Research Article

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An effective, novel, and cheap carbon paste electrode for naproxen estimation

https://doi.org/10.1515/rev-ac-2022-0041
received October 11, 2021; accepted June 05, 2022

Abstract: Herein, a carbon paste electrode (CPE) modified with poly(reduced-o-nitrobenzoic acid [r-o-NBA]) supported in graphene quantum dots (GQDs) was fabricated for the first time. The fabricated electrode’s surface morphology and composition were characterised by scanning electron microscope and transmission electron microscope. The poly(r-o-NBA)/GQDs/CPE showed high electrocatalytic activity towards the oxidation of naproxen (NPX) using cyclic and differential pulse voltammetric methods. The effect of scan rate on the oxidation peak of NPX suggests that the electrode process was typically diffusion-controlled. In addition, the effect of pH reflects the participation of protons in the oxidation process of NPX. The peak current is linearly proportional to the concentration of NPX ranging from 1.0 to 100.0 µM, with the correlation coefficient (R²), sensitivity, limit of detection (LOD), and limit of quantification (LOQ) being 0.9995, 0.419 µA·µM⁻¹·cm⁻², 0.672, and 2.241 µM, respectively. Using chronoamperometry, the diffusion coefficient of NPX at the poly(r-o-NBA)/GQDs/CPE was estimated to be 5.36 × 10⁻⁶ cm²·s⁻¹. The proposed electrode has good reproducibility, stability, and high selectivity for NPX oxidation. The obtained recovery range (96.7–102.0%) means that the proposed sensor performed satisfactorily when applied for the detection of NPX in its pharmaceutical formulations.

Keywords: naproxen, modified carbon paste electrode, graphene quantum dots, cyclic voltammetry, differential pulse voltammetry, chronoamperometry

1 Introduction

Naproxen (NPX), also known as 2-(6-methoxynaphthalen-2-yl)propanoic acid, is a non-steroidal anti-inflammatory drug. The importance of NPX as a non-steroidal anti-inflammatory comes from its analgesic and antipyretic properties [1]. NPX is commonly used in the treatment of severe pain, fever, inflammation caused by rheumatoid arthritis, ankylosing spondylitis, primary dysmenorrhea, and degenerative joint disease [2,3]. NPX acts in the inhibition of the cyclooxygenase enzyme, which prevents the biosynthesis of certain prostaglandins [4]. Therefore, accurate quantification of NPX is essential and has attracted much attention.

In recent years, the most frequently used conventional methods of NPX detection have been spectrophotometry [5,6], spectrofluorimetry [7,8], capillary electrophoresis [9], and chromatography techniques [10,11]. These methods are undoubtedly precise, but they require protracted analysis, time-consuming detection processes, and professional operators [12,13]. However, it is important to remember that chromatographic methods can be used to estimate more than one analyte at a time.

The electrochemical methods, on the other hand, are among the various sensors used in recent years for NPX detection due to their high sensitivity, portability, selectivity towards electroactive species, simple preparation methods, and quick response [14,15]. Unfortunately, the electrochemical determination of NPX on a bare electrode suffers from a poor response and high overpotential. Therefore, a variety of modified electrodes can provide some useful advantages in electrochemical responses.

Graphene quantum dots (GQDs) consist of thin sheets of graphene that can provide a large surface area, high
electrocatalytic activity, speedy electron transfer rate, and high sensitivity of the electrode [16,17]. The new zero-dimensional compound (GQDs) consists of single or multiple layers of graphene with a thickness and a diameter of less than 30 and 20 nm, respectively [17]. The absence of electrode fouling is an important factor for the modified electrodes [18]. Therefore, their low cytotoxicity, high surface area, and excellent solubility make GQDs excellent candidates for the modification of different substrates (such as glass, carbon, and graphite). Furthermore, a polymeric thin film can increase the modified electrodes’ stability, reproducibility, and active sites [19]. A polymer film of reduced-o-nitrobenzoic acid (r-o-NBA) can be easily formed on the surface of carbon paste electrode (CPE) through electropolymerisation. To the best of our knowledge, the application of a polymer film of r-o-NBA on GQDs/CPE to detect NPX as reported here is the first of its kind.

