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Fullerene modified single-use electrodes as a convenient biosensor platform for electrochemical monitoring of drug-DNA interaction

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ABSTRACT: Fullerene enriched disposable electrodes were developed and used as a biosensor platform for electrochemical monitoring of drug-DNA interaction. The surface of pencil graphite electrode (PGE) was modified with fullerene in order to enhance electrode surface for efficient dsDNA immobilization. The surface of fullerene modified PGEs (f-PGEs) was characterized using scanning electron microscopy (SEM), and electrochemical impedance spectroscopy (EIS). The behavior of dsDNA layer onto f-PGE surface was investigated by EIS measurements in $Fe(CN_6)^{4-/3-}$ redox system. After optimization of several experimental parameters, the suitability of the constructed electrodes as a sensor platform for monitoring of drug-DNA interaction has been examined. The reproducibility of the biosensor was also tested in the presence of dsDNA immobilization. Consequently, the developed fullerene based biosensor offers suitable platform for the electrochemical analysis of drug-DNA interaction sensitively.

KEYWORDS: Fullerene; pencil graphite electrodes; electrochemical biosensor; electrochemical impedance spectroscopy; drug-DNA interaction.

1. INTRODUCTION

Fullerene is a unique carbon structure that brings a new level to nanomaterial applications. This nanostructure has unique physical and chemical properties and readily available with high purity [1,2]. Researchers have been investigating the prospect to use this third allotrope of carbon, which has many conjugated electrons, as a mediator in the design of various sensors. Fullerene-modified electrodes have been shown to be an excellent working electrode with great properties such as a large electroactive surface area, strong electrical conductivity, and biocompatibility [3-5]. The enormous surface area of the fullerene nanomaterial, which is due to its spherical shape, is highly desired characteristic in biosensors and sensor systems [6-12]. Due to the ability of lowering the potential of electro-reduction of redox substrates and increasing the reaction rates, fullerenes have been used to improve the sensitivity, selectivity, and reproducibility of electrochemical biosensors [13,14]. Thus, fullerenes have attracted great interest in recent years in the design of novel biosensing systems. For instance, Hernandez *et al*. [15] developed a low-cost electrochemical methodology for the quantification of ciprofloxacin in beef samples with nafion and fullerene modified carbon paste electrode (N-F/CPE) by cyclic voltammetry (CV) and differential pulse voltammetry (DPV) techniques. The analytical performance of the proposed methodology was resulted in LOD of 1.0 µM, a LOQ of 3.0 µM and repeatability of 5.38 %. Materon *et al*. [16] reported fullerene (C_{60}), reduced graphene oxide (rGO) and Nafion (NF) (C_{60}-rGO-NF/SPE) modified screen printed electrodes to determine the antibiotic metronidazole (MTZ). Under optimized conditions, the C_{60}-rGO-NF/SPE sensor exhibited a linear response in square wave voltammetry for MTZ concentrations from 2.5 x 10^{-7} to 34 x 10^{-6} M, with a detection limit of 2.1 x 10^{-7} M. The developed sensor also applied to determine MTZ in serum and urine samples [16]. Kong *et al*. [17] developed an electrochemical sensor which was based on the delaminated titanium carbide nanosheet (d-$Ti_3C_2T_x$) and fullerene composite modified glassy carbon electrode (d-$Ti_3C_2T_x$/C_{60}/GCE). The prepared electrode showed electrocatalytic activity for the oxidation of baicalein which has a variety of beneficial pharmacological effects such as anti-inflammatory, antioxidant, anti-microbial, etc. The detection of baicalein showed a linear range of 0.015-4.0 µM with a detection limit of 0.005 µM [17]. For the selective

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determination of phenolic compounds, namely, catechol and hydroquinone, an electrochemical sensor that is based on platinum nanoparticles (Pt NPs) and fullerene composite was constructed by modifying Pt/fullerene composite on the surface of a pyrolytic graphite electrode by Zhu *et al*. [18]. The sensor exhibited high electrocatalytic activities and large peak-to-peak separation toward the oxidation of catechol and hydroquinone by DPV, as well as a wide linear concentration range, high sensitivity, and low limit of determination.

