A pencil graphite electrode modified with poly nicotinamide as a framework for the electrochemical detection of propranolol hydrochloride

A Santhy, S Beena*, U S Krishnanunni Namboothiri, S Anupriya and C V Sreeranjini

Department of Chemistry, Amrita School of Arts and Sciences, AmritaVishwa Vidyapeetham, Amritapuri Campus, Clappana P.O, Kollam, 690525, India

Email-id: beenas@am.amrita.edu

Abstract: Herein, a novel polymer film modified pencil graphite electrode as an electrochemical sensor for the propranolol hydrochloride (PROP) is reported. A poly nicotinamide modified pencil graphite (Poly-NA-PGE) electrode was used for the electrochemical detection of propranolol hydrochloride using differential pulse voltammetry. The modified electrode was characterized by Scanning Electron Microscopy. Furthermore, the experimental parameters like pH of the supporting electrolyte, concentration of the nicotinamide and polymerisation cycles were optimized. The cyclic voltammetry of propranolol hydrochloride showcased an irreversible oxidation peak at 0.9361V. The sensor showed a linear range from 1µM – 20µM with a correlation co-efficient of 0.99825. The repeatability of the electrode was excellent with an RSD of 3.5%. The sensor was utilized effectively for the determination of propranolol from the commercially available pharmaceutical tablet.

1. INTRODUCTION

Propranolol hydrochloride is an anti-hypertensive drug associated with the treatment of disorders in the function. The structure of PROP is shown in figure 1. The successive utilization of PROP in the treatment Haemangiomas was reported[1, 2]. PROP is being used as a dominant medication in the treatment of various conditions such as heart dysrhythmia, migraine, portal hypertension, nerve disorders, overactive thyroid and tumour of adrenal gland for over 50 years[3]. The analysis of drugs from pharmaceutical formulations is of great importance in industries for quality control and the monitoring of drug manufacturing processes. Numerous analytical methods have been developed so far for the determination of PROP including colorimetry[4], spectrophotometry[5-7] and chromatography[8] due to the therapeutic importance of the drug. Various electroanalytical techniques were also reported in the literature for the determination of PROP[9-11]. Among all these quantification techniques, electrochemical techniques offered more sensitivity and reliability in sample consumption and miniaturization process[12].

As per our knowledge, the electrochemical sensing of PROP was not reported on pencil graphite electrode (PGE). The PGE is a commercially available cost-effective electrode for electrochemical sensing in contrast to other carbon-based electrodes[13]. So, hereby we are putting forward a novel electrochemical sensor on a poly nicotinamide modified PGE for the detection of PROP from pharmaceutical tablets.
Figure 1. structure of propranolol hydrochloride

2. EXPERIMENTAL

2.1. Reagents and solutions
The PROP tablets (Ciplar LA-40) were brought from a local pharmaceutical store. The anhydrous NaH$_2$PO$_4$ and Na$_2$HPO$_4$ for the preparation of phosphate buffer (PBS) were procured from Merck. Nicotinamide was supplied from LobaChemie. The pure drug sample of PROP was donated by KVSR Siddhartha College of Pharmaceutical Sciences, India. A local stationery store supplied pencil lead with a diameter of 0.7 mm marketed by Cello Pvt. Ltd. Preparation of all solutions were done with Millipore water and all reagents utilized for the experiments were of analytical reagent grade.

2.2. Instrumentation
An electrochemical workstation, A CHI 610E (CH Instruments, USA), equipped with a customary three electrode system was used for complete electrochemical measurements at room temperature. The poly NA-PGE was used as the working electrode, Ag/AgCl electrode (1M KCl) served as reference electrode and a Pt wire as the counter electrode.

2.3. Voltammetric procedure
A 1.0 mM stock solution of PROP was prepared in 10 mL de-ionised water. Appropriate amounts of analyte solution were added to the electrochemical cell containing 10 mL 0.1 M PBS 7 to get the desired working concentration range. Then the electrochemical analysis was rendered using DPV technique with a pulse width of 25 ms and pulse amplitude of 50 mV. For preparing the real sample solution, 15 tablets of Ciplar LA-40 was finely crumbled using a mortar and pestle. Furthermore a 1 mM solution of the tablet was prepared using this finely crushed powder using deionized water. The solution was then sonicated for 5 minutes, filtered using ordinary filter paper and used for analytical validation of PROP.

2.4. Preparation of modified PGE
A pencil lead enveloped was with a teflon tape exposing a length of 4 mm without teflon covering. The uncovered portion acts as the working surface of the PGE. Then the working surface is immersed in a solution of 1mM nicotinamide in 0.1 M PBS of pH 7.4 for electropolymerisation[14]. The electropolymerisation was done using cyclic voltammetry (CV) in a potential window of -0.8 V to 1.8 V at a scan rate of 100 mV/s for 10 consecutive cycles. Finally, the electrode was properly washed with de-ionized water for further use.