In this study, our interest was to further improve the properties of the CPE with poly(r-o-NBA) supported in GQDs to facilitate the detection of NPX. It was investigated whether the presence of a polymer film of r-o-NBA along with GQDs makes CPE a sensitive electrode for NPX determination in real samples.

2 Experimental section

2.1 Chemical reagents and solutions

NPX (98.0%), hydrochloric acid (HCl, 32.0%), and sulphuric acid (H2SO4, 98.0%) were purchased from Sigma-Aldrich. Citric acid (CA), sodium hydroxide, monosodium phosphate, and disodium phosphate were procured from El-Nasr Pharmaceutical Chemicals (Egypt). In our experiments, all the chemical reagents were of analytical grade unless otherwise stated and were used directly without any further purification. All solutions were freshly prepared using ultrapure water (18.2 MΩ cm−1) at room temperature. A buffer solution of 0.1 M NaH2PO4–Na2HPO4 (phosphate-buffered saline [PBS], pH 7.0) was used as the supporting electrolyte. The NPX stock solution was prepared daily by dissolving an exact amount of NPX in PBS, with a concentration of 1.0 mM of NaOH and HCl solutions being used to adjust for the desired pH.

2.2 Apparatus and cell

The electrochemical experiments were performed using an EG&G Princeton Applied Research Potentiostat/Galvanostat model 263A (USA) in a three-electrode microcell (model K0264), in which a highly pure platinum wire (model K0266) and Ag/AgCl saturated with KCl (model K0265) were utilised as auxiliary and reference electrodes, respectively. At the same time, a bare CPE and the poly(r-o-NBA)/GQDS/CPE were used as the working electrode. A CyberScan pH 500 Meter (EuTech, India) was employed to adjust pH values. The synthesized GQDs were characterised by a Fourier-transform infrared spectrometer (FT-IR; JASCO [FT/IR-4100]) and powder X-ray diffraction (XRD; X’Pert Powder; Malvern Panalytical B.V., The Netherlands). The surface morphology of the working electrode was probed with a scanning electron microscope (SEM; QUANTA FEG250) and a transmission electron microscope (TEM; JEOL 2100 HRTEM 200V, Tokyo, Japan). Ultra-performance liquid chromatographic analysis was utilised using LC-20ADXR liquid chromatography (Shimadzu, Japan).

2.3 Synthesis and characterisation of GQDs

The GQDs were synthesised by directly pyrolysing CA, as described by Dong et al. [20]. In brief, a balloon flask containing 2.0 g of CA was slowly heated to 200°C. The colour of the molten CA changed from pale yellow to orange in 30 min, implying the formation of GQDs. The orange liquid obtained was added drop by drop into 100 mL of 1 M HCl. The prepared GQDs were characterised by FT-IR using a PerkinElmer Spectrum-100. As shown in Figure 1a, the FT-IR of the synthesized GQDs exhibits absorption of functional groups characteristic of the hydrophilic regions. The absorption bands at near ~3,429, 2,854, 1,629, and 1,275 cm−1 are attributed to stretching vibration of OH, CH, CO, and COC, respectively. This means the surface of GQDs contains hydroxyl, alkyl, carboxyl, and carbonyl groups [20]. In addition, the XRD analysis of GQDs is shown in Figure 1b to investigate the crystalline nature of GQDs. As can be seen, there are two diffraction peaks centred at around 9.5° and 25.1° (2θ), which correspond to amorphous carbon. The appearance peak with a high degree (as a result of the carbonisation of CA) was corresponding to an interlayer d-spacing of 0.36 nm. The UV-Vis absorption spectra for the synthesized GQDs in the wavelength range of 200–500 nm are shown in Figure 1c. The GQDs display two absorption peaks at wavelengths of 210 and 262 nm, as can be seen. It can be observed that the GQDs exhibit two absorption peaks near ~210 and 262 nm. The first one may be attributed to the absorption of graphene derivatives. While the other one originates from a π–π* transition of aromatic C=C bonds.
2.4 Fabrication of the bare CPE and the poly(r-o-NBA)/GQDs/CPE