Understanding how drug molecules interact with DNA has become a hot topic of research in the fields of chemistry, molecular biology, and medicine. It is also an important aspect of pharmacology, as it aids in the understanding of drug action processes and the development of more efficient and specifically targeted drugs with fewer side effects [19]. Such interactions are studied using a variety of spectroscopic techniques, such as, UV-Visible, Infrared (IR), Raman spectroscopies or atomic force microscopy (AFM), electrophoresis, mass spectrometry etc. [20]. However, these techniques take time and require expensive instrumentation and long sample preparation times. Electrochemical methods have been proven to be a facile and convenient technique for the sensitive identification of biologically essential organic compounds that undergo oxidation and reduction reactions, such as drugs and related substances in pharmaceuticals and body fluids. Electroanalytical techniques are extremely useful in the field of drug analysis because of their low cost, fast analysis time, and excellent sensitivity and specificity. Impedimetric biosensors have been utilized for detection a number of biomolecules. In this regard, Katz and Willner [21] recently published a study of impedance spectroscopy for exploring biomolecular interactions at conductive and semi-conductive surfaces, as well as immunosensors, nucleic acid sensors, and enzyme based biosensors.

The objective of the current work is to develop a sensitive and convenient nucleic acid biosensor for electrochemical monitoring of drug-DNA interaction. Within our knowledge, fullerene modified single-use graphite electrode was developed for the first time herein as a sensing platform and applied for electrochemical monitoring of drug-DNA interaction through the measurement of impedance. For this purpose, double stranded DNA was immobilized onto the surface of fullerene modified single-use pencil graphite electrodes (f-PGEs) to obtain nanomaterial-based biosensor. Then, drug-DNA interaction was monitored with f-PGE biosensor by measuring charge transfer resistance (Rct) value via electrochemical impedance spectroscopy (EIS). Lumazine was chosen as a model drug for this assay. Analytical performance including reproducibility of the biosensor was tested and discussed.

2. RESULTS and DISCUSSION

To develop an efficient electrochemical assay, selection of a proper electrode material is a crucial step. Thus, a variety of electrode types were used in conjunction with nanostructures for different sensing applications [1-18]. Due to their lower background currents, superior sensitivity, reproducibility, amendable electroactive surface area, cost effective and ease of disposability, pencil graphite electrode has gain considerable attention in recent years. Herein, the single-use pencil graphite electrode (PGE) surface was functionalized with fullerene which exhibited the superior improvement of the electrode properties compared with the bare pencil graphite electrode. The surface morphologies of bare PGE, f-PGE and dsDNA immobilized f-PGE were investigated by SEM. Figure 1 shows the topographies of each PGEs at different steps. As fullerenes can be clearly seen in Fig. 1-c,d,e,f, dsDNA molecules can also be distinguished as network structure at some parts of f-PGE in Fig. 1-e,f.

Since the concentration of fullerene is of great importance for the effectiveness of electrode surface modification, three different concentrations, 500, 700 and 900 µg/mL were employed to test the optimal condition (Figure 2). The semicircle diameter (Rct) related to the electron-transfer-limited process was measured and evaluated. When fullerene was applied to PGE surface, a larger semicircle domain was observed, indicating a higher Rct on the f-PGE. This was due to the fact that a thicker fullerene layer would increase the electron-transfer distance between the redox probe $[Fe(CN)_6]^{4-/3-}$ and the electrode, resulting in an increment at electron transfer resistances [22,23]. The Rct values were recorded as 78.5 ± 10.6 Ohm (RSD %, 13.5 %, n =3), 146.5 ± 16.2 Ohm (RSD %, 11.1 %, n =3) and 158 ± 85.5 Ohm (RSD %, 53.9 %, n =3), after modification of 500, 700 and 900 µg/mL fullerene onto PGE, respectively. In the presence of 900 µg/mL fullerene, the highest Rct value was obtained (Figure 2d), nevertheless the relative standard deviation (RSD %) was too high (RSD %, 53.9 %), which makes these results statistically insecure. This may indicate that the modification efficiency is low due to the presence of high amount (900 µg/mL) of fullerene on the surface. Since the most reproducible Rct value was obtained with 700 µg/mL fullerene (Figure 2c), it was chosen as optimum concentration for effective surface modification.

