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β-cyclodextrin coated graphene oxide nanoadsorbents on the hollow fiber-solid phase microextraction and electrochemical monitoring of acetaminophen

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ABSTRACT

A new sensitive sensor for simultaneous pre-concentration and electrochemical detection of acetaminophen has been developed and validated with the help of ionic liquid mediated hollow fiber pencil graphite electrode modified with graphene oxide coated with β-cyclodextrin. Differential pulse voltammetry was used for the electrochemical analyte monitoring. Factors affecting the extraction process and method of statistical factors, such as recovery, reproducibility, and selectivity was optimized. Two Linear ranges were obtained in the ranges of 0.1–50.0 and 50–500 μM. The detection limit was 30 nM and the relative standard deviations for five repeated experiments of acetaminophen (in the different concentrations) were found to be within the range of 2.7%–3.6%. Finally, this sensor was used for single-step simultaneous purification and determination of acetaminophen in pharmaceutical formulations with satisfactory results.

Keywords: Acetaminophen; Hollow fiber-pencil graphite hybrid electrode; β-cyclodextrin coated graphene oxide; Ionic liquid

1. Introduction

A (N-acetyl-P-aminophenol) acetaminophen (AC), generally known as paracetamol, is one of the analgesic and antipyretic drugs. Medical control (blood, urine, and plasma as biological fluids) and quality control analysis (in pharmaceutical formulations), the extension of sensitive, efficient, and simple analytical procedures for the designation of AC are important [1]. In recent years, for the determination of AC in pharmaceutical formulations and biological fluids some methods including spectrophotometry [2], high-performance liquid chromatography [3], chemiluminescence [4], and electrochemisty [5] have been used. But, electrochemical sensors, particularly owing to their simplicity of preparation, fast response, high selectivity, and sensitivity has attracted the researcher's attention [6].

The electrochemical methods using chemically modified electrodes (CMEs) have been widely used as sensitive and selective analytical methods for the detection of the trace amounts of biologically important compounds. One of the most important properties of CMEs has been their ability to catalyze the electrode process via significant decreasing of overpotential respect to unmodified electrode. With respect to the relatively selective interaction of the electron mediator with the target analyte in a coordination fashion, these electrodes are capable to considerably enhance the selectivity in the electroanalytical methods [7–13].

Recently, a new method called hollow fiber solid–liquid phase microextraction (HF-SLPME) provided by Es'haghi group in which they combined hollow fiber liquid phase microextraction [14] with solid phase extraction and benefited from the advantages of both methods [15,16]. In this technique, microextraction the performance was improved because of the incorporation of organic solvents contained inside piece of polypropylene hollow fiber with nanocomposites which improved by chemically surface

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modification methods. These incorporated nanoparticles in the membrane system could operate as a nanoscale solid phase extractor with high surface area. It has provided high enrichment factor of analyte. The method has been successfully used for many analytes separation such as drugs (analgesics such as acetaminophen), environmental targets, food and beverages, and peptides [15].

We used from this history and merged it with electrochemical methods to achieve and design a powerful new sensor for simultaneous preconcentration (due to the use of hollow fiber for analytes preconcentration) and determination (due to the use of electrochemical instruments) of the target analyte. We established the electrical contact between the fiber and sample solution via pencil graphite electrode (PGE) that were put inside the fiber and connected to copper wire for electrochemical signal record. PGE have the same benefits, such as high electrochemical reactivity, mercantile availability, disposability, good mechanical hardness, ease of modification, low technology, and low cost [17]. In addition, we require an additional component to establish electrical connection between the sample solution and the electrodes.

Common organic solvents are existing which already used for HF-LPME but cannot be used here. Because of these solvents cannot be able to establish the electrical connection between the sample solution and the electrode. For this reason, we have used ionic liquids (ILs). Room-temperature ionic liquids (RTILs) have surprising properties such as electrolytic conductivity, low volatility, adjustable viscosity, and miscibility. RTILs have proved to be excellent materials for applications in electrochemistry and highly used in this field because of their matchless physicochemical properties [18,19].

Also, we used the β-Cyclodextrin functionalized graphene oxide as a modifier for improves the sensitivity and selectivity. β-CDs are able to trap various organic, inorganic, and biological guest molecules via their cavity and form host-guest inclusion complexes with them [20]. β-CDs have many electroanalytical applications due to the creation of an inclusion complex [21,], molecular recognition [22], and selective preconcentration of analytes at the electrode [23].

In recent years, enormous scientific regards have attracted to graphene oxide (GO). It has specific properties such as large surface area, many combining sites, and easy dispersion that it has become a suitable choice for sensors manufacturing. For this reason, GO is combined with various nanocomposites such as metals [24], metal oxides [25], conducting polymers [26], and some other functional materials for the construction of modified sensors. When we functionalized GO with β-CD, the constructed new materials possess unique properties of both such as large surface area, high conductivity, high supramolecular recognition, and enrichment capability properties [27].

