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Research Article

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Layered Yttrium Oxide Reinforced Graphene Oxide Electrode Surface for Voltammetric Determination of Paracetamol

Parasetamolün Voltametrik Tayini için Katmanlı İtriyum Oksit Takviyeli Grafen Oksit Elektrot Yüzeyi

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ABSTRACT

In this study, graphene oxide (GO) was synthesized by the Hummers method starting from graphite. Also, yttrium(III) oxide (Y_2O_3, YO) was synthesized with the sol-gel method and was characterized by Fourier transform infrared spectroscopy (FTIR), X-Ray diffraction (XRD), scanning electron microscopy (SEM) and transmission electron microscopy (TEM) techniques. The sensor performance of the modified electrode against the paracetamol analyte was investigated by cyclic voltammetry (CV) and differential pulse voltammetry (DPV). As a result of the optimized voltammetric methods calculated the linear working range was 0.25-10.0 µM and the limit of detection (LOD) value was 19.0 nM. With the DPV method, advanced analytical parameters such as stability, reproducibility, and selectivity were studied. Moreover, the performance of the new sensor to detect paracetamol in real tablet samples was examined.

Key Words

Paracetamol detection, rare earth metals, carbon-based materials, electrochemical method.

ÖZ

Bu çalışmada grafitten yola çıkılarak Hummers yöntemiyle grafen oksit (GO) sentezlendi. Ayrıca sol-jel yöntemiyle itriyum(III) oksit (Y_2O_3, YO) sentezlendi ve Fourier dönüşümlü kızılötesi spektroskopisi (FTIR), X-Işını kırınımı (XRD), taramalı elektron mikroskobu (SEM) ve geçirimli elektron miktroskobu (TEM) teknikleriyle karakterize edildi. Modifiye elektrotun parasetamol analite karşı sensör performansı, dönüşümlü voltametri (CV) ve diferansiyel puls voltametrisi (DPV) ile araştırıldı. Optimize edilmiş voltametrik yöntemler sonucunda hesaplanan doğrusal çalışma aralığı 0.25-10.0 µM ve algılama limiti (LOD) değeri 19.0 nM olarak bulundu. DPV yöntemi ile stabilite, tekrarlanabilirlik ve seçicilik gibi ileri analitik parametreler üzerinde çalışıldı. Ayrıca yeni sensörün performansı gerçek tablet örneklerindeki parasetamolü tayin edebilmek için incelendi.

Anahtar Kelimeler

Parasetamol tespiti, nadir toprak metalleri, karbon bazlı malzemeler, elektrokimyasal yöntem.

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INTRODUCTION

Paracetamol ((N-(4-hydroxyphenyl) acetamide), PCM) is a compound with strong analgesic and antipyretic effects [1]. PCM is widely used in the treatment of migraines, muscle aches, colds, and coughs [2]. It is reported that the use of this drug in different forms (injection, tablet, or syrup) is approximately 30000-35000 tons every year. In addition to having complications such as acute kidney and liver failure, it also carries great risks in terms of environmental pollution [3]. For these reasons, interest in PCM detection continues with innovative methods that can provide sensitive and selective responses in environmental and clinical samples.

Current detection methods for PCM include high-performance liquid chromatography (HPLC) [4], electrophoresis [5], and spectrophotometry techniques [6]. Although these methods provide many advantages such as cheapness and sensitive properties, different approaches are needed in addition to these methods [7, 8]. To provide this innovation, electrochemical and optical sensor systems are widely preferred for the detection of many analytes [9-12]. Among these methods, the electrochemical detection mechanism comes to the forefront by offering cheap, easy, instrumentation and on-site analysis of the analyte [13,14]. These good properties were intended to be integrated into the present study, so the electrochemical method was preferred for PCM detection.

Carbon-based nanoparticles [10], quantum dots [15], metals [16], metal oxides [17], and polymers [18] are generally used to increase sensitivity in electrochemical sensors. Carbon-based nanoparticles, which have subclassifications such as single or multi-walled carbon nanotubes, graphene, graphene oxide (GO), and carbon quantum dots, have been used in different composite systems, allowing the design of sensitive sensors that can be used in a wide range of areas [19]. GO, an oxidized graphene sheet, contains sp^2 domains originating from the graphene structure and sp^3 domains because it has oxygen-containing groups. Having a very large surface area together with its good mechanical, thermal, and electronic properties allows it to find applications in a wide range of areas such as energy [20], sensor [21], and biomaterials [22,23]. Carbon-based materials are frequently encountered in studies conducted for the determination of paracetamol by the electrochemical method. Considering current studies, GO has been used for PCM detection together with structures such as palladium [24], zeolite [25], and titanium oxide (TiO_2) [26]. Yang et al. developed a molecularly imprinted electrochemical paracetamol sensor. It has been stated that many improvements have been made thanks to this electrode, in which gold/palladium (AuPd) nanoparticles are used together with ionic liquid functionalized 3D graphene-carbon nanotubes. However, it has been underlined that it needs improvement in storage and selectivity features to better meet practical sensor demands [27]. There is an improvement in sensor properties with the addition of different nanoparticle structures to the composite system.

Rare earth metals, including yttrium, and their oxide forms are of great interest for obtaining new surfaces in the development of electrochemical sensors. Among these oxide compounds, yttrium oxide (YO) attracts great attention and is used in different application areas thanks to its distinctive features such as porous structure, chemical stability, and large surface area [28].

In this study, optimized amounts of the GO@YO composite system, which is thought to increase the affinity of the PCM analyte, were coated on the GCE surface by drop-casting. The synthesized structures were characterized in detail physically, chemically, and morphologically. The newly obtained electrode surface was analyzed by cyclic voltammetry (CV) and differential pulse voltammetry (DPV) methods for PCM detection and determination of the electrochemical mechanism. It has been determined that the properties of the sensor have improved after the GO@YO modification. The recovery properties of tablet real samples, including reproducibility, stability, and selectivity, which are important parameters in sensor studies, were also examined by the DPV method. In addition, the easy preparation procedure and relatively inexpensive cost are also advantageous. The results showed that the newly designed electrochemical PCM sensor has sensitive, stable, and selective properties.

MATERIALS and METHODS

Chemicals

Glucose ($C_6H_{12}O_6$), ascorbic acid ($C_6H_8O_6$), uric acid ($C_5H_4N_4O_3$), urea (CH_4N_2O), sulfuric acid (H_2SO_4), potassium permanganate ($KMnO_4$), hydrogen peroxide (H_2O_2), yttrium(III) nitrate hexahydrate ($Y(NO_3)_3{\cdot}6H_2O$), ethylene glycol, citric acid, graphite, potassium dihydrogen phosphate (KH_2PO_4), dipotassium hydrogen phosphate (K_2HPO_4), potassium hexacyanoferrate(III) ($K_3[Fe(CN)_6]$), potassium hexacyanoferrate(II) trihydrate ($K_4[Fe(CN)_6].3H_2O$), N,N′-dimethylformamide (DMF), and paracetamol ($C_8H_9NO_2$) were obtained from Sigma-Aldrich, USA. No purification process was applied to the chemicals.

Characterization methods

Fourier transform infrared (FTIR, Perkin Elmer Spectrum 100 spectrophotometer, USA), and X-ray diffraction (XRD, Rigaku, Japan) spectroscopy were used for the chemical characterization of the synthesized structures. Surface morphological characterizations were observed with scanning electron microscopy (SEM, FEI-Nova) and transmission electron microscopy (TEM) images obtained with the Hitachi (HT-7700, Japan). Electrochemical analysis was carried out by an electrochemical analyzer system of CHI440B model CH Instruments (USA) at room temperature. All sensor measurements were performed with a three-electrode system consisting of a working electrode (modified GCE), reference electrode (silver/silver chloride, Ag/AgCl), and counter electrode (platinum (Pt) wire).

Synthesis of GO

For the synthesis, the traditional Hummers' method used for GO obtained from graphite by strong oxidizers in an acidic environment was preferred. The following work was taken as a reference for the synthesis procedure [29]. In brief, graphite was used as the starting material and the reaction procedure started by first dispersing graphite in H_2SO_4. Then, $NaNO_3$ was added to the medium while keeping the temperature constant at 4°C. As a second step, $KMnO_4$ was added to the medium as an oxidizer and the reaction medium was stirred with a magnetic stirrer for approximately 1 hour at 45°C. To terminate the reaction, distilled water and H_2O_2 were added to the medium. The resulting product was washed with pure water, precipitated in a centrifuge, and dried completely in an oven at 50°C.

Synthesis of YO

A study in the literature was followed with some modifications for the synthesis of YO by the sol-gel method [30]. $Y(NO_3)_3.6H_2O$ and citric acid starting materials were dissolved in 25 mL and 10 mL of distilled water, respectively. After dissolution was completed, the two solutions were mixed and stirred at room temperature with the aid of a magnetic stirrer. The addition of ethylene glycol to the medium was made considering the citric acid:ethylene glycol molar ratio (1:1, n:n). Stirring was continued and gelation was achieved by bringing the temperature to about 200°C. In the last step, the gel was exposed to a temperature of 300°C in an oven to burn organic residues and calcined in a furnace at 750°C to obtain crystalline YO.

Electrode Modification and Electrochemical Measurements

All electrochemical measurements were taken in 0.05 M, pH 7.0 phosphate buffer solution (PBS). PBS was prepared using salts KH_2PO_4 and K_2HPO_4 salts. The GCE surface was cleaned with slurries of alumina powders of different sizes (0.03 µm, 0.05 µm, and 0.1 µm). It was then washed with distilled water and ethanol, respectively, and dried at room temperature. 3.0 µL of the GO dispersion prepared by sonication in 1.0 mg/mL DMF for about 10 minutes was dropped onto the polished electrode surface and allowed to dry at room temperature. A 3.0 µL drop of 1.0 mg/mL YO dispersion, which was prepared by dispersing in distilled water for about 10 minutes, was dropped on the surface of the obtained GO/GCE electrode. The modified final version, GO@YO/GCE, was also made ready for use after drying at room temperature. CV measurements were performed at a scan rate of 100 mV/s between 0.0 and 1.0 V. DPV analyses were noted from 0.0 to 0.8 V at a pulse period of 0.5 s, an amplitude of 0.05 V, and a pulse width of 0.2 s. Three replications were made for the electroanalytical measurements.

Preparation of real sample

A commercially available PCM tablet was crushed into a powder form. The obtained powder from PCM was dissolved in 0.05 M PBS medium at pH 7 and then filtered through filter paper and stored in the refrigerator at +4°C. Before the electroanalytical measurements, it was diluted with PBS with the same properties at the desired ratio and used. The remaining solution was stored in the refrigerator for later use [2].

RESULTS and DISCUSSION

Characterization of GO and YO nanoparticles

The FTIR spectrum was used for the chemical characterization of the synthesized GO and YO structures. In addition, the XRD spectrum was taken for materials because in order to get more accurate and clear information. The obtained spectra are given in Figure 1. Figure

1a shows the FTIR spectrum for GO. The broad peaks between 3100-3600, 1640, 1444, and 1050 cm^{-1} detected in the spectrum are due to C–H stretching, C=C stretching, C-H stretching, C-OH and C-O stretching. It was observed that these peaks supported strong groups containing oxygen and were found to be compatible with the literature [31]. The FTIR spectrum of the YO structure is also given in Figure 1b. The peak at 557 cm^{-1}, which supports the presence of Y-O bond, was determined in accordance with the literature [32]. The peaks observed at approximately 1510 and 1406 cm^{-1} can be considered as stretching peaks indicating the formation of citric acid complexes with Y ions [30]. According to the XRD spectrum shown in Figure 1c, it was determined that the YO sample obtained after calcination had a good crystal structure and characteristic diffraction peaks supporting the presence of pure-phase YO, which supports the ICDD PDF 41-1105 standard data [33]. In addition, the peaks at 2θ=10.66° and 42.62° in the XRD spectrum of GO also support the structure [34].

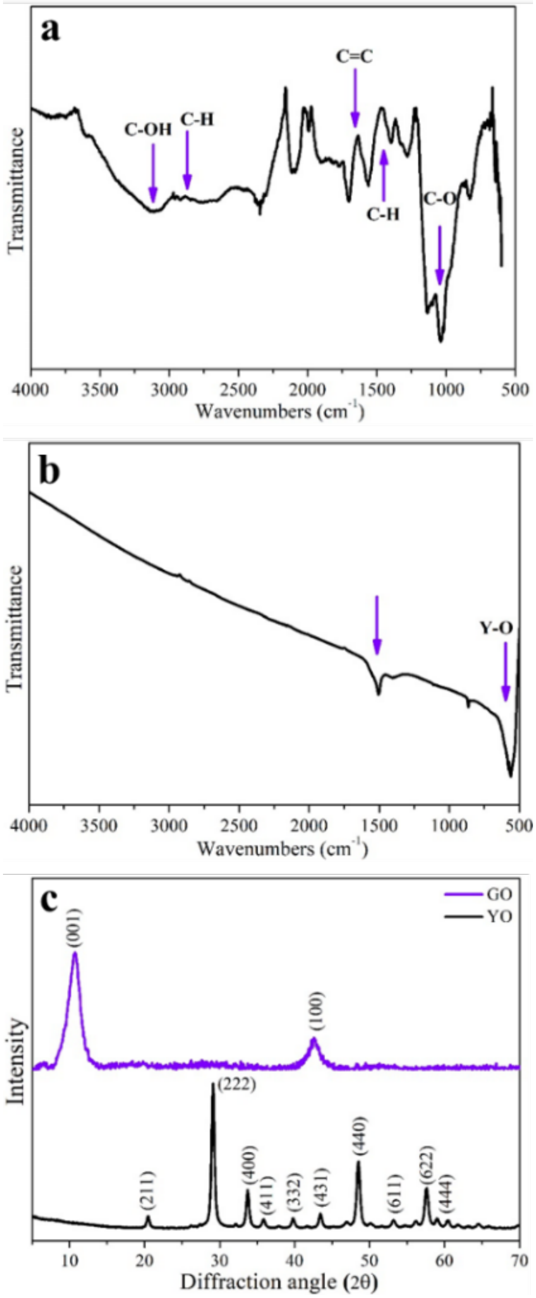


Figure 1. FTIR spectra of a) GO, b) YO, and c) XRD spectra of YO and GO.

SEM and TEM images determined for the morphological characterization of YO nanoparticles are given in Figure 2. The surface image obtained from SEM (Figure 2a) analysis highlights an irregular structure. However, TEM images (Figure 2b-c) better represent the nanoparticle structure. The average particle size of the ImageJ program YO was calculated to be 30±4 nm.

Optimization parameters of the working electrode

Optimization studies make a great contribution to getting the best performance from any developed sensor. Therefore, for this study, the optimizations of GO and YO, which are the components used in electrode modification, were carried out. Line graphs of numerical values obtained from CV are given in Figure 3. In the optimization study, first of all, the amount of GO was optimized by considering the steps in the coating procedure. In the optimization study performed at five different concentrations, 0.25, 0.50, 1.00, 2.00, and 4.00 mg/mL, it was observed that the peak current value increased up to 1.0 mg/mL. However, it was determined that there was a decrease in the peak current value due to the problems that may be caused by the closure of the surface (Figure 3a). After determining the optimum value for GO, the amount of YO coated on it was evaluated for five different concentrations: 0.25, 0.50, 0.75, 1.00, and 2.00 mg/mL (Figure 3b). While the peak current value increased up to 1.0 mg/mL, no significant change was observed in the peak current value afterward. As a result of the optimization, 1.0 mg/mL was accepted as the optimum for both components and these amounts were used for all electrochemical studies.

Electrochemical characterization of the GO and YO-modified electrode

In Scheme 1, the electrochemical reaction mechanism of the electrode preparation process is given. The first and second steps represent coating the cleaned GCE surface first with GO and then with YO. The third step includes the electrochemical redox reaction of PCM,

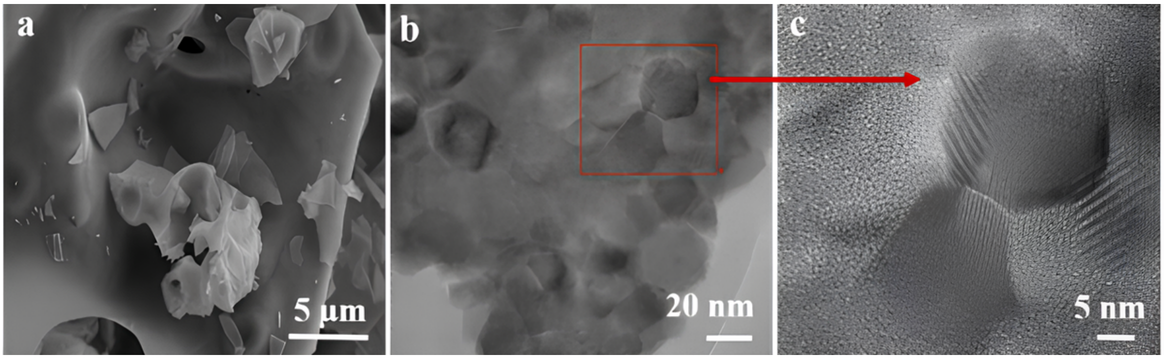


Figure 2. a) SEM and b, c) TEM images of YO nanoparticles.

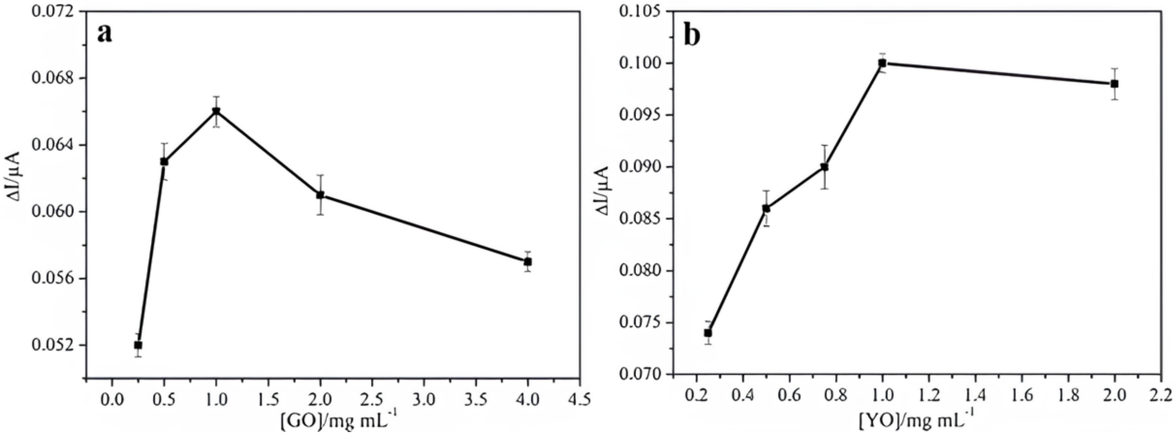
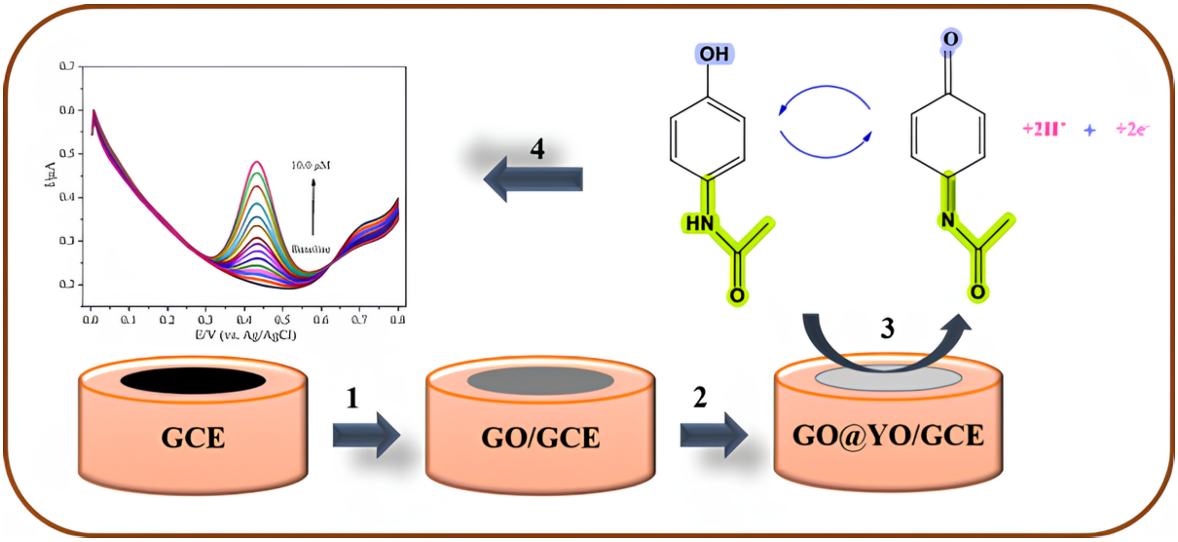


Figure 3. Optimizations of GO@YO/GCE sensor a) GO and b) YO concentrations.



Scheme 1. GO@YO/GCE electrode preparation and electrochemical PCM detection mechanism.

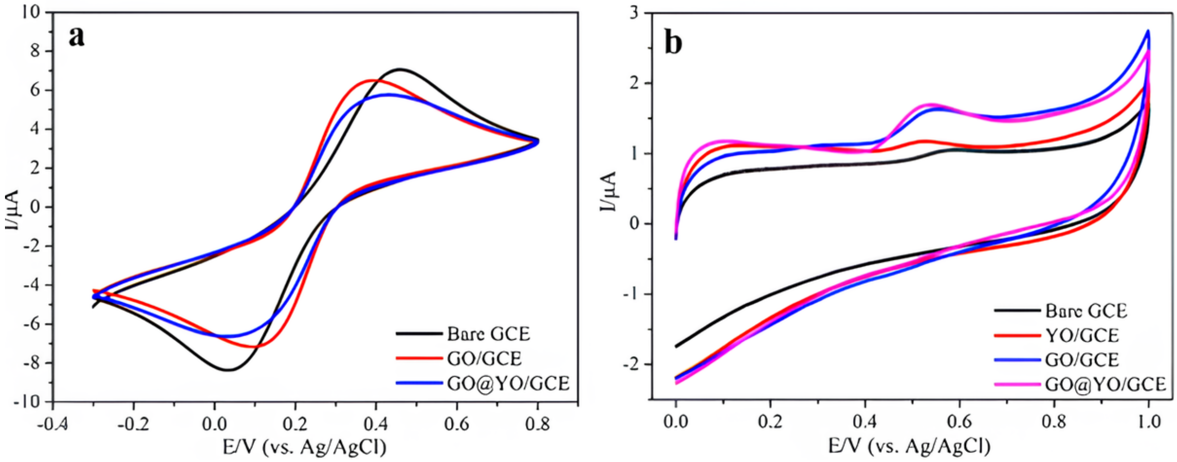


Figure 4. a) CV responses of different groups in 5.0 mM $[Fe(CN)_6]^{3-/4-}$ containing 0.1 M KCl and b) in 7.5 μM PCM containing a pH of 7.0 PBS.

and the fourth step includes the DPV results obtained within the scope of the study. In more detail, the oxidation mechanism of PCM is as follows: The electro-oxidation reaction for PCM starts in the phenolic group. In other words, an intermediate radical ion is formed by separating H from the hydroxy group in the PCM structure. In order to form the final product, which is then stabilized, an H separation occurs in the amide group and the oxidation reaction is completed [35].

To determine the effect of the designed sensor component, electrochemical characterization was performed in 0.1 M potassium chloride (KCl) containing 5.0 mM ferro/ferri cyanide ($[Fe(CN)_6]^{3-/4-}$) solution, and the redox performances of bare GCE, GO/GCE, and GO@YO/GCE were evaluated (Figure 4a). We are of the opinion that there is no significant difference in the oxidation peak current values, and this may be due to the fact that the coated structures are oxide. However, with the shift of the peak potentials in the modified electrodes compared to the bare GCE, it can be concluded that the new electrode acts as a catalyst for better performance [13]. In Figure 4b, the electrochemical responses of the components constituting the final sensor against the analyte in PBS containing 7.5 μM PCM were investigated. According to the peak current values obtained, in the measurements made against paracetamol at the same concentration, it was determined that GO/GCE showed 2.86 times higher peak current values compared to unmodified GCE, and GO@YO/GCE showed 4.31 times higher peak current values. These results support that the newly modified electrode gives more sensitive electrochemical results against PCM.

Effect of the scan rate

In order to evaluate the electrochemical reaction mechanism of GO@YO/GCE, different scanning rates were taken by the CV method in a PBS medium in the presence of PCM, and the obtained voltammograms are given in Figure 5a. The correlation between the CV peak current value and the scan rate peak current value for the PCM is given in Figure 5b. A linear increase was determined in line with the data in the graph ($y=0.4533x + 0.3728$, $R^2 = 0.9904$). The slope of the graphs of $\upsilon^{1/2}$ versus I_{pa} (Figure 5c) was evaluated to determine whether the electrochemical detection was diffusion-controlled or adsorption-controlled. It has been observed that there is a linear relationship between the peak current (I_p) and the square root of the scan rate ($\upsilon^{1/2}$) at scan rates between 50-500 mV/s. The linear regression determined for Figure 5c is $y=0.1174x + 0.5269$, $R^2 = 0.9898$. As a result, it was stated that the redox reaction for PCM was diffusion-controlled [36]. In the literature, PCM sensors are widely diffusion controlled. For example, Li et al. developed an electrode based on multi-walled carbon nanotubes that can detect levodopa, paracetamol, and L-tyrosine analytes. It has been explained that all oxidation peak currents of all three analytes increase linearly with the square root of the scanning rate, and therefore the electrochemical reaction is diffusion-controlled [37].

Analytical performance

The analytical performances of the GO@YO/GCE sensor at different PCM concentrations were examined by the DPV method and the obtained voltammograms are presented in Figure 6a. As seen from the voltammograms, the peak currents at 0.432 V increased linearly with the

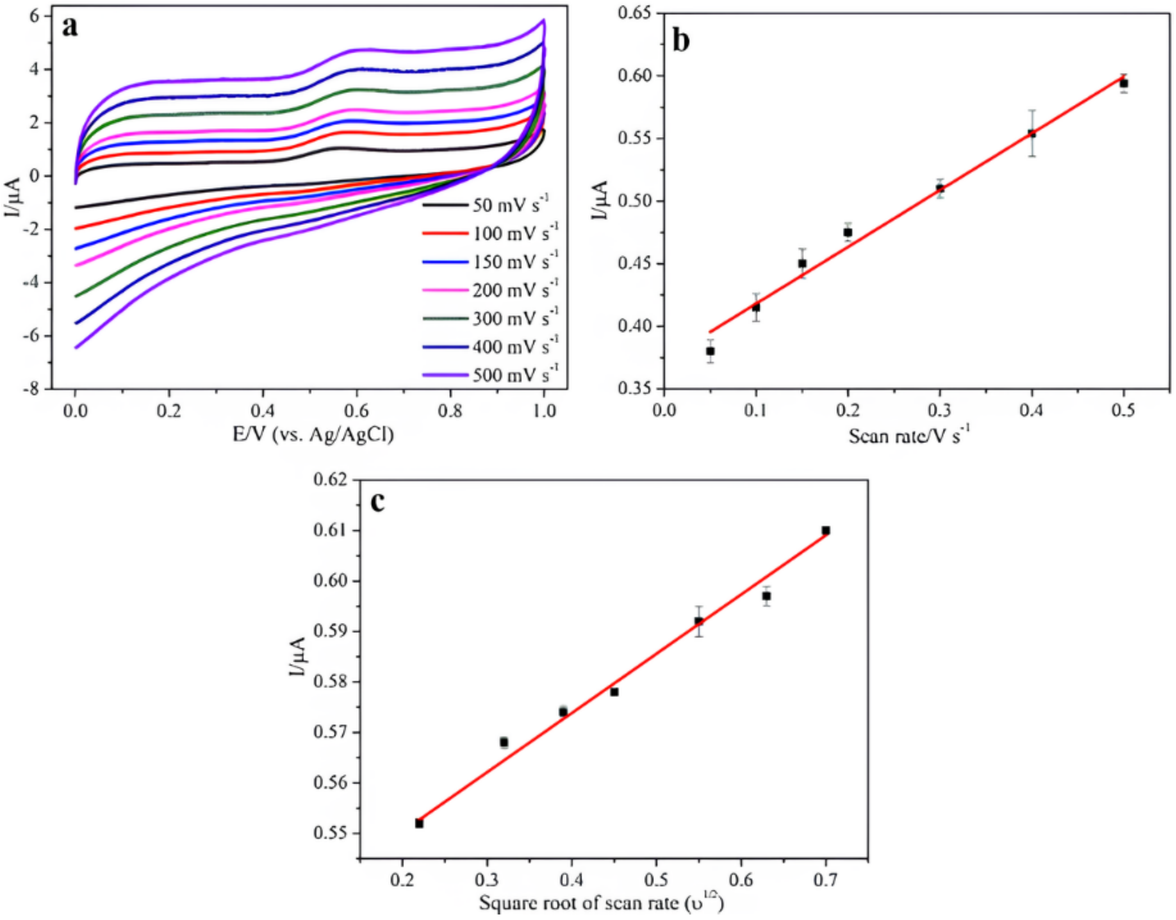


Figure 5. a) CVs of GO@YO/GCE at different potential scan rates, b) dependence of the oxidation peak current, and c) graph of $\upsilon^{1/2}$ versus Ipa on the scan rate.

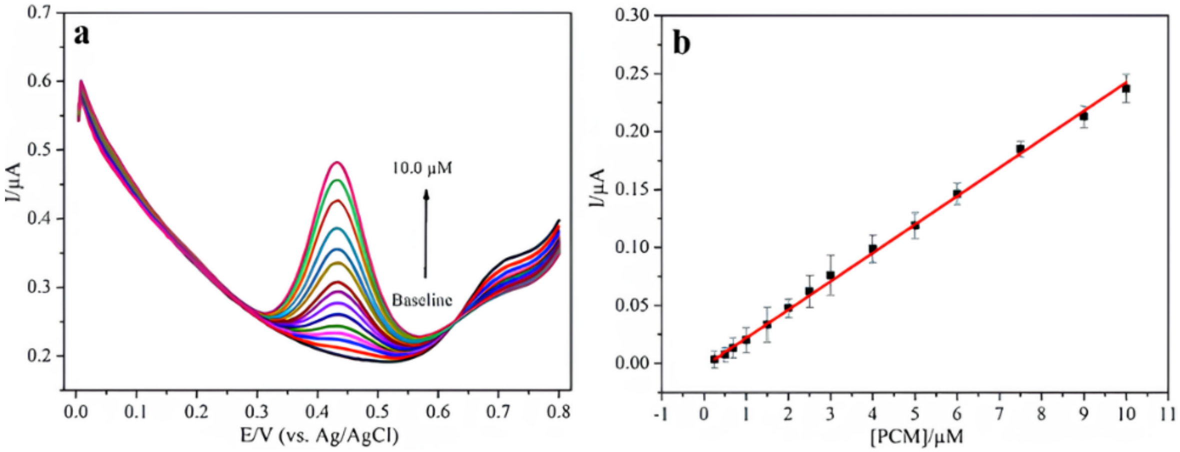


Figure 6. a) DPV responses at increasing concentrations of PCM on the GO@YO/GCE and b) calibration graph.

increase in PCM concentration. The correlation between PCM concentration and peak current values given in Figure 6b also supports this linear relationship between 0.25-10.0 μM. The linear regression equation was determined as I(μA)= 0.0245C (μM) + 0.0026 (R^2 = 0.9987). As a result of data obtained from DPV results for PCM, the limit of detection (LOD) and limit of quantification (LOQ) were calculated as 19.0 nmol/L and 62.7 nmol/L.

In Table 1, the analytical outputs for the PCM sensor studies were compared with those of other PCM sensors [38-42]. While selecting the studies, sensors containing GO or reduced GO were preferred. Among the current studies in Table 1, the fact that the current study is relatively simple in its preparation procedure is seen as an advantage. In addition, considering the LOD values, very low values were determined in this study compared to the literature. The LOD value of the electrode modified with graphene oxide/Zn-metal organic framework is lower than in this study, but the narrow linear working range is seen as a disadvantage. Moreover, recoveries calculated from real sample analyses show similar characteristics to literature studies. Therefore, it can be said that the performance of the new PCM sensor obtained has advantages over the literature. In addition, in a study, a GO-Y_2O_3 composite structure was synthesized by the hydrothermal method, and a carbon paste consisting of graphite and paraffin oil was mixed into the electrode [43].

However, the characteristics such as the low chemical and mechanical resistance of the carbon paste electrode are stated as disadvantages [44]. In addition to its disadvantages, the component of oil, which is a petroleum refining product, is not stable. This can lead to the incorporation of undesirable compounds into the measurement medium. Also, the non-conductiveness of the oil component is another limiting factor. Because a non-conductive component weakens the electrochemical response of the sensor [45]. Differently, in the aforementioned study, the sensor components were synthesized in the same environment. This may also pose some obstacles to optimization. As a matter of fact, while the LOD value was found to be 1.45 μM in the study, it was found to be 19.0 nM in the current study. In the GO@YO/GCE sensor, each component was synthesized separately and coated on the electrode surface layer by layer. In addition, the individual optimization of each component and the use of GCE, which exhibits more stable properties as an electrode, both make this work different and provide better performance. Devadas et al. also used yttrium hexacyanoferrate on reduced GO structure for electrochemical PCM detection. They calculated the LOD value as 80 nM in their determination with CV and linear sweep voltammetry techniques [46]. As observed, different forms of similar structures have been evaluated in various composite systems and contributions have been made to the literature.

Stability and reproducibility

In the system containing 7.5 μM PCM in PBS medium, the stability of the sensor was determined based on 10 consecutive measurements taken with the GO@YO/GCE sensor. The obtained voltammograms are given in Figure 7a and the %RSD value was calculated as 2.71%. Finally, the stability of the designed PCM sensor was found to be sufficient (<5%).

Table 1. Comparisons of electrochemical PCM sensors.

Working Electrode	LOD (nM)	Linear range (μm)	Real Samples	Recovery (%)	Ref
Multi-walled carbon nanotube/ GO/poly(threonine) composite	160	5-50	Tablet formulation and human serum	96.0-101.0%	(38)
Ferrocene-functionalized GO	210	2–200	Human urine samples	98.80-101.82%	(39)
Electroreduced GO-cobalt phthalocyanine Polymer Nanocomposite	104	7.0–90	Synthetic urine samples	96.0-101.0%	(40)
A GO/Zn-metal organic framework	14.0	0.05–1.3	Human urine samples and drug tablets	90% and 110%	(41)
Hollow Fe_3O_4-reduced GO-Nanocomposites	110	0.5-100	Tablets	100.52-101.43%	(42)
Carbon paste electrode with a GO-Y_2O_3 nanocomposite	1450	7-400	Commercial pharmaceutical sample	100.13-104.86%	(43)
Flower-like yttrium hexacyanoferrate particles/ reduced GO/glassy carbon electrode	80	10-1000	Commercial paracetamol tablets	95.0-98.0%	(46)
GO@YO/GCE	19.0	0.25-10	Tablet	96.4%-100.9%	This work

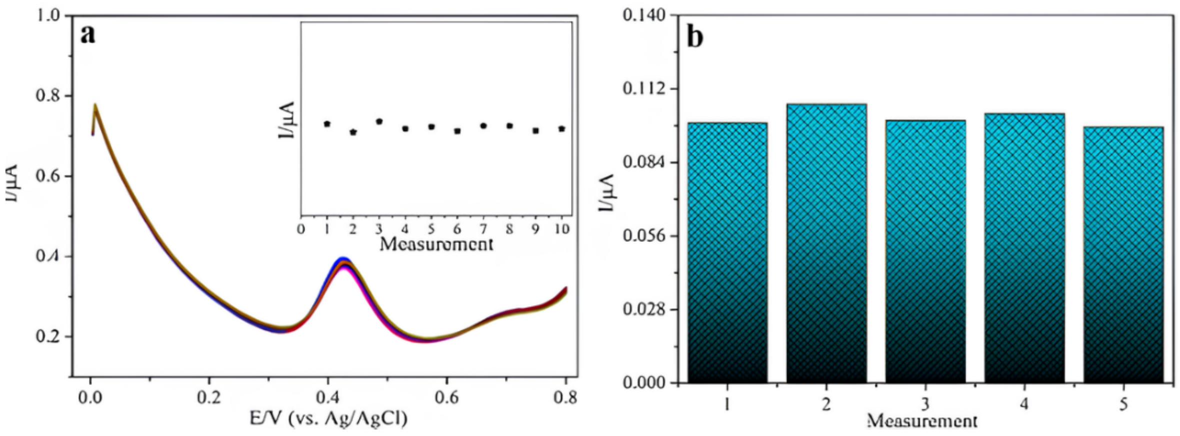


Figure 7. a) DPV voltammograms for consecutive 10 measurements and b) reproducibility test for 5 measurements of GO@YO/GCE.

The reproducibility of a sensor is an important parameter and for this purpose, the DPV responses of five sensors taken in the measurement medium containing 5.0 μM PCM were recorded and analyzed to test the GO@YO/GCE sensor. The column chart drawn according to the calculated data is given in Figure 7b, and the %RSD value was determined as 3.36%. These results show the reproducibility of the sensor with good accuracy.

Effect of the interferences

The selectivity of the developed PCM sensor (GO@YO/GCE) was investigated to evaluate the effect of various inhibitory substances such as urea, uric acid, glucose, and ascorbic acid. First, 30 eqv. interfering agents were added to PBS and analyzed by DPV in a PCM-free medium. As seen in the voltammograms given in Figure 8a, no peak formation was observed. Afterward, the peak current value was calculated by adding 7.5 μM PCM to

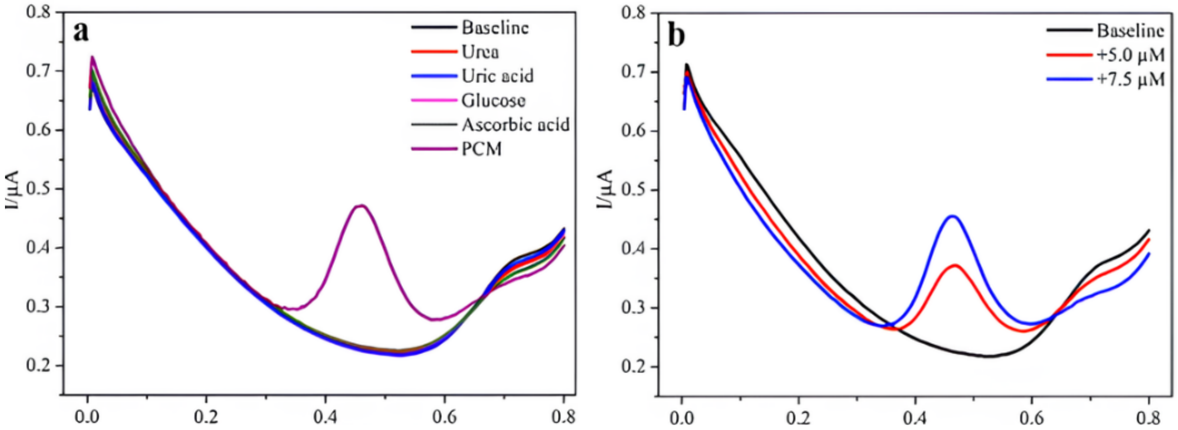


Figure 8. DPV results of a) selectivity and b) real sample analysis with the GO@YO/GCE electrode against PCM.

Table 2. Determination of PCM by GO@YO/GCE sensor with DPV in a commercial tablet.

Real Sample	Added (µM)	Found (mM)	Recovery (%)
Tablet	0	-	-
	5.0	4.82±0.15	96.4
	7.5	7.57±0.32	100.9

the measurement medium. The relative error calculated after three repetitive electrochemical measurements was found to be 3.47%. Selected interfering species have been widely preferred in the literature for the evaluation of PCM selectivity. For example, Gürsoy et al. developed a graphene-supported poly(3-aminophenyl boronic acid) surface for electrochemical PCM detection. In the selectivity study conducted with the DPV method, they used uric acid and glucose as the species that could interfere and did not detect any interference [47]. Bhangoji et al. also used NaCl, KCl, glucose, uric acid, ascorbic acid, and dopamine as the species that can interfere with the PCM analyte and tested them by the amperometric method. According to the data they obtained, it was stated that the species with the potential to interfere show a negligible peak current value [48]. Thus, it has been determined that the studies conducted for GO@YO/GCE are compatible with the literature.

Real sample analysis

Sensitive, easy, and accurate detection of PCM in pharmaceutical tablets is important. For this reason, tablets were preferred for real sample analysis in this study, and the appropriate calculated volume was added to PBS. The obtained voltammograms are given in Figure 8b and the numerical values calculated are given in Table 2. When the voltammogram is examined, it is observed that first of all, the fixation of the PBS baseline without PCM is ensured for the correct determination of the amount, and there is no electrochemical response of the PCM as expected. Then, PCM was added to the PBS as the first concentration of 5.0 µM and after the measurement was taken, the second concentration was 7.5 µM PCM. Thus, the amount of PCM for two additions was determined and its accuracy was determined by spike and recovery tests. According to the data obtained, the % recovery values were determined as 96.4% and 100.9%. Therefore, it can be said that the new electrochemical sensor developed within the scope of the study is successful for high-accuracy PCM determination in the tablet sample. When current studies are examined, there are many studies in which the tablet is used as a real sample. In the study of Prasad et al., the tablet was used as one of the PCM recovery samples, and the values were determined as 96.00%-98.40% [38].

CONCLUSION

As a result, GO and YO structures synthesized by Hummers and sol-gel methods, respectively, were used for the first time in GCE modification to develop a PCM sensor with good electroanalytical properties. It was determined that this new composite system, which was developed as a paracetamol sensor by electrochemical method, showed good sensitivity and electrocatalytic effect compared to the unmodified GCE. In other words, in the measurements made against paracetamol at the same concentration, the peak current value was 2.86 times higher for GO/GCE and 4.31 times higher for GO@YO/GCE compared to unmodified GCE. It has been observed that this sensor with a linear operating range of 0.25-10.0 µM has a quasi-reversible redox mechanism and a diffusion-controlled process. In addition, the LOD value was calculated as 19.0 nM. The newly developed conductive composite system exhibited reproducible, stable, and selective properties. In addition, as a real sample analysis, the recovery test of the PCM value contained in the tablet was performed and a good result was calculated with the 96.4-100.9% value. Apart from its good analytical properties, it has a relatively inexpensive and easy process that can be compared with other methods presented in the literature, which may enable it to be preferred as an alternative method.

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