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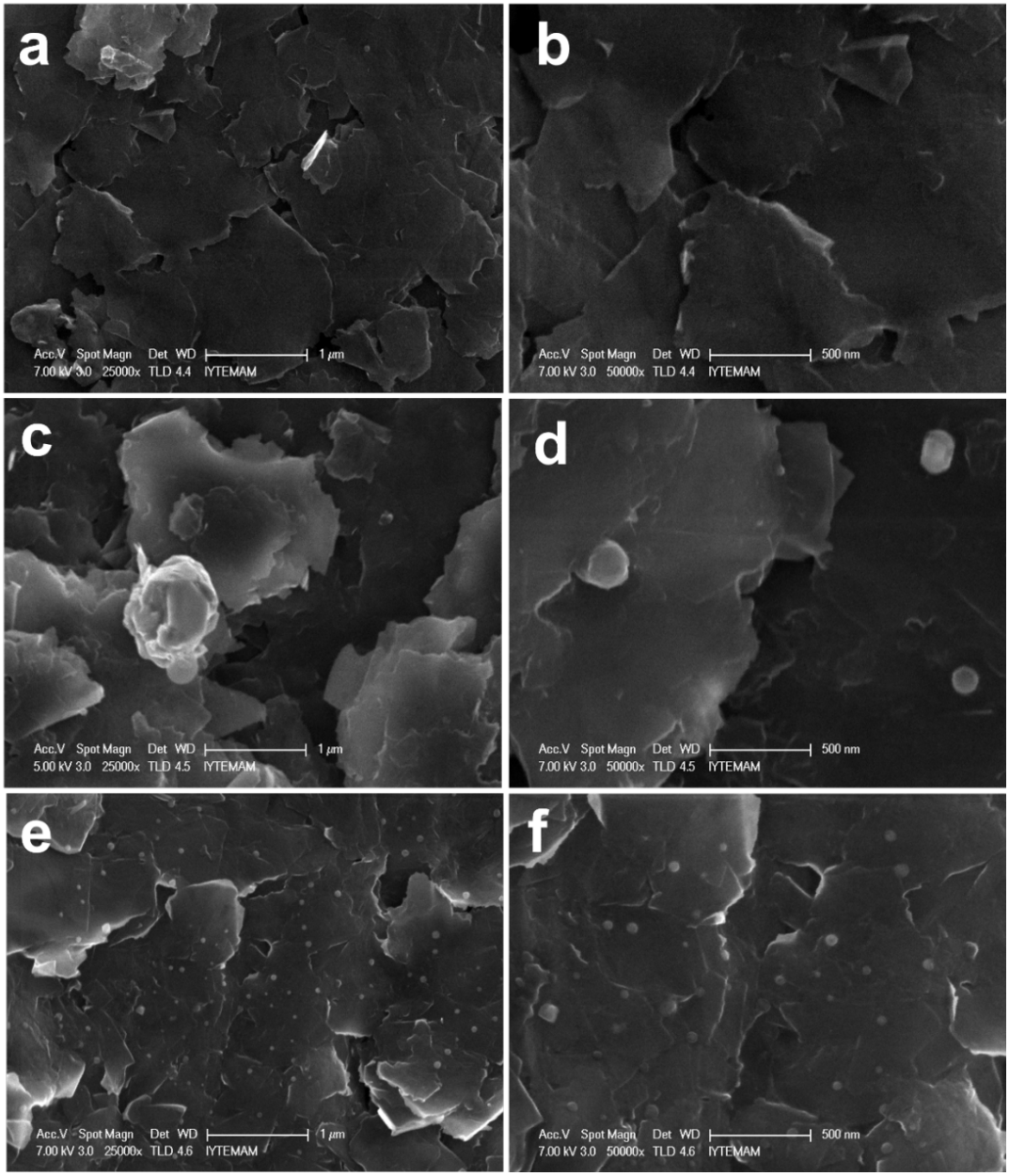

Figure 1. SEM images of PGE (a, b), f-PGE (c, d) and 50 µg/mL dsDNA immobilized f-PGE (e, f) with resolutions of 1 µm and 500 nm.

The Nyquist diagrams of bare PGE and f-PGE in the presence and absence of dsDNA immobilization are shown in Figure 3. The average Rct value of PGE was measured as 55.25 ± 6.51 Ohm (RSD %, 11.8 %, n =8). After fullerene modification onto the PGE surface, 2.6-fold increase at the Rct value was recorded and measured as 146.50 ± 16.27 Ohm (RSD %, 11.1 %, n =8). Due to the charge repulsion between negatively charged phosphate backbone of the DNA and $[Fe(CN)_6]^{3-/4-}$ the electron transfer ability was reduced at the electrode surface on the surface of dsDNA/f-PGE [24-29]. The Rct was measured as 3153 ± 401.4 Ohm (RSD %, 12.7 %, n =4) after immobilization of dsDNA into the surface of f-PGE. Immobilization of dsDNA onto the surface of f-PGE resulted in a 21.5-fold increase in Rct value, whereas immobilization of dsDNA onto the surface of bare PGE (dsDNA/PGE) resulted in a 14.9-fold increase. According to the method described by Janek *et al*. [30], the apparent fractional coverage values (θ_R^{IS}) were calculated for dsDNA/PGE and dsDNA/f-PGE as 0.934 and 0.954, respectively. The θ_R^{IS} values were more than 0.9, indicating that the modification of fullerene was performed successfully. In comparison to PGE, the higher θ_R^{IS} value with f-PGE demonstrated that more coverage was acquired at the surface of f-PGE.

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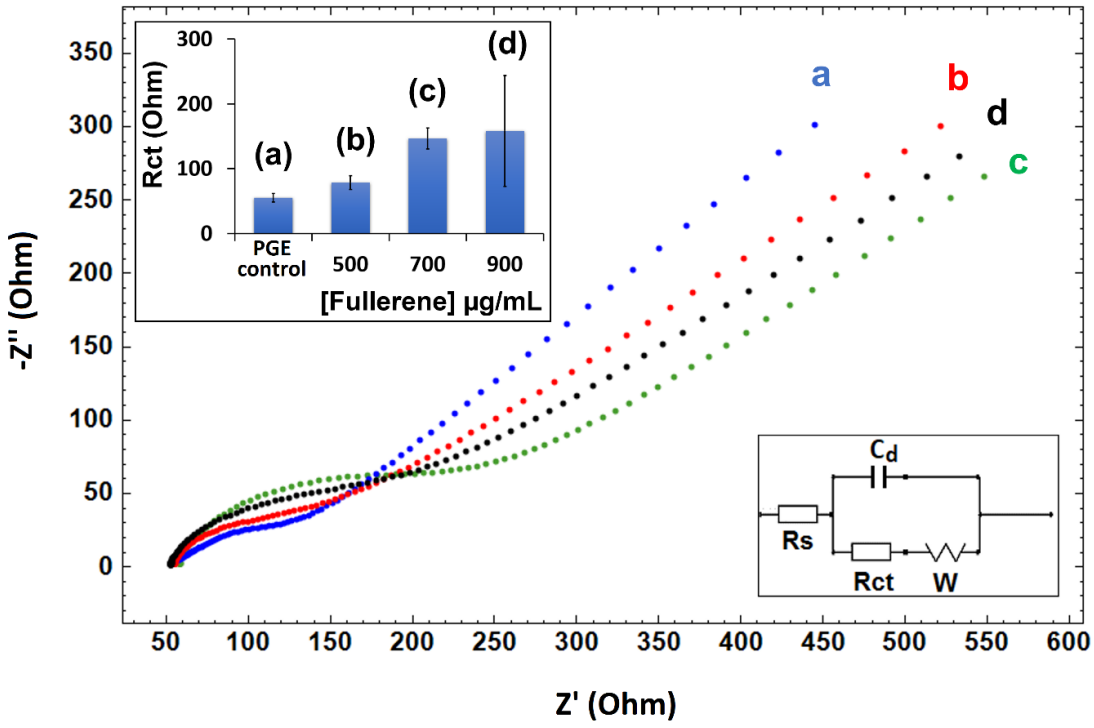

Figure 2. Nyquist diagrams of (a) bare PGE (in the absence of fullerene), (b) 500 µg/mL, (c) 700 µg/mL, (d) 900 µg/mL fullerene modified PGE. Histograms representing the average Rct values (n=3) recorded by (a) base PGE, (b) 500 µg/mL, (c) 700 µg/mL, (d) 900 µg/mL fullerene modified PGE.

Since the highest and the most reproducible Rct value as 798 ± 84 Ohm (RSD %, 10.5 %, n=3) was achieved in the presence of 10 µg/mL dsDNA (Table 1), this concentration was chosen as the best dsDNA concentration for interaction study.

The limit of detection (LOD) was calculated as 1.09 µg/mL in the linear concentration range between 2.5 and 10 µg/mL dsDNA with the equation reported by Miller and Miller [31]. The equation was *Rct (Ohm) = 16.63* C_{dsDNA} *(µg/mL) + 634,* and the regression coefficient R^2 of the linear curve was 0.99 as shown in Figure S1.

Table 1. The average Rct values (n=3) with RSD % measured after immobilization of dsDNA in its various concentrations on f-PGE.

[dsDNA] µg/mL	The average Rct	RSD %
2.5	671.5 ± 95.4	14.2
5	778.6 ± 180.7	23.2
7.5	687 ± 45	6.58
10	798 ± 84	10.5
15	664 ± 164	24.7

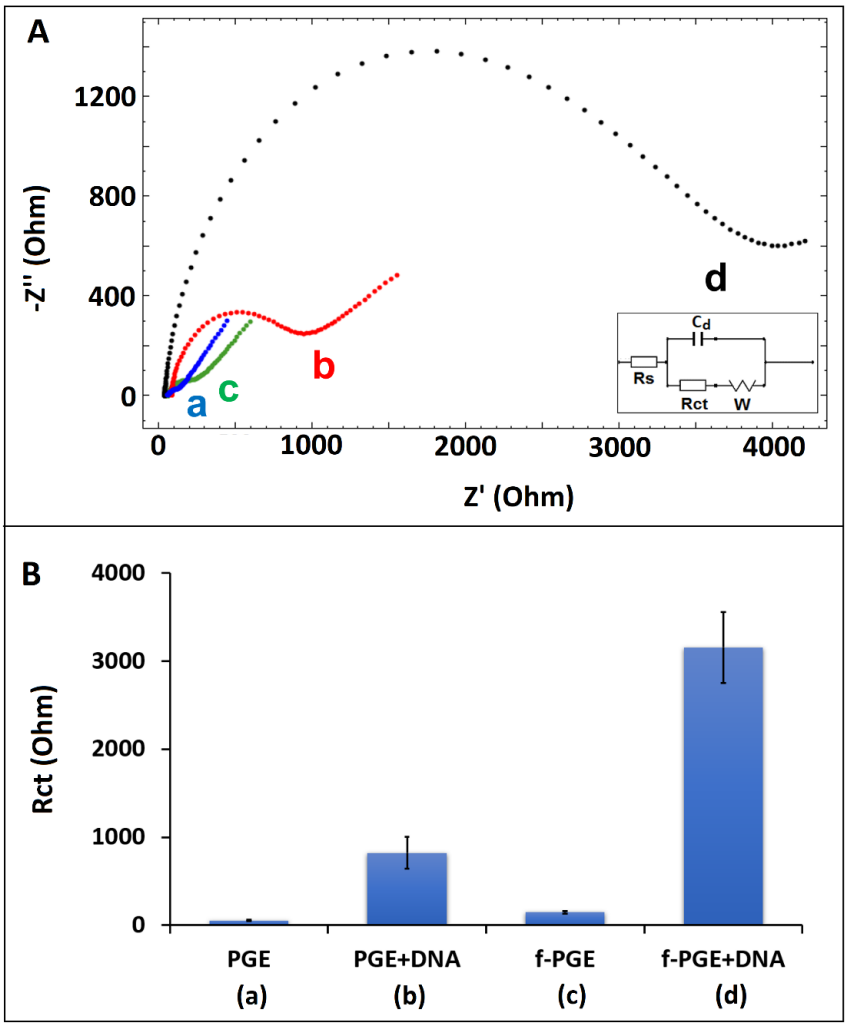

Figure 3. A. Nyquist diagrams of (a) PGE, (b) dsDNA/PGE, (c) f-PGE, (d) dsDNA/f-PGE. **B.** Histograms representing the average Rct value (n=3) recorded by PGE, dsDNA/PGE, f-PGE, and dsDNA/f-PGE.

Prior to drug-DNA interaction studies, the reproducibility of the fullerene-based biosensor was tested. 10 µg/mL dsDNA was immobilized onto the surfaces of five different f-PGEs and measurements were carried out under the same conditions. Similar Rct values, 760 Ohm, 715 Ohm, 921 Ohm, 831 Ohm, 855 Ohm were recorded with each f-PGEs and relative standard deviation (RSD %) was 9.8 %. These tests revealed that the proposed biosensor had a high level of reproducibility.

Next, the interaction of LMZ and dsDNA at f-PGEs in case of different interaction times was explored by EIS. The LMZ concentration was chosen as 2 µg/mL which was used in our previous work [24]. After 10 µg/mL dsDNA immobilization on f-PGE, Rct value was measured as 798.66 ± 84.3 Ohm (RSD %, 10.5 %, n =3) (Fig. 4b), which was 5.4-fold higher than the one measured by f-PGE (Fig. 4a). This increase at Rct could be due to increment of negative charges of dsDNA on the electrode. After interaction 2 µg/mL LMZ with 10 µg/mL dsDNA during 5, 15 and 30 min, the increase ratios were calculated as, 25.3 %, 36.1 % and 46.5 %, respectively. An increase in the negativity of electrode surface may occur due to the charge repulsion between LMZ and dsDNA following the intercalation. As a result of the increase in negative charges at the electrode surface, the resistance increased, as previously observed in the studies related to nucleic acid ligands [22-29, 32, 35].

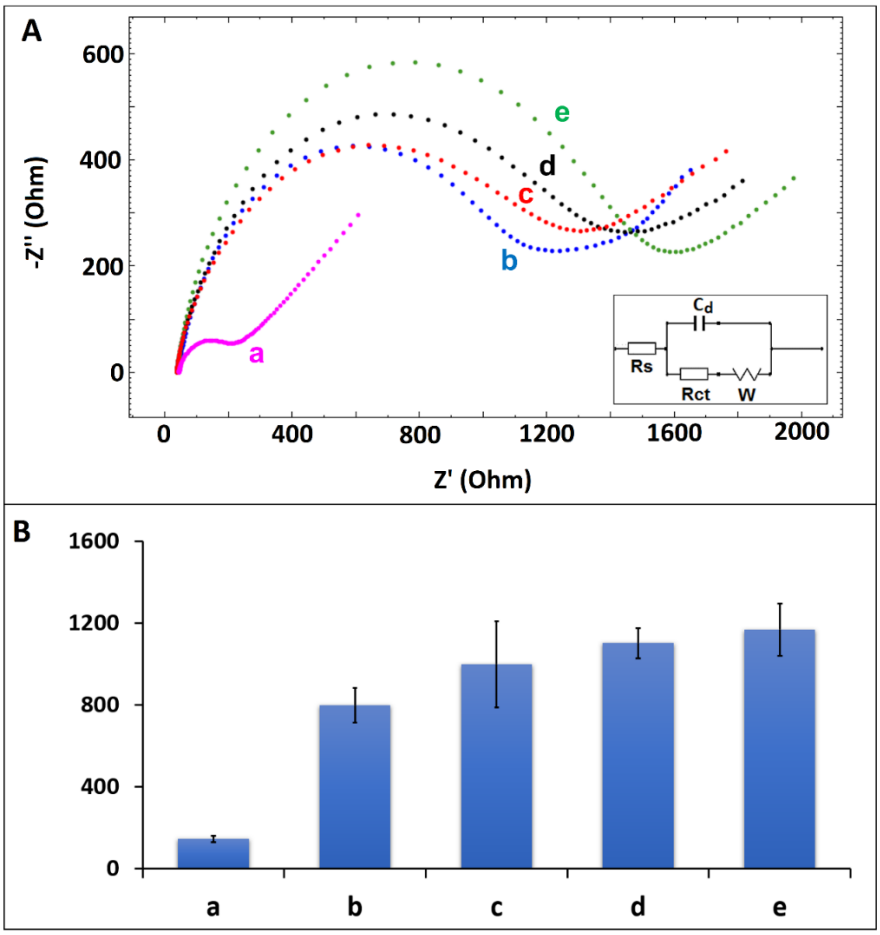

Figure 4. (A) Nyquist diagrams recorded with (a) f-PGE, (b) 10 µg/mL dsDNA immobilized f-PGE before interaction, after interaction with 2 µg/mL LMZ during (c) 5 min, (d) 15 min, (e) 30 min. (B) Histograms related to the average Rct values (n=3) measured with (a) f-PGE, (b) 10 µg/mL dsDNA immobilized f-PGE before interaction, after interaction with 2 µg/mL LMZ during (c) 5 min, (d) 15 min, (e) 30 min.

3. CONCLUSION

Herein, fullerene modified single-use graphite electrode was used for the first time as a sensing platform and applied for monitoring of drug-DNA interaction through the measurement of impedance. This fullerene-based biosensor platform showed a good analytical performance in terms of low detection limit, