



Article

Ultrasensitive Electrochemical Sensor Based on SnO₂ Anchored 3D Porous Reduced Graphene Oxide Nanostructure Produced via Sustainable Green Protocol for Subnanomolar Determination of Anti-Diabetic Drug, Repaglinide

Ayyapayya Mathad ¹, Karuna Korgaonkar ¹, Seetharamappa Jaldappagari ^{1,*} and Shankara Kalanur ^{2,*}¹ Department of Chemistry, Karnatak University, Dharwad 580003, India² Hydrogen Research Institute (IRH), Université du Québec à Trois-Rivières, 3351 Boulevard des Forges, Trois-Rivières, QC G9A 5H7, Canada

* Correspondence: drjseetharamappa@kud.ac.in (S.J.); shankara.kalanur@uqtr.ca (S.K.)

Abstract: Herein, we have reported on a simple, environmentally friendly, and ultra-sensitive electrode material, SnO₂@p-rGO, used in a clean sustainable manner for rapid electrochemical determination of an anti-diabetic agent, repaglinide (RPG). Three-dimensional porous reduced graphene oxide nanostructure (p-rGO) was prepared via a low-temperature solution combustion method employing glycine. The aqueous extract of agricultural waste “cotton boll peel” served as stabilizing and reducing agents for the synthesis of SnO₂ nanoparticles. The structural and morphological characterization was carried out by XRD, Raman, SEM, EDX, FTIR, absorption, and TGA. The oxidation process of RPG was realized under adsorption controlled with the involvement of two protons and electrons. The sensor displayed a wider linearity between the concentration of RPG and oxidation peak current in the ranges of 1.99×10^{-8} – 1.45×10^{-5} M and 4.99×10^{-8} – 1.83×10^{-5} M for square-wave voltammetric and differential pulse voltammetric methods, respectively. The lower limit of detection value of 0.85×10^{-9} M was realized with the SWV method. The proposed sensor was applied for the quantification of RPG in fortified urine samples and pharmaceutical formulations. Furthermore, the sensor demonstrated reproducibility, long-term stability, and selectivity in the presence of metformin and other interferents, which made the proposed sensor promising and superior for monitoring RPG.

Keywords: Porous reduced graphene oxide; SnO₂ nanoparticles; sensor; repaglinide



Citation: Mathad, A.; Korgaonkar, K.; Jaldappagari, S.; Kalanur, S.

Ultrasensitive Electrochemical Sensor Based on SnO₂ Anchored 3D Porous Reduced Graphene Oxide Nanostructure Produced via Sustainable Green Protocol for Subnanomolar Determination of Anti-Diabetic Drug, Repaglinide. *Chemosensors* **2023**, *11*, 50. <https://doi.org/10.3390/chemosensors11010050>

Academic Editor: Chunsheng Wu

Received: 5 December 2022

Revised: 29 December 2022

Accepted: 3 January 2023

Published: 6 January 2023

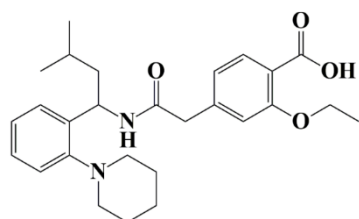


Copyright: © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Type 2 diabetes mellitus is the most prevalent metabolic ailment worldwide, affecting nearly 8% of young people and growing explosively over the last few years, with predictions that by 2030, there would be around 400 million cases [1]. The disorder results from increasing β cell malfunction in the presence of chronic insulin resistance that causes a progressive deterioration in plasma glucose homeostasis. Repaglinide (RPG) (Scheme 1), a novel rapid-acting meglitinide analog, is an oral hypoglycemic drug from the class of carbamoylmethylbenzoic acids. It is safe and efficacious. Therefore, it is widely prescribed to control postprandial glucose excursion in type 2 diabetic patients. It is particularly beneficial when metformin cannot be administered owing to side effects and fails to control blood glucose levels effectively or blood glucose levels cannot be managed by exercise or diet alone. Although the insulinotropic action of RPG is partly comparable to sulfonylureas, it displays distinct pharmacological properties in terms of structure, binding profile, mechanisms of excretion, and duration of action [2]. REP decreases hyperglycemia by stimulating the pancreas by depolarization of β cells [3] via ATP-sensitive potassium channel blockage at the plasma membrane, resulting in Ca²⁺ influx through voltage-dependent channels,

which stimulates Ca^{2+} dependent exocytosis of insulin-containing granules and subsequent release of insulin [4]. It shows a fast onset of dose-dependent blood-glucose-lowering effect after rapid and complete absorption from the gastrointestinal tract [5], and subsequently, the drug is removed rapidly through biliary excretion without accumulation in the plasma after multiple doses. Hence, RPG is well tolerated in type 2 diabetic patients who are elderly patients and patients with renal or hepatic impairment. Given the biological importance of RPG, the monitoring of it in biological fluids is crucial. Hence, efforts have been made to develop low-cost sensors for clinical use.



Scheme 1. Structure of repaglinide.

For the determination of RPG in dosage forms, raw material, and plasma, a number of analytical methods have been reported. These include HPLC [6–8], HPLC integrated with electrochemical detection [9], ultra-violet [10], liquid chromatography–tandem mass spectrometric (LC-MS/MS) [11,12], reversed-phase thin-layer chromatographic (RPTLC) [13], spectrophotometric [14], and reversed-phase-HPLC [15] methods.

However, most of the reported methods involve complicated and costly instruments, lengthy pretreatment processes, and laborious sample preparations. In addition, they require trained technicians. The regular analysis of RPG thus demands a straightforward, sensitive, and inexpensive method. Therefore, electrochemical sensing methods are better alternatives. They have received more and more attention because they are simple, sensitive, economical, and rapid for the determination of traces of electroactive analytes [16–20]. However, the reported electrochemical methods [21,22] for the assay of RPG have low sensitivity or require more time for the fabrication of electrochemical sensors. In view of developing a simple, ultrasensitive, and eco-friendly sensor utilizing inexpensive environmentally friendly reagents, we have fabricated $\text{SnO}_2/\text{p-rGO}$ on GCE for the assay of RPG at trace level.

Graphene is a single sheet of an sp^2 hybridized two-dimensional form of carbon allotrope. As a first created 2D material, it became a cornerstone in the field of materials science research. This was motivated by its exquisite and unique physical and chemical properties, leading to a wide spectrum of applications. It has been explored in the areas of photonics, electronics, sensors, catalysis, energy generation and storage, electroensing, metrology, environment, and bioapplications [23,24]. It is a highly appealing electrode material for a wide range of applications due to its superior properties, including high thermal and electronic conductivity, larger surface area, promising mechanical strength, and ease of chemical functionalization. Conversion of 2D graphene sheets into three-dimensional (3D) graphene not only avoids undesirable aggregation phenomena but also introduces desirable features of fast electronic and ionic transportation, strong mechanical properties, and higher specific area [25]. Amongst the types of nanostructures, 3D reduced porous graphene has received substantial attention from scientists recently because of its advantages, such as larger accessible surface area, enhanced catalytic activity due to higher pore volume, stronger mechanical strength, and higher conductivity [26].

The unique properties of p-rGO have highly promising applications in electrochemical energy storage [27], supercapacitors [28], fuel cells [29], electrocatalysis [30], and electrochemical sensors [31,32]. In 3D porous graphene, graphene layers are self-assembled or have holes in structures. In comparison with GO, 3D porous graphene demonstrates excellent conductivity because of the partial loss of oxygen-based surface groups and defects present in the basal plane [33]. The 3D pore structure enables easy access and

diffusion of molecules and ions throughout its structure [34]. Consequently, fast electron and mass transport kinetics occur in comparison to the original graphene, which enhances its electrochemical sensing performance. With these advantages, it has attracted growing attention as a sensing material for small drug molecules. The low-temperature solution combustion method is simple, is almost instantaneous, is inexpensive, does not require costly/toxic reagents, and is an environmentally benign method to produce huge porous surfaces in graphene-based material for electrochemical applications [35].

Additionally, reduced graphene oxide offers huge benefits in terms of capacity, activity, and electrical stability owing to its unique structure, lattice defects, and negative charge [36]. The better conductivity of rGO than that of graphene oxide is because of the loss of oxygen-based surface functional groups and the presence of defects in the basal plane [37], which restores the aromatic network of sp^2 -carbon with notable dielectric loss. An environment-friendly and inexpensive greener synthesis route for rGO is extremely important for safe application. In order to minimize the hazardous effects of certain reducing agents, a few environmentally benign reducing agents such as glucose [38], microorganisms [39], ascorbic acid, and certain amino acids [40] have been used in the recent past for the synthesis of rGO on a large scale. Amino acids and their derivatives offer specific merits due to their biocompatible and non-toxic nature. Given this, it was planned to synthesize the p-rGO material just by heating the homogeneous mixture of graphene oxide and glycine fuel suspension at 250 °C for 30 s. The present work explores glycine simultaneously as a greener reducing agent for the reduction of GO and as a fuel for combustion to produce porous microstructure in rGO.

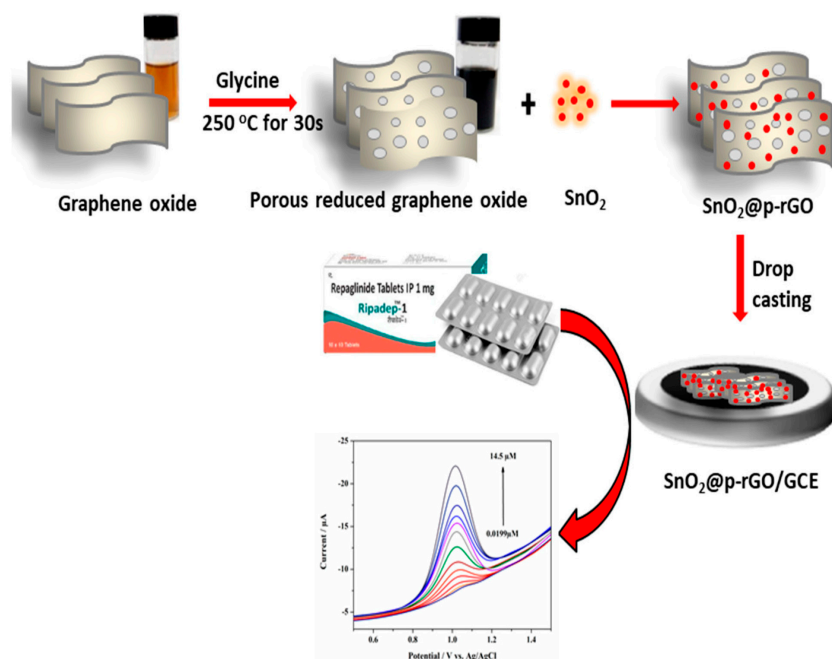
Furthermore, the electrochemical properties of rGO can be effectively enhanced further by combining with other nanostructured functional materials such as metal oxide nanoparticles [26]. Metal-oxide-nanoparticles-decorated nanocomposites were reported to enhance electrochemical sensing performance [41]. Among different metal oxide nanoparticles, tin oxide (SnO_2) nanoparticles have garnered much scientific interest as important n-type semiconductors with a vital band gap of 3.6 eV. They are broadly utilized in numerous applications such as photo electronics, microelectronics, super capacitors, solar cells, biosensors, gas sensing, lithium-ion batteries, and field emission studies [42]. There is increased use of SnO_2 as an electrode modifier material, and SnO_2 in combination with rGO has recently been employed successfully as a sensing material [43] due to its astonishing features such as high conductivity, biocompatibility, excellent band gap, economical nature, abundant availability, the existence of oxygen vacancy defects, and the most chemically and thermally stable oxidation state [43]. Furthermore, SnO_2 -based nanomaterials play a significant role in catalysis due to their intrinsic redox nature.

Green synthesis for the preparation of nanoparticles has attracted much interest on account of its merits such as a straightforward and fast reaction process, safe nature, environmentally benign status, ease in manufacturing, inexpensive nature, and low-temperature, short time, and mild reaction conditions [44]. The green synthesis of metal oxide nanomaterials using plant extracts provided promising and sustainable alternative approaches to conventional synthetic methods. The plant extracts contain phytochemicals (i.e., secondary metabolites) such as terpenoids, alkaloids, antioxidants, flavonoids, and amino acids. These exist in seeds, peels, fruits, and leaves that function as capping and reducing agents for the reduction of metal ions [22]. Given green chemistry, the preparation of SnO_2 via a simple sustainable procedure is worthwhile for sensor applications. In view of this, the tetragonal structured SnO_2 nanoparticles were synthesized via a green synthesis route using an aqueous extract of agricultural waste cotton boll peels. This extract with major constituents such as ascorbic acid, pyrogallol, gallic acid, and ellagic acid can act as both a reducing and capping mediator [45].