Fabrication of CPE was performed by grinding graphite powder and paraffin wax, which was heated till melting, in the ratio of 70:30 (w/w) in a mortar and pestle for 25 min. After homogenisation, the paste was carefully packed into the cavity of the Teflon tube and smoothed on a soft paper. Furthermore, a copper wire inserted into the tube served to provide electrical contact. A CPE was modified with GQDs by hand mixing 60% graphite powder and 10% GQDs with 30% paraffin wax, while the polymer film of r-o-NBA could be formed by immersing the GQDs/CPE in 0.1 M PBS (pH = 7.0) containing 5.0 mM

Figure 1: FT-IR spectrum (a), XRD pattern (b), and UV-Vis absorption (c) of GQDs.
monomer of o-NBA. Then, the potential was cycled between 0.8 and −1.5 V (vs Ag/AgCl) for 8.0 cycles at a scan rate of 100 mV s⁻¹. The poly(r-o-NBA)/GQDs/CPE was thoroughly rinsed with ethanol and deionised water to remove unreacted monomer before drying at room temperature.

2.5 Pharmaceutical sample preparation

Five sodium NPX tablets (containing various species) were accurately weighed and ground to a fine powder to prepare a 0.1 M NPX stock solution in a 25 mL volumetric flask containing PBS (pH = 7.0). After analysis by the proposed sensor, the percent recovered was estimated, relating the concentration of the analyte found to the concentration expected.

3 Results and discussion

3.1 Electropolymerisation of o-NBA on the surface of GQDs/CPE

The electropolymerisation of o-NBA was performed on the surface of GQDs/CPE by cyclic voltammetry (CV). In an aqueous medium, o-NBA exists as o-nitrobenzoate with a pKa value of 3.41 [21]. Figure 2 depicts the CVs of 5.0 mM o-NBA in 0.1 M PBS (pH = 7.0) at a scan rate of 100 mV s⁻¹. As can be seen in the first scan, three reductive and one oxidative peak appeared at potentials of around −0.32, −0.58, −0.86, and 0.04, respectively. This means the reduction of nitrobenzoate to hydroxylamine benzoate is represented by PC1. At the same time, further reduction of the formed hydroxylamine benzoate to an aminobenzoate is represented by PC2 [22]. Also, the cathodic peak (PC) was paired with the anodic peak (PA) and corresponded to the redox of nitrobenzoate [23]. Furthermore, all the peak currents increased gradually with the enhancement of cyclic sweep, indicating the polymer film’s continuous growth.

3.2 Characterisation of the bare CPE and the poly(r-o-NBA)/GQDs/CPE

SEM is one of the important techniques used to study the surface morphology of thin films. Therefore, Figure 3 shows the SEM images of a bare CPE (Figure 3a) and the poly(r-o-NBA)/GQDs/CPE (Figure 3b). It is clear from Figure 3a that the surface of the bare CPE reveals a randomly arranged flakes-like structure with ridges and grooves. Moreover, a very thin film of paraffin wax can be seen covering the graphite particles. However, the SEM image of the poly(r-o-NBA)/GQDs/CPE (Figure 3b) revealed a completely different structure morphology, which is disclosed to be uniform. A homogeneous dispersion of the composites with scaly shape on the surface of the CPE can be observed. In addition, the TEM image was used to confirm the decoration of the poly(r-o-NBA) at the prepared GQDs/CPE (Figure 3c). As is observed, GQDs exhibit spherical shape, with a diameter ranging from 4 to 15 nm and are covered with a polymer film of r-o-NBA [24,25].

