019.05.008.

[7] Reddy YVM, Sravani B, Agarwal Sh, Guptha VK, Madhavi G. Electrochemical sensor for detection of uric acid in the presence of ascorbic acid and dopamine using the poly(DPA)/\(\text{SiO}_2@\text{Fe}_2\text{O}_3\) modified carbon paste electrode. J Electroanal Chem. 2018;1572–6657(18):30319. doi: 10.1016/j.jelechem.2018.04.059.

[8] Behpour M, Ghoreishi SM, Honarmand E. A gold nanoparticle-modified carbon paste electrode as a sensor for simultaneous determination of acetaminophen and atenolol. Int J Electrochem Sci. 2010;5:1922–33.

[9] Ghanavari M, Madrakian T, Afkhami A, Ghoorchian A. A modified carbon paste electrode based on \(\text{Fe}_2\text{O}_3\) at multivalled carbon nanotubes@polyacrylonitrile nanofibers for determination of imatinib anticancer drug. J Appl Electrochem. 2020;50:281–94. doi: 10.1007/s10800-019-01388-x.

[10] Babaei A, Mirzakhani S, Khalilzadeh B. A sensitive simultaneous determination of epinephrine and tyrosine using an iron (n) doped zeolite-modified carbon paste electrode. J Braz Chem Soc. 2009;20(10):1862–9.

[11] Sharma S, Jadon N, Jain R. Development of electrochemical sensor for simultaneous quantification of atenolol and losartan potassium. Nanosci Technol. 2018;5(2):1–13. doi: 10.15226/2374-8414/5/2/00156.

[12] Arvand M, Vaziri M, Vejdani M. Electrochemical study of atenolol at a carbon paste electrode modified with mordenite type zeolite. Mater Sci Eng C. 2010;30:709–14. doi: 10.1016/j.msec.2010.03.002.

[13] Hardman JG, Limbird LE, Gilman AG. Goodman and Gilman’s – the pharmacological basis of therapeutics. 1995, 9th edn. New York: McGraw-Hill; 1996. doi: 10.1177/096032719601500711.

[14] Sartori ER, Meideiros RA, Rocha-Filho RC, Fatibello-Filho O. Square-wave voltammetric determination of propranolol and atenolol in pharmaceuticals using a boron-doped diamond electrode. Talanta. 2010;81:1418–24. doi: 10.1016/j.talanta.2010.02.046.

[15] Kellner R, Mermet JM, Otto M, Valcarcel M, Widmer HM. Analytical chemistry: a modern approach to analytical science. 2nd edn. Weinheim: Wiley-VCH; 2004. p. 124–97.
[16] Uslu B, Ozkan SA. Electroanalytical methods for the determination of pharmaceuticals: a review of recent trends and developments. Anal Lett. 2011;44:2644–702. doi: 10.1080/00032719.2011.553010.

[17] Sweetman SC, editor. Martindale: the complete drug reference. 35th edn. London: Pharmaceutical Press; 2007. p. 723–4. doi: 10.3163/1536-5050.100.1.018.

[18] Ashoka NB, Swamy BEK, Jayadevappa H. Nanorod TiO2 sensor for dopamine: a voltammetric study. N J Chem. 2017;41:11817–27. doi: 10.1039/C7NJ02188G.

[19] Fadillah G, Saleh TA, Wahyuningsih S. Enhanced electrochemical degradation of 4-nitrophenol molecules using novel Ti/TiO2-NiO electrodes. J Mol Liq. 2019;289:111108. doi: 10.1016/j.molliq.2019.111108.

[20] Hegde RN, Kumara Swamy BE, Sherigara BS, Nandibewoor ST. Electro oxidation of atenolol at a glassy carbon electrode. Int J Electrochem Sci. 2008;3:302–14.

[21] Bishop E, Hussein W. Electroanalytical studies of beta-adrenergic blocking agents; N-isopropylethanolamine derivates; procainamide. Analyst. 1984;109:65–71.

[22] Radi A, Wassel AA, El Ries MA. Adsorptive behavior and voltammetric analysis of propranolol at carbon paste electrode. Chem Analityczna. 2004;49:51–8.

[23] Manani G, Morris M, Caudle S, Wanekaya A, Mugweru A. Electrocatalytic oxidation of propranolol using microwave synthesized graphene decorated with gold nanoparticles and single walled carbon nanotubes. Chem Mater Res. 2013;3(11):39–48. ISSN: 2224-3224 (Print)/ISSN: 2225-0956 (Online).

[24] Baranowska I, Koper M. Electrochemical behavior of propranolol and its major metabolites, 4’-hydroxypropranolol and 4’-hydroxypropranolol Sulfate, on glassy carbon electrode. J Braz Chem Soc. 2011;22:1601–9.

[25] Deng B, Yin H, Liu Y, Ning X. Pharmacokinetics of propranolol hydrochlorid in human urine by capillary electrophoresis coupled with electrochemiluminescence. Anal Sci. 2015;27:55–9.

[26] Taylor KML, Rieter WJ, Lin W. Manganese-based nanoscale metal–organic frameworks for magnetic resonance imaging. J Am Chem Soc. 2008;130(44):14358–59. doi: 10.1021/ja803777x.

[27] Omidinia E, Shadjoua N, Hasanzadehb M. (Fe3O4)-graphene oxide as a novel magnetic nanomaterial for non-enzymatic determination of phenylalanine. Mater Sci Eng C. 2013;33(8):4624–32. doi: 10.1016/j.msec.2013.07.023.

[28] Saghafiroushousa L, Hasanzadeh M, Shadjoua B, Khalizadeh B. Deposition of new thia-containing Schiff-base iron(II) complexes onto carbon nanotube-modified glassy carbon electrodes as a biosensor for electrooxidation and determination of amino acids. Electrochim Acta. 2011;56(3):1051–61.

[29] Kasim EA, Ghandour MA, El-Haty MT, Ahmed MM, Pharm J. Determination of verapamil by adsorptive stripping voltammetry in urine and pharmaceutical formulations. Biomed Anal. 2002;30:921–9. doi: 10.1016/S0731-7085(02)00322-9.

[30] Semaan FS, Cavalheiro ETG, Brett CMA. Electrochemical behavior of verapamil at graphite/polyurethane composite electrodes: determination of release profiles in pharmaceutical samples. Anal Lett. 2009;42:1119–35. doi: 10.1080/00032710902890470.

[31] Dos Santos SX, Cavalheiro ETG, Brett CMA. Analytical potentialities of carbon nanotube/silicone rubber composite electrodes: determination of propranolol. Electroanalysis. 2010;22:2776–83. doi: 10.1002/elan.201000262.

[32] Gossler DK. Cyclic voltammetry; simulation and analysis of reaction mechanisms. Synth React Inorg Metal-Organ Chem. 1994;24(7):1237–8. doi: 10.1080/00945719408001398.

[33] Bard AJ, Faulkner LR. Electrochemical methods. Fundamentals and applications. New York: Wiley; 1980.