3. RESULTS AND DISCUSSIONS

3.1. Characterization of poly NA-PGE
The morphological characterization of the poly NA-PGE was done by Scanning Electron Microscopy (SEM). The figure 2 demonstrates the SEM micrographs of bare PGE and poly NA-PGE. The figure 2A shows a smooth flake like appearance of the PGE surface, whereas the figure 2B represents a rougher surface of the PGE after modification. This uneven surface of the modified PGE implies the formation of poly nicotinamide film on the PGE surface.
3.2. Electrochemical behaviour of PROP on poly NA-PGE
Cyclic voltammetry (CV) was initially used for studying the electrochemical characteristics of PROP. The PROP showed an irreversible oxidation peak at 0.98 V in 0.1 M PBS 7 in a potential range of 0.2 V to 1.2 V at a scan rate of 80 mV/s (figure 3). The oxidation peak observed on the poly NA-PGE may be due to the oxidation of secondary alcoholic group in the PROP as in the previous literature [9]. The electrochemical response of 5 µM PROP on the modified electrode was analysed with different scan rate using CV. As scan rate increases from 40 mV/s to 120 mV/s (figure 4A), a linear response of current was obtained with the linear regression equation $I_{pa} (\mu A) = 0.2596 + 0.002213 \cdot \nu$ (mV/s), $R^2 = 0.99395$ (figure 4B) was obtained. Owing to the linear nature of the peak current versus scan rate plot, electrochemical oxidation of the PROP follows an adsorption-controlled nature on poly NA-PGE.

![SEM images of (A) bare PGE (B) poly NA-PGE](image1)

**Figure 2. SEM images of (A) bare PGE (B) poly NA-PGE**

![CV of (a) poly NA-PGE alone 0.1 M PBS 7 (b) poly NA-PGE with 5 µM PROP in 0.1 M PBS 7, scan rate 80 mV/s](image2)

**Figure 3. CV of (a) poly NA-PGE alone 0.1 M PBS 7 (b) poly NA-PGE with 5 µM PROP in 0.1 M PBS 7, scan rate 80 mV/s**

3.3. Comparison of the modified PGE and unmodified PGE by DPV
The electro oxidation of PROP was done on bare PGE and the modified PGE by DPV of 5 µM PROP in 0.1 M PBS (pH 7) and is given in figure 5. As seen in the figure, an enhancement in the peak current was obtained for modified PGE than the bare PGE.

3.4. Optimization of operational parameters
3.4.1. pH study for the electrochemical detection of PROP
The most important parameter in the electroanalytical study of an analyte is the pH of the supporting electrolyte. So, we analysed the response of 5 µM PROP in PBS with pH ranging from 4 – 8 (figure 6A). The best response was obtained at neutral pH and PBS with pH 7 were considered for the further analysis.
3.4.2. Effect of nicotinamide concentration and polymerization cycle

Electropolymerisation was done with varying concentrations of nicotinamide such as 0.5 mM, 1 mM, 1.5mM and 2 mM to optimize the current for 5 µM PROP in PBS 7 (figure 6B). The oxidation peak current obtained was maximum for 1mM monomer and was selected for further studies. Moreover, we analysed the effect of polymerization cycles on the electro oxidation of PROP from 5 to 15 cycles. Based on the current response 10 cycles was selected for analytical studies.

3.4.3. Calibration curve and repeatability of the electrode

DPV study was used for the analytical application of the developed sensor. The DPV response of PROP under the optimized conditions were evaluated from 1µM – 20 µM concentration (figure 6C). As shown in the figure 6D, the poly NA-PGE electrode shows a linearity with respect to the current in the concentration range of 1µM – 20 µM (I_pA(µA) = 4.80224 + 0.71458 C (µM)), R^2 = 0.99038. The repeatability of the electrode was verified by measuring the electrochemical response of 5µM PROP in PBS with pH 7 for three different electrodes. A signal change with an RSD of only 3.5% was obtained suggesting the repeatability of the sensor.

![Figure 4](image1.png)

Figure 4. (A) CV of 5 µM PROP with different scan rates on poly NA-PGE (B) Plot of scan rate versus current

![Figure 5](image2.png)

Figure 5. (A):(a) and (b) DPVs of bare PGE without and with 5µM PROP (B): (a) and (b) DPVs of poly NA-PGE without and with5µM PROP

| Sample          | Amount added (µM) | Amount observed (µM) | % error |
|-----------------|-------------------|----------------------|---------|
| Ciplar LA tablet| 5                 | 4.66                 | 6.6%    |

Table 1. Determination of PROP from Ciplar LA tablet using Poly NA-PGE electrode
Figure 6. (A) Plot of pH versus current (B) Variation of current with monomer concentration (C) DPV of PROP in 0.1M PBS 7 (D) calibration plot

Table 2. Comparative study of some of the existing electrochemical sensors for PROP with our work

| Electrode                  | Concentration range (µM) | Supporting electrolyte | Reference |
|---------------------------|--------------------------|------------------------|-----------|
| Pt/MWCNT/GCE              | 0.68 – 38                | 0.1 M PBS 7            | [9]       |
| CuO/CPE                   | 10-104                   | 0.15 M B R Buffer      | [10]      |
| Ta – C: N electrode       | 0.9 – 9.8                | 0.5 M H₂SO₄            | [11]      |
| BDD                       | 0.2 – 9                  | 0.1 M H₂SO₄            | [15]      |
| 3D – hybrid/Au            | 0.1 – 20                 | 0.07 M PBS 7.4         | [16]      |
| Pd/MWCNT/nafion           | 200 – 2500               | 0.05 M H₂SO₄           | [17]      |
| Poly NA - PGE             | 1 – 20                   | 0.1 M PBS 7            | Present Work |

3.4.4. Pharmaceutical application and comparative study with reported works.

The developed sensor was efficaciously applied to determine the PROP content from the pharmaceutical tablets using DPV and the results are displayed in table 1. The obtained concentration of the tablet Ciplar LA was compared with the added concentration and a good result was obtained with a percentage error of 6.6%. Also, the present work was compared with few of the literature reports for the electrochemical studies of PROP and is given in table 2. It highlights that our work is novel, as the poly nicotinamide modified PGE was used for the determination of PROP from real sample.

4. CONCLUSION

A novel and cost-effective electrochemical sensor for the antihypertensive drug propranolol hydrochloride was reported. Electrode modification was done by the electropolymerisation of nicotinamide on the PGE. The morphological studies of the electrode were done by SEM. A linear range in the concentration range of 1µM – 20 µM was obtained in the DPV studies. The electrode exhibited good repeatability with an RSD of 3.5% and was applied analytically to determine the PROP from pharmaceutical formulations with an error of only 6.6%.
ACKNOWLEDGMENTS

The authors thankfully acknowledge KVSR Siddhartha College of Pharmaceutical Sciences, India, for providing the propranolol hydrochloride as a gift sample. Also acknowledge Amrita Centre for Nano Sciences, Kochi for the SEM analysis.

REFERENCES

[1] Mousa W, KuesK, HaasE, Lauerer P, Pavlakovic H, Schön M and Zutt M 2010 J Dtsch Dermatol Ges. 8 184-86
[2] Dezsi CA, and Szentes V 2017 Am J Cardiovasc Drugs 17 361-73
[3] Srinivasan A, 2019 Ann Indian Acad Neurol 22 21-26
[4] Idowu O S, Adegoke O A, and Olaniyi A A 2004 Journal of AOAC International 87 573-78
[5] Gowda B G, Seetharamappa J and MelwankiM B 2002 Analytical sciences 18 671-74
[6] Khalil S and BorhamN 2000 Journal of pharmaceutical and biomedical analysis 22 235-40
[7] GotardoM A, Tognolli JO, PezzaH R and Pezza L 2008 Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 69 1103-09
[8] El-Saharty Y 2003 Journal of pharmaceutical and biomedical analysis 33 699-709
[9] KunZ, Yi H, Chengyun Z, Yue Y, ShuliangZ and YuyangZ 2012 Electrochimica Acta 80 405-12
[10] Shadjou N, Hasanzadeh M, Saghatforoush L, Mehdizadeh R and Jouyban A 2011 Electrochimica Acta 58 336-47
[11] LourencaoBC, SilvaT A, Fatibello-FilhoO and SwainG M 2014 Electrochimica Acta 143 398-406
[12] Krishnan RG, GreeshmaS, Morris D S, Rameshan S S and BeenaS 2019 Materials Today: Proceedings 18 3314-20
[13] Rejithamol R, Keerthi P and BeenaS 2019 Materials Today: Proceedings 18 5081-86
[14] Teradale A, GaneshP and DasS 2018 Anal. Bioanal. Electrochem 10 203-219
[15] SartorierER, MedeirosR A, Rocha-FilhoR Cand Fatibello-Filho O 2010 Talanta 81 1418-24
[16] Łuczak T 2019 Ionics 25 5515-25
[17] Gioia D and Casella IG 2016 Sensors and Actuators B: Chemical 237 400-407