Consequently, rational integration of SnO_2 on p-rGO can be a promising approach to significantly improve its sensing performance due to its individual merits and synergistic interactions between two components [46]. p-rGO sheets not only support anchoring SnO_2 nanocrystals without aggregation but also can effectively improve the electron transfer

rate at the electrode by forming p–n junctions at the interfaces of n-type SnO_2 and p-type p-rGO [47], thereby promoting the electrode reaction. These nano-Schottky barriers can be controlled by the reduction or oxidation of electroactive analyte. Since the work function of p-rGO is lesser than that of SnO_2 , electrons released during the oxidation of RPG are moved to GCE via p-rGO due to their greater mobility. The concentration of electrons rises upon successive addition of RPG, which causes the barrier to become forward biased and raise the peak current at the SnO_2 @p-rGO composite modified GCE. Therefore, SnO_2 anchored p-rGO might serve as an ultrasensitive sensing interface for the determination of RPG.

The current study describes the sustainable greener synthetic protocol for the efficient synthesis of SnO_2 nanoparticles using cotton boll peel extract. For the production of porous architecture and reduction of GO, glycine was utilized as an eco-friendly reagent. Herein, we have proposed a sensitive electrochemical sensor based on an SnO_2 anchored p-rGO modified electrode (Scheme 2). The enhanced sensing performance and lower limit of detection ($8.50 \times 10^{-10} \text{ mol L}^{-1}$) in terms of electrochemical sensing of RPG and its quantification at a subnanomolar level was realized at SnO_2 @p-rGO/GCE, as the fabricated electrode material demonstrated excellent conductivity, larger surface area, and higher porosity. Further, the structure and morphology of electrode material were characterized by XRD, Raman, SEM-EDX, UV-Vis, TGA, FTIR, cyclic voltammetry, and electrochemical impedance. The performance of the fabricated sensor was evaluated for repeatability and reproducibility. The practical applications of the proposed methods were established by analyzing RPG in biological fluids and pharmaceutical formulations. The fabricated electrochemical sensor demonstrated greater selectivity, repeatability, and long-term stability.



Scheme 2. Schematic representation of fabrication process of modified electrode.

2. Materials and Methods

2.1. Chemicals and Reagents

RPG and tin chloride dihydrate ($\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$) were obtained from Sigma Aldrich, St. Louis, MI, USA. A $500 \mu\text{M}$ stock solution of RPG was prepared by dissolving a calculated amount of RPG in methanol, diluted as needed with phosphate buffer solution and refrigerated at 4°C . Agro-waste cotton peels were collected from the cotton field of Yarikoppa village, Dharwad district, Karnataka, India. The drug formulation (labeled 0.5 and 1 mg per tablet) used in the present study was obtained from the local market. The supporting electrolyte used in this study was phosphate buffer solution of pH 3.0.

2.2. Apparatus

A computer-controlled CHI6136E electrochemical workstation (CH Instruments Ltd. Co., Austin, TX, USA) operating on a three-electrode system was used to perform electrochemical experiments. Differential pulse voltammograms were recorded with a differential scan rate range of 0–1.5 with a pulse width of 50 ms and a pulse amplitude of 50 mV. To record square-wave voltammograms, a scan rate of 74.2 mVs^{-1} , potential increment of 4.95 mV, and pulse amplitude of 25.0 mV were maintained.

2.3. Material Characterization

EIS spectra were obtained on the electrochemical interface (model CHI6136E, CH Instruments Ltd. Co., Austin, TX, USA) operating on a conventional three-electrode system. A SmartLab Se, Rigaku X-ray diffractometer with $\text{Cu K}\alpha$ radiation ($1.5406 \text{ \AA}$) and Bragg's diffraction angle (2θ) of $5\text{--}90^\circ$ was employed to record the XRD patterns. FTIR spectra were obtained from a Nicolet Fourier transform infrared (FTIR) spectrophotometer (Nicolet 5700, Nicolet, Green Bay, WI, USA) in KBr medium in the mid-IR range of $4000\text{--}400 \text{ cm}^{-1}$. The NXR-FT-Raman spectrophotometer, (Nicolet 5700, Nicolet, Green Bay, WI, USA) was employed to record Raman spectra. Both elemental composition and surface morphologies of $\text{SnO}_2/\text{p-rGO}$ were examined on a JEOL (Model JSM-IT1500LA, Akishima, Japan) scanning electron microscope (SEM) with an energy dispersive X-ray analysis (EDX) facility with a magnification of 100 KX. A UV-Vis double-beam spectrophotometer (model AU-2701, Bengaluru, India) was used to record absorption spectra of samples using a 1.0 cm quartz cell. Thermogravimetric analysis (TGA) in the temperature range of $25\text{--}700^\circ\text{C}$ was carried out on a SDT-Q600 (TA Instruments, New Castle, DE, USA).

2.4. Preparation of p-rGO

In a typical synthesis of porous reduced graphene oxide, the modified Hummers method [48] was followed to prepare graphene oxide by the oxidation of graphite powder, and the low-temperature solution combustion method was then used to produce p-rGO [49]. Briefly, GO (6 mg/mL) was sonicated for 30 min in 15 mL double-distilled water to disperse it. Then, 2 g of glycine was added to the aqueous suspension of GO for the combustion process. This mixture was then heated on a hot plate (150°C) until a thick colloidal suspension was obtained. It was maintained at 250°C for 30 s in the oven. The fuel (glycine) was ignited, which resulted in the evolution of many gases from GO, leaving a black voluminous porous solid. The resulting product was washed with distilled water several times and then with ethanol. Finally, it was dried at 60°C , and the final product was labeled as p-rGO. The fabrication procedure for the modification of electrode is represented pictorially in Scheme 2.

2.5. Preparation of Cotton Peel Extract

The aqueous agro-waste cotton peel extract was prepared according to the reported method with a slight modification [45]. Freshly collected cotton boll peels were washed 3–4 times with distilled water and dried in air. Peels were cut into small pieces and ground to powder using an electric mixer. The aqueous extract was prepared by dispersing 3 g of cotton boll peel powder in 100 mL distilled water and then heating it to 80°C for 30 min in a water bath. Eventually, the aqueous extract was cooled to room temperature. Finally, it was filtered using Whatman filter paper No. 1 and then refrigerated at 4°C . The pH of the extract was found to be 3.5.

2.6. Green Synthesis of Tin Oxide Nanoparticles Utilizing Cotton Boll Peel Extract

Tin chloride dihydrate (0.329 g) was dissolved in 20 mL distilled water, and then, 20 mL aqueous extract of cotton boll peel was introduced drop-wise into tin chloride solution with stirring at 80°C . Following 30 min of heating, the light-yellow-colored solution turned to brown. The resulting mixture was then cooled to room temperature and subsequently centrifuged at 6000 rpm for 30 min. After washing with distilled water and ethanol several

times, the residue was carefully collected. Eventually, the residue was dried at 60 °C and subjected to calcination at 200 °C for 4 h to obtain SnO₂ nanoparticles.

2.7. Preparation of SnO₂@p-rGO and Fabrication of SnO₂@p-rGO/GCE

SnO₂@p-rGO nanocomposite was prepared by sonication of the mixture containing a colloidal suspension of SnO₂ (1 mg/ mL) and p-rGO (2 mg/mL) solution in 1:2 for 4 h at room temperature. The resulting homogeneous suspension was designated as SnO₂@p-rGO. Prior to each electrochemical measurement, the glassy carbon electrode was pretreated by abrading its surface with slurry of alumina powder (0.05 µm) on a polishing pad. It was then rinsed thoroughly with distilled water to yield a clean and smooth electrode surface. Later, the electrode was subjected to ultrasonication in distilled water for 30 s and finally dried in the air. A simple drop-casting method was adopted to prepare modified electrode. To fabricate a modified GCE, 5 µL (1.0 mg/mL) of SnO₂@p-rGO suspension was dropped on the clean surface of GCE and dried under the IR lamp to obtain the desired modified electrode, SnO₂@p-rGO/GCE.

2.8. Assay of Tablets

RPG containing tablets equivalent to prepare a stock solution of 1 mM were weighed and powdered. The amount of homogenized powder was dissolved in 50 mL methanol. Then, it was sonicated for 20 min. By properly diluting with the supporting electrolyte, the desired working solutions were prepared. It was then analyzed by DPV and SWV methods. Utilizing the regression equation deduced from the calibration graph, the recovery of RPG was calculated.

2.9. Quantification of RPG in Human Urine Samples

A 1 mL urine sample (drug-free) collected from healthy volunteers was combined with 1 mL RPG solution (1 mM) to obtain the stock solution for the analyte. An appropriate aliquot of urine that had been fortified with analyte was diluted with a PBS of pH 3. Then, it was taken into the electrochemical cell, and voltammograms were recorded at SnO₂@p-rGO/GCE using the DPV and SWV methods. Furthermore, the calibration plot was used to calculate the recovery of RPG.

3. Results and Discussion

3.1. Mechanism of Formation of p-rGO and SnO₂ Nanoparticles

The 3D nanostructured porous graphene was prepared by a low-temperature solution combustion method. When a colloidal suspension of GO was heated at 250 °C in the presence of glycine as a fuel, the glycine was ignited and generated a huge amount of gas in the graphene oxide suspension. When the combustion process was finished within 30 s, the suspension was converted to black powder with enlarged volume. At 250 °C, the glycine was ignited, and it reacted with epoxy, hydroxyl, and carboxyl groups (oxidizers) on the GO surface, which resulted in the reduction of GO. The reduction reaction mainly took place due to the nucleophilic attack of a -COO⁻ group of glycine on hydroxyl/epoxy group(s) present on the GO surface, forming an intermediate that yielded rGO and other decarboxylation products [50]. As a result, large amounts of bubbles of CO₂, N₂, and H₂O vapor were generated in between graphene oxide sheets of GO suspension, and pores were formed by the bubbles between layers of graphene sheets. The pores formed in the architecture have uneven sizes, since the bubbles formed during combustion have different sizes. The product, labeled as p-rGO, has a foam-like structure with several pores and enlarged volume compared to the GO suspension. The possible mechanism in the formation of SnO₂ nanoparticles is presented in Scheme S1. The water-soluble phyto-constituents with hydroxyl groups present in the agro-waste cotton boll peels aqueous extract reduced Sn²⁺ in the precursor to form Sn nanoparticles and stabilized them. Subsequently, the calcination of the residue yielded SnO₂ nanoparticles [51,52].

3.2. Structural and Morphological Characteristics

Scanning electron microscopic (SEM) images were recorded to understand the surface morphology and microstructures of GO, SnO₂, p-rGO, and SnO₂@p-rGO composite. The surface morphology of GO (Figure 1A) consisted of thin flexible stacked sheet-like texture, indicating its layered microstructure. Figure 1C presents an SEM image of SnO₂ nanoparticles, which shows the spherical morphology of SnO₂ nanoparticles with sizes in the range of 4–12 nm. The average size of SnO₂ nanoparticles was 7.8 nm, which matched with the average crystallite size obtained from XRD data. The interconnected 3D porous network-like morphological structure possessing pores with diameters ranging from nanometer to micrometer was observed in p-rGO (Figure 1B), which could provide a larger exposed surface area and electrically conductive pathway. This facilitated efficient charge transfer and mass transfer. It is reported that the interconnected 3D carbon porous network of graphene would be beneficial for the enhancement of electrochemical response when used for electrochemical sensor application [32,53]. A rough porous surface with highly dense and uniformly distributed SnO₂ nanoparticles on p-rGO microstructure was evident for hybrid SnO₂@p-rGO (Figure 1D). This increased the stability of individual p-rGO sheets by reducing the restacking of p-rGO sheets and also increased the interfacial surface area. The introduction of porosity with a 3D network in p-rGO and the attachment of SnO₂ nanoparticles to a p-rGO sheet created a high density of active sites with increased interfacial surface area. Consequently, it improved the contact between the analyte and p-rGO modified electrode surface. Hence, the electrochemically active molecules would obtain more active sites for the electron transfer reaction.

The elemental composition of SnO₂@p-rGO nanocomposite was investigated by EDX. The peaks corresponding to O, C, and Sn were observed in the EDX spectrum (Figure 1E), which revealed the purity of prepared electrode material. The percentage of these elements in the composite is given in the inset of Figure 1E.

XRD patterns of GO, p-rGO, SnO₂, and SnO₂/p-rGO are displayed in Figure 1F. The XRD pattern of GO showed a typical intense peak at $2\theta = 10.2^\circ$ (Figure 1F, a), attributable to the (001) plane with an interlayer d-spacing of 0.34 nm [54], indicating the successful preparation of GO by oxidation of graphite [39]. The peak at 24.4° for p-rGO (Figure 1F, c) due to the reflection from the (002) plane ensured that GO was transformed into graphene 2D sheets (porous reduced GO) after combustion and poor ordering of the reduced GO nanosheets along their stacking direction [53]. The diffraction pattern of SnO₂ nanoparticles (Figure 1F, b) represented nine reflections at $2\theta = 26.59, 33.84, 37.72, 51.96, 57.64, 61.85, 65.45, 71.60, \text{ and } 78.91^\circ$, which corresponded to the planes (110), (101), (200), (211), (220), (310), (301), (202), and (321), respectively (JCPDS card no. 41-1445) [55]. The characteristic peaks of pure SnO₂ could be indexed as tetragonal rutile structures for SnO₂ (space group of P42/mnm (136)). The mean crystallite size of SnO₂ nanocrystals calculated from the (110) peak using Scherrer's formula was an ultrafine 7 nm. However, the diffraction pattern of SnO₂/p-rGO nanocomposite (Figure 1F, d) displayed all the peaks corresponding to SnO₂ nanoparticles. However, no obvious peak ascribed to p-rGO was noticed in the XRD pattern, which could be due to the overlapping of the crystallographic (002) plane of p-rGO with the (110) plane of SnO₂ [56].

Raman spectroscopy was employed to understand the structural changes during the conversion of GO to p-rGO and formation SnO₂@p-rGO (Figure 2A). Raman spectra of p-rGO (Figure 2A, a) exhibited two Raman peaks at nearly 1310 and 1598 cm⁻¹, which were characterized by the disorder-induced D band and graphitic G band, respectively [57]. The D band originated from the edges, structural disorders, and defects of the graphitic structure, while the G band arose from the first-order scattering of the E_{2g} mode of graphitic carbon (sp²) [56]. The Raman spectra of the SnO₂@p-rGO (Figure 2A, b) composite contained D and G bands at 1310 and 1612 cm⁻¹, respectively. The blue shift of 13 cm⁻¹ in the G band of the composite was observed relative to the G band of the pure p-rGO. It could be owing to the electronic interaction between the SnO₂ nanoparticles and porous graphene sheets. Further, other Raman peaks situated at the low-frequency region at 495

and 653 cm^{-1} revealed the existence of E_g and A_{1g} vibrational modes of SnO_2 nanoparticles deposited on p-rGO nanosheets [58]. The estimated value of the ratio of D to G band (I_D/I_G) of the SnO_2 @p-rGO (1.21) was higher than that of the bare p-rGO (1.09), indicating the decreased sp^2 carbon domain and a higher degree of defects (C_{sp^3}). It was caused by increased vacancies, more edges and defects on the porous nanosheets surface of p-rGO [25], the porosity of the p-rGO matrix, and SnO_2 nanoparticles on the surface of graphene sheets [59].

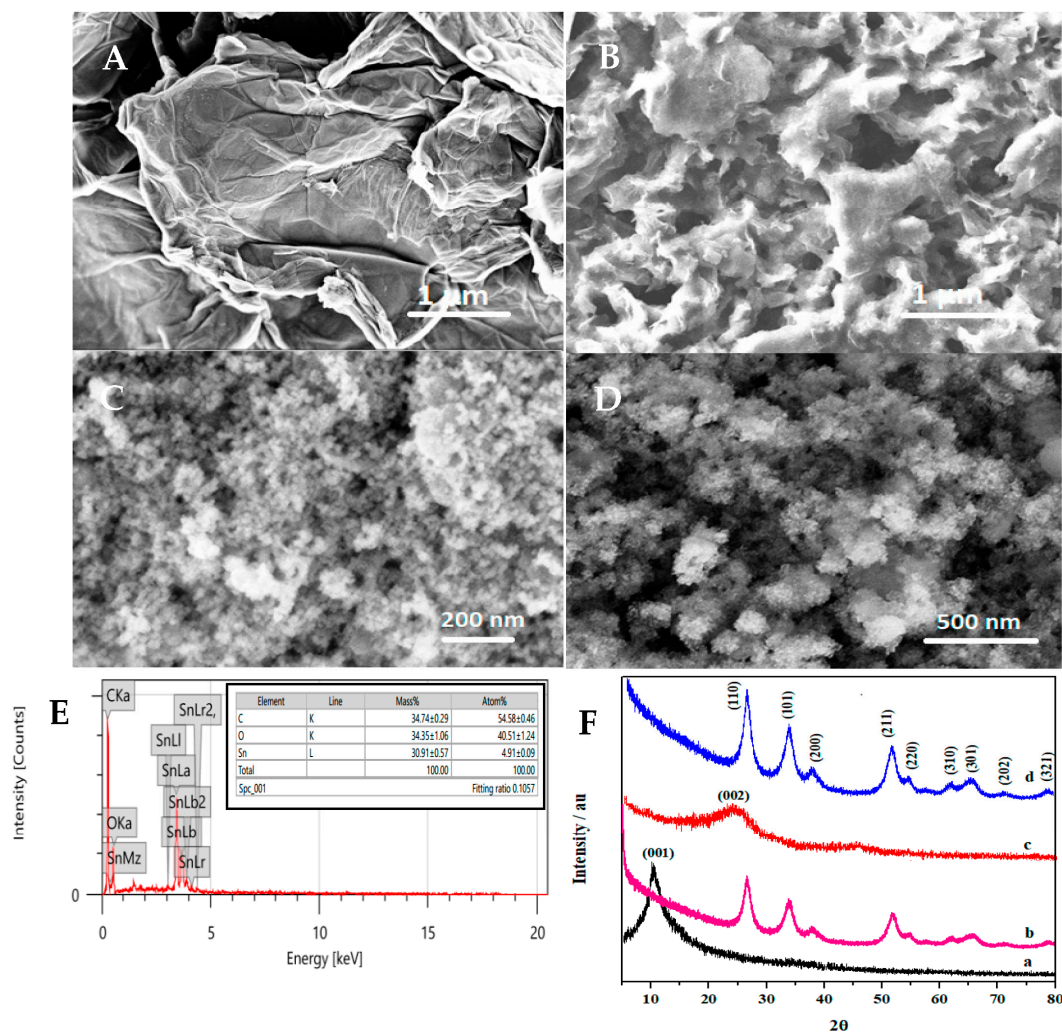


Figure 1. SEM images of (A) GO, (B) p-rGO, (C) SnO_2 (Inset: particles size distribution histogram), and (D) SnO_2 @p-rGO. (E) EDX micrograph of SnO_2 @p-rGO; inset graph represents elemental composition of SnO_2 @p-rGO. (F) Powder XRD pattern of GO (a), SnO_2 (b), p-rGO (c), and SnO_2 @p-rGO (d).

FTIR spectra (Figure 2B) were recorded to characterize the functional groups present in the sample. The FTIR spectrum of p-rGO (Figure 2B) consisted of bands at $3100\text{--}3500\text{ cm}^{-1}$ (O-H stretching vibration), 2924 and 2852 cm^{-1} (stretching vibrations of C-H), 1722 cm^{-1} (C=O stretching of carboxylic acid groups), 1630 cm^{-1} (aromatic C=C stretching), 1300 cm^{-1} (C-OH stretching of epoxide groups), and 1057 cm^{-1} (C-O stretching), which confirmed the existence of oxygenated functional groups such as carboxyl, hydroxyl, carboxylic, and epoxide groups on the p-rGO surface. Even though the process of combustion was accompanied by the reduction of GO, there were still plenty of functional groups on the surface of partially reduced graphene oxide (p-rGO) [60]. The FTIR spectrum of SnO_2 @p-rGO (Figure 2B) clearly showed the representative bands of p-rGO with reduced intensity. In addition, the characteristic absorption peak positioned at 467 cm^{-1} was attributed to the stretching vibrations of the terminal Sn-OH, while the band at 570 cm^{-1} corresponded

to the E_u mode of SnO_2 (the anti-symmetric stretching modes of Sn–O–Sn) [61], thereby demonstrating that the SnO_2 nanoparticles were anchored on p-rGO.

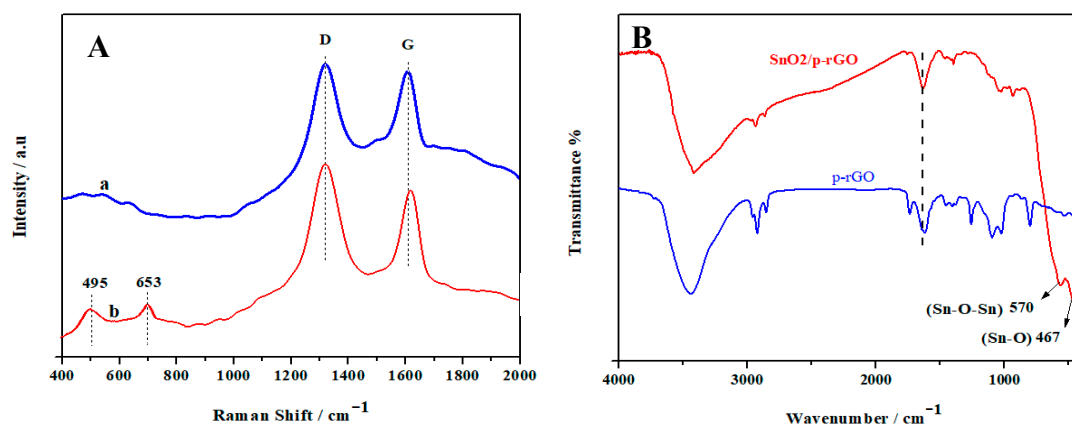


Figure 2. (A) Raman spectra and (B) FTIR spectra of p-rGO (a) and $\text{SnO}_2/\text{p-rGO}$ (b).

Absorption spectral data confirmed the formation of $\text{SnO}_2/\text{p-rGO}$. The p-rGO dispersion displayed a wavelength of maximum absorption at nearly 260 nm (as shown in Figure S1a) that corresponded to π to π^* electronic transition of aromatic C–C conjugated double bonds. In addition to this peak, another absorption peak at 330 nm was also observed for the $\text{SnO}_2/\text{p-rGO}$ composite (Figure S1c), which was the characteristic peak of SnO_2 (Figure S1b) [58]. These absorption bands confirmed the deposition of SnO_2 on p-rGO nanosheets.

The presence of SnO_2 on p-rGO was evaluated by thermogravimetric analysis (TGA), and the corresponding thermograms are presented in Figure S2. Two obvious weight loss processes were observed from TGA profiles for both p-rGO (Figure S2a) and $\text{SnO}_2/\text{p-rGO}$ (Figure S2b) samples. The initial decline and sharp drop observed in thermograms at nearly 230 $^{\circ}\text{C}$ were due to the loss of adsorbed water and pyrolysis of the various oxygen-based functional groups on the p-rGO surface. The abrupt mass loss in the second stage at nearly 400 $^{\circ}\text{C}$ was mainly attributed to the decomposition of the carbon skeleton of a p-rGO [62]. The loss in mass was about 22 and 46 wt. % for p-rGO and $\text{SnO}_2/\text{p-rGO}$, respectively, when the temperature reached 600 $^{\circ}\text{C}$ [63]. Based on TGA results, approximately 24 wt. % of SnO_2 was anchored on p-rGO surface in the $\text{SnO}_2/\text{p-rGO}$ composite.

3.3. Electrochemical Characterization of Modified GCEs

The electrochemical performance of the electrode in terms of acceleration of electron/charge transfer process and the electrocatalytic activity was examined by cyclic voltammetry (CV) using 1 mM ferro/ferricyanide solution as a standard redox probe in 0.1 M potassium chloride electrolyte. Cyclic voltammograms were recorded at bare GCE and modified electrodes (Figure 3A). The heterogeneous electron transfer (HET) rate, a function of peak separation (ΔE_p) of the cathodic and anodic peaks, is a crucial attribute when investigating the electrocatalytic efficiency of the sensor material [64]. The lower the ΔE_p value, the faster the HET rate and the better the conductivity of electrode material in sensing applications. A reversible redox peak was observed for the redox probe with the ΔE_p value of 85 mV and I_p value of $\sim 14.20 \mu\text{A}$ at bare GCE (Figure 3A, a). The SnO_2 nanoparticles-based electrode showed a greater peak current ($I_p = 30.45 \mu\text{A}$ and $\Delta E_p = 79 \text{ mV}$) (Figure 3A, b) compared to that of the bare electrode, indicating its good conductive nature. At p-rGO/GCE, the ΔE_p was observed to be reduced to 75 mV, and I_p increased considerably to $41.87 \mu\text{A}$ (Figure 3A, c), which was due to the larger electroactive surface area and excellent conductivity of p-rGO. However, the voltammogram of the probe at $\text{SnO}_2/\text{p-rGO}/\text{GCE}$ shows the grafting of SnO_2 nanostructures on a p-rGO/GCE platform that not only amplified the peak signal remarkably ($I_p = 51.75 \mu\text{A}$) but also decreased the peak potential difference (ΔE_p) to 70 mV (Figure 3A, d). These results

suggest enhanced electron transfer kinetics and electrocatalytic activity at the surface of the $\text{SnO}_2/\text{p-rGO}/\text{GCE}$ sensor, which could be due to the enhanced electrochemical performance caused by a larger electroactive surface area with high edge density and excellent conductivity of the porous structure of p-rGO. The highest electrochemical response noted was closely related to the synergistic effect of SnO_2 and p-rGO. The corresponding CV results are presented in Table 1.

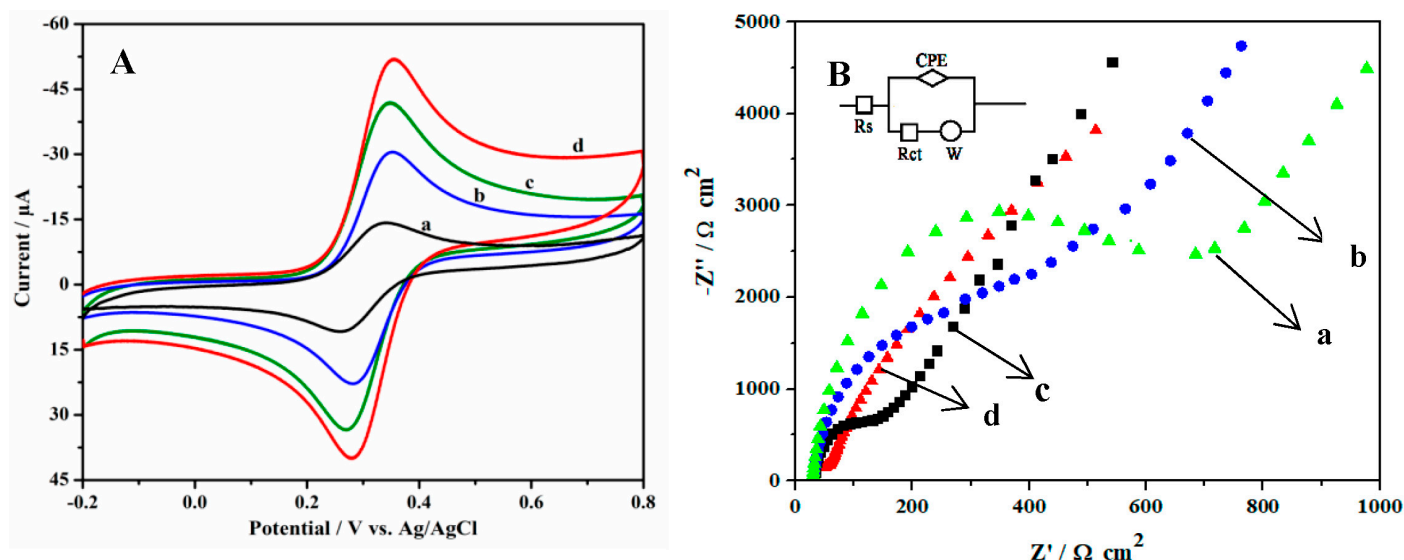


Figure 3. (A) Cyclic voltammograms and (B) impedance spectra of 1 mM $[\text{Fe}(\text{CN})_6]^{3-/4-}$ at bare GCE (a), SnO_2 (b), p-rGO (c), and $\text{SnO}_2/\text{p-rGO}$ (d) in 0.1 M KCl. Inset in (B) shows equivalent circuit for modified GCE.

Table 1. Electrochemical characteristics of different modified electrodes.

Modified GCE	Voltammetric Results			Impedance Spectroscopic Results				
	Area (cm^2)	ΔE_p (mV)	I_p (μA)	R_{ct} ($\Omega \text{ cm}^2$)	R_s ($\Omega \text{ cm}^2$)	CPE ($\mu\text{F cm}^{-2}$)	n	W_0 ($\text{k}\Omega \text{ cm}^2$)
$\text{SnO}_2/\text{p-rGO}/\text{GCE}$	0.594	70	51.72	28.7	1.11	4.137	0.890	2.45×10^{-4}
p-rGO/GCE	0.115	75	41.87	162.3	1.06	3.120	0.871	1.56×10^{-4}
SnO_2/GCE	0.088	79	30.45	486.5	1.12	3.326	0.823	1.21×10^{-4}
Bare GCE	0.058	85	14.20	738.6	1.18	4.372	0.798	1.26×10^{-4}

The electroactive surface area is one of the key factors that affect the sensitivity of the electrochemical sensor, owing to the increased interaction between the analyte and interface of the sensor. To examine the electro-active surface area of the modified platform, CV experiments were performed for the standard probe solution of $\text{K}_4[\text{Fe}(\text{CN})_6]$ under variable scan rates (10–350 mV/s). Further, the active surface areas of $\text{SnO}_2/\text{p-rGO}/\text{GCE}$, p-rGO/GCE, SnO_2 , and bare GCE were obtained from voltammograms using the Randles–Sevcik equation shown below [65]:

$$i_p = (2.69 \times 10^5) n^{3/2} A D^{1/2} C \sqrt{\nu}$$

where ' I_p ' is the peak current, ' n ' is the number of electrons transferred in the redox process ($n = 1$), ' D ' is the diffusion coefficient ($7.6 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$), ' A ' is the surface area of the electrode, ' C ' is the concentration of the redox probe, and ν is the scan rate. From the slope value of the graph of I_p vs. $\sqrt{\nu}$, the real surface areas of bare GCE, SnO_2 , p-rGO/GCE, and $\text{SnO}_2/\text{p-rGO}/\text{GCE}$ were calculated to be 0.058, 0.088, 0.115, and 0.594 cm^2 , respectively. The material $\text{SnO}_2/\text{p-rGO}/\text{GCE}$ exhibited more extensive active sites (larger effective surface area), which were beneficial to adsorb more analyte molecules, promoting the

sensing reaction that resulted in rapid charge transfer kinetics at the interface and hence an enhanced current response at $\text{SnO}_2@\text{p-rGO}/\text{GCE}$.

In order to assess the conductance and interfacial charge transfer property of the proposed electrode, the EIS technique was used. Figure 3B shows the EIS scans as Nyquist plots for $[\text{Fe}(\text{CN})_6]^{3-/4-}$ at GCE (Figure 3B, a), SnO_2 (Figure 3B, b), $\text{p-rGO}/\text{GCE}$ (Figure 3B, c), and $\text{SnO}_2@\text{p-rGO}/\text{GCE}$ (Figure 3B, d). Nyquist plots were constructed to measure charge transfer kinetics at the electrode surface. The plots consisted of broader semicircle curves in the medium frequencies and inclined lines at lower frequencies. The semicircle diameter measures interfacial electron transfer resistance (R_{ct}), which governs the electron transfer kinetics of the electrode reaction [66]. From Figure 3B, it was observed that the diameter of the semicircle for bare GCE ($R_{\text{ct}} = 738.6 \Omega$) was wider than that for SnO_2 ($R_{\text{ct}} = 486.5 \Omega$), demonstrating a low rate of the electron transfer ability of GCE and conductive nature of SnO_2 . The $\text{p-rGO}/\text{GCE}$ displayed much lower impedance ($R_{\text{ct}} = 162.3 \Omega$) to the electron transfer process than SnO_2/GCE , indicating that p-rGO with 3D porous microstructure and high edge density was highly conductive and could effectively promote the charge transfer at the interface. However, for the $\text{SnO}_2@\text{p-rGO}/\text{GCE}$ electrode, a nearly straight line with a very smaller semicircle curve ($R_{\text{ct}} = 28.7 \Omega$) was noticed confirming the excellent conductivity of $\text{SnO}_2@\text{p-rGO}$. This was mainly due to the presence of highly conductive and unique porous structural material ($\text{SnO}_2@\text{p-rGO}$) on the electrode surface that has an open porous microstructure and a 3D interpenetrating network that allowed the electrolyte to access almost all the graphene sheets. Further, small pores in p-rGO offered lesser inner-pore resistance, facilitating the transfer of electrons and the diffusion of ions during an electrochemical reaction [67]. The ohmic resistance signified the excellent conductive nature of $\text{SnO}_2@\text{p-rGO}/\text{GCE}$ compared to other electrodes. The EIS findings validate the results of CV.

3.4. Electrochemical Behavior of RPG at Bare GCE and Modified GCEs

To examine the electrochemical behavior of RPG, cyclic voltammograms were recorded for an RPG solution (10 μM) in PBS of pH 3 at bare GCE (Figure 4, a), SnO_2/GCE (Figure 4, b), $\text{p-rGO}/\text{GCE}$ (Figure 4, c), and $\text{SnO}_2@\text{p-rGO}/\text{GCE}$ (Figure 4, d). RPG exhibited an irreversible anodic peak at all three electrodes with varied peak currents (I_{pa}) and anodic peak potentials (E_{pa}). At bare GCE, the peak appeared at 1.28 V (peak a₁) with the lowest current due to the slow electron transfer kinetics between the electrolyte and electrode surface. At SnO_2/GCE , RPG exhibited higher I_{p} compared to that at bare GCE (with $E_{\text{p}} = 1.20$ V) due to the conductive nature of SnO_2 . However, the E_{p} value was observed at 1.156 V with notable enhancement in the current signal at $\text{p-rGO}/\text{GCE}$ compared to that at GCE, owing to the presence of conductive p-rGO with a larger electroactive surface area. Further, RPG exhibited significant enhancement in the peak current (~28-fold) at a lower anodic peak potential ($E_{\text{p}} = 1.09$ V) at $\text{SnO}_2@\text{p-rGO}/\text{GCE}$ compared to that at bare GCE. This indicated that the $\text{SnO}_2@\text{p-rGO}/\text{GCE}$ catalyzed and facilitated the interface electron transfer when the electrochemical oxidation of RPG occurred. The superior sensing performance and improved electrocatalytic activity observed at $\text{SnO}_2@\text{p-rGO}/\text{GCE}$ towards the oxidation of RPG was due to the 3D porous structure, higher surface area, and excellent conductivity of the $\text{SnO}_2@\text{p-rGO}/\text{GCE}$ electrode.

The 3D porous network in $\text{SnO}_2@\text{p-rGO}/\text{GCE}$ provided highly conductive multiplexed pathways for better diffusion of the electrolyte along with the analyte to access the active electrode material. This increased the enrichment of analyte at electrode. The presence of SnO_2 nanoparticles on p-rGO led to even more active sites as well as more exposed edges within the p-rGO network, which are favorable for transferring electrons [67]. The lower Fermi level energy of SnO_2 compared to p-rGO facilitated the electron move from SnO_2 to p-rGO . Therefore, the electron transfer rate was faster [57]. Good conductivity and morphological uniqueness of $\text{SnO}_2@\text{p-rGO}$ synergistically contributed to excellent electrochemical performance of $\text{SnO}_2@\text{p-rGO}/\text{GCE}$, and it is thus acknowledged as a promising electrode for further experiments.

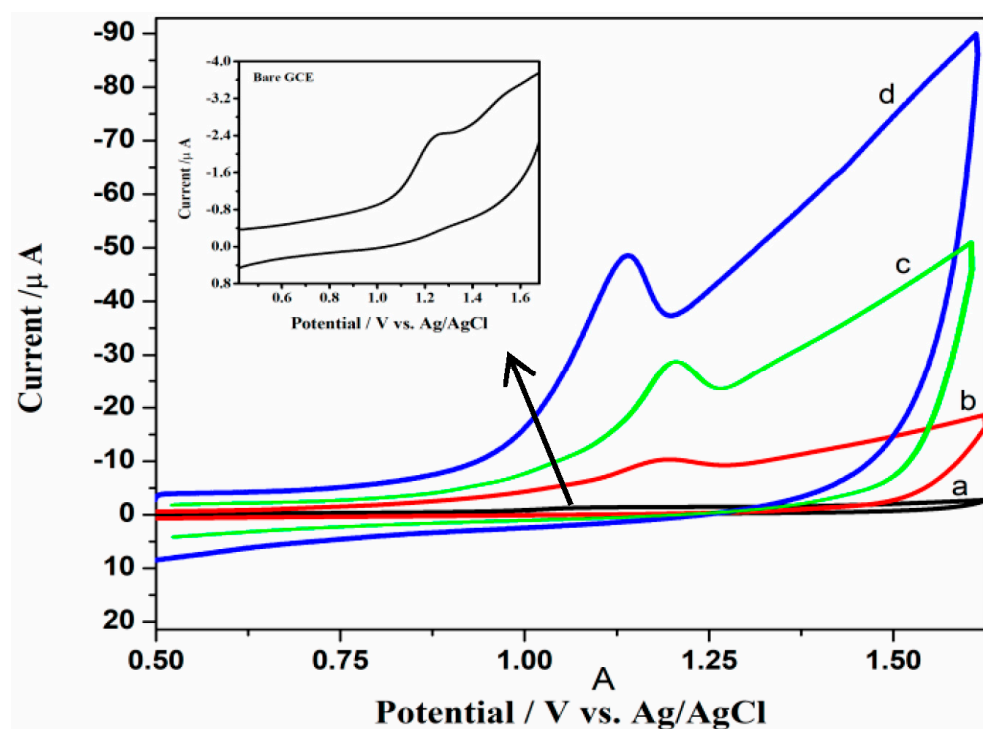


Figure 4. Cyclic voltammograms of 10 μM RPG at bare GCE (a), SnO_2 (b), p-rGO (c), and $\text{SnO}_2/\text{p-rGO}$ (d) in phosphate buffer of pH 3.

