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# GLASSY CARBON ELECTRODE MODIFIED WITH POLY(TAURINE)/$TiO_2$-GRAPHENE COMPOSITE FILM FOR DETERMINATION OF ACETAMINOPHEN AND CAFFEINE

*A novel electrochemical sensor poly(taurine)/$TiO_2$-graphene nanocomposite modified glassy carbon electrode (PT/$TiO_2$-Gr/GCE) was fabricated. This sensor was based on an electrochemically polymerized taurine layer on a $TiO_2$-graphene modified glassy carbon electrode. The electrochemical behavior of acetaminophen and caffeine at the modified electrode was studied by cyclic voltammetry and differential pulse voltammetry. The results showed that the oxidation peak currents of acetaminophen and caffeine were linear with their concentrations in the range of $1\times10^{-7}$-$9\times10^{-5}$ M and $2.5\times10^{-5}$-$2\times10^{-4}$ M, respectively. The detection limits of acetaminophen and caffeine were $3.4\times10^{-8}$ M and $5.0\times10^{-7}$ M, respectively (S/N = 3). This modified electrode showed good sensitivity and stability, which has promising potential applications in electrochemical sensors and biosensors design.*

*Keywords: taurine; $TiO_2$-graphene nanocomposite; acetaminophen; caffeine; electropolymerization.*

Acetaminophen (*N*-acetyl-*p*-aminophenol or paracetamol), an antipyretic and analgesic drug, is widely used in the world. It is used mainly as an effective medicine for the relief pain and reduction of fever and a suitable alternative for patients who are sensitive to aspirin [1-5]. Caffeine (3,7-dihydro-1,3,7--trimethyl-1*H*-purine-2,6-dione) is a natural alkaloid *N*-methyl derivative of xanthine, and is extensively present in foods such as coffee, tea, cola nuts, yerba-mate, guarana berries and cacao bean. Caffeine ingestion exerts many physiological effects, such as stimulation of the central nervous system, diuresis and gastric acid secretion [2]. The unique properties of caffeine are also applied in analgesic preparations. Therefore, acetaminophen and caffeine often occur together in analgesic pharmaceutical formulations.

Generally, limited use of acetaminophen and caffeine does not exhibit any harmful side effects. However, overdosed ingestions of acetaminophen lead to the accumulation of toxic metabolites, which may cause severe and sometimes fatal heptatotoxicity and nephrotoxicity, which in some cases associate with renal failure [4-7]. Caffeine is considered to be a risk factor for cardiovascular diseases and may have behavior effects such as depression and hyperactivity. Therefore, in analgesic preparation *ca*. 200 mg per day of dosage is generally recommended [8]. It is vital to establish a simple, sensitive, accurate methodology for simultaneous determination of acetaminophen and caffeine. Some methods including titrimetry [9], spectrophotometry [10-12], liquid chromatography [13-15] and electrochemistry [3,4,6, 16-22] have been developed for the individual estimation of two molecules. Only a few methods have been reported for the determination of acetaminophen and caffeine. Lau *et al*. used perchloric acid-methanol (1:1) as the solvent and electrolyte to improve the sensitivity and peak separation of acetaminophen and caffeine. Obviously, it is difficult to make quantitative determination due to the addition of easily evaporating methanol [23]. Zen and Ting used a nafion/ruthenium oxide pyrochlore chemically modified electrode for the simultaneous determination of acetaminophen and caffeine in drug formulation by square-wave voltammetry. The experiments were completed in 0.05 M perchloric acid, high cost reagent with controlled sale [8]. Fatibello-Filho *et al*. used a boron-doped diamond

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(BDD) electrode for acetaminophen and caffeine simultaneous determination. However, prior to the experiments, this electrode was cathodically pretreated in a 0.5 mol $L^{-1}$ $H_2SO_4$ solution [2]. Sanghavi *et al.* used an *in situ* surfactant-modified multi-walled carbon nanotube paste electrode for simultaneous determination of acetaminophen and caffeine. An accumulation potential of -0.7 V and an accumulation duration time of 300 s were used for stripping voltammetric analysis [24].

Recently, graphene (Gr) was found to be an ideal two-dimensional (2D) catalyst support to anchor metal and semiconductor catalyst nanoparticles because of its unique two-dimensional geometric structure, large surface area, and high mobility of charge carriers [25]. Being a famous semiconductor, $TiO_2$ has received much attention due to its nontoxicity, long-term stability, low cost and mutifunctions [26]. Most recently, we reported the $TiO_2$-Gr nanocomposite prepared by hydrothermal method using graphene as templates to immobilized $TiO_2$ nanoparticles. The as-prepared $TiO_2$-Gr exhibited remarkable electrocatalytic activity toward dopamine oxidation [23]. Taurine is a well-known dissociated amino acid, which exhibits important physiological functions and pharmacological characteristics. It has been widely used as a food nutrition enhancer and common drug. Taurine possesses electron-rich N atoms and high electron density of sulfonic groups. Hence, the poly(taurine) (PT) film is negatively charged and is propitious to adsorb acetaminophen and caffeine from the solution. PT modified electrodes have been reported and have shown good electrochemical performance [27, 28]. In this work, we report about the fabrication of PT modified electrode by electrochemical polymerization of taurine on the $TiO_2$-Gr-modified glassy carbon electrode (PT/$TiO_2$-Gr/GCE) and the application of the modified electrodes for simultaneous detection of acetaminophen and caffeine.

## EXPERIMENTAL

### Chemicals and materials

Graphite powder (320 mesh, spectrum pure) was purchased from Sinopharm Chemical Reagent Co., Ltd., China. Titanium isopropoxide ($Ti(O^iPr)_4$) was obtained from Aladdin Chemistry Co., Ltd., China. Acetaminophen and caffeine were purchased from Alfa Aesar and used without further purification. Taurine was purchased from Shanghai No. 1 Chemical Company (Shanghai, China). The phosphate buffer solution (PBS) was prepared using $Na_2HPO_4$ and $NaH_2PO_4$. Double distilled water was used to prepare all solutions used in the present work.

### Apparatus

All electrochemical experiments were carried out with a CHI660D electrochemical workstation (CH Instruments, Shanghai). A conventional three-electrode system was used for all electrochemical experiments, which consisted of a platinum wire as counter electrode, an Ag/AgCl/3M KCl as reference electrode, and a bare or modified glassy carbon electrode (3mm diameter) as working electrode. All pH measurements were measured with a PHS-3C digital pH meter (Shanghai Rex Instrument Factory, Shanghai, China). A Hitachi S-4800 scanning electron microscope (SEM) was used.

### Preparation of $TiO_2$-graphene nanocomposite

Graphene oxide was synthesized from graphite powder according to the modified Hummers method [29,30]. Gr was obtained by the chemical reduction of a colloidal suspension of exfoliated graphene oxide sheets in water with hydrazine hydrate [31]. To prepare $TiO_2$-Gr nanocomposite, Gr (50 mg), titanium isopropoxide (0.2 mL) and $H_2SO_4$ (1 M, 2 mL) was firstly added into a 25-mL Teflon-sealed autoclave. This resultant mixture was ultrasonicated for 10 min, and then the autoclave was kept in oven for 24 h at the temperature of 170 °C. Finally, black powder of $TiO_2$-Gr nanocomposite was obtained by filtration, rinsed thoroughly with deionized water and methanol, and dried in vacuum [25].

### Preparation of the modified electrodes

The as-prepared $TiO_2$-Gr nanocomposite (1.5 mg) was dispersed in DMF (4.0 mL) to form a homogenous suspension. Before modification, glass carbon electrode (GCE) was polished to a mirror-like with 0.3 and 0.05 μM of alumina slurry, and then washed successively with ultrapure water, anhydrous alcohol and ultrapure water in an ultrasonic bath and dried in $N_2$ flow. The $TiO_2$-Gr film-modified GCE ($TiO_2$-Gr/GCE) was prepared by dropping 6 μL of the resultant suspension on the cleaned GCE, and dried at room temperature.

The PT/GCE and PT/$TiO_2$-Gr/GCE were prepared as follows. Cyclic voltammetry (CV) was used to form polymerization film on the bare GCE and $TiO_2$-Gr/GCE, respectively. The polymeric film was deposited by cyclic sweeping from -1.5 to 2.0 V at 100 $mVs^{-1}$ for 10 cycles in PBS (pH 7.0) containing $2.0\times10^{-3}$ M taurine. The obtained electrodes were individually noted as PT/GCE and PT/$TiO_2$-Gr/GCE.

### Serum sample preparation

Human blood serum samples were obtained from healthy volunteers. The samples were centrifuged at 4000 rpm for 30 min at room temperature. Then 1.2 mL of acetonitrile was added to remove serum protein, followed by fortification with acetaminophen and caffeine. After vortexing for 1 min, the mixture was centrifuged for 10 min at 10000 rpm to remove the serum protein residues. The supernatant was taken carefully and appropriate volumes of this supernatant were transferred into the electrochemical glass cell and diluted up to the volume with the PBS.

## RESULTS AND DISCUSSION

### Surface morphology of $TiO_2$-graphene and poly(taurine)/$TiO_2$-graphene composite

The surface morphologies of $TiO_2$-Gr and PT/$TiO_2$-Gr composite were examined by SEM observation (Figure 1). In Figure 1A, it can be seen that $TiO_2$ was formed in a highly faceted morphology on the substrates of Gr with *ca.* 20-30 nm diameter for the clusters. As shown in the SEM images, the as-prepared $TiO_2$-Gr nanocomposite exhibited considerable edge plane defect structures. These edge plane defects have shown to be essentially responsible for the high electron transfer kinetics and the electrocatalytic activity of Gr, which contributed significantly to the electrochemical property of the present $TiO_2$-Gr nanocomposite as well. Figure 1B depicts the SEM image of the PT/$TiO_2$-Gr composite, showing that a layer of PT was formed on the $TiO_2$-Gr surface.

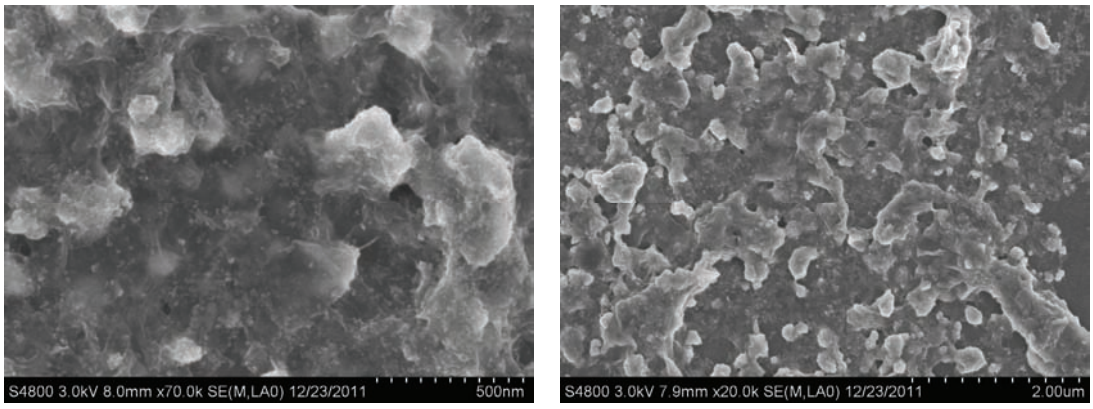
### The electropolymerization of taurine at the $TiO_2$-graphene/GCE

In the previous reports, repeated cyclic voltammetry was used for the electrochemical formation of PT film. The potential scan range was the most important factor. If the positive value for polymerization was below 1.6 V or if the negative one was above -0.8 V, no polymer reaction occurred [26]. Therefore, we selected the potential range of -1.5 and 2.0 V as the electropolymerization potential window in this work.

Figure 2 shows CVs of electrochemical polymerization of taurine on the $TiO_2$-Gr/GCE. One obvious reduction peak was observed at -0.7 V. An increase in cycle number results in the enhancement of the peak currents and a slight shift of potential peak, which was reflecting the continuous growth of the film. It could be observed that the film growth was faster for the first four cycles than for the other cycles. After modification, a shiny and light green color was found on the electrode surface. These facts indicated taurine was deposited on the surface of $TiO_2$-Gr film modified GCE by electropolymerization. The inset of Figure 2 shows CVs of electrochemical polymerization of taurine on the GCE, and a similar phenomenon was obtained.

### Effect of different electrodes

In the present study, the electrochemical behavior of the mixture containing acetaminophen and caffeine on the aforementioned electrodes (bare GCE, $TiO_2$-Gr/GCE, PT/GCE, PT/$TiO_2$-Gr/GCE) was investigated using the CV. Figure 3 depicts CVs curves of the acetaminophen and caffeine (0.1 mM) in PBS (0.1 M, pH 7.0) at a scan rate of 100 $mVs^{-1}$. A well shaped oxidation peak and a poorly defined reduction peak on the bare GCE was observed (curve a). The height of the reduction peak was lower than that of the oxidation peak. For caffeine, the oxidation peak was characterized by an extraordinarily asymmetric shape and no obvious reduction peak was observed on the reverse scan, indicating that the oxidation was irreversible. The oxidation peak potentials of acetaminophen and caffeine at bare GCE are 461




(A) (B)

*Figure 1. SEM of $TiO_2$-Gr (A) and PT/$TiO_2$-Gr (B).*

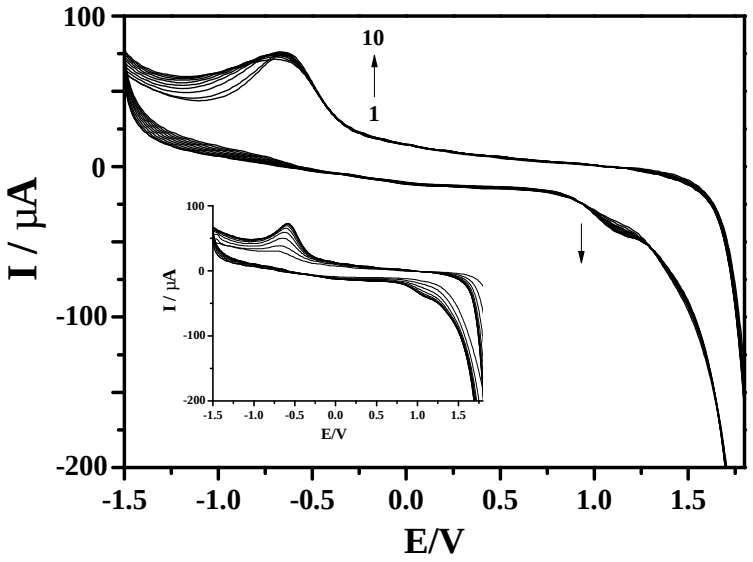



*Figure 2. Cyclic voltammograms for the polymerization of taurine on the $TiO_2$-Gr/GCE. Inset: cyclic voltammograms for the polymerization of taurine on bare GCE. Scan rate of 100 mV $s^{-1}$. The supporting electrolyte: 0.1 M phosphate buffer (pH 7.0).*

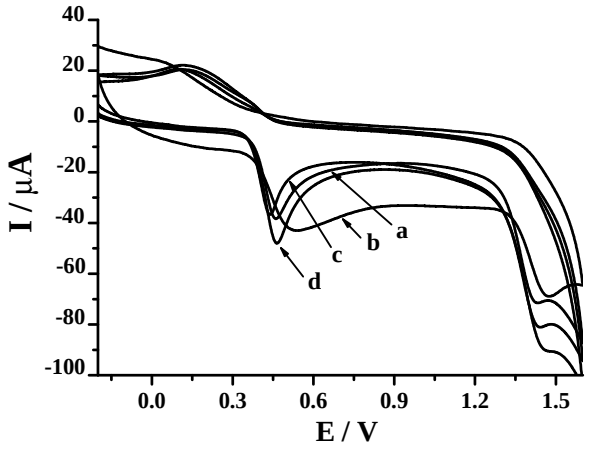



*Figure 3. Cyclic voltammetric curves of 110 μM acetaminophen and 320 μM caffeine in PBS (pH 7.0) on the different electrode: a) bare GCE, b) $TiO_2$-Gr/GCE, c) PT/GCE and d) PT/$TiO_2$-Gr/GCE.*

and 1433 mV, respectively. Compared to bare GCE, the oxidation peak potential of acetaminophen at the PT/GCE (curve c) shifted 23 mV negatively, and the peak current decreased slightly. However, caffeine showed the oxidation peak current increased slightly without the change of peak potential. To $TiO_2$-Gr/ /GCE, acetaminophen and caffeine demonstrated broad oxidation peaks at 539 and 1476 mV, respectively. The charging current was obviously larger than that at both the above electrodes (curve b). Also, the peak current of acetaminophen enhanced slightly. The highest improvement of the oxidation peak currents of acetaminophen and caffeine was obtained at the PT/$TiO_2$-Gr/GCE (curve d). These phenomena indicated that the enhancement effect may be due to the synergetic effect of PT and $TiO_2$-Gr. The PT film might facilitate the adsorption of acetaminophen and caffeine from the solution to the modified electrode surface through physical adsorption by the improvement of area of the modified electrode. Moreover, the coarseness of the modified electrode surface also contributed to this.

### Effect of scan rate

The effect of scan rate was also studied at the PT/$TiO_2$-Gr/GCE. Figure 4 showed that the oxidation peak shifted to a more positive value for both compounds, and the reduction peak of acetaminophen shifted to more negative values with increasing scan rates that had concurrent increases in current. For acetaminophen, the plot of the anodic peak current ($i_p$) *vs.* the square root of scan rate showed excellent

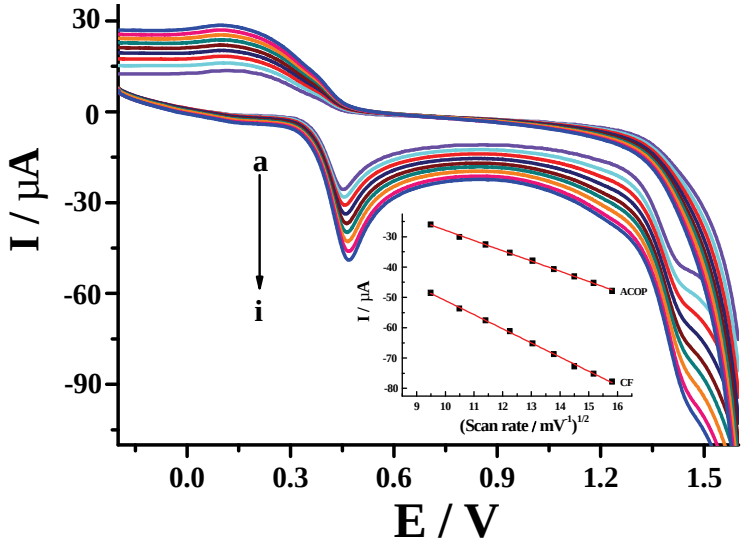



*Figure 4. Cyclic voltammetric response of the PT/$TiO_2$-Gr/GCE to 70 μM acetaminophen and 210 μM caffeine in 0.1 M BPS (pH 7.0) at various scan rates (a-r): 90, 110, 130, 150, 170, 190, 210, 230 and 250 mV $s^{-1}$. Inset: peak current vs. $v^{1/2}$.*

linearity over the range of 90-250 mV $s^{-1}$, the corresponding equation was: $i_p$ (μA) = -3.38($v$ / mV $s^{-1}$)$^{1/2}$ + + 5.927 ($R$ = 0.999) (inset a of Figure 4). Similarly, as shown in inset to Figure 4, the oxidation peaks currents of caffeine increased linearly with the increase of square root of scan rate, the corresponding equation was: $i_p$ (μA) = -4.658($v$ / mV $s^{-1}$)$^{1/2}$ - 4.637 ($R$ = = 0.999). This revealed that the oxidation processes of acetaminophen and caffeine on the surface of PT/ /$TiO_2$-Gr/GCE were under diffusion control.

### Effects of supporting electrolyte

The electrode reaction can be affected by the buffer solution. The effect of different electrolyte on the current responses was investigated. Some electrolytes including KHP-NaOH, $NH_4Cl$, $NaH_2PO_4$-$Na_2HPO_4$, BR, $NaNO_3$, KCl and $NH_3$-$NH_4Cl$ (each 0.1 M) were studied. The results showed that high current peaks and good peak shape were obtained in phosphate buffer. Therefore, this solution was applied in the subsequent studies.

### Effect of pH

The effect of varying pH of buffer solution on the electrochemical behavior of acetaminophen and caffeine at PT/$TiO_2$-Gr/GCE was performed using CV in 0.1 M PBS. Figure 5 depicts the response of peak current and potential of acetaminophen and caffeine to pH. The anodic and cathodic peak potentials were shifted negatively when the solution pH was increased (Figure 5D). The anodic peak current of acetaminophen increased from pH 3.0 to 7.0 and reached the maximum at pH 7.0, and then decreased again with higher pH value (Figures 5A and 5C). The anodic peak current of caffeine increased from pH 3.0 to 7.0 and kept almost unchanged in the pH range of 7.0-9.0 (Figure 5B). To obtain the high response signal for acetaminophen and caffeine, the solution of pH 7.0 was used for the optimal supporting electrolyte.

### Effect of $TiO_2$-graphene amount

The effect of $TiO_2$-Gr amount was investigated. When the amount of $TiO_2$-Gr suspension (0.375 mg $mL^{-1}$) increased from 0 to 6 μL, the oxidation peak current of acetaminophen and caffeine increased notably. However, when it exceeded 6 μL, the oxidation peak currents conversely showed gradual decline. Therefore, 6 μL of $TiO_2$-Gr suspension was selected for the fabrication of the electrochemical sensor in this work.

### Simultaneous determination of acetaminophen and caffeine

Under the optimal experiment conditions, the simultaneous determination of acetaminophen and caffeine was carried out at PT/$TiO_2$-Gr/GCE. The experiment was performed by changing the equal concentrations of acetaminophen and caffeine over the range from $5\times10^{-7}$ to $1\times10^{-4}$ M. The differential pulse voltammetric results (Figure 6) showed two well-distinguished anodic peaks at potentials of 396 and 1372 mV, corresponding to the oxidation for acetaminophen and caffeine, respectively. The peak current values were proportional to the concentrations of acetaminophen and caffeine in the mixture. The insert of Figure 6 showed the relationship between the anodic currents and the concentrations of acetaminophen (curve a) and caffeine (curve b). The oxidation

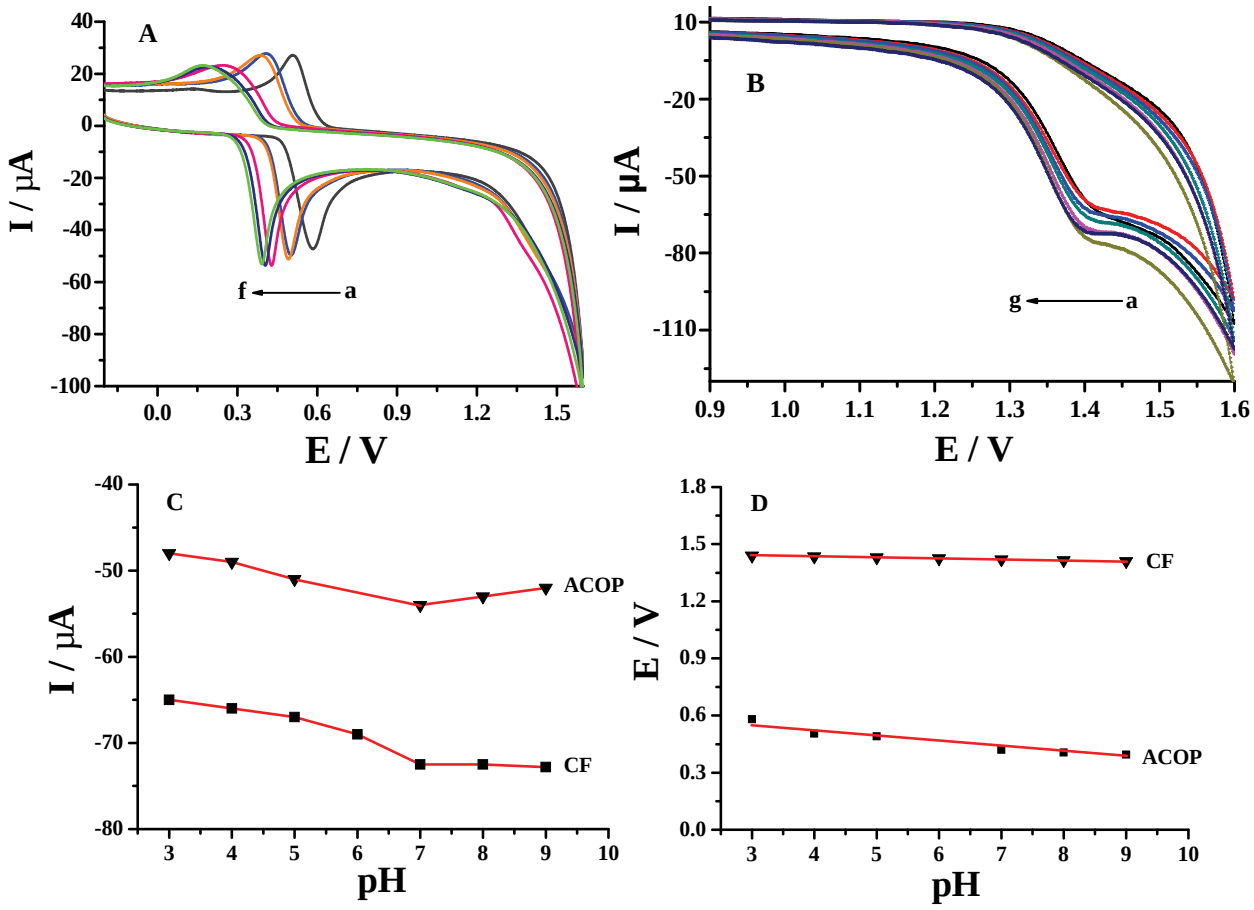



*Figure 5. A) Cyclic voltammograms of 160 μM of acetaminophen at PT/$TiO_2$-Gr/GCE with different pH values of PBS (0.1 M) (a-f): pH 3, 4, 5, 7, 8 and 9; B) cyclic voltammograms of 390 μM caffeine at PT/$TiO_2$-Gr/GCE with different solution pH values (a-f): pH 3, 4, 5, 6, 7, 8 and 9; C) peak current vs. pH value; D) peak potential vs. pH value.*

peak current of acetaminophen was proportional to its concentration over the range from 0.5 to 100 μM, obeying the following equation: $I$ (μA) = -0.302($C$ / / μM) - 6.143 ($R$ = 0.991). The oxidation peak current of caffeine was proportional to its concentration over the range from 0.5 to 100 μM, obeying the following equation: $I$ (μA) = -0.186($C$ / μM) + 0.255 ($R$ = 0.994). The detection limits of acetaminophen and caffeine were $3.4\times10^{-8}$ and $5.0\times10^{-7}$ M, respectively. A comparison of the detection methods are shown in Table 1, which includes the limit of detection and the linear range. Table 1 indicates that the proposed sensor exhibited low detection limit and wide measurement range. The reason might be as follows: firstly, the excellent electrical conductivity of Gr enhanced the charge transport; secondly, the formation of the PT film increased the adsorb amount of analytes.

### Individual determination of acetaminophen and caffeine

For further investigation of electrochemical response when both substances are present in the solution, the DPV experiments were performed in solutions containing variable concentration of one species and constant concentration of the other one. The separate determination of acetaminophen in the concentration range of $1.0\times10^{-7}$-$9.0\times10^{-5}$ M was accomplished in solutions containing caffeine at the fixed concentration of $3.0\times10^{-5}$ M. As shown in Figure 7A, the peak current of acetaminophen clearly increased gradually while that of caffeine remained fairly constant, suggesting that the change of acetaminophen did not have significant influence on the peak currents and peak potentials of the caffeine. On the other hand, the separate determination of caffeine in the concentration range of $2.5\times10^{-5}$-$2.0\times10^{-4}$ M was accomplished in solutions containing acetaminophen at the fixed concentration of $1.0\times10^{-6}$ M. As shown in Figure 7B, the peak current of caffeine increased gradually while that of acetaminophen remained fairly constant. Furthermore, the peak currents of acetaminophen or caffeine increased linearly with the increase of concentration in the presence of a constant concentration of the other compound (insert in Figure 7A

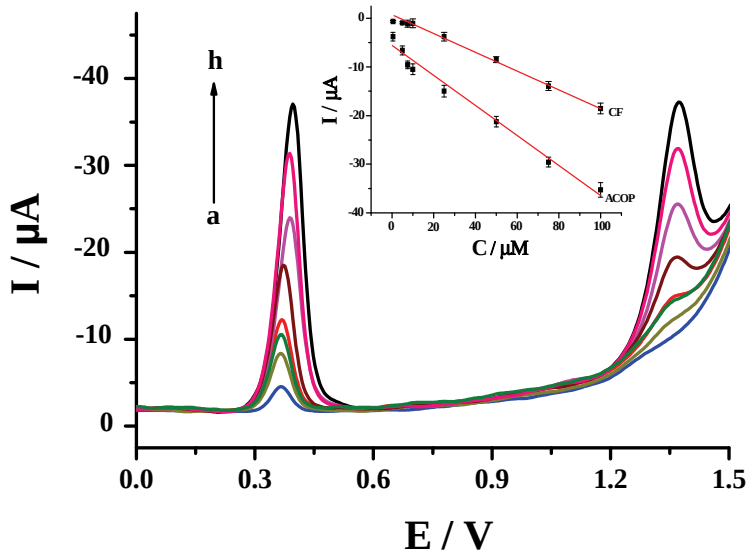



*Figure 6. Differential pulse voltammograms of PT/TiO$_2$-Gr/GCE in 0.1 M PBS (pH 7.0) containing equal concentrations of acetaminophen and caffeine: a) 0.5, b) 5, c) 7.5, d) 10, e) 25, f) 50, g) 75 and h) 100 μM. Inset: calibration plots of the oxidation peak current versus different concentration of acetaminophen and caffeine.*

and 7B). The calibration equations were $i_{pa}$ (μA) = = -0.543(*C* / μM) - 2.432 (*R* = 0.990) and $i_{pa}$(μA) = = -0.179(*C* / μM) - 0.654 (*R* = 0.993) for acetaminophen or caffeine, respectively. The detection limits were $3.4\times10^{-8}$ and $5.0\times10^{-7}$ M, respectively. Hence, it was confirmed that for the oxidation of acetaminophen and caffeine at PT/TiO$_2$-Gr/GCE, the other component did not give interference to the electrochemical signal.

### Interference study

Under the optimized conditions, the influence of various foreign species on the simultaneous determination of acetaminophen and caffeine (50 μM) was investigated in PBS (pH 7.0). It was found that the common ions such as $Na^+$, $K^+$, $Fe^{3+}$, $Cu^{2+}$, $Al^{3+}$, $Cl^-$, $NO_3^-$, $H_2PO_4^-$, $HPO_4^{2-}$, $CO_3^{2-}$, and $SO_4^{2-}$ had almost no interference with acetaminophen and caffeine detection. As for the common interferences in pharmaceutical samples for the determination of acetaminophen and caffeine, 10-fold sodium carbonate, saccharin, citric acid, ascorbic acid, glucose, uric acid had no obvious interference with the current response of acetaminophen and caffeine (signal change below 5%).

### Stability, reproducibility and repeatability

In order to investigate the stability of PT/TiO$_2$-Gr/GCE, the reproducibility was tested. Repetitive CV

*Table 1. Comparison of electrochemical sensors for acetaminophen (ACOP) and caffeine (CF)*

| Modified electrode | Linear range, μM | *LOD* / μM | Reference |
|---|---|---|---|
| Screen-printed carbon electrode | ACOP: 2.5-1000 | ACOP : 0.1 | [1] |
| Carbon-doped diamond electrode | ACOP: 0.5-83; CF: 0.5-83 | ACOP: 0.49; CF: 0.035 | [2] |
| Palladium nanoclusterspolyfuran/platinum electrode | ACOP: 0.5-100 | ACOP: 0.0764 | [3] |
| ZrO$_2$ nanoparticles/carbon paste electrode | ACOP: 1.0-2500 | ACOP: 0.912 | [4] |
| Graphene/GCE | ACOP: 0.1-20 | ACOP: 0.032 | [6] |
| Nafion/ruthenium oxide pyrochlore/GCE | ACOP: 5-250; CF: 10-250 | ACOP: 2.2; CF: 1.2 | [8] |
| Poly(taurine)/multiwalled carbon nanotube/GCE | ACOP: 1.0-100 | ACOP: 0.5 | [17] |
| Nafion-ruthenium oxide pyrochlore/GCE | CF: 5-200 | CF: 2.0 | [19] |
| Nafion/GCE | CF: 0.995-10.6 | CF: 0.798 | [20] |
| Carbon nanotubes/carbon-ceramic electrode | ACOP: 0.2-100.0 | ACOP: 0.12 | [21] |
| Dowex50wx2 and gold nanoparticles/glassy carbon paste electrode | ACOP: 0.0334-42.2 | ACOP: 0.0047 | [22] |
| *In situ* surfactant-modified multi-walled carbon nanotube paste electrode | ACOP, CF: 0.291-62.7 | ACOP: 0.0258; CF: 0.0883 | [24] |
| PT/TiO$_2$-GR/GCE | ACOP, CF: 0.05-100 | ACOP: 0.034; CF: 0.5 | This work |

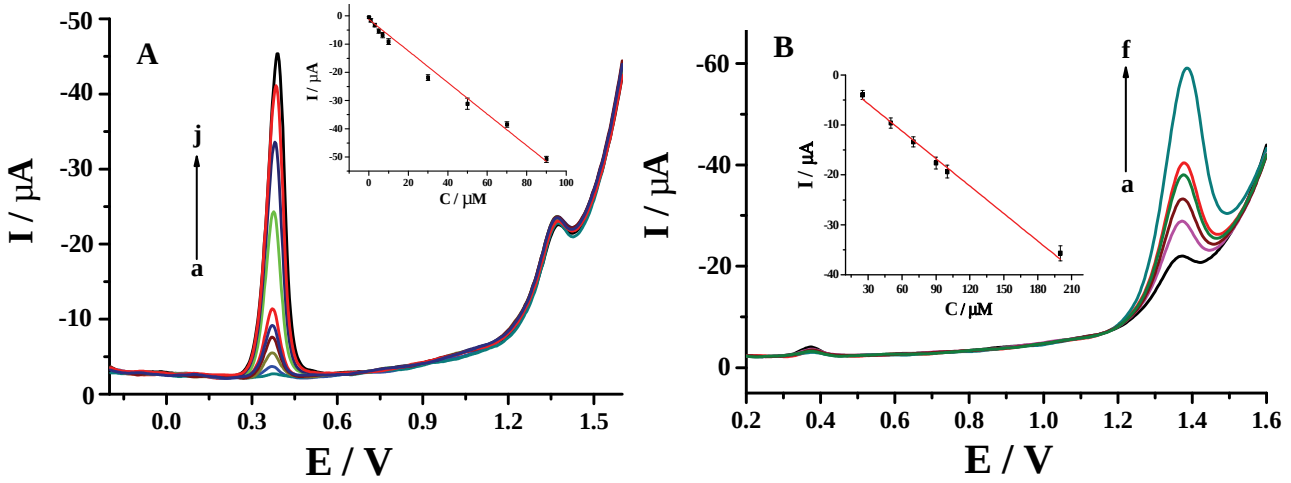



*Figure 7. A) Differential pulse voltammograms of PT/$TiO_2$-Gr/GCE in 0.1M BPS (pH 7.0) containing 30 μM caffeine and different concentrations of acetaminophen: a) 0.1, b) 1, c) 3, d) 5, e) 7, f) 10, g) 30, h) 50, i) 70 and j) 90 μM. Inset: plot of oxidation peak current as a function of acetaminophen concentration. B) Differential pulse voltammograms of PT/$TiO_2$-Gr/GCE in 0.1 M BPS (pH 7.0) containing 1 μM acetaminophen and different concentrations of caffeine: a) 25, b) 50, c) 70, d) 90, e) 100 and f) 200 μM. Inset: plot of oxidation peak current as a function of caffeine concentrations.*

measurements were performed 20 times in 0.1 M PBS (pH 7.0). The relative standard deviations (RSD) were 1.81 and 3.17% for acetaminophen (100 μM) and caffeine (100 μM), respectively. This result suggested that this sensor had a good reproducibility and did not undergo surface fouling during the voltammetric measurements. The stability of PT/$TiO_2$-Gr/GCE towards the catalytic oxidation of acetaminophen (100 μM) and caffeine (100 μM) was examined as well. The CVs of this binary solution were recorded after this electrochemical sensor has been dipped into PBS (pH 7.0) for 2 weeks. The anodic current responses of acetaminophen and caffeine individually decreased 4.25 and 4.83%, indicating that the good stability of developed sensor. Furthermore, the repeatability between multiple PT/$TiO_2$-Gr modified glassy carbon electrodes was carried out by parallel determining of 100 μM acetaminophen and caffeine mixture. The RSD was 3.29% for 6 independent glassy carbon electrodes modified with PT/$TiO_2$-Gr.

## Analytic application

In order to testify the performance of this modified electrode in real sample analysis, four serum samples from the hospital affiliated to our university were examined by the developed electrochemical sensor and the high-performance liquid chromatography (HPLC) method, respectively. The concentrations of acetaminophen and caffeine were measured by the standard addition method, and the results showed that no acetaminophen and caffeine were found in the four serum samples. To test the reliability of the measurements, a known amount of acetaminophen and caffeine standard was spiked in the serum samples, and then analyzed with a standard addition method. The obtained results were shown in Table 2. The recoveries were in the range of 95.6% to 103.5%. It was in accordance with the result obtained by using HPLC, which indicated the developed was reliable and feasible.

*Table 2. Determination of acetaminophen and caffeine in human serum samples*

| Serum sample | | Detected by PT/$TiO_2$-GR/GCE | | | | Detected by HPLC | |
|---|---|---|---|---|---|---|---|
| | | Added, μM | Found, μM | *RSD* / % | Recovery,% | Found, μM | *RSD* / % |
| 1 | ACOP | 5 | 4.86 | 2.6 | 97.2 | 5.11 | 1.5 |
| | CF | 10 | 9.56 | 2.4 | 95.6 | 9.82 | 1.8 |
| 2 | ACOP | 30 | 30.72 | 3.1 | 102.4 | 29.1 | 2.1 |
| | CF | 50 | 49.05 | 2.4 | 98.1 | 49.2 | 1.6 |
| 3 | ACOP | 80 | 77.36 | 3.6 | 96.7 | 78.6 | 2.2 |
| | CF | 120 | 124.2 | 1.9 | 103.5 | 125.1 | 2.7 |
| 4 | ACOP | 150 | 152.4 | 2.2 | 101.6 | 147.3 | 1.8 |
| | CF | 200 | 195.6 | 1.8 | 97.8 | 197.5 | 2.0 |

## CONCLUSION

In this work, a novel type of polymer/$TiO_2$-Gr-modified glassy carbon electrode was prepared and used for the simultaneous determination of acetaminophen and caffeine. The modified electrode exhibited many desirable properties including excellent stability, reproducibility, high sensitivity, low detection limit and satisfactory linear range. Furthermore, its ease to construct, low cost and no treatment before use make it feasible to be applied in routine determination.

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NAUČNI RAD

# ELEKTRODA OD STAKLASTOG UGLJENIKA MODIFIKOVANA POLI(TAURIN)/$TIO_2$-GRAFEN KOMPOZITNIM FILMOM ZA ODREĐIVANJE ACETAMINOFENA I KOFEINA

*Napravljena je nova elektroda od staklastog ugljenika modifikovana poli(taurin)/$TiO_2$-grafen nanokompozitnim filmom (PT/$TiO_2$-Gr/GCE). Ovaj senzor je zasnovan na elektrohemijskoj polimerizaciji taurinskog sloja na $TiO_2$ grafen modifikovanoj elektrodi od staklastog ugljenika. Elektrohemijsko ponašanje acetaminofena i kafeina na modofikovanim elektrodama je proučavano cikličnom volatmetrijom i diferencijalnom pulsnom voltametrijom. Rezultati pokazuju da oksidacioni pik struje ima zadovoljavajuću linearnost u opsegu koncentracija od $1\times10^{-7}$-$9\times10^{-5}$ M za acetaminofen i $2.5\times10^{-5}$-$2\times10^{-4}$ M za kafein. Limit detekcije za acetaminofen je $3.4\times10^{-8}$ M, a za kofein $5.0\times10^{-7}$ M. Ova modifikovana elektroda je pokazala dobru osetljivost i stabilnost, pa ima obećavajuću potencijalnu primenu kao dobar elektrohemijski senzor i biosenzor.*

*Ključne reči: taurin; $TiO_2$-grafen nanokomposit; acetaminofen; Kofein; elektropolimerizacija.*