Recently, nanocomposites are made of β-CD and GO hybrid, attract the regard of researches in greater scope for example in the detection of organophosphate pesticides [28], imidacloprid [29], heavy metal ions [30], and phenolic pollutants [31]. Also, it should be considered another wonderful combination and it is ILs-GO blend. The unique physicochemical confidants of ILs give those highly applied in electrochemistry, universally in ILs-carbon nanomaterial (ILs-CNM) forms. The synergistic combination of both components eventuates in remarkable betterment for many electrochemical applications, including energy storage devices and sensor electrodes [22]. This paper proffers a quick, plain, and cheap manner for the selective extraction and sensitive determination of trace levels of acetaminophen using carrier assisted H.F coupled with the DPV principles using ionic liquid interceded hollow fiber-pencil graphite hybrid electrode (H.F/PGE), modified with β-cyclodextrin functionalized graphene oxide.

2. Experimental

2.1. Chemicals and reagents

Acetaminophen (1-butyl-3-methylimidazolium hexafluorophosphate) [$BMIMPF_6$] and β-Cyclodextrin (β-CD) was procured from Sigma-Aldrich Company (St. Louis, USA). Our nanoparticles (GO and GO-O) were prepared in the author's laboratory. Epichlorohydrin (ECH), sulfuric acid, analytical graphite, phosphoric acid, $KMnO_4$, and H_2O_2, all were purchased from Merck (Darmstadt, Germany). We also used 0.05 mol/L phosphate buffer (PBS, prepared from NaH_2PO_4, and Na_2HPO_4) to pH control of feed solution. The accurel Q 3/2 polypropylene hollow fiber membrane used here was obtained from Membrana (Wuppertal, Germany, the inner diameter was 600 μm, the wall thickness was 200 μm, and the pore size was 0.2 μm). All reagents were at least analytical grade all over the work, and de-ionized three-time distilled water were used. By untangling of the suitable value of acetaminophen in de-ionized (DI) water, 0.01 M stock solutions of acetaminophen were prepared. Working standard solutions were obtained by proper dilution of the stock standard solution.

2.2. Electrochemical measurements

Autolab (Eco Chemie B.V., Netherlands) PGSTAT30 potentiostat/galvanostat (driven by the NOVA software, Version 1.8) were accomplished to all the differential pulse voltammetry (DPV) measurements. The electrochemical cell subtends of working, reference, and an auxiliary electrode that included a home-made ionic liquid interceded hollow fiber – pencil graphite hybrid electrode (HF-PGE), Ag/AgCl, and platinum wire. A Metrohm pH-meter (model 691, Switzerland) was used for pH measurements. 15.0 mL of the sample solution was added to the voltammetry cell. We optimized the voltammetry experimental variables such as; scan rate of potential, deposition time, equilibrium time, voltage step, voltage step time, and stirring speed of the solution.

2.3. GO and GO-O synthesis

Hummers method was used for GO procurement and refinement [32]. For the preparation of homogenous GO suspension, the GO which synthesis in the previous step was interspersed in 40 mL of deionized water by ultrasonication. Then toward pH adjustment to 9.5, we use of 10% NaOH solution. After pH adjustment, 1.5 mL of epichlorohydrin

(ECH) was added dropwise to the suspension. To gain a solid product, first the reaction mixture was stirred by a magnet at 60°C for 3 h. Second, centrifuge at 14,000 rpm for 10 min and washed three times with distilled water. Epoxy functionalized graphene oxide (GO-O) was produced.

2.4. Preparation of GO-β-CD

0.5 g of β-CD was added to dispersed GO-O in 60 mL of carbonate buffer with pH = 10. GO-β-CD was prepared after stirring the previous solution at 60°C for 3 h, centrifuge at 14,000 rpm for 10 min, washed three times with warm water and freeze-drying [33].

2.5. Manufacturing of the hollow fiber-pencil graphite electrode (HF-PGE/BMIMPF6/GO-β-CD)

First, hollow fiber was divided into 2 cm pieces and 1.7 cm of it was incorporated with graphite pencils rod (O.D. 0.7 mm and 2.5 cm length) attentively. But segments with 2.0 cm length washed with acetone for pollutions elimination and dried in the air before inserting the graphite. The end of hollow fibers was blocked with heat. At this stage, the HF-PGE electrode has been created. In the second stage, a homogenous suspension of GO-β-CD (3.0 mg) and ionic liquids (0.5 mL) was prepared in the conical tube. Finally, before analysis, we sonicated the constructed HF-PGE which put on the homogenous suspension. At the end stage, HF-PGE was bringing off the conical tube and washed twice with 1–2 mL deionized water. Now it is ready for the voltammetric measurements.

2.6. Real sample preparation

2.6.1. Urine sample preparation

Urine samples were taken from healthy volunteers and kept in a refrigerator instantly. Samples were then diluted with PBS (pH 2.0) and do not need any further treatment. The diluted urine samples were spiked with a known concentration of AC.

2.6.2. Serum sample preparation

A blank human serum sample (drug-free) was provided by a healthy volunteer who not exposed to any drug for at least 10.0 months. The real serum sample was stored frozen until assay. The following method was used to prepare all the serum samples: according to the method of Suh et al. [34], to eliminate protein and other substances, 5.0 mL of human serum sample was placed in a10.0 mL glass tube and 5.0 mL of 15.0% (w/v) zinc sulfate solution-acetonitrile (50/40, v/v) was added. The glass tube was vortexed for 20.0 min, maintained at 4.0°C for 15.0 min followed by centrifugation at 4,000.0 rpm for 5.0 min. Then, the supernatant was collected in the same tube and this solution was used for later analyses.

2.7. General approach

After manufacturing of the hollow fiber-pencil graphite electrode, it is modified with β-cyclodextrin functionalized graphene oxide (HF-PGE/BMIMPF$_6$/GO-β-CD) and 15-mL volume of PBS with pH 2 was alienated into the voltammetric cell. We optimized the voltammetry experimental variables such as; scan rate of potential, deposition time, equilibrium time, voltage step, voltage step time, and stirring speed of the solution, then the DPV mode was used for taking of AC voltammograms. The deposition potential of AC was tested from 0.0 to 1.2 V. For the on-line preconcentration time of analyte, extracting time study was performed 5 min before applying of potential. Because of avoiding any carryover, we used each HF-PGE only once.

3. Results and discussion

3.1. Characterization of GO, GO-O, GO-β-CD, and HF-PGE/BMIMPF$_6$/GO-β-CD

Fig. 1 highlights the generic way for the gaining of the GO-β-CD composites. In the first step, reaction between ECH and –OH groups on the GO introduced the epoxide functional groups onto the surface of GO (i.e., GOO) under alkaline conditions. This step has two important effects, increases the chemical activity of GO, and provided suitable binding arms. In the second step, to the formation of β-CD modified GO ultimate product (GO-β-CD), β-CD was reacted with GO-O under alkaline conditions through a ring-opening reaction. Three materials (GO, GO-O, and GO-β-CD) have different colors (yellow, brown–black, and black). Fig. 2 shows the FT-IR spectra of GO, GO-O, and GO-β-CD. Two changes indicate the successful adherence of ECH onto GO: first, more intense of the C–O stretching band at 1,034 cm^{-1} in the spectrum of GO–O than in GO and second, a new C–H stretching bands become visible at 2,923 cm^{-1}. Modification with β-CD shows several changes in the GO-β-CD spectrum that confirm its molecules are covalently bonded to the surface of GO: coupled C–O/C–C stretching vibrations at 1,034 and 1,074 cm^{-1}, C–H/O–H bending vibrations at 1,420 cm^{-1} and CH$_2$ stretching vibrations at 2,942 and 2,870 cm^{-1}. For further characterization of GO-β-CD formation, scanning electron microscopy (SEM) images of GO and GO-β-CD were taken. From the SEM images, it was obvious that GO-β-CD, with a mean diameter around 40–50 nm is uniformly was formed. These results are shown in Fig. 3. Also, we taken SEM images of GO-β-CD modified HF-PGE before and after impregnated with a homogenized mixture of GO-β-CD and ionic liquid. It was obvious that GO-β-CD is uniformly deposited on to HF-PGE modified surface due to the expansion of the hollow fiber and increase of its pores diameter from nanometers to micrometers. This result is shown in Fig. 4.

3.2. Electrochemical behaviors of different electrodes

Electrochemical behavior of AC on PGE and modified electrodes was considered using differential pulse voltammetry. Differential pulse voltammograms (DPVs) of 50 μM AC in 0.1 M PBS (pH 2) at the surface of PGE (a), HF-PGE/BMIMPF$_6$ (b), HF-PGE/BMIMPF$_6$/GO (c), and HF-PGE/BMIMPF$_6$/GO-β-CD electrodes (d) which were started from 0.0 V and terminated at 1.2 V are shown in Fig. 5. Oxidation peak current of AC was enhanced by modification of the

HF-PGE electrode with GO and GO-β-CD that the following reasons can be cited for it: large surface area, many combining sites, and easy dispersion of the graphene oxide, inclusion complex formation ability of β-CD and preconcentration potency of H.F for the analytes (due to its porous surface). The accumulation of the drug (AC) at the surface of the modified electrode was raised by the synergistic effect of these factors and finally the kinetic of the electrode process was increased.

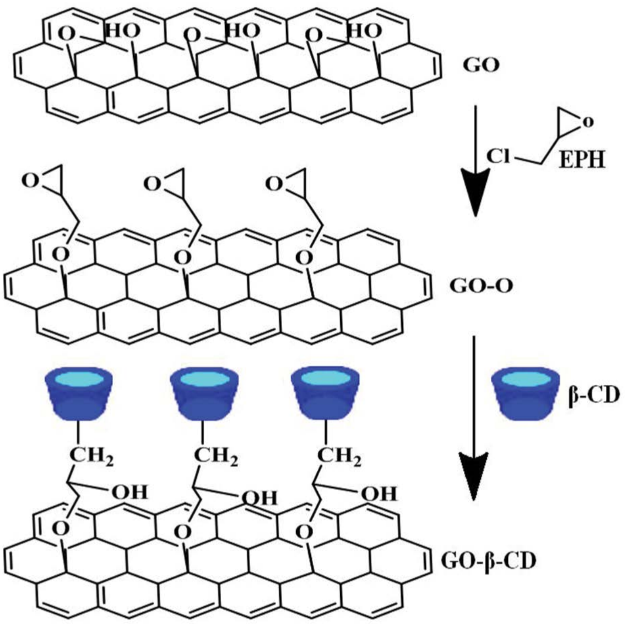

Fig. 1. Projection of the β-CD functionalized graphene oxide preparation.

3.3. Optimization of the operational conditions

3.3.1. Effect of pH

To assess the effect of pH on the AC responses on the HF-PGE/ BMIMPF$_6$/GO-β-CD, we studied the electrochemical behavior of AC (50 μM) in PBS (0.1 mol/L) in the pH range of 2.0–12.0 using DPV (Fig. 6). By increasing pH of solution oxidation peaks of AC shift to negative potentials, that indicates the participation of proton(s) in the oxidation reaction. Dependence of the oxidation peaks potential to solution pH was found to equations that characterized by slopes of 52 mV per decade for AC (Fig. 6C). The proximity of this slope to Nernstian value (59.1 mV), disclosing that the ratio of the electron and proton involved in the reactions is equal. The AC oxidation mechanism on the H.F-PGE/GO-β-CD is shown in Fig. 7. On the other hand, the decrease of peak currents of AC with increasing the solution pH shown in Fig. 6B. The agglomeration of AC on the electrode was mainly owing to the formation of a hydrogen bond between AC and [BMIM]PF$_6$ in acidic pHs. Also, the stability of acetaminophen in higher pH 7.0 disappears, and it is difficult for the electrochemical reactions of acetaminophen in a basic solution. For this reason, a slightly acidic condition is suggested for the oxidation of acetaminophen. Although, due to acetaminophen performance at body pH, researchers have like to this species is most response at neutral pH. Therefore, pH 2.0 was chosen to make the required sensitivity to AC in the following experiments.

3.3.2. Effect of preconcentration times

Differential pulse voltammetry (DPV) was used as a sensitive method for the quantitative detection of the AC at the proposed electrode. Unlike conventional methods of differential pulse anodic stripping voltammetry (DPASV), we have

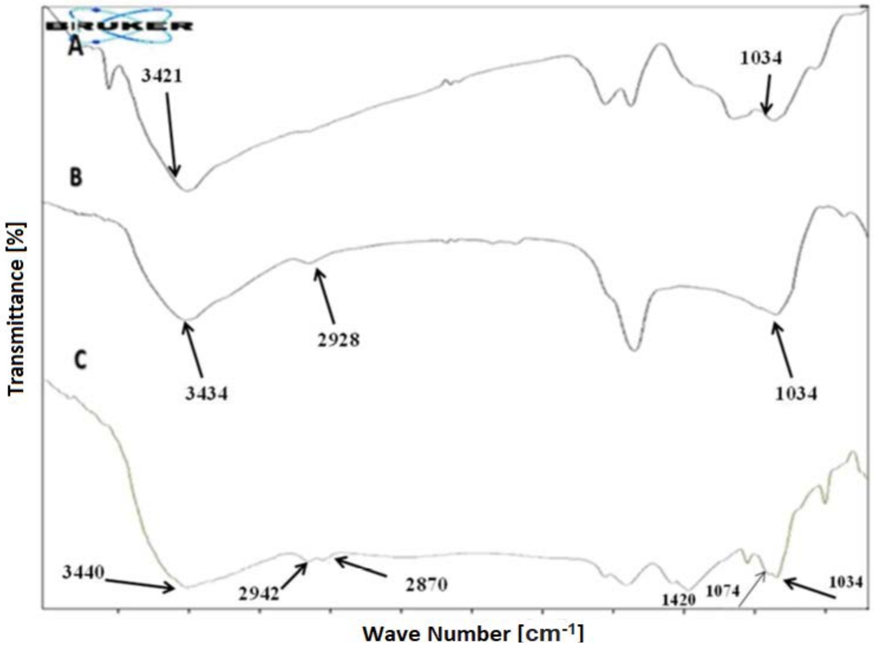

Fig. 2. FTIR spectra of (A) GO, (B) GO-O, and (C) GO-β-CD.

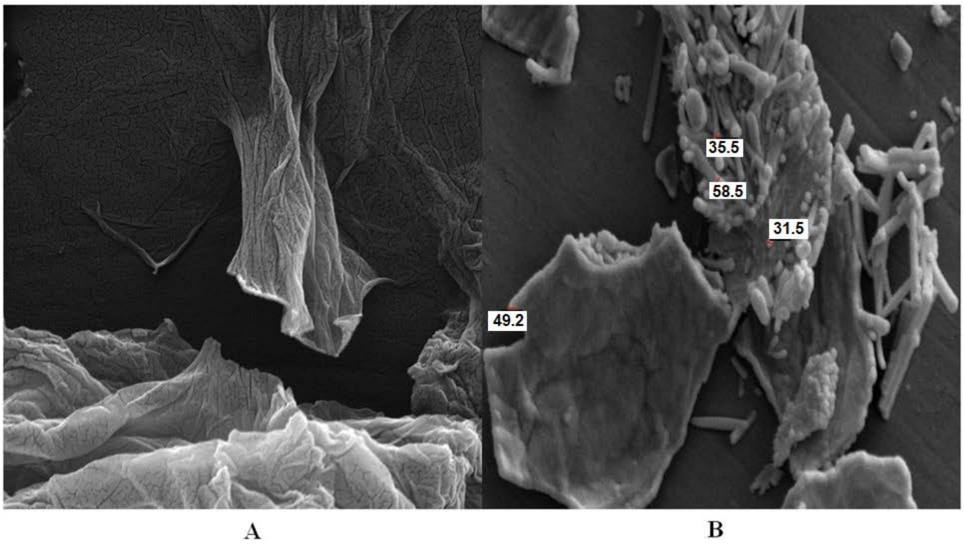

Fig. 3. SEM images of GO (A) and GO-βCD (B).

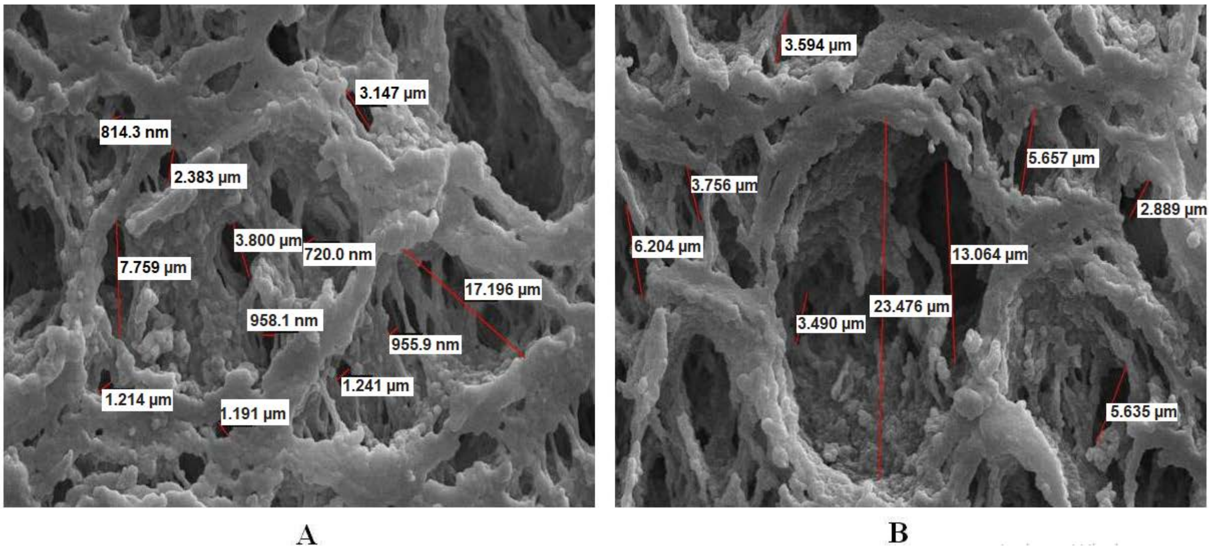

Fig. 4. SEM image of empty hollow fiber (A), satiated hollow fiber with a homogenized mixture of GO-β-CD and ionic liquid (B).

not used from accumulation potential in this work. Because the extraction time is given to the electrode to AC trapped in H.F and its supported liquid membrane (SLM) only by a diffusion mechanism. The efficacy of extraction time was also considered on the peak current of 50 μM AC. To choose the most favorable time of the extraction, extraction time was differing from 1 to 60 min. By increasing the extraction time up to 5 min, the anodic peak current increased and gently leveling off at periods longer than 5 min (Fig. 8). This leveling off in peak current could possibly be due to the following factors: the passive back diffusion of target molecules into (SLM) and donor phase (sample solution), which has been previously reported [35] and presumably saturation of the electrode pores. Thus, the extraction time of 5 min was selected as the optimum value throughout the work that it can integrate high sensitivity with low analysis time.

3.4. Calibration curve

Calibration curves were plotted in the obtained optimal conditions and parameters (n = 5). The DPV was started from 0.0 V and terminated at 1.2 V. As explained earlier, we do not use accumulation potential. After 5 min as the extraction time, the DPV responses of the HF-PGE/BMIMPF$_6$/GO-β-CD were acquired. Two working concentration ranges were exhibited by the suggested electrode 0.1 (100 nM)–50.0 μM (R^2 = 0.996) and 50–500 μM (R^2 = 0.997) for AC. The linear regression equations as follows:

$$\mathrm{IP}\left(\mu A\right) = 0.041C_{\mathrm{AC}}\left(\mu A\right) + 0.398\times10^{-6} \quad (1)$$

$$\mathrm{IP}\left(\mu A\right) = 0.020C_{\mathrm{AC}}\left(\mu A\right) + 1.548\times10^{-6} \quad (2)$$

The limits of detection (LOD) and quantification (LOQ) were calculated by use of kS_b/m equation, where $k = 3$ for LOD and 10 for LOQ, S_b display the standard deviation of the peaks current of the blank ($n = 5$) and m representing the slope (sensitivity, in μA/μM). Both LOD and LOQ values are found to be 30 and 98.3 nM, respectively, which these values indicate the sensitivity of the proposed method.

3.5. Interferences

The maximum concentration of the interfering substance that AC measurement error is less than 5% was defined as the tolerance limit. Disparate inorganic ions and organic compounds identified or anticipated to render a voltammetric response with the proposed modified electrode, or with a chance of either interacting with AC or generating a peak nearby to the studied analyte peak were investigated to explore the selectivity of the proposed method. For this aim, the voltammetric behavior of 50 μM of AC in the presence of various metal ions and organic compounds was studied at optimum conditions. AC commonly coexists with ascorbic acid (AA) and dopamine (DA) in biological fluids. Fortunately, the anodic peak of AC exhibits good separations from AA and DA peaks. Therefore, the presence of AA and DA can't cause disturbance to measure of AC and satisfactory selectivity with the detection of AC in the presence of AA and DA can be observed. The results revealed that the change in peak current was less than ±5% for500-fold inorganic ions, such as Mg^{2+}, Ca^{2+}, Zn^{2+}, Pb^{2+}, Cd^{2+}, Ni^{2+}, Cu^{2+}, K^{+}, $Cr_2O_4^{-}$, Cl^{-}, NO_3^{-}, and SO_4^{2-}. Tolerance limit for organic compounds such as L-tryptophan, tyrosine, cysteine, uric acid, lactose, glucose, sucrose was about 100-fold compared to AC. Consequently, the selectivity of the suggested method is acceptable and this method can be selectively used to determination of AC in pharmaceutical products and biological fluids.

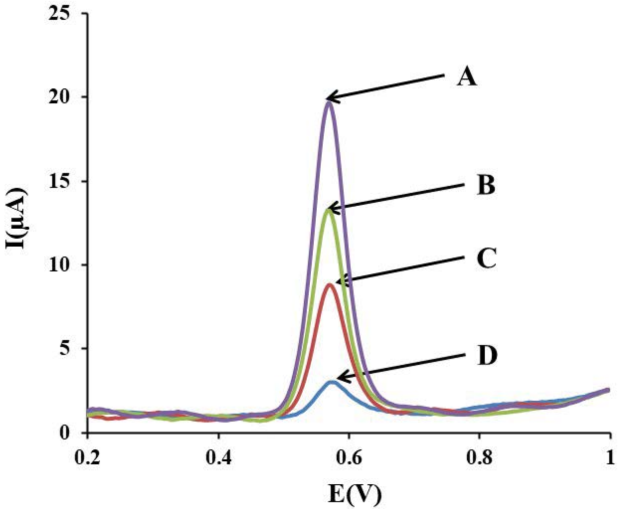

Fig. 5. Differential pulse voltammograms (DPVs) of 50 μM AC in 0.1 M PBS (pH 2) at the surface of PGE (A), HF-PGE/BMIMPF$_6$ (B), HF-PGE/BMIMPF$_6$/GO (C), and HF-PGE/BMIMPF$_6$/GO-β-CD electrodes (D) which were started at 0.0 V and terminated at 1.2 V.

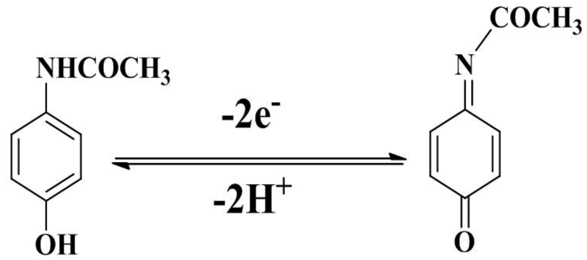

Fig. 7. AC oxidation mechanism on the H.F-PGE/GO-β-CD.

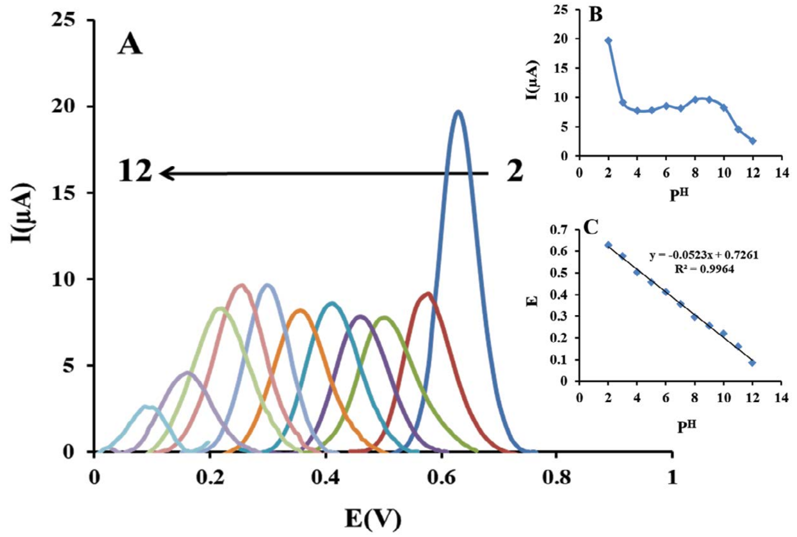

Fig. 6. (A) Differential pulse voltammograms (DPVs) of 50 μM AC in 0.1 M PBS with different pHs (2.0–12.0). In sets (B and C) are the variations of peak current and potential vs. pH min extraction times. In sets (B) are the variation of peak current vs. time.

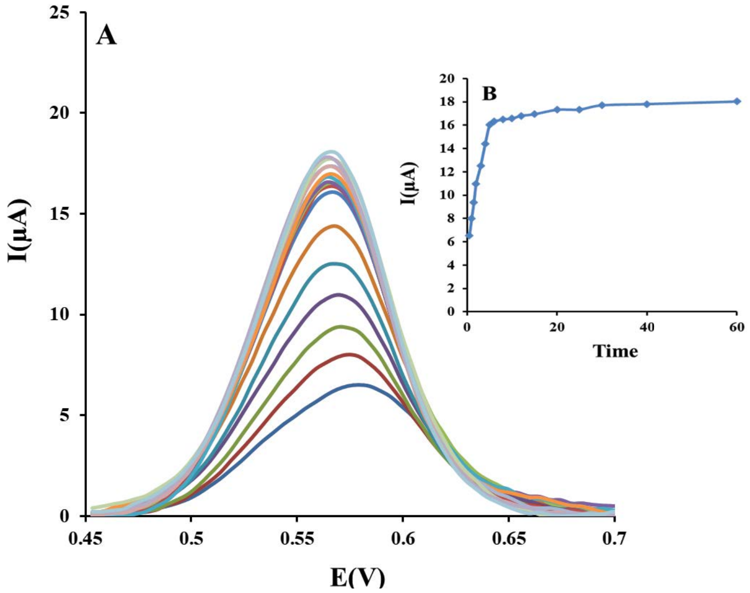

Fig. 8. (A and B) Differential pulse voltammograms (DPVs) of 50 µM AC in 0.1 M PBS (pH 2) from 1 to 60.

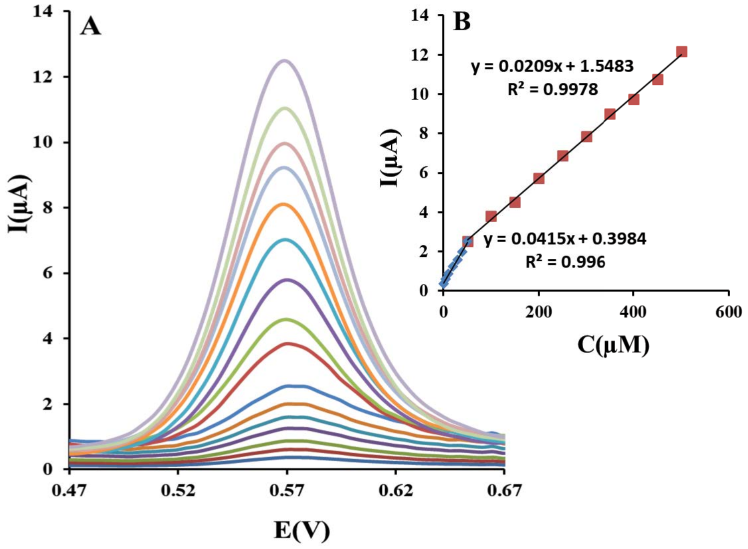

Fig. 9. (A) Differential pulse voltammograms (DPVs) of (0.1–500 µM) AC in 0.1 M PBS (pH 2). In sets (B) are the variation of peak current vs. concentrations.

3.6. Method validation

In order to assign the reproducibility of the suggested sensor, the anodic current of 50 µM of AC under optimum conditions were determined at five modified electrodes newly prepared. The peak current was nearly constant and relative standard deviation RSD% was found to be within the range of 2.7%–3.6%. For examination of interday repeatability, a modified electrode used in the DPV determination of 50 µM of AC in 5 various days. 1.69% was obtained for RSD% that exhibits the stability of the electrode response pending applying and storage in a long time course. Great stability was showed for the prepared electrode during a course of 4 weeks when kept in laboratory condition. The

Table 1
Determination of AC in urine and serum samples using our suggested sensor

Sample	Added (µM)	Found (µM)[a]	RR (%)[b]
	0.0	Not detected	–
Urine	1.0	0.976 ± 0.01	97.6 ± 0.01
	5.0	5.220 ± 0.03	104.4 ± 0.02
	0.0	Not detected	–
Serum	1.0	0.982 ± 0.05	98.2 ± 0.06
	5.0	4.850 ± 0.04	97.1 ± 0.03

[a] Average values of five determinations ± standard deviations.
[b] Relative recovery percent.

Table 2
Comparison of analytical parameters of the proposed electrode with other sensors

Electrode	Methods	Limit of detection (μM)	Linear range (μM)	pH	References
MWCNTs – CHT/GCE[a]	DPV[h]	0.17	1–145	7.0	[15]
SWCNT/CCE[b]	DPV	0.12	0.2–150	7.0	[36]
ERG/GCE[c]	DPV	1.2	5–800	7.4	[37]
Carbon ionic liquid	DPV	0.3	1–2,000	4.6	[38]
C–Ni/GCE[d]	DPV	0.6	2–230	3.0	[39]
Gr/$CoFe_2O_4$[e]	SWV[i]	0.025	0.03–12.0	7.0	[40]
$NiFe_2O_4$/Gr/CPE[f]	SWV	0.003	0.01–9	7.5	[41]
GCE/AgNPs-PHEMA-CMK-1[g]	DPV	0.005	0.015–7.5 and 0.03–10.8	7.0–8.0	[42]
HF-PGE/[BMIM]PF_6/GO-β-CD	DPV	0.030	0.1–50.0 and 50–500	2.0	This work

[a] Multiwalled carbon nanotube/chitosan modified glassy carbon electrode.
[b] Single-walled carbon nanotube-modified carbon–ceramic electrode.
[c] Electrochemically reduced graphene glassy carbon electrode.
[d] Carbon-coated nickel magnetic nanoparticles modified glass carbon electrode.
[e] Graphene/$CoFe_2O_4$ nanocomposite.
[f] Graphene/$NiFe_2O_4$ nanocomposite.
[g] Glassy carbon electrode with an ordered mesoporous carbon (OMC)/poly(2-hydroxyethyl methacrylate) (PHEMA)/Ag nanoparticle composite.
[h] Differential pulse voltammetry.
[i] Square wave voltammetry.

favorable decrease in the peak current for AC (less than 5% after this course) confirmed its excellent stability.

3.7. Application to real samples

For the applicability appraisal of the proposed sensor, it was employed to determine the concentration of AC in urine and blood plasma samples. For this aim, the samples were prepared as explained in section 2.6 (Real sample preparation) and analyzed using the standard addition method, and the results of this work which were spiked with different amounts of the drug are tabloid in Table 1. The obtained values reveal that the sensor is interference-free from urine and serum sample matrices. The DPV method was used for the determination of AC in real samples such as urine and human plasma. Accordingly, the method is capable for the determination of AC in samples with different matrices. The values presented in Table 1 are the average recovery of five repetitious measurements of AC with standard addition method for urine and serum samples. The results show that this sensor might have the potential to use in the detection of AC and the accuracy and precision were satisfactory in the measurement of AC in real samples.

4. Conclusions

This research presented the results achieved by in-house fabricated electrode (HF-PGE) for electrochemical DPV analysis of AC. The coupling of a three-electrode configuration system with differential pulse voltammetry has prepared tools of a comparatively cheap in place sensor for trace levels of Ac. In this work, we coupled separation based on the fabricated membrane with electrochemistry method to make and design a powerful method for simultaneous preconcentration and monitoring of the electroactive analyte. We introduced a new modified electrode based on ionic liquid mediated hollow fiber-pencil graphite hybrid electrode, modified with β-cyclodextrin functionalized graphene oxide (HF-PGE/BMIMPF_6/GO-β-CD) for simultaneous *in-situ* preconcentration and electrochemical detection of AC in real samples by DPV. The proposed electrode presented greater sensitivity and selectivity in the measurement of AC. Meanwhile, the new electrode displayed nice reproducibility and stability. The synergistic combination of both components (H.F/BMIMPF_6 and GO-β-CD) cause a remarkable enhancement in the area of the electrode together with the effective separation of AC in H.F pores and a considerable increase in sensitivity and detection limit of the HF-PGE/BMIMPF_6/GO-β-CD compared to other reported sensors (Table 2). Determination of trace amounts of AC in pharmaceutical and clinical preparations with satisfactory results is promising due to the high sensitivity of the modified electrode.

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