3.3 Electrochemical response of NPX at various electrodes

The electrochemical response of NPX at the bare CPE, the GQDs/CPE, and the poly(r-o-NBA)/GQDs/CPE was investigated by CV in a potential window ranging from −0.5 to 1.5 V (vs Ag/AgCl). Figure 4 depicts CVs of 0.5 mM NPX in 0.1 M PBS with pH 7.0 at a scan rate of 100 mV s⁻¹ for the bare CPE (Figure 4a), the GQDs/CPE (Figure 4b), and the poly(r-o-NBA)/GQDs/CPE (Figure 4c). As can be observed, there is no response for the bare CPE towards NPX. However, the presence of GQDs caused a well-defined oxidative peak that appeared at 0.88 V, with no apparent peak found in the reverse scan. This potential value for NPX oxidation

![Figure 2: CVs of 5.0 mM o-NBA in 0.1 M PBS (pH = 7.0) at the GQDs/CPE with a scan rate of 100 mV s⁻¹.](image-url)
Figure 3: (a) SEM image of the bare CPE, (b) SEM image of the poly(\(\alpha\)-NBA)/GQDs/CPE, and (c) TEM image of the poly(\(\alpha\)-NBA)/GQDs/CPE.

Figure 4: CVs of 0.5 mM NPX in 0.1 M PBS (pH = 7.0) using a bare CPE (a), the GQDs/CPE (b), and the poly(\(\alpha\)-NBA)/GQDs/CPE (c) at a scan rate of 100 mV s\(^{-1}\).
may be as a result of the formation of a cation that is stabilised through the resonance structures of the methoxy-naphthyl ring. This behaviour indicates the totally irreversible electrode process for the oxidation reaction of NPX. Under identical conditions, the peak current signal of NPX was significantly enhanced on the poly(η-o-NBA)/GQDs/CPE. This might be attributed to the more active sites caused by the composite. In addition, the polymer film improved the conductivity and facilitated electron transfer between NPX and the electrode surface.

3.4 Effect of scan rate

The effect of scan rate helps understand the nature of the electrocatalytic process. Figure 5 depicts the voltammetric response of 0.5 mM NPX in 0.1 M PBS (pH 7.0) using the poly(η-o-NBA)/GQDs/CPE at various scan rates. It is revealed that the anodic peak current of NPX goes on increasing over the scan rate of 20–200 mV s⁻¹. In addition, the oxidation peak potential shifted to more positive values as the scan rate was increased, which verified the irreversible oxidation of NPX. The inset of Figure 5 displays the linear dependence of the anodic peak current on the square root of scan rate. The regression line equation can be represented as:

\[ I_p(\mu A) = 12.991v^{1/2}(mV \cdot s^{-1})^{1/2} + 20.62 \]  

with \( R^2 = 0.9995 \), suggesting that the electrode process for NPX was typically diffusion-controlled [26,27].

3.5 Effect of pH

It is known that the pH of the buffer solution has an important role in the analyte’s current response. Therefore, the effect of pH on the peak current and peak potential of NPX was investigated using 0.1 M PBS in the pH range (3.0–9.0), as shown in Figure 6a. Results revealed that the peak potential of NPX decreased linearly along with an increase in the pH value. The regression line equation \( E_p (V) = 0.189 - 0.013 \text{pH} \) with \( R^2 = 0.9982 \) (far from the theoretical slope, 59 mV per pH unit) indicates that proton was not involved in NPX oxidation [28,29]. In addition, with the increase in pH values, the anodic peak current of NPX goes on increasing up to 7.0, then decreases. Thus, pH of 7.0 was used as an optimal value for the electrochemical oxidation of NPX at the poly(η-o-NBA)/GQDs/CPE.

![Figure 5: CVs of 0.5 mM NPX in 0.1 M PBS (pH = 7.0) on poly(η-o-NBA)/GQDs/CPE at different scan rates from a to h (20, 30, 50, 60, 80, 100, 150, and 200 mV s⁻¹). Inset: the plot of \( I_p \) versus \( v^{1/2} \).](image-url)
Tafel curve (Figure 6b) was employed to determine the number of electrons involved in the electrochemical oxidation of NPX. Thus, the Tafel slope of 0.323 V was obtained, which means that the electrochemical oxidation process of NPX involves a one-electron transfer. According to the aforementioned results, a reaction oxidation mechanism of NPX was proposed as shown in Scheme 1, which is in agreement with previously reported data [28,29].

