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Electrochemical determination of anticancer drug, flutamide in human plasma sample using a microfabricated sensor based on hyperbranchedpolyglycerol modified graphene oxide reinforced hollow fiber-pencil graphite electrode

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ABSTRACT

Flutamide (FLT) is a non-steroidal anti-androgen drug that has a specific anti-androgenic activity so that it is used in the treatment of prostate cancer. FLT may also be used to treat excess androgen levels in women. A sensitive electrochemical sensor based on hyperbranchedpolyglycerol functionalized- graphene oxide developed, using ionic liquid mediated hollow fiber-pencil graphite electrode (HF/HBP-GO/PGE) as a working electrode for determination of an anticancer drug, flutamide (FLT. In this design, a two centimeter piece of porous polypropylene hollow fiber membrane was impregnated with ionic liquid (1-Pentyl-3-methylimidazoliumbromide), and a graphite rod modified with hyperbranchedpolyglycerol/graphene oxide (HBP-GO), was located inside the fiber lumen. The modified electrode exhibits sorption activity, high sensitivity, stability and applicability over a wide range of concentration of FLT. The morphology and the electrochemical properties of the modified electrode were characterized by scanning electron microscopy (SEM) and cyclic voltammetry (CV). The effect of the amount of graphene oxide (GO), scan rate, pH, concentration of ionic liquid, extraction time and agitation rate on electrochemical behavior of flutamide molecules was investigated. The square wave voltammetric method showed a linear behavior over the drug concentration range 0.1–110 μM. The limit of detection (LOD) and the limit of quantification (LOQ) were found to be 0.029 μM and 0.099 μM, respectively. The proposed sensor was applied for determination of FLT in human plasma sample with satisfactory results.

1. Introduction

Flutamide (FLT), 4-nitro-3-trifluoromethyl-isobutilanilide (Fig. 1), is a widely used nonsteroidal anti-androgen drug for treatment of prostate cancer [1]. FLT works by blocking the effects of testosterone, which is a natural hormone that helps the prostate cancer to grow and spread, thereby slowing the growth and spread of prostate cancer [2]. It has also been used in the treatment of male-to-female transsexuals. After human oral administration, FLT is quickly metabolized to produce about 10 metabolites, mainly 2-hydroxyflutamide and 3-trifluoromethyl-4-nitroaniline [3]. This drug and its primary hydroxyl metabolite decrease the metabolism of C-19 steroids by cytochrome P-450 system at the target cells in the secondary sex organ [4]. Plasma testosterone levels increase in male which partially overcomes the direct and androgen action of FLT. It is palliative in advanced prostatic carcinoma [5].

Different instrumental methods have been reported for determination of FLT including high-performance liquid chromatography (HPLC) [6–8], gas chromatography (GC) [9], photochemistry [10], spectrofluorimetry [11], spectrophotometry [12], flow-injection analysis [13], polarography [14–16] and voltammetry [17,18]. Among these instrumental techniques for flutamide analysis, the electrochemical methods are very attractive in this field, because of their simplicity, high sensitivity and selectivity, low costs and also low reagent consumption. Electrochemical pretreatment of pencil graphite electrode (PGE) seems to be a simple, less time consuming and more applicable strategy in comparison with the other modification procedures of the electrode surface. Pencil electrodes have been used successfully for a variety of electrochemical analysis methods [19–21] due to their good reproducibility and low cost of the commercially available graphite lead which is the basis of PGE. Moreover, unlike conventional carbon electrodes, PGEs do not require any polishing prior to use. Although PGE is

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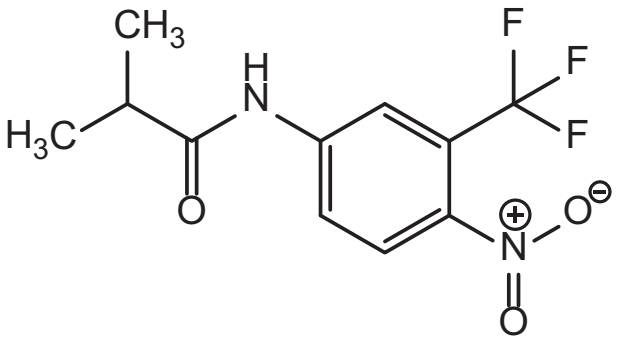


Fig. 1. Structure of flutamide.

relatively new type of carbon electrode, it has been successfully applied to the cathodic and anodic voltammetry by virtue of its high electrochemical reactivity, low technology, and ease of modification [22–24].

Pharmaceutical residues are usually present in environmental water samples at trace levels. Thus, a sample isolation and pre-concentration technique is necessary before their analysis. Among the available techniques, solid phase microextraction (SPME) is one of the most interesting methods [25,26]. SPME as a solvent free process is fast, portable and easy to use technique, but SPME suffers from some drawbacks such as frangible fiber, limited lifetime, high desorption temperature and sample carry over effect. Therefore, the present work aimed to develop the SPME technique by inserting the nanoparticles into the pores of polypropylene hollow fibers via an organic solvent or ionic liquid as a solid/liquid membrane. The idea was to have a membrane based, functionalized nanoparticles that acts as analyte trap, lead in higher selectivity and enrichment, because the nanoparticles act as solid sorbents in SPME fibers [27–29].

Among various nanoparticles, graphene oxide has attracted robust scientific and technological interest in recent years due to superior mechanical strength, low density, high surface area, electrical conductivity and high heat conductivity [30–37]. Graphene oxide also has aqueous processing capabilities, and surface functionalizability, which are due to its chemical structures composed of small sp^2 carbon domains surrounded by sp^3 carbon domains and oxygen containing hydrophilic functional groups [37]. Many applications have been reported based on its mechanical, electrical and chemical properties. Some of these applications are in the area of fuel cells [30,31], biosensors [32,33], electrochemical sensors [34,35], nanosensors [36] and nanocatalysts [37].

In the present work a modified working electrode based on hollow fiber-pencil graphite electrode was introduced for extraction and in-situ determination of the analyte. This solid-liquid phase microextraction mode is made through the use of a piece of polypropylene hollow fiber that protects the pencil graphite rod and acts as the electrode in an electrochemical detection system, square wave voltammetry (SWV). All of the extraction and detection process of the analyte were done on the fabricated working electrode. The electrode surface was modified with hyperbranchedpolyglycerol/graphene oxide nanocomposite [38].

In this new application, the role of the background solvent is important, because it allows the analyte to penetrate into the membrane. The solvent also should be consistent with the structure of the fiber, such that it should not leave the fiber pores. Many solvents were tested and finally an ionic liquid (1-Pentyl-3-methylimidazoliumbromide) was selected as the best carrier.

2. Experimental

2.1. Materials and methods

2.1.1. Standards and reagents

FLT was purchased from the Sobhanoncology Pharmaceutical Company (Rasht, Iran) and it was of pharmaceutical quality. All of the solvents and another chemical reagents were of analytical grade and they supplied by Merck chemical company (Darmstadt, Germany). Graphite powder (< 150 μm, 99.99%) was purchased from Sigma-Aldrich. *n*-methylimidazole and 1-bromopentane were purchased from Sigma–Aldrich (St. Louis, MO) and used without further purification except when is mentioned specifically. Q3/2 Accurel polypropylene microporous hollow fiber membrane (200 μm wall thickness, 600 μm inner diameter, 0.2 μm pore size, 75% porosity) was obtained from Membrana (Wuppertal, Germany). A stock standard solution of flutamide(1.0×10^{-2} M) was prepared in ethanol and stored in a refrigerator at 4 °C. The working standard solutions were prepared by appropriate dilution of the stock standard solution with 0.04 M Britton Robinson buffer (BR)), pH 8.0. A 0.04 M BR buffer solution was prepared using a mixture of orthophosphoricacid, boric acid and acetic acid. The pH of buffer solution was adjusted using dilute solutions of HCl or NaOH. Milli-pore deionized water was used in this study.

2.1.2. Apparatus

Voltammetric measurements were performed using a μAutolab electrochemical system (Metrohm) equipped with a NOVA software. All measurements were carried out in a three-electrode measuring cell; an Ag/AgCl/KCl (3.5 M) as reference electrode, a platinum wire as a counter electrode and the home-made hollow fiber pencil graphite electrode (HF- PGE) as a working electrode. The voltammograms of flutamide was obtained by CV and SWV mode. The volume of the solution introduced in the voltammetry cell was 5.0 mL. The reference and counter electrodes were purchased from Azar Electrode Company, Urmia. Iran. An Ultrasonic Processor, model UP 400S, made in Germany was used for functionalizing the surface of graphene oxide with HBP. The FT-IR spectra were recorded using a Buck Scientific M-500 Fast-Scan IR spectrometer (East Nor-walk, CT, USA). A Metrohm 780 pH-meter equipped with a combined glass electrode (Herisau, Switzerland) was used for determination the pH values of the solutions during the experiments. Scanning electron microscopic (SEM) images were obtained by a (JEOL JEM2000, Nikon, Japan) instrument.

2.2. Synthesis of ionic liquid

The ionic liquid1-Pentyl-3-methylimidazoliumbromide, was synthesized by direct reaction of *n*-methylimidazole and 1-bromopentane [39]. *N*-methyl imidazole and 1-bromopentane were placed into a three-neck flask equipped with a mechanical stirrer and reflux condenser which was immersed in a silicon oil bath set at 140 °C and the mixture was refluxed at this temperature. After 10 min, the reaction flask was removed from the oil bath and allowed to cool under stirring for 10 min. Once again, the flask was placed into the oil bath at 140 °C for another 15 min to produce the 1-pentyl-3-methylimidazoliumbromide. The contents of the flask were dried under vacuum at 100–120 °C. The FT-IR Spectra of IL, 1-penthyl-3-methyl-imidazolium bromide has been presented in Fig. 2.

The IR spectrum of [PMIM] Br IL showed three absorption bands due to the C H of aromatic and aliphatic at 3078, 2926 and 2854 cm^{-1}, respectively. Also, the [PMIM] Br IL structure was confirmed by appearance of characteristics C=== stretching at 1570 cm^{-1}in the IR spectrum.

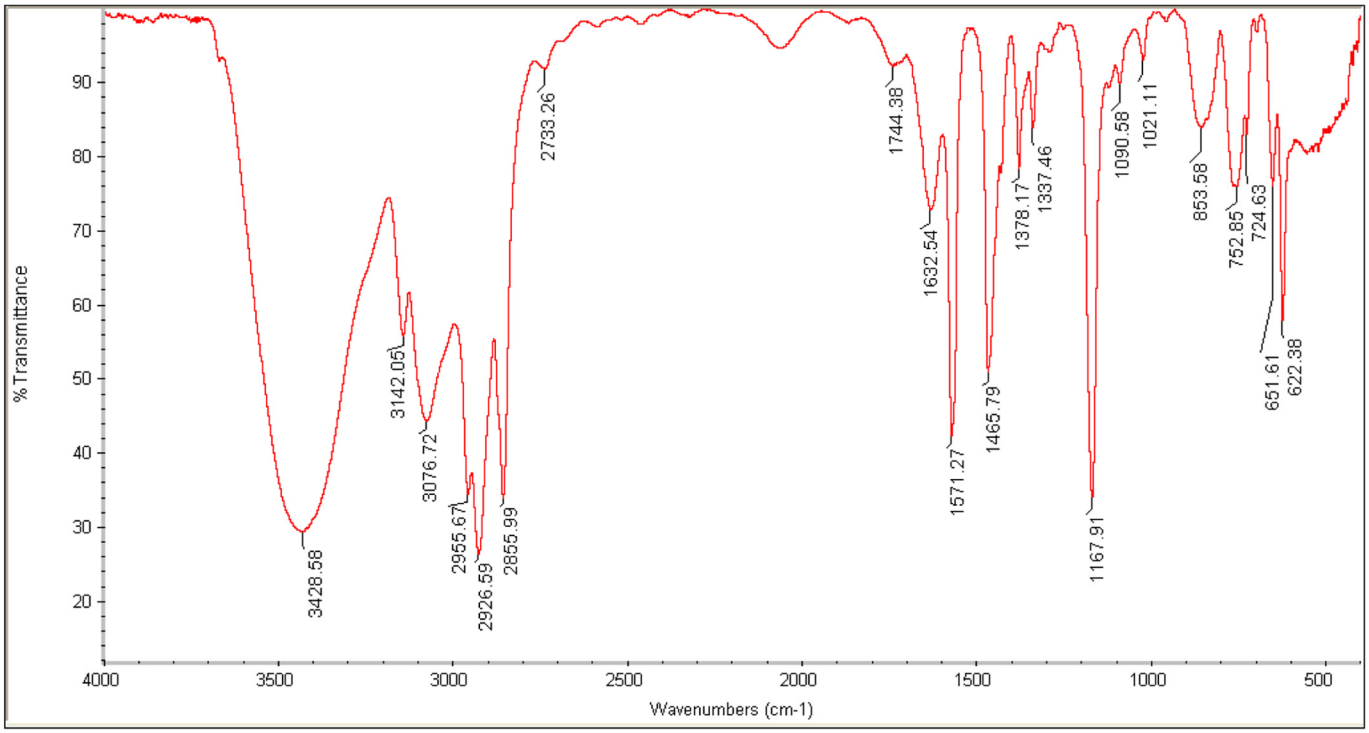


Fig. 2. FT-IR spectrum of: 1-penthyl-3-methyl-imidazolium bromide IL.

2.3. Synthesis and functionalization of graphene oxide with HBP

GO was prepared from graphite powders using a modified Hummer's method [40]. Although sometimes the pure graphene oxide can be used in extraction and removal of organic and inorganic pollutants without the need for further fictionalization, but it is needed to modify the surface of graphene oxide by attaching some functional groups in order to obtain a specific surface in separation purposes. HBP synthesized by Masoodi et al. in Payame Noor University of Mashhad (2nd International Symposium Frontiers in Polymer Science 29–31 May 2011, Lyon, Franc, the synthesis of Azo (PAMAM − DIPA Core (G1)) 2 Dendrimer). For functionalizing the surface of the graphene oxide, 1.0 g HBP, 1.0 g graphene oxide and 5 mL thionyl chloride were added in a round-bottom flask. The solution was stirred at reflux condition for 8.0 h. After completion the reaction, 50.0 mL of ethanol was added to the solution and it was allowed to cool at room temperature. The precipitated products were separated by filtration and washed with ethanol. The proposed mechanism for the reaction is shown in Fig. 2.

Fig. 3 shows the FT-IR analysis to characterize the HBP functionalized with graphene oxide (HBP-GO).

2.4. Preparation of HBP-GO/PGE

First, the graphite pencils rod (HiWe, 2B of 0.5 mm in diameter and 6 cm length) leads were cleaned before each use in a simple consistent manner. They were washed in deionized water for 10 min and cleaned in acetone for 5 min to remove organic impurities followed by thorough rinsing deionized water for 5 more min and then dried in room temperature. 7 mg of functionalized GO was dispersed in 5 mL of deionized water and sonicated for 20 min. The pretreated PGEs were immersed in this solution for 1 h and then dried in room temperature. Functionalized GO was physically adsorbed to the PGE surface, via their penetration into graphite micro-pores.

2.5. Fabrication of the hollow fiber supported graphite electrode (HF-PGE)

Polypropylene hollow fibers were cut into segments with length of 2.0 cm. The fiber segments were washed in deionized water for 10 min and cleaned with acetone for 5 min to remove impurities and directly dried in air. The free end of hollow fiber was closed by heating. 0.02 M of ionic liquid solution (1-pentyl-3-methylimidazoliumbromide) was prepared in 1-octanol. Then, the pretreated HFs sonicated in mixture of

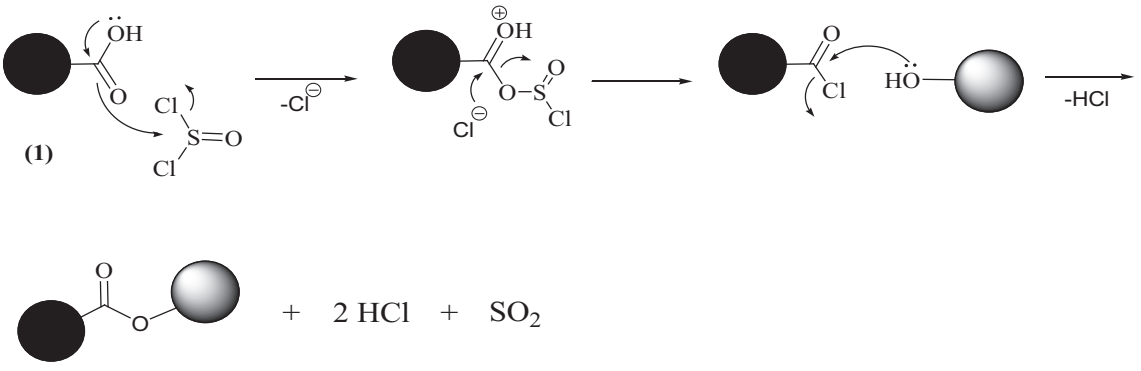
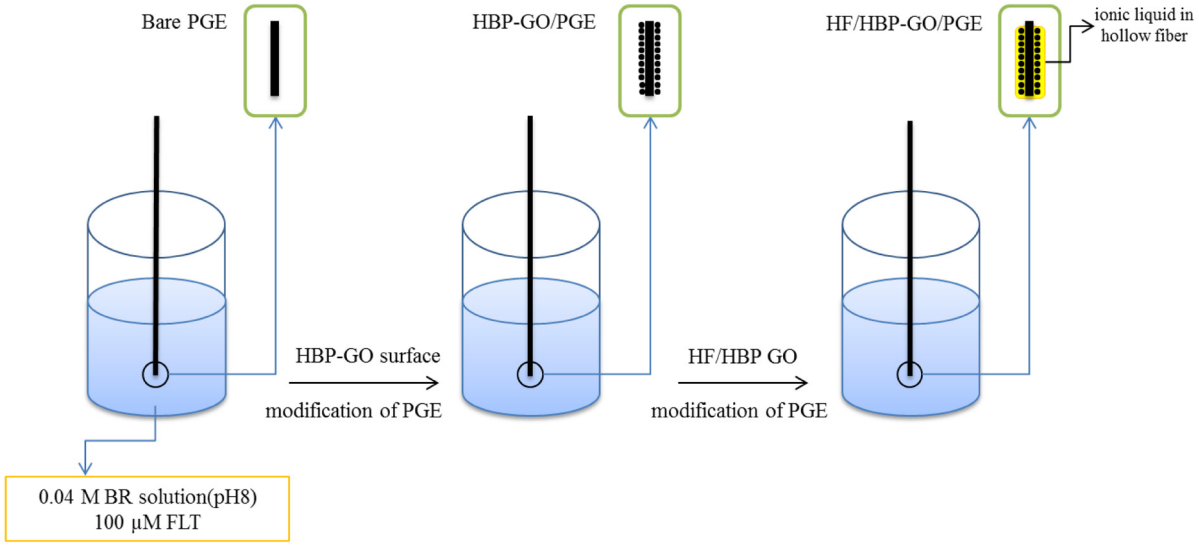


Fig. 3. Proposed mechanism of graphene oxide functionalization.



Scheme 1. Flow chart of fabrication of HF-PGE.

ionic liquid and 1-octanol for a few mints to fill the membrane pores of the hollow fiber wall. 1-octanol is compatible with polypropylene and easily occupies the pores. 2 cm of modified graphite pencils rod (HBP-GO/PGE) was inserted carefully into the prepared segment. Hollow fiber because of its porous nature, while establishing the connection between the solution and the electrodes, it also protects the surface of functionalized GO modified pencil graphite electrode. Each HF-PGE was used only once to avoid any memory effect. Schematic of the fabrication of HF-PGE is showed in Scheme 1.

3. Results and discussion

3.1. Characterization of (HBP-GO/PGE)

The surface morphologies of unmodified PGE, HBP-GO/PGE and HF-PGE were explored using SEM analysis (Fig. 5A, B and C). The clustered HBP-GO molecules can be clearly seen at the surface of PGE in contrast to unmodified ones. The surface roughness and brightness of PGEs increased after the modification of HBP-GO (Fig. 4B) onto PGE surface comparison to the ones obtained by using unmodified electrode (Fig. 5A). Moreover, it was clearly seen that the sharpness of the sheets increased due to the graphite sheets were covered with hyperbranchedpolyglycerol (Fig. 5B). This was a firm proof that the immobilization of HBP-GO onto the surface of PGEs was successfully achieved.

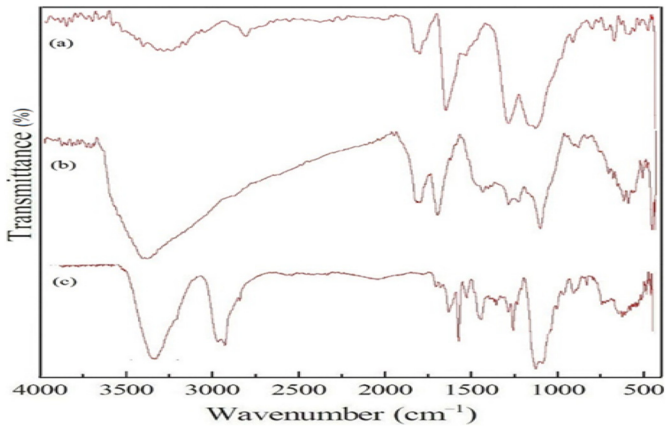


Fig. 4. FT-IR spectra of; a) HBP-GO, b) GO, and c) HBP [38].

3.2. Electrochemical behavior of FLT

Fig. 6, shows a cyclic voltammogram of 100 µM solution of FLT in Britton-Robinson buffer (pH 8) at PGE electrode. In the forward scan, one cathodic peak, in the potential range −1.2 to −0.2 V, owing to the reduction of the nitro group to hydroxylamine with the four electrons addition was observed and no peak was noticed in the reverse scan suggesting that the reduction of flutamide at PGE is irreversible.

Nevertheless, there was a slight anodic peak at −0.5 V. This anodic peak is not negligible and it may be attributed to the oxidation of (hydroxylamine) reduced product.

Scheme 2, shows the proposed reduction mechanism of FLT molecule. The cyclic voltammogram of flutamide at PGE electrode showed only one cathodic peak at −0.60 V but the oxidation peak was not observed in the potential range − 1.2 to −0.2 V. However, Brahman et al. [18] mentioned that the single cathodic peak of flutamide splits into two peaks in more concentrated solutions and/or different media or various electrodes. The splitting of this peak, may be assigned to the formation of radical species at the electrode surface. The cyclic voltammograms of 100 µM solution of FLT at different fabricated electrodes are shown in Fig. 7. As is evident in this Figure, a weak reduction peak, around −0.60 V is observed at the bare PGE electrode that imply FLT reduction at the bare GCE was slow due to the slow electron transfer (A). But, the activity was considerably improved with the HBP-GO/PGE (B). As can be seen from Fig. 7(C), the cyclic voltammogram of flutamide demonstrates that the reduction peak current of the drug molecules increases significantly in the presence of the ionic liquid at the surface of the HF-PGE electrode compared to the other fabricated electrodes. It is clear that the addition of the ionic liquid exerts a significant enhancing effect on the electrochemical reduction of the flutamide molecules because ionic liquid could improve the electrical conductivity and chemical stability. So it leads to decrease of over potential in the process and enhancement of the peak current is observed.

The electrocatalytic effect of HF-PGE was also studied by Square wave voltammetry as since, Square wave voltammetry is more sensitive than cyclic voltammetry; detailed studies are carried out using square wave voltammetry.