3.5. Effect of pH and Supporting Electrolyte

The pH of the medium influences the electrochemical performance of a sensor. The peak potential (E_p), current (I_p), and shape of peak significantly depend on the pH of the buffer solution. Thus, the effect of pH was assessed to understand the number of protons that participated in the electrode process and to choose the best pH for achieving a higher sensitivity for the determination of RPG. Therefore, buffer solutions of different pH (from 2.0 to 10) were used as the supporting electrolyte, and cyclic voltammograms were recorded (Figure S3A). A linear negative shift in the oxidation potential was noticed with an increase in pH of the medium (Figure S3A). In addition to the first oxidation peak, the new oxidation peak appeared for pH beyond 4. This shift in the first oxidation peak potential confirmed the participation of H^+ ions in the electrode process. Further, the graph of E_p vs. pH (Figure S3B) indicated breaks at pH 4 and 6 for linear segments, which was probably owing to a change in the protonation–deprotonation equilibrium of RPG. The breaks were close to $p^{\text{Ka}1}$ (3.9) and $p^{\text{Ka}2}$ (6.0) of RPG.

The plots of E_p vs. pH yielded slopes of 52.5 mV per pH (pH 2–4), 63.3 mV per pH (pH 4–6), and 65.0 mV per pH (pH 6–10), in three different regions. These values are close to the expected slope value of 59 mV/pH, indicating that an identical number of electrons and protons have taken part in the electro-oxidation of RPG [43].

$$E_{pa} [\text{V}] = -0.0525 [\text{pH}] + 1.287; R^2 = 0.9899 \text{ (pH 2.0–4.0)}$$

$$E_{pa} [\text{V}] = -0.0633 [\text{pH}] + 1.032; R^2 = 0.9825 \text{ (pH 4.0–6.0)}$$

$$E_{pa} [\text{V}] = -0.065 [\text{pH}] + 0.982; R^2 = 0.9825 \text{ (pH 6.0–10.6)}$$

It was further observed in Figure S3A that the maximum peak current for RPG was observed at pH 3.0. Thus, electrochemical responses were recorded in different buffer solutions, viz. H_2SO_4 , acetate buffer, Britton–Robinson buffer, and PBS at pH 3.0. By taking into consideration peak current, peak potential, and shape of peak, PBS was found to be the most favorable buffer medium for the electro-oxidation of RPG, and it was used for subsequent work.

3.6. Optimization of the Sensing Response

Charge transfer kinetics in the electrode reaction and the mass transfer mechanism through the porous modifier film were examined by varying the thickness of the modifier film on the electrode surface. For this, different volumes of SnO₂@p-rGO suspension (1 mg/mL) were drop-casted on GCE, and cyclic voltammograms of RPG were recorded. A significant increase in the anodic peak current was noticed with an increase in the amount of the modifier from 1 to 5 µL (Figure S4A). Beyond 5 µL, a thick film of modifier on the electrode would obstruct the diffusion of the analyte through the modifier, which led to a decrease in the peak current of RPG. Therefore, 5 µL of SnO₂@p-rGO suspension was used as an optimal amount to fabricate the modified electrode towards the electro-oxidation of RPG. The effect of the accumulation time on the peak current of 10 µM RPG was studied in PBS of pH 3.0. As shown in Figure S4B, the peak current of RPG was raised with an increase in the accumulation time from 30 to 280 s, and a maximum peak current was reached at 120 s, suggesting that the adsorption equilibrium was reached. An accumulation time of beyond 120 s led to desorption of RPG, and thus, the optimal time was set at 120 s. Therefore, the suspension of 5 µL, accumulation time of 120 s, and PBS of pH 3.0 were maintained throughout the investigation.

3.7. Scan Rate Studies

In order to inspect the electro-oxidation of RPG at the SnO₂@p-rGO/GCE surface, the impact of scan rate (ν) on the voltammetric response was investigated by recording cyclic voltammograms of 10 µM RPG solution at SnO₂@p-rGO/GCE in the 10 to 350 mV s⁻¹ scan rate ranges. With increases in the scan rate, not only did the oxidation peak currents increase, but their peak potentials were moved towards a positive potential window. The plot of peak current vs. the scan rate (ν) revealed the linear relationship. The corresponding regression equation is presented below:

$$I_{pa} (\mu A) = 3.826 \times 10^{-4} (\nu) - 6.811 \times 10^{-6}; (R^2 = 0.989)$$

The linear regression equation for the plot of the log I_{pa} versus log ν (Figure 5B) equation is indicated below:

$$\log i_{pa} = 1.092 \log \nu - 3.469; R^2 = 0.99$$

The electrode process followed the adsorption-controlled behavior, as evident from the slope value of 1.092, which is close to the theoretical value of 1.0, known to characterize an ideal adsorption-controlled electrode process [68]. According to Laviron's theory, the relationship between E_p and scan rate (ν) is outlined below [69]:

$$E_{pa} = E^{\circ'} - RT/\alpha nF [\ln (RTk_s)/(\alpha nF) + \ln \nu] \text{ (for an irreversible electrode process)}$$

where $E^{\circ'}$ is the formal standard potential; ν , T , R , and F stand for their usual meaning; and α , n , and k_s are the electron transfer coefficient, the number of electrons involved, and the HET rate constant, respectively. The values of ' n ' and ' k_s ' were calculated using the value of the slope of the linear plot of E_{pa} versus $\ln \nu$. The intercept of the plot was used to determine the value of $E^{\circ'}$ for RPG at SnO₂@p-rGO/GCE. The values of ' k_s ' and ' αn ' were calculated to be 1.095 s⁻¹ and 1.11. The value of ' α ' was typically assumed to be 0.5 for an irreversible oxidation process [70], and the value of ' n ' was calculated to be 2.22. Based on these findings, we have proposed that RPG has undergone two electrons' irreversible oxidation at SnO₂@p-rGO/GCE followed by the loss of two protons.

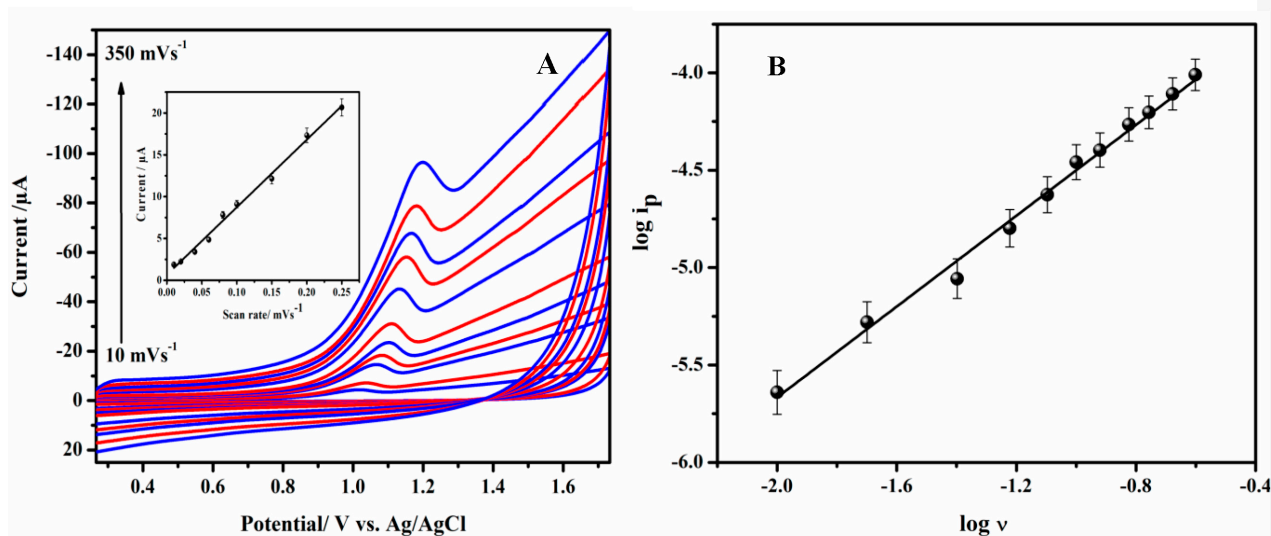
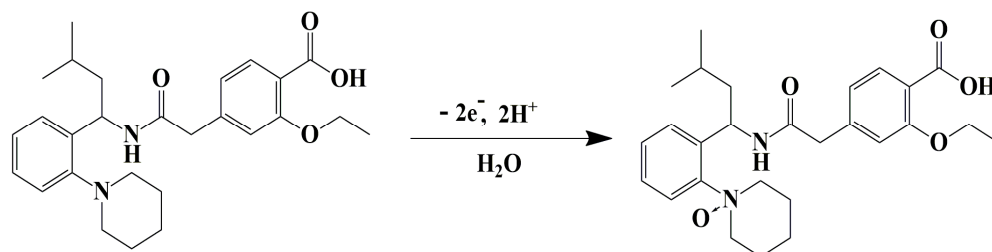


Figure 5. (A) Cyclic voltammograms of 10 μM RPG (at pH 3) at the scan rate range of 10–350 mV s^{-1} and (B) dependence of $\log I_{pa}$ on $\log \nu$.

3.8. Electrode Reaction Mechanism

The probable mechanism for the oxidation of RPG at $\text{SnO}_2@\text{p-rGO}/\text{GCE}$ is proposed based on the results of the experiments, and the same is presented in Scheme 3. It is proposed that the RPG has undergone oxidation with the loss of two electrons and two protons at $\text{SnO}_2@\text{p-rGO}/\text{GCE}$. Taking into account the experimental data, the electrochemical oxidation behavior of piperidine, and previous reports for other piperidine-containing compounds [71,72], we suppose that the nitrogen atom in the piperidine moiety of RPG has undergone oxidation. The oxidation has followed the two-step oxidation mechanism. RPG was electrochemically oxidized by two electrons to yield piperidine N-oxide at $\text{SnO}_2@\text{p-rGO}$ over the investigated pH range.



Scheme 3. Plausible mechanism of oxidation of RPG.

3.9. Construction of Calibration Curve

Because of RPG's enhanced electrochemical response at $\text{SnO}_2@\text{p-rGO}/\text{GCE}$, new electrochemical methods for its quantification were developed. In the current work, sensitive square-wave voltammetric and differential pulse voltammetric methods for the determination of RPG were established under optimal conditions. As seen in Figure 6A,B, the current responses increased linearly with increased concentrations of RPG on $\text{SnO}_2@\text{p-rGO}/\text{GCE}$ in the ranges of 4.99×10^{-8} – $1.83 \times 10^{-5} \text{ mol L}^{-1}$ and 1.99×10^{-8} – $1.45 \times 10^{-5} \text{ mol L}^{-1}$ for DPV and SWV methods, respectively. Below are the corresponding regression expressions:

$$I_p (\mu\text{A}) = 0.9259 [\text{RPG}] + 2.306 \times 10^{-7}, R^2 = 0.994 \quad (\text{For DPV method})$$

$$I_p (\mu\text{A}) = 0.9523 [\text{RPG}] + 4.463 \times 10^{-8}, R^2 = 0.988 \quad (\text{For SWV method})$$

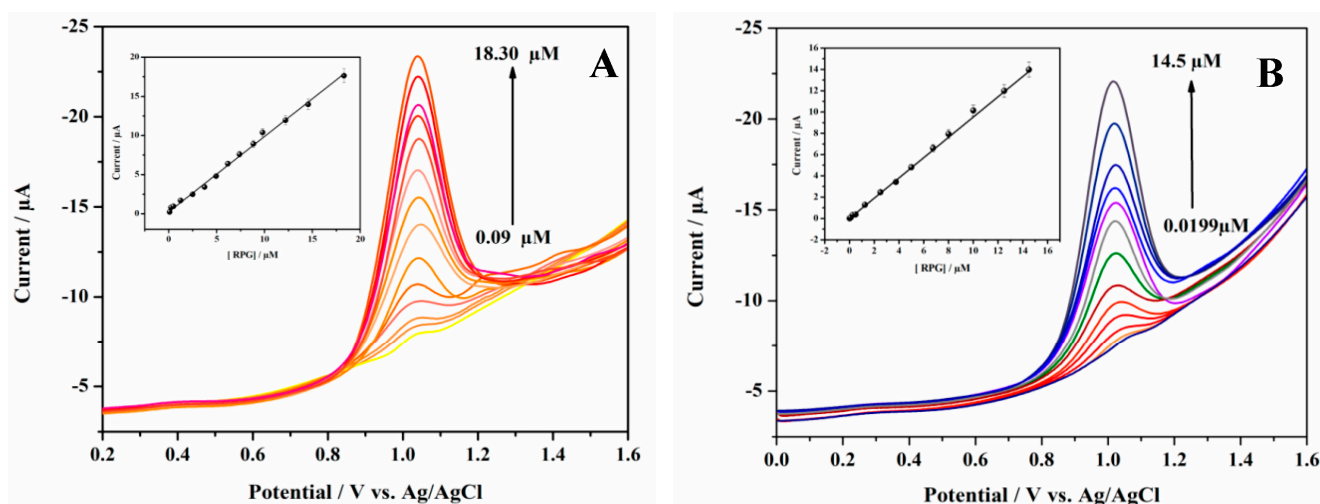


Figure 6. (A) Differential pulse and (B) square-wave voltammograms for increasing concentration of RPG in phosphate buffer of pH 3 and respective calibration plots (Inset).

The limit of detection (LOD), the limit of quantification (LOQ), and linear ranges are critical figures of merit indicative of the performance of an electrochemical sensor and ensure the practical implementation of the designed sensor. Therefore, the developed electroanalytical methods for the assay of RPG were successfully validated by assessing the values of analytical parameters such as LOD, LOQ, RSD, and selectivity. The LOD and LOQ values for DPV and SWV methods were determined and are given in Table 2. LOD values of $9.02 \times 10^{-9} \text{ mol L}^{-1}$ and $8.50 \times 10^{-10} \text{ mol L}^{-1}$ for DPV and SWV methods, respectively, were achieved. These values were noticed to be lower than those of the reported methods (Table 3). These results highlight the high sensitivity of the proposed procedures. The SWV method demonstrated greater sensitivity in terms of LOD and LOQ compared to the DPV method. It allows rapid determination with higher sensitivity and selectivity, as it could suppress background and non-faradaic currents.

Further, better sensitivity was noticed at $\text{SnO}_2/\text{p-rGO}/\text{GCE}$. This could be attributed to the existence of numerous pores in p-rGO (for catalytic activity) and increased surface area, which facilitated rapid charge transfer at the electrode surface [73]. Furthermore, the proposed methods' inter-day and intra-day assays were examined by recording differential pulse and square-wave voltammograms of five replicates of RPG on the same day and three separate days. RSD values for inter-day and intra-day assay results were calculated to be 2.45% and 1.74% for DPV method and 2.19% and 2.23% for SWV method, respectively (Table 2). Low RSD values indicated that the proposed methods are precise.

Table 2. Characteristics of the calibration plot for the determination of RPG.

Parameters	DPV	SWV
Linearity range, mol L^{-1}	4.99×10^{-8} – 1.83×10^{-5}	1.99×10^{-8} – 1.45×10^{-5}
LOD, mol L^{-1}	9.02×10^{-9}	8.50×10^{-10}
LOQ, mol L^{-1}	3.00×10^{-8}	2.83×10^{-9}
Inter-day assay, RSD * (%)	2.45	2.19
Intra-day assay, RSD * (%)	1.74	2.23

* Average of 5 determinations.

Table 3. Comparison of analytical range and detection limits of the proposed methods with those of reported methods.

Method	Linearity Range	LOD	LOQ	Ref.
HPLC ^a	5–50 µg/mL	0.73 µg/mL	2.21 µg/mL	[6]
HPLC	0.5–3 µg/mL	0.056 µg/mL	0.172 µg/mL	[7]
HPLC	50–2000 ng/mL	-	20 ng/mL	[8]
HPLC-EC ^b	-	0.017 µg/mL	0.051 µg/mL	[9]
HPLC-UV ^c	0.1–0.5 µg/mL	-	-	[10]
LC-MS/MS ^d	-	1.0 ng/mL	-	[12]
RPTLC ^e	0.6–3.6 µg/10 µL	0.08 µg/10 µL	0.27 µg/10 µL	[13]
RP-HPLC ^f	110–550 ng/mL	-	110 ng/mL	[15]
Differential pulse voltammetry				
Carbon paste electrode, CPE	0.36–1.44 µg/mL	0.0161 µg/mL	0.203 µg/mL	[19]
Glassy carbon electrode, GCE	0.18–1.81 µg/mL	0.048 µg/mL	0.160 µg/mL	
MIP-PoDB/PoPD/GCE ^g	0.002–0.452 µg/mL	0.8 ng/mL	-	[20]
DPV (SnO ₂ @p-rGO/GCE)				
Square-wave voltammetry	0.02–8.14 µg/mL	4.08 ng/mL	13.5 ng/mL	
SWV (SnO ₂ @p-rGO/GCE)	0.009–6.56 µg/mL	0.38 ng/mL	1.28 ng/mL	Proposed work

^a High-performance liquid chromatography method; ^b High-performance liquid chromatography–Electrochemical method; ^c High-performance liquid chromatography–Ultraviolet method; ^d Liquid chromatography–tandem mass spectrometric method; ^e Reversed phase thin-layer chromatographic method; ^f Reversed-phase-HPLC method; ^g Electropolymerized o-dihydroxy benzene (o-DB) and o-phenylenediamine (o-PD) modified GCE.

3.10. Reproducibility and Stability of SnO₂@p-rGO/GCE

To verify the repeatability and stability of SnO₂@p-rGO/GCE, five modified electrodes were constructed using identical technique, and their performances were examined by monitoring the peak current of 10 µM RPG by CV in PBS of pH 3.0. Peak currents had a relative standard deviation (RSD) of less than 2.06% (average of five observations on each electrode). The RSD for five replicate SWV measurements with a single electrode for 10 µM RPG was found to be 2.3%. The findings show that the developed sensor has greater reproducibility and repeatability in both fabrication and voltammetric measurements. The stability of SnO₂@p-rGO/GCE was evaluated over 3 weeks. During this period, the peak current was recorded regularly. Up to 15 days of storage, no appreciable drop in peak current was detected. Further, $97.3 \pm 0.4\%$ response of the initial peak current was retained in the next 7 days. This revealed that the thin film of the SnO₂@p-rGO/GCE modifier on the GCE surface has long-term stability (for 3 weeks) for sensing RPG.

3.11. Determination of RPG in Urine Samples

The practical implication of the developed SWV and DPV methods was further established by determining RPG in untreated human urine samples. The recovery of RPG was examined using the standard addition protocol by adding known dosages of pure RPG to drug-free urine samples of healthy volunteers obtained upon their written consent and recording voltammograms. The calibration curve was utilized to calculate the amount of RPG in urine samples. The findings of the urine sample analysis are summarized in Table 4. The percentage recovery ranged from 98.0 to 99.6%, with RSD values ranging from 1.5 to 3.02%. These results demonstrate the electrode's high repeatability in real sample analysis, confirming the electrode's potential for practical utility.

Table 4. Results of analysis of RPG in spiked human urine samples.

Proposed Method	Amount of RPG Added, μM	n	Amount Found, μM	Average Recovery (%)	RSD, %
DPV	0.1	5	0.098	98.0	3.02
	0.25	5	0.248	99.2	1.95
	0.5	5	0.495	99.0	2.56
SWV	0.1	5	0.099	99.0	2.50
	0.25	5	0.249	99.6	1.50
	0.5	5	0.497	99.4	2.38

3.12. Determination of RPG in Pharmaceutical Formulations

The fabricated sensor, $\text{SnO}_2/\text{p-rGO}/\text{GCE}$, was successfully used in practice for the determination of RPG in tablets. The stock solution of the tablet sample was prepared as given in the experimental section. By proper dilution, the working tablet solution was prepared. Then, under optimal circumstances, differential pulse and square-wave voltammograms were recorded. For recovery studies, the standard addition method was used. Higher average recovery (97.60–99.60%) (Table 5) demonstrated the efficacy of the suggested approaches. Low RSD readings (below 3.0%) indicated that the recommended procedure was precise.

Table 5. Results of analysis of RPG in pharmaceutical formulations by DPV and SWV methods.

	DPV		SWV	
	Eurepa MF1 ^b	Ripadep ^c	Eurepa MF1	Ripadep
Labeled amount, mg	0.5	1	0.50	1.00
Amount found, mg	0.485	0.996	0.49	0.997
Recovery, %	97.00	99.6	98.00	99.70
RSD ^a , %	2.34	1.98	2.51	2.86
t-Value at 95% confidence level	1.64	-	0.16	-
F-Value at 95% confidence level	2.37	-	4.39	-
Pure RPG added, mg	0.25	0.3	0.25	0.3
Amount found, mg	0.244	0.294	0.248	0.299
Recovery, %	97.60	98.00	99.20	99.60
RSD ^a , %	2.46	3.06	2.60	2.76

^a Average of 5 replicates; ^b Torrent Pharmaceuticals Ltd., Ahmedabad, India; ^c Globus Labs.

By applying Student's *t*-test and the variance ratio F-test, the results of analysis of proposed methods were statistically compared to those obtained by the reported methods in the literature [6]. The results reveal that there was no notable difference in the accuracy of the suggested and reported procedures, as evidenced by the Student's *t*-test values (Table 5), which were less than the tabulated value (2.132) at a 95% confidence level. Since F-calculated values (Table 5) were less than the tabulated value (6.39) at a 95% confidence level, we propose that there was no appreciable difference in precision between the reported and proposed methodologies.

3.13. Selectivity and Interference Studies

To investigate the selectivity of the proposed method using a newly developed sensor, $\text{SnO}_2/\text{p-rGO}/\text{GCE}$, the effect of possible electroactive interfering species in the determination of RPG was evaluated. For this purpose, differential pulse and square-wave voltammograms of 5 μM RPG solutions were recorded in the presence of some chosen biologically active molecules. The SWV of 5 μM RPG in the presence of metformin and glucose at bare GCE and $\text{SnO}_2/\text{p-rGO}/\text{GCE}$ is shown in Figure 7. No peak corresponding glucose was noticed at bare GCE in PBS of pH 3, while a broad peak was observed for RPG and metformin. Three well-resolved anodic peaks were found at $\text{SnO}_2/\text{p-rGO}/\text{GCE}$. The

first one was due to oxidation of glucose to glucolactone that hydrolyses to gluconic acid in water to yield an anodic peak at 0.26 V. The second peak, noticed at 0.905 V, was attributed to the conversion of the imino group of guanidine moiety into N-hydroxy imino group of metformin, while the third peak corresponded to oxidation of RPG at 1.09 V.

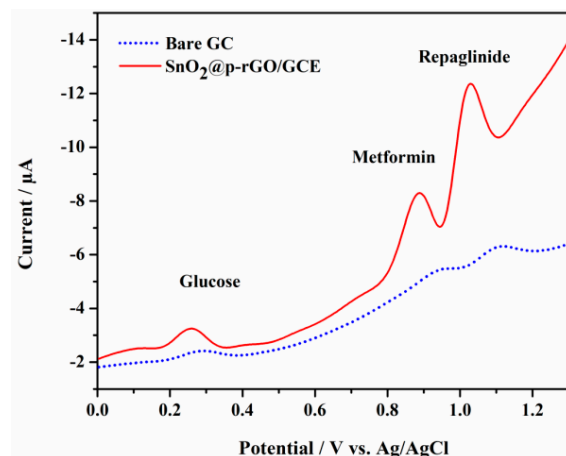


Figure 7. SWV of PBS solution (pH 3) containing 5 μM RPG with metformine and glucose monitored at bare GCE and $\text{SnO}_2@\text{p-rGO}/\text{GCE}$.

Further, the effect of chosen interferences, viz. ascorbic acid, lactose, glucose, acacia, uric acid, and metformin, was examined in the determination of RPG under optimal conditions. As shown in Table S1, several folds of the aforementioned interferences did not significantly influence the peak current response of RPG. The results suggest that the proposed electrochemical sensor could be utilized to determine RPG selectively.

4. Conclusions

In summary, a facile, inexpensive, and sustainable protocol was developed for the fabrication of an electrochemical sensor, $\text{SnO}_2@\text{p-rGO}/\text{GCE}$, that could be used for the determination of RPG. Glycine and aqueous extract of empty cotton boll peels were utilized to prepare p-rGO and SnO_2 . The morphological and structural characterization of $\text{SnO}_2@\text{p-rGO}$ was performed by XRD, SEM-EDX, Raman, FTIR, TGA, UV-vis, CV, and EIS measurements. The proposed electrochemical sensor exhibited selectivity and sensitivity for the determination of RPG due to the synergism between the larger surface area of SnO_2 nanoparticles and the superior electronic characteristics of p-rGO. The pH-dependent irreversible oxidation peak was observed at all due to electro-oxidation of RPG with the participation of two electrons and two protons. The effect of pH and scan rate studies confirmed the adsorption-controlled electrode process. Between the DPV and SWV methods, the lower LOD of $8.50 \times 10^{-10} \text{ mol L}^{-1}$ was realized with the SWV method. This method exhibited linearity in the range of 1.99×10^{-8} to $1.45 \times 10^{-5} \text{ mol L}^{-1}$ RPG. The sensing platform, $\text{SnO}_2@\text{p-rGO}/\text{GCE}$, was successfully demonstrated for the assay of RPG in pharmaceutical formulations and RPG-fortified urine samples with precise results and satisfactory recoveries. Therefore, the $\text{SnO}_2@\text{p-rGO}/\text{GCE}$ could be a good electrode for sensitive determination of RPG in clinical diagnostics and pharmaceutical industries.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/chemosensors11010050/s1>. Figure S1: UV-visible absorption spectra of p-rGO (a), SnO_2 (b), and $\text{SnO}_2@\text{p-rGO}$ (c); Figure S2: TGA curves for p-rGO (a) and $\text{SnO}_2/\text{p-rGO}$ (b); Figure S3: (A) Cyclic voltammograms of 10 μM RPG at different pH and (B) plot of E_p vs. pH; Figure S4: (A) Dependence of peak current on the amount of $\text{SnO}_2/\text{p-rGO}$ suspension and (B) accumulation time; Scheme S1: Plausible mechanism for the formation of SnO_2 nanoparticles by cotton boll peel extract; Table S1: Tolerance of interferences in the determination of $2.26 \mu\text{g mL}^{-1}$ RPG using proposed sensor by SWV method.