3.6 Effect of NPX concentration

Differential pulse voltammetry (DPV) is one of the voltammetric techniques with high sensitivity and better resolution [30,31]. Accordingly, DPV was used to measure NPX at different concentrations. In this method, the poly(r-o-NBA)/GQDs/CPE was immersed in 0.1 M PBS (pH = 7.0) containing various concentrations of NPX as shown in Figure 7. As a result, the rise in NPX concentration from 1.0 to 100 µM led to an obvious increase in the anodic peak current. Furthermore, the inset of Figure 7 depicts the calibration curve obtained by plotting the anodic peak current versus NPX concentration. A good linear equation was calibrated as:

\[ I_p(\mu A) = 0.419C(\mu M) + 0.325 \]  

with the correlation coefficient \( R^2 \), sensitivity, limit of detection (LOD; 3\( \sigma \)), and limit of quantification (LOQ; 10\( \sigma \)) being
0.9995, 0.419 µA·µM⁻¹·cm⁻², 0.672, and 2.241 µM, respectively. As shown in Table 1, the poly(r-o-NBA)/GQDs/CPE has a lower detection limit for NPX compared to the other reported electrodes.

### 3.7 Chronoamperometry studies

Chronoamperometry, which measures current versus time in response to a potential pulse, was employed to study the electrochemical oxidation of NPX at the poly(r-o-NBA)/GQDs/CPE. Figure 8 displays the chronoamperograms of 0.1 M of PBS (pH = 7.0) containing different concentrations of NPX (0.5–3.0 mM). Under diffusion control, a linear dependence of the current on $t^{-1/2}$ was obtained for various concentrations of NPX (Figure 8a). The resulting slopes of these relationships were then plotted versus the NPX concentration, as shown in Figure 8b. Using the slopes and the Cottrell equation [34]:

$$I = \frac{nFAD}{4\pi RT} \frac{1}{2} \left( \frac{D}{v} \right)^{1/2} \sqrt{t}$$

With $I$ as the current, $n$ as the number of electrons, $F$ as the Faraday constant, $A$ as the electrode area, $D$ as the diffusion coefficient, $R$ as the gas constant, $T$ as the temperature, and $v$ as the scan rate.

### Table 1: Analytical parameters of several reported electrodes for the determination of NPX

| Method               | Electrode                                      | Linear range (µM) | Sensitivity (µA·µM⁻¹) | LOD (µM) | Reference |
|----------------------|------------------------------------------------|-------------------|------------------------|----------|-----------|
| Square-wave voltammetry | ZnO/multi-walled carbon nanotubes (MWCNT)/CPE | 1.0–200           | 0.256                  | 0.23     | [26]      |
| DPV                  | Graphite electrode                             | 1.96–18.18        | 4.19                   | 0.68     | [27]      |
| Linear sweep voltammetry | Poly(-serine)-glassy carbon electrode (GCE) | 4.3–65.0          | 0.28                   | 0.69     | [28]      |
| Amperometry (AMP)    | Shorter diameter-MWCNT/GCE                     | 10.0–1,000        | 0.050                  | 1.90     | [29]      |
| DPV                  | Grapene oxide/GCE                              | 10.0–1,000        | 0.60                   | 1.94     | [30]      |
| AMP                  | MWCNT–GCE                                      | 10.0–100          | 0.394                  | 0.60     | [31]      |
| DPV                  | MWCNTs-Gr-II/GCE                               | 1.0–100           | —                      | 0.125    | [32]      |
| DPV                  | Pt electrode                                   | 4.0–100           | 0.114                  | 1.0      | [33]      |
| DPV                  | Poly(r-o-NBA)/GQDs/CPE                         | 1.0–100           | 0.419                  | 0.672    | This work |
In $F_\text{A DC} \pi t b$

where the bulk concentration and the diffusion coefficient are represented by $C_b$ (mol·cm$^{-3}$) and $D$ (cm$^2$·s$^{-1}$), respectively, and the other symbols have their usual meaning.

The $D$ value of NPX at the poly(r-o-NBA)/GQDs/CPE was estimated to be $5.36 \times 10^{-6}$ cm$^2$·s$^{-1}$.