3.3. Optimization of the experimental conditions

3.3.1. Influence of the amount of graphene oxide

The effect of the amount of graphene oxide is illustrated in Fig. 8.

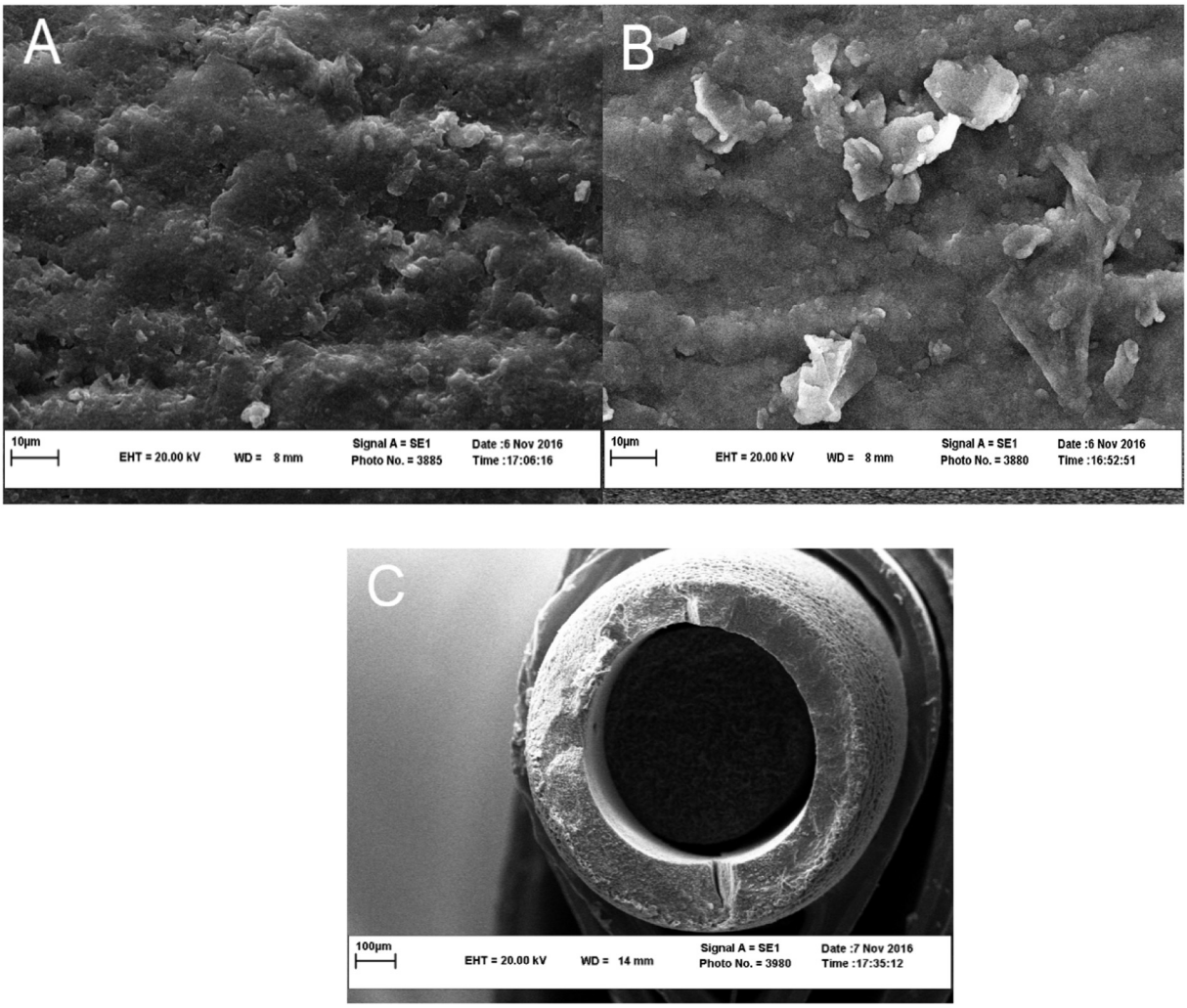


Fig. 5. SEM images of unmodified PGE (A), HBP-GO modified PGE (B) and polypropylene hollow fiber impregnated with ionic liquid (C) at the identical acceleration voltage as 2.0 kV in.

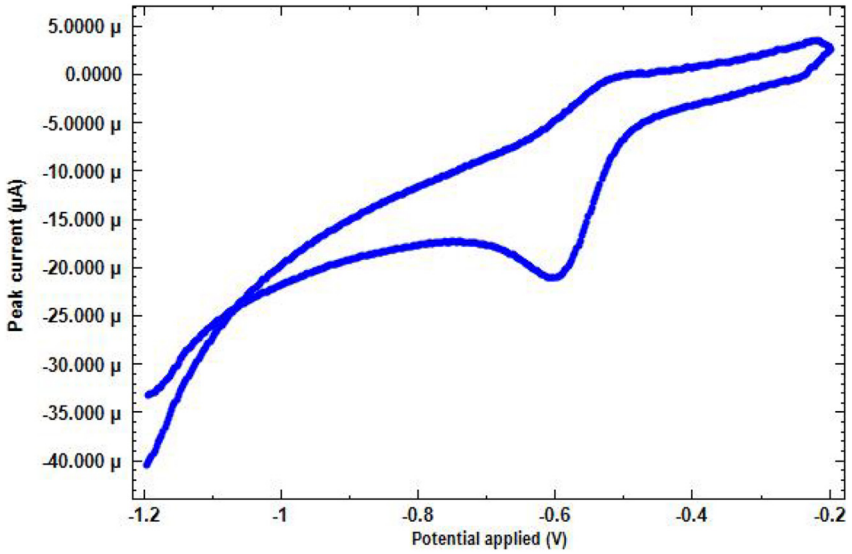
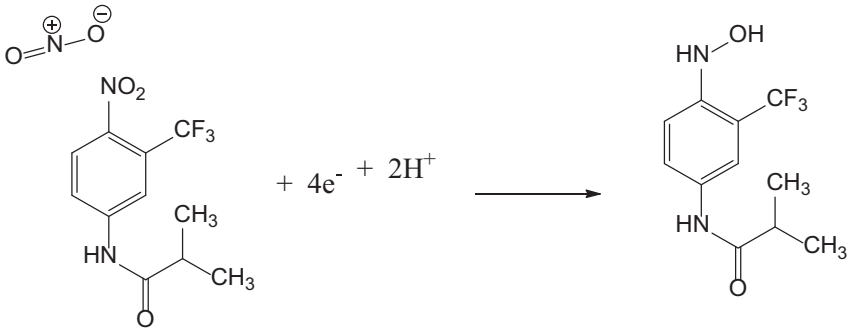


Fig. 6. Cyclic voltammogram of 100 μM solution of FLT in 0.04 M BR solution (pH 8) at bare PGE electrode.



Scheme 2. Electrochemical reduction of flutamide molecule (adapted from Ref. [43]).

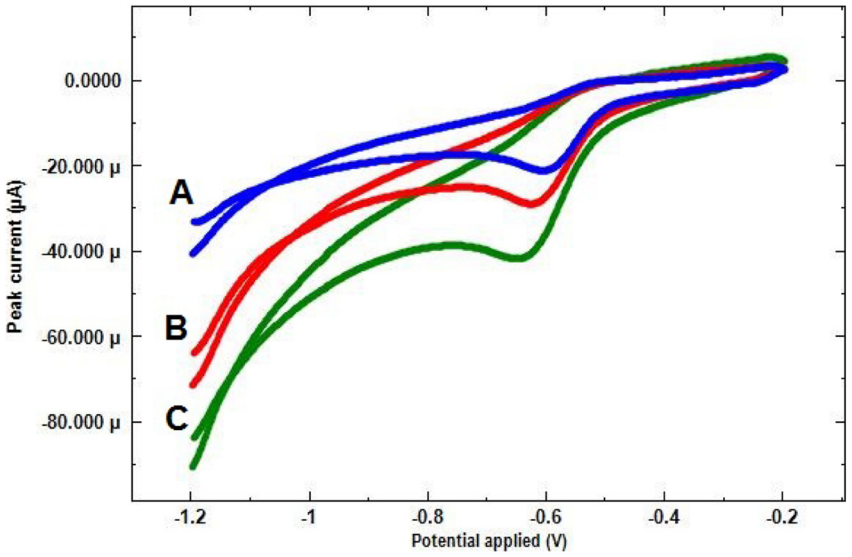


Fig. 7. Cyclic voltammogram of 100.0 µM of FLT in 0.04 M BR solution (pH 8) at bare PGE electrode (A), HBP-GO/PGE electrode (B) and HF-PGE electrode(C).

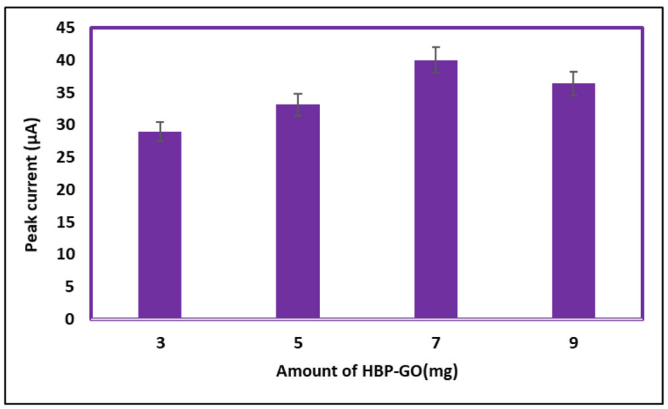


Fig. 8. The change of the reduction peak current of FLT with the amount of HBP-GO for 100 µM solution of FLT in 0.04 M BR buffer solution (pH 8) at HBP-GO/PGE with scan rate 100 mV s^{-1}.

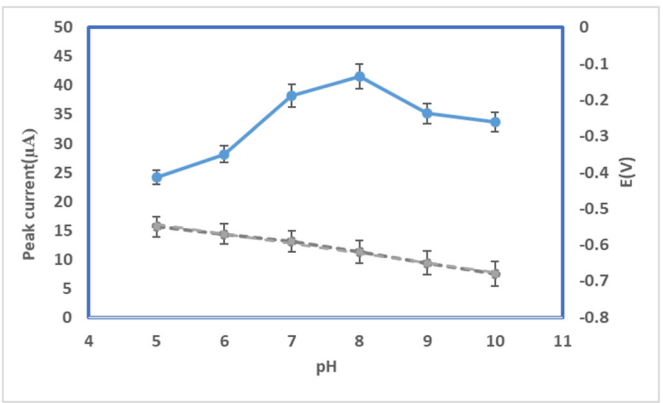


Fig. 9. Effect of pH values on the peak current and peak potential of FLT molecules using of HBP-GO/PGE in the presence of 100 µM FLT at a scan rate of 100 mV s^{-1}.

The peak current of FLT reduction at the surface of HF-PGE increases with increasing the amount of GO up to 7 mg. The reason is that an increase of GO amounts improves the conductivity and electron transfer properties of the HF-PGE for reduction of FLT molecules. However, with further increase in the amount of GO, a decrease in catalytic activity is observed. This is due to an increase in the thickness of the GO film on the surface of the electrode which results in a decrease in its electrical conductivity.

3.3.2. *Influence of pH*

The FLT redox behavior depended on the pH value of the buffer solution. Therefore, the effect of the pH of the solution was investigated over the pH range of 5–10 (Fig. 9). The results showed that the cathodic potential of FLT shifted to more negative values with increasing pH, indicating that with the solution of greater alkalinity, further reduction of nitro group is not facilitated owing to the non-availability of the protons. Consequently, the pH of supporting electrolyte applied a significant influence on electroreduction of FLT at the surface of the

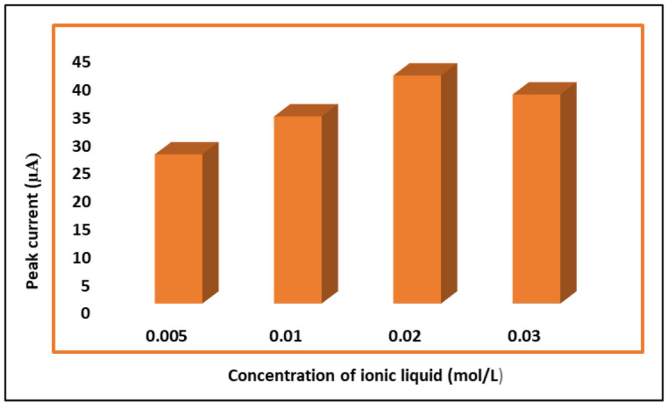


Fig. 10. Effect of ionic liquid concentration on the reduction peak current of FLT Molecules using HBP-GO/PGE in 100 μM solution of FLT in 0.04 M BR buffer solution (pH 8) with scan rate 100 mV s^{-1}.

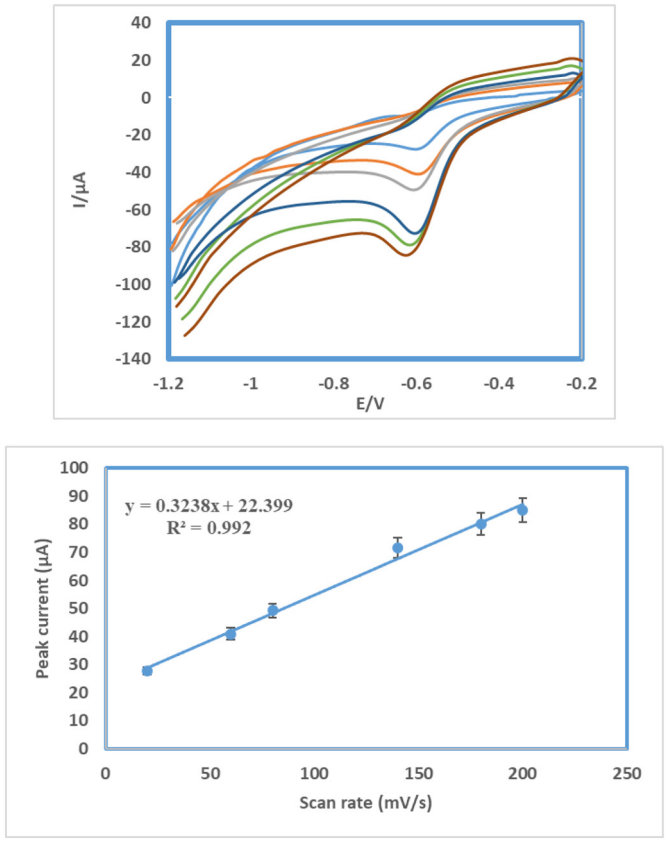


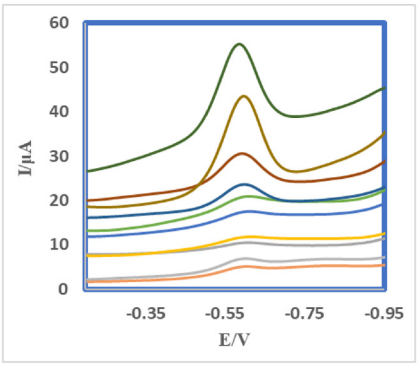
Fig. 11. (A) Plot of peak current versus E_p for the reduction of FLT (100 μM) at HBP-GO/PGE at different scan rates from 20 to 200 mV s^{-1}. (B) Plot of peak current peak current versus scan rate in 0.04 M BR buffer solution (pH 8).

modified electrode.

The results showed that the cathodic peak current of FLT had its maximum at pH 8.0.

3.3.3. Influence of ionic liquid concentration

As is depicted in Fig. 10, the concentration of the ionic liquid influences the reduction peak current of the FLT molecules. The reduction peak current increases with concentration of ionic liquid up to 0.02 mol L^{-1}, but at higher concentration the intensity of the peak decreases. It seems, that at low concentration of the ionic liquid a small amount of HBP-GO is deposited at the surface of the electrode which results in a low peak.



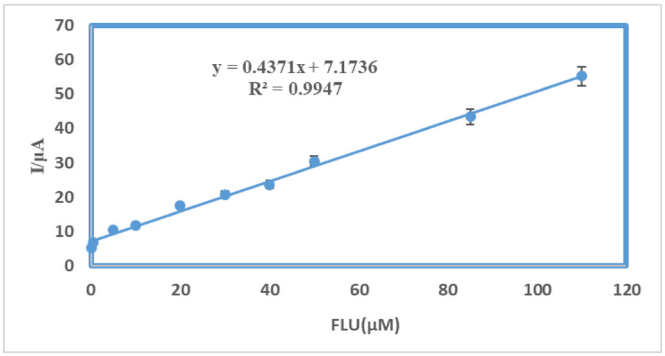


Fig. 12. (A) Squarewave voltammograms for various concentrations of FLT in the range of 0.1–110 μM. (B) Linear calibration curve of peak current vs. FLT concentration (0.1–110 μM) at HF-PGE.

3.3.4. Effect of the scan rate

The effect of scan rate on the redox reaction of 100 μM solution of FLT at HF-PGE was investigated in the range of 20 to 200 mV s^{-1} scan rates with cyclic voltammetry (Fig. 11A). It was found that the reduction peak current is proportional to the scan rate, suggesting that the reduction of the FLT molecules at HF-PGE is adsorption-controlled. Linear plots of peak current (I_p) versus square root of the scan rate ($\gamma^{1/2}$) should be obtained for diffusing electro-active species; whereas species adsorbed on the electrode surface should result in linear plots of peak current (I_p) versus scan rate [41] (Fig. 11B).

The peaks potential (Ep) of FLT moved to a more negative potential with increasing the scan rate, which confirms the irreversibility of the process. In these study 100 mV s^{-1} was chosen as the scan rate because at this value the sensitivity was relatively high and the voltammetric curves were well-shaped with relatively narrow peak width.

3.3.5. Effect of the other parameters

Extraction time is an important factor in the solid phase microextraction process and must be optimized. Mass-transfer is a time-dependent process, and its rate affects the equilibrium conditions [42]. Since SPME is an equilibrium extraction mode, the maximum amount of analyte that can be extracted by the sorbent is achieved at equilibrium. Based on the results, from 0.0 to 900.0 s, as the length of electrode stays in the cell was higher; response to analyte was more associated with higher currents along with a steep slope. During this time, analyte had the opportunity to accumulate into the hollow fiber pores. Then, by applying a cathodic potential, analyte that was concentrated into hollow fiber, on the graphite surface was reduced. Therefore, 900 s were chosen as the optimum extraction time. Extra extraction times did not have much effect on the outcome.

In the extraction, agitation speed has a direct effect on increasing the contact area between two phases and causes the mass transfer are well done. So, we study the effect of agitation speed on the extraction, with different speeds of 200,400, 600 and 800 rpm. The results showed that the extraction efficiency has highest value at the lowest agitation

Table 1
Analytical performance of fabricated HF-PGE method for detection of flutamide in solutions.

Compound	Linear range(μM)	R^2	Regression equation	LOD(μM)	LOQ(μM)	RSD% (n = 5)
Flutamide	0.1–110	0.9947	Y = 0.4371X + 7.1736	0.029	0.099	3.4

Table 2
Comparison of detection of limits (LOD) for determination of FLT in some electrochemical measurements.

Electrode	Method	LOD (μM)	Ref
Hanging mercury drop electrode	CASV[a]	0.19	[17]
Modified CPE	DPV/CV	0.18	[18]
Nano-Ag/Modified GCE	CV	9.33	[43]
Hanging mercury drop electrode	SWV/CV[b]	0.42	[44]
HF-PGE	DPV/CV	0.026	This work

[a] CASV: cathodic adsorptive stripping voltammetry.
[b] SWCASV: square wave adsorptive stripping voltammetry.

Table 3
Interference study for the determination of FLT under the optimized conditions.

Species	Signal change (%)
Glucose	−1.65
Sucrose	−1.90
Caffeine	+4.64
Urea	−2.34
Oxalic acid	+2.70
Ascorbic acid	−0.76

Table 4
Voltammetry determination of FLT in human plasma sample.

Sample	Spiked (μM)	Found (μM)	Recovery (%)
Plasma	5.0 (n = 3)	4.5	90.0
	30.0 (n = 3)	29.1	97.0

speed. Since higher speeds cause the air bubbles around the hollow fiber. Therefore, the agitation speed of 200 rpm was selected as the optimal parameter.

3.4. Validation of the proposed method

The determination of FLT at HF-PGE was carried out in 0.04 M solution of BR (pH 8.0) by Square wave voltammetry (SWV) (Fig. 12A). The correlation coefficient, repeatability, linearity, limit of detection (LOD) and limit of quantitation (LOQ) for trace amount of FLT were determined experimentally under the optimized experimental conditions. The results are summarized in Table 1. The calibration curves for trace concentrations of FLT drug present a good linear response in the concentration range between 0.1 μM to 110 μM (Fig. 12B). The limits of detection and quantification were found to be 0.029 μM and 0.099 μM, respectively. The relative standard deviation (RSD) was obtained for five replicate measurements and it was found to be: 3.4% which shows a satisfactory reproducibility of the proposed modified electrode for determination of FLT in solutions. The limit of detection (LOD) obtained in this work with those obtained by the other electrochemical measurements for determination of FLT in solutions, are compared in Table 2. As is evident in this table, the value of LOD obtained in this work is lower or comparable with those obtained in the other electrochemical determination of FLT. (See Table 3.)

3.5. Effect of interferences

The effect of some potential interferences existing in biological fluids such as glucose, sucrose, urea, caffeine, oxalic acid and ascorbic acid on determination of FLT was investigated by analyzing a standard solution of 10 μM FLT under the optimum experimental conditions. The results showed that the presence of a 100 fold concentration of the interferences in solution does not show any significant interfere with the determination of FLT using the proposed modified electrode and the peak current variation caused by them was < 5%. The results are given in Table.

3.6. Analysis of real sample

The practical feasibility of the proposed electrode was investigated for determination of FLT in spiked human plasma samples by standard addition method.

The drug-free human blood plasma samples which obtained from a local medical diagnostic laboratory; Mashhad, Iran, were used for analysis after pretreatment by centrifugation (3500 rpm for 10 min). A 2.0 mL aliquot of prepared solutions was spiked with certain amounts of FLT. Then these solution were diluted with the electrolyte buffer to give a working concentration of FLT (5.0 and 30.0 μM).

The results given in Table 4, confirm that the new fabricated-PGE, modified electrode is a novel and sensitive electrochemical sensor for determination of FLT in human plasma sample.

4. Conclusions

A novel electroanalytical producer based on hyperbranchedpolyglycerol functionalized-graphene oxide, using ionic liquid mediated hollow fiber- pencil graphite electrode as working electrode has been developed for determination of trace amount of flutamide as anticancer drug in human plasma sample. In the optimized experimental conditions, the results indicate that the fabricated HF-PGE electrochemical sensor is a sensitive and reproducible for determination of flutamide using cycle voltammetry (CV) and Square wave voltammetry (SWV). GO reacted with HBP via its functional groups using thionyl chloride. HBP-GO modified PGE was supported by a macroporous polypropylene membrane wall that impregnated with the ionic liquid (1-Pentyl-3-methylimidazoliumbromide). Polypropylene wall pores are the channels in which the analyte, nanosorbent and ionic liquid are in contact with each other. Meanwhile, the pores can cause a kind of dimensional selectivity to the analyte molecules. The proposed method is flexible, simple, sensitive and unexpansive. The disposable nature of the hollow fiber totally eliminates the possibility of sample carry over and ensures a high reproducibility. The results displayed that the HF-PGE/DPV can provide one-step simultaneous purification, preconcentration, extraction, back-extraction and determination of electroactive analytes such as organic compounds and metal ions and the advantage over the conventional SPME coatings that often do not allow such effective extraction of polar analytes from the same sample.

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