Author Contributions: A.M.: Conceptualization, data curation, software, formal analysis, writing—original draft preparation. K.K.: Software, formal analysis. S.J.: Supervision, funding acquisition, methodology, investigation, project administration, resources, validation. S.K.: Visualization and editing. All authors have read and agreed to the published version of the manuscript.

Funding: Council of Scientific and Industrial Research (CSIR), New Delhi, Ref. No. 01(3068)/21/EMR-II dated 23-08-2021.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: We thank the CSIR, New Delhi, for financial support to carry out this work. Thanks are also due to SAIF, Karnatak University, Dharwad, for instrumental facilities.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Gumieniczek, A.; Berecka, A. Analytical Tools for Determination of New Oral Antidiabetic Drugs, Glitazones, Gliptins, Gliflozins and Glinides, in Bulk Materials, Pharmaceuticals and Biological Samples. *Open Chem.* **2016**, *14*, 215–242. Available online: https://doi.org/10.1515/CHEM-2016-0023/ASSET/GRAPHIC/J_CHEM-2016-0023_FIG_007.JPG (accessed on 25 November 2022). [CrossRef]
2. Fuhendorff, J.; Rorsman, P.; Kofod, H.; Brand, C.L.; Rolin, B.; MacKay, P.; Shymko, R.; Carr, R.D. Stimulation of Insulin Release by Repaglinide and Glibenclamide Involves both Common and Distinct Processes. *Diabetes* **1998**, *47*, 345–351. [CrossRef]
3. Kim, J.M.; Seo, S.W.; Han, D.G.; Yun, H.; Yoon, I.S. Assessment of Metabolic Interaction between Repaglinide and Quercetin via Mixed Inhibition in the Liver: In Vitro and In Vivo. *Pharmaceutics* **2021**, *13*, 782. [CrossRef] [PubMed]
4. Ding, D.; Wang, M.; Wu, J.X.; Kang, Y.; Chen, L. The Structural Basis for the Binding of Repaglinide to the Pancreatic KATP Channel. *Cell Rep.* **2019**, *27*, 1848–1857.e4. [CrossRef] [PubMed]
5. Jirovský, D.; Bartošová, Z.; Skopalová, J.; Maier, V. Electrochemical Characterization of Repaglinide and Its Determination in Human Plasma Using Liquid Chromatography with Dual-Channel Coulometric Detection. *J. Chromatogr. B* **2010**, *878*, 3243–3248. [CrossRef]
6. Dhole, S.M.; Amnerkar, N.D.; Khedekar, P.B. Comparison of UV Spectrophotometry and High Performance Liquid Chromatography Methods for the Determination of Repaglinide in Tablets. *Pharm. Methods* **2012**, *3*, 68–72. [CrossRef]
7. Patel, D.; Patel, L.J.; Patel, M. Development and Validation of Stability Indicating Method for the Determination of Repaglinide in Pharmaceutical Dosage Form Using High Performance Liquid Chromatography. *Int. J. ChemTech Res.* **2011**, *3*, 539–546.
8. Lakshmi, K.S.; Rajesh, T. Separation and Quantification of Eight Antidiabetic Drugs on a High-Performance Liquid Chromatography: Its Application to Human Plasma Assay. *ISRN Pharm.* **2011**, *2011*, 1–7. [CrossRef]
9. Gumustas, M.; Coskun, G.; Ozkan, S.A. Selective and sensitive determination of repaglinide in pharmaceuticals by voltammetric and lc methods. *Rev. Roum. Chim.* **2015**, *60*, 477–490.
10. Gandhimathi, M.; Ravi, T.K.; Renu, S.K. Determination of Repaglinide in Pharmaceutical Formulations by HPLC with UV Detection. *Anal. Sci.* **2003**, *19*, 1675–1677. [CrossRef]
11. Wang, M.; Miksa, I.R. Multi-Component Plasma Quantitation of Anti-Hyperglycemic Pharmaceutical Compounds Using Liquid Chromatography-Tandem Mass Spectrometry. *J. Chromatogr. B Analyt. Technol. Biomed. Life Sci.* **2007**, *856*, 318–327. [CrossRef]
12. Ho, E.N.M.; Yiu, K.C.H.; Wan, T.S.M.; Stewart, B.D.; Watkins, K.L. Detection of Anti-Diabetics in Equine Plasma and Urine by Liquid Chromatography-Tandem Mass Spectrometry. *J. Chromatogr. B Analyt. Technol. Biomed. Life Sci.* **2004**, *811*, 65–73. [CrossRef]
13. Gumieniczek, A.; Berecka, A.; Hopkała, H. Quantitative Analysis of Repaglinide in Tablets by Reversed-Phase Thin-Layer Chromatography with Densitometric UV Detection. *JPC—J. Planar Chromatogr.—Mod. TLC* **2007**, *18*, 155–159. [CrossRef]
14. Goyal, A.; Singhvi, I. Visible Spectrophotometric Methods for Estimation of Repaglinide in Tablet Formulation. *Indian J. Pharm. Sci.* **2006**, *68*, 656–657. [CrossRef]
15. Tatiparthi, R.; Ramanjireddy, T.; Dhachinamoorthi, D.; Chandrasekhar, K.B. Pharmacokinetic Study of Repaglinide Floating Drug Delivery System in Rabbits by RP-HPLC Method Improving the Outpatient Medication Adherence towards the Chronic Diseases by Sending SMS to Remind the Dosing Instructions in Local Languages View Project Herbal Medicine Use: Clinical and Economic Outcomes View Project Pharmacokinetic Study of Repaglinide Floating Drug Delivery System in Rabbits by RP HPLC Method. *Artic. J. Chin. Pharm. Sci.* **2012**, *21*, 162–168. [CrossRef]
16. Li, G.; Qi, X.; Wu, J.; Xu, L.; Wan, X.; Liu, Y.; Chen, Y.; Li, Q. Ultrasensitive, Label-Free Voltammetric Determination of Norfloxacin Based on Molecularly Imprinted Polymers and Au Nanoparticle-Functionalized Black Phosphorus Nanosheet Nanocomposite. *J. Hazard. Mater.* **2022**, *436*, 129107. [CrossRef] [PubMed]

17. Li, G.; Wu, J.; Qi, X.; Wan, X.; Liu, Y.; Chen, Y.; Xu, L. Molecularly Imprinted Polypyrrole Film-Coated Poly(3,4-Ethylenedioxythiophene): Polystyrene Sulfonate-Functionalized Black Phosphorene for the Selective and Robust Detection of Norfloxacin. *Mater. Today Chem.* **2022**, *26*, 101043. [[CrossRef](#)]
18. Ozcelikay, G.; Kaya, S.I.; Ozkan, E.; Cetinkaya, A.; Nemutlu, E.; Kır, S.; Ozkan, S.A. Sensor-Based MIP Technologies for Targeted Metabolomics Analysis. *TrAC Trends Anal. Chem.* **2022**, *146*, 116487. [[CrossRef](#)]
19. Mathad, A.S.; Seetharamappa, J.; Kalanur, S.S. β -Cyclodextrin Anchored Neem Carbon Dots for Enhanced Electrochemical Sensing Performance of an Anticancer Drug, Lapatinib via Host-Guest Inclusion. *J. Mol. Liq.* **2022**, *350*, 118582. [[CrossRef](#)]
20. Bilge, S.; Karadurmus, L.; Atici, E.B.; Sinağ, A.; Ozkan, S.A. A Novel Electrochemical Sensor Based on Magnetic Co_3O_4 Nanoparticles/Carbon Recycled from Waste Sponges for Sensitive Determination of Anticancer Drug Ruxolitinib. *Sens. Actuators B Chem.* **2022**, *367*, 132127. [[CrossRef](#)]
21. Genidy, G.; Kamal, A.; Nabi, M.A. Electrochemical Determination of the Antidiabetic Drug Repaglinide. *Yakugaku Zasshi* **2008**, *128*, 171–177.
22. Roushani, M.; Jalilian, Z. Development of Electrochemical Sensor Based on Glassy Carbon Electrode Modified with a Molecularly Imprinted Copolymer and Its Application for Detection of Repaglinide. *Electroanalysis* **2018**, *30*, 2712–2718. [[CrossRef](#)]
23. Wang, Q.; Wang, X.; Chai, Z.; Hu, W. Low-Temperature Plasma Synthesis of Carbon Nanotubes and Graphene Based Materials and Their Fuel Cell Applications. *Chem. Soc. Rev.* **2013**, *42*, 8821–8834. [[CrossRef](#)] [[PubMed](#)]
24. Kemp, K.C.; Seema, H.; Saleh, M.; Le, N.H.; Mahesh, K.; Chandra, V.; Kim, K.S. Environmental Applications Using Graphene Composites: Water Remediation and Gas Adsorption. *Nanoscale* **2013**, *5*, 3149–3171. [[CrossRef](#)] [[PubMed](#)]
25. Huang, X.; Qian, K.; Yang, J.; Zhang, J.; Li, L.; Yu, C.; Zhao, D. Functional Nanoporous Graphene Foams with Controlled Pore Sizes. *Adv. Mater.* **2012**, *24*, 4419–4423. [[CrossRef](#)] [[PubMed](#)]
26. Karaman, C.; Karaman, O.; Atar, N.; Yola, M.L. Tailoring of Cobalt Phosphide Anchored Nitrogen and Sulfur Co-Doped Three Dimensional Graphene Hybrid: Boosted Electrocatalytic Performance towards Hydrogen Evolution Reaction. *Electrochim. Acta* **2021**, *380*, 138262. [[CrossRef](#)]
27. Yang, Y.; Ma, G.; Huang, J.; Nan, J.; Zhen, S.; Wang, Y.; Li, A. Hollow MnO_2 Spheres/Porous Reduced Graphene Oxide as a Cathode Host for High-Performance Lithium-Sulfur Batteries. *J. Solid State Chem.* **2020**, *286*, 121297. [[CrossRef](#)]
28. Van Hoa, N.; Dat, P.A.; Van Hieu, N.; Le, T.N.; Minh, N.C.; Van Tang, N.; Nga, D.T.; Ngoc, T.Q. Rapid and Efficient Synthesis of High-Porous Reduced Graphene Oxide/ NiCo_2S_4 Nanocomposites for Supercapacitor Application. *Diam. Relat. Mater.* **2020**, *106*, 107850. [[CrossRef](#)]
29. Qiu, H.J.; Guan, Y.; Luo, P.; Wang, Y. Recent Advance in Fabricating Monolithic 3D Porous Graphene and Their Applications in Biosensing and Biofuel Cells. *Biosens. Bioelectron.* **2017**, *89*, 85–95. [[CrossRef](#)]
30. Zamani, P.; Higgins, D.C.; Hassan, F.M.; Fu, X.; Choi, J.Y.; Hoque, M.A.; Jiang, G.; Chen, Z. Highly Active and Porous Graphene Encapsulating Carbon Nanotubes as a Non-Precious Oxygen Reduction Electrocatalyst for Hydrogen-Air Fuel Cells. *Nano Energy* **2016**, *26*, 267–275. [[CrossRef](#)]
31. Saisahas, K.; Soleh, A.; Somsiri, S.; Senglan, P.; Promsuwan, K.; Saichanapan, J.; Kanatharana, P.; Thavarungkul, P.; Lee, K.; Chang, K.H.; et al. Electrochemical Sensor for Methamphetamine Detection Using Laser-Induced Porous Graphene Electrode. *Nanomaterials* **2021**, *12*, 73. [[CrossRef](#)] [[PubMed](#)]
32. Mahmood, F.; Sun, Y.; Wan, C. Biomass-Derived Porous Graphene for Electrochemical Sensing of Dopamine. *RSC Adv.* **2021**, *11*, 15410–15415. [[CrossRef](#)] [[PubMed](#)]
33. Karaman, C.; Aktaş, Z.; Bayram, E.; Karaman, O.; Kizil, C. Correlation between the Molecular Structure of Reducing Agent and PH of Graphene Oxide Dispersion on the Formation of 3D-Graphene Networks. *CS J. Solid State Sci. Technol.* **2020**, *9*, 071003. [[CrossRef](#)]
34. Yin, S.; Niu, Z.; Chen, X. Assembly of Graphene Sheets into 3D Macroscopic Structures. *Small* **2012**, *8*, 2458–2463. [[CrossRef](#)] [[PubMed](#)]
35. Huang, X.; Sun, B.; Su, D.; Zhao, D.; Wang, G. Soft-Template Synthesis of 3D Porous Graphene Foams with Tunable Architectures for Lithium- O_2 Batteries and Oil Adsorption Applications. *J. Mater. Chem. A* **2014**, *2*, 7973–7979. [[CrossRef](#)]
36. Hassan Oghli, A.; Soleymannpour, A. Ultrasensitive Electrochemical Sensor for Simultaneous Determination of Sumatriptan and Paroxetine Using Molecular Imprinted Polymer/Sol-Gel/Polyoxometalate/RGO Modified Pencil Graphite Electrode. *Sens. Actuators B Chem.* **2021**, *344*, 130215. [[CrossRef](#)]
37. Mehmandoust, M.; Erk, N.; Karaman, O.; Karimi, F.; Bijad, M.; Karaman, C. Three-Dimensional Porous Reduced Graphene Oxide Decorated with Carbon Quantum Dots and Platinum Nanoparticles for Highly Selective Determination of Azo Dye Compound Tartrazine. *Food Chem. Toxicol.* **2021**, *158*, 112698. [[CrossRef](#)]
38. Xu, C.; Shi, X.; Ji, A.; Shi, L.; Zhou, C.; Cui, Y. Fabrication and Characteristics of Reduced Graphene Oxide Produced with Different Green Reductants. *PLoS ONE* **2015**, *10*, e0144842. [[CrossRef](#)]
39. Fan, M.; Zhu, C.; Feng, Z.Q.; Yang, J.; Liu, L.; Sun, D. Preparation of N-Doped Graphene by Reduction of Graphene Oxide with Mixed Microbial System and Its Haemocompatibility. *Nanoscale* **2014**, *6*, 4882–4888. [[CrossRef](#)]
40. Wang, J.; Salihi, E.C.; Šiller, L. Green Reduction of Graphene Oxide Using Alanine. *Mater. Sci. Eng. C* **2017**, *72*, 1–6. [[CrossRef](#)]
41. Karimi-Maleh, H.; Karimi, F.; Fu, L.; Sanati, A.L.; Alizadeh, M.; Karaman, C.; Orooji, Y. Cyanazine Herbicide Monitoring as a Hazardous Substance by a DNA Nanostructure Biosensor. *J. Hazard. Mater.* **2022**, *423*, 127058. [[CrossRef](#)] [[PubMed](#)]

42. Huang, Z.; Zhu, J.; Hu, Y.; Zhu, Y.; Zhu, G.; Hu, L.; Zi, Y.; Huang, W. Tin Oxide (SnO₂) Nanoparticles: Facile Fabrication, Characterization, and Application in UV Photodetectors. *Nanomaterials* **2022**, *12*, 632. [[CrossRef](#)] [[PubMed](#)]
43. Sharma, A.; Ahmed, A.; Singh, A.; Oruganti, S.K.; Khosla, A.; Arya, S. Review—Recent Advances in Tin Oxide Nanomaterials as Electrochemical/Chemiresistive Sensors. *J. Electrochem. Soc.* **2021**, *168*, 027505. [[CrossRef](#)]
44. Singh, J.; Dutta, T.; Kim, K.H.; Rawat, M.; Samddar, P.; Kumar, P. ‘Green’ Synthesis of Metals and Their Oxide Nanoparticles: Applications for Environmental Remediation. *J. Nanobiotechnol.* **2018**, *16*, 84. [[CrossRef](#)]
45. Narasaiah, B.P.; Banoth, P.; Sohan, A.; Mandal, B.K.; Dominguez, A.G.B.; Valladares, L.D.L.S.; Kollu, P. Green Biosynthesis of Tin Oxide Nanomaterials Mediated by Agro-Waste Cotton Boll Peel Extracts for the Remediation of Environmental Pollutant Dyes. *ACS Omega* **2022**, *7*, 15423–15438. [[CrossRef](#)]
46. Saadat Niavol, S.; Milani Moghaddam, H. SnO₂ Nanoparticles/Reduced Graphene Oxide Nanocomposite for Fast Ethanol Vapor Sensing at a Low Operating Temperature with an Excellent Long-Term Stability. *J. Mater. Sci. Mater. Electron.* **2021**, *32*, 6550–6569. [[CrossRef](#)]
47. Cheng, J.P.; Wang, J.; Li, Q.Q.; Liu, H.G.; Li, Y. A Review of Recent Developments in Tin Dioxide Composites for Gas Sensing Application. *J. Ind. Eng. Chem.* **2016**, *44*, 1–22. [[CrossRef](#)]
48. Hummers, W.S.; Offeman, R.E. Preparation of Graphitic Oxide. *J. Am. Chem. Soc.* **1958**, *80*, 1339. [[CrossRef](#)]
49. Li, Y.; Zhang, L.; Hu, Z.; Yu, J.C. Synthesis of 3D Structured Graphene as a High Performance Catalyst Support for Methanol Electro-Oxidation. *Nanoscale* **2015**, *7*, 10896–10902. [[CrossRef](#)]
50. Kumar, A.; Khandelwal, M. Amino Acid Mediated Functionalization and Reduction of Graphene Oxide—Synthesis and the Formation Mechanism of Nitrogen-Doped Graphene. *New J. Chem.* **2014**, *38*, 3457–3467. [[CrossRef](#)]
51. Suresh, K.C.; Surendhiran, S.; Manoj Kumar, P.; Ranjith Kumar, E.; Khadar, Y.A.S.; Balamurugan, A. Green Synthesis of SnO₂ Nanoparticles Using Delonix Elata Leaf Extract: Evaluation of Its Structural, Optical, Morphological and Photocatalytic Properties. *SN Appl. Sci.* **2020**, *2*, 1735. [[CrossRef](#)]
52. Narasaiah, B.P.; Mandal, B.K. Remediation of Azo-Dyes Based Toxicity by Agro-Waste Cotton Boll Peels Mediated Palladium Nanoparticles. *J. Saudi Chem. Soc.* **2020**, *24*, 267–281. [[CrossRef](#)]
53. Niu, X.; Li, X.; Chen, W.; Li, X.; Weng, W.; Yin, C.; Dong, R.; Sun, W.; Li, G. Three-Dimensional Reduced Graphene Oxide Aerogel Modified Electrode for the Sensitive Quercetin Sensing and Its Application. *Mater. Sci. Eng. C* **2018**, *89*, 230–236. [[CrossRef](#)]
54. Feng, H.; Cheng, R.; Zhao, X.; Duan, X.; Li, J. A Low-Temperature Method to Produce Highly Reduced Graphene Oxide. *Nat. Commun.* **2013**, *4*, 1539. [[CrossRef](#)]
55. Zhao, Y.; Li, H.; Li, Y.; Ma, Y.; Yang, H.; Liu, H.; Ren, X.; Zhao, H. Layered SnO₂ Nanorods Arrays Anchored on Reduced Graphene Oxide for Ultra-High and Ppb Level Formaldehyde Sensing. *Sens. Actuators B Chem.* **2021**, *346*, 130452. [[CrossRef](#)]
56. Sha, R.; Badhulika, S. Facile Green Synthesis of Reduced Graphene Oxide/Tin Oxide Composite for Highly Selective and Ultra-Sensitive Detection of Ascorbic Acid. *J. Electroanal. Chem.* **2018**, *816*, 30–37. [[CrossRef](#)]
57. Fadillah, G.; Wicaksono, W.P.; Fatimah, I.; Saleh, T.A. A Sensitive Electrochemical Sensor Based on Functionalized Graphene Oxide/SnO₂ for the Determination of Eugenol. *Microchem. J.* **2020**, *159*, 105353. [[CrossRef](#)]
58. Choudhari, A.; Bhanvase, B.A.; Saharan, V.K.; Salame, P.H.; Hunge, Y. Sonochemical Preparation and Characterization of RGO/SnO₂ Nanocomposite: Electrochemical and Gas Sensing Performance. *Ceram. Int.* **2020**, *46*, 11290–11296. [[CrossRef](#)]
59. Bansode, S.R.; Khare, R.T.; Jagtap, K.K.; More, M.A.; Koinkar, P. One Step Hydrothermal Synthesis of SnO₂-RGO Nanocomposite and Its Field Emission Studies. *Mater. Sci. Semicond. Process.* **2017**, *63*, 90–96. [[CrossRef](#)]
60. Tao, Y.; Kong, D.; Zhang, C.; Lv, W.; Wang, M.; Li, B.; Huang, Z.H.; Kang, F.; Yang, Q.H. Monolithic Carbons with Spheroidal and Hierarchical Pores Produced by the Linkage of Functionalized Graphene Sheets. *Carbon N. Y.* **2014**, *69*, 169–177. [[CrossRef](#)]
61. Li, G.; Shen, Y.; Zhou, P.; Hao, F.; Fang, P.; Wei, D.; Meng, D.; San, X. Design and Application of Highly Responsive and Selective RGO-SnO₂ Nanocomposites for NO₂ Monitoring. *Mater. Charact.* **2020**, *163*, 110284. [[CrossRef](#)]
62. Huang, J.; Meng, C.; Wang, H.; Ren, H.; Lu, X.; Joo, S.W. Preparation of Cross-Linked Porous SnO₂ Nanosheets Using Three-Dimensional Reduced Graphene Oxide as a Template and Their Gas Sensing Property. *J. Alloys Compd.* **2022**, *910*, 164763. [[CrossRef](#)]
63. Yu, X.; Wu, Q.; Zhang, H.; Zeng, G.; Li, W.; Qian, Y.; Li, Y.; Yang, G.; Chen, M. Investigation on Synthesis, Stability, and Thermal Conductivity Properties of Water-Based SnO₂/Reduced Graphene Oxide Nanofluids. *Materials* **2018**, *11*, 38. [[CrossRef](#)] [[PubMed](#)]
64. Alizadeh, M.; Mehmandoust, M.; Nodrat, O.; Salmanpour, S.; Erk, N. A Glassy Carbon Electrode Modified Based on Molybdenum Disulfide for Determination of Folic Acid in the Real Samples. *J. Food Meas. Charact.* **2021**, *15*, 5622–5629. [[CrossRef](#)]
65. Mehmandoust, M.; Çakar, S.; Özacar, M.; Salmanpour, S.; Erk, N. Electrochemical Sensor for Facile and Highly Selective Determination of Antineoplastic Agent in Real Samples Using Glassy Carbon Electrode Modified by 2D-MoS₂ NFs/TiO₂ NPs. *Top. Catal.* **2021**, *65*, 564–576. [[CrossRef](#)]
66. Yu, L.; Zhang, Q.; Yang, B.; Xu, Q.; Xu, Q.; Hu, X. Electrochemical Sensor Construction Based on Nafion/Calcium Lignosulphonate Functionalized Porous Graphene Nanocomposite and Its Application for Simultaneous Detection of Trace Pb²⁺ and Cd²⁺. *Sens. Actuators B Chem.* **2018**, *259*, 540–551. [[CrossRef](#)]
67. Yu, X.; Sheng, K.; Shi, G. A Three-Dimensional Interpenetrating Electrode of Reduced Graphene Oxide for Selective Detection of Dopamine. *Analyst* **2014**, *139*, 4525–4531. [[CrossRef](#)]

68. Laviron, E.; Roullier, L. General Expression of the Linear Potential Sweep Voltammogram for a Surface Redox Reaction with Interactions between the Adsorbed Molecules: Applications to Modified Electrodes. *J. Electroanal. Chem. Interfacial Electrochem.* **1980**, *115*, 65–74. [CrossRef]
69. Laviron, E. General Expression of the Linear Potential Sweep Voltammogram in the Case of Diffusionless Electrochemical Systems. *J. Electroanal. Chem. Interfacial Electrochem.* **1979**, *101*, 19–28. [CrossRef]
70. Bourlinos, A.B.; Stassinopoulos, A.; Anglos, D.; Zboril, R.; Karakassides, M.; Giannelis, E.P. Surface Functionalized Carbogenic Quantum Dots. *Small* **2008**, *4*, 455–458. [CrossRef]
71. Grimshaw, J. Chapter 6—Oxidation of Aromatic Rings. *Electrochem. React. Mech. Org. Chem.* **2000**, 203–218. Available online: <https://books.google.co.in/books?hl=en&lr=&id=kGWj4pLZY6wC&oi=fnd&pg=PP1&dq=+Oxidation+of+Aromatic+Rings.+by++Grimshaw,+&ots=2PcmIf0mjA&sig=RLSwtcuhEBpcuUcheExLQ8vyZzU#v=onepage&q=Oxidation%20of%20Aromatic%20Rings.%20by%20%20Grimshaw%2C&f=false> (accessed on 22 November 2022).
72. Özkan, S.A.; Özkan, Y.; Şentürk, Z. Electrooxidation of Pimozide and Its Differential Pulse Voltammetric and HPLC–EC Determination. *Anal. Chim. Acta* **2002**, *453*, 221–229. [CrossRef]
73. Zhang, H.; Bo, X.; Guo, L. Electrochemical Preparation of Porous Graphene and Its Electrochemical Application in the Simultaneous Determination of Hydroquinone, Catechol, and Resorcinol. *Sens. Actuators B Chem.* **2015**, *220*, 919–926. [CrossRef]

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.