### 3.8 Reproducibility and stability

The reproducibility of the poly(r-o-NBA)/GQDs/CPE towards the NPX detection was investigated. The reproducibility of the fabricated electrode was evaluated daily by successive measurements of seven solutions of 0.1 M PBS (pH = 7.0) containing 0.5 mM of NPX as shown in Figure 9, leading to a relative standard deviation of 2.73%. Moreover, the long-term stability of the modified electrode was evaluated. Over 5 weeks, the anodic peak signal decreased by 2.3% when the poly(r-o-NBA)/GQDs/CPE was kept in 0.1 M PBS at room temperature. The absence of any major change in the current response of NPX indicates that the proposed electrode has good reproducibility and high stability.

### 3.9 Interference effect

To appraise the selectivity of the poly(r-o-NBA)/GQDs/CPE, the influence of several interferences on the detection of NPX was investigated. Various interference species were individually added to 0.1 M PBS (pH = 7.0) containing 0.5 mM of NPX. The results indicated that the common

$$I = nFAD^{1/2}C_b\tau^{-1/2}t^{-1/2}$$

where the bulk concentration and the diffusion coefficient are represented by $C_b$ (mol·cm$^{-3}$) and $D$ (cm$^2$·s$^{-1}$), respectively, and the other symbols have their usual meaning.

The $D$ value of NPX at the poly(r-o-NBA)/GQDs/CPE was estimated to be $5.36 \times 10^{-6}$ cm$^2$·s$^{-1}$.
ions such as Na⁺, K⁺, Ca²⁺, Mg²⁺, NO₃⁻, SO₄²⁻, and Cl⁻ did not show interference with NPX detection. CA, tartaric acid, glucose, lactose, alanine, and cysteine have no obvious interference in NPX determination. Not only this, but also no notable response to ibuprofen, diclofenac, and meloxicam was observed, as summarised in Table 2.

### 3.10 Sample analysis

According to the obtained results, the poly(r-o-NBA)/GQDs/CPE could be applied to the quantitative analysis of pharmaceutical forms (tablets, 250 and 500 mg) containing NPX. The standard addition method was used to obtain the various concentrations of NPX, and the results are given in Table 3. Satisfactory recoveries ranging from 96.7% to 102.0% were obtained, which indicates the accuracy of the proposed method. Moreover, two pharmaceutical samples of NPX were analysed using the proposed DPV and high-performance liquid chromatography (HPLC) methods, and the results are summarised in Table 4. The data confirmed that the proposed method is in strong agreement with the HPLC method. Therefore, the poly(r-o-NBA)/GQDs/CPE based on the proposed method can be successfully applied for NPX detection in pharmaceutical tablets.

### 4 Conclusion

A simple and cost-effective electrochemical modification was employed to further improve the properties of the CPE. Herein, a CPE was modified with synthesised GQDs and a polymer film of r-o-NBA, and its surface was characterised with SEM and TEM analyses. The fabricated poly(r-o-NBA)/GQDs/CPE showed favourable electrocatalytic behaviour towards the NPX oxidation. The peak current of NPX increased with an increase in the scan rate in the range of 20–200 mV·s⁻¹. Also, a linear dependence of the anodic peak current versus NPX concentration was obtained from 1.0 to 100 µM using the DPV technique. The values of correlation coefficient (R²), sensitivity, LOD (3σ), and LOQ (10σ) were calculated to be 0.9995, 0.419 µA·µM⁻¹·cm⁻², 0.672, and 2.241 µM, respectively. According to the chronoamperometry study, the diffusion coefficient of NPX at the poly(r-o-NBA)/GQDs/CPE was calculated to be 5.36 × 10⁻⁶ cm²·s⁻¹. Good reproducibility, stability, and high selectivity were achieved for the fabricated electrode in NPX detection in the real sample.

**Acknowledgments:** The authors extend their appreciation to the Deanship of Scientific Research at Imam Mohammad Ibn Saud Islamic University for funding this work through Research Group No. RG-21-09-72.

**Author contributions:** Mohamed Abd-Elsabour: experimental work, writing – original draft, writing – review and editing; Mortaga M. Abou-Krisha: writing – review and editing, formal analysis; Abdulrahman G Alhamzani: visualisation, writing; Tarek A. Yousef: writing – review and editing, formal analysis, project administration.

**Conflict of interest:** The authors state no conflict of interest.

**Data availability statement:** All data are included in the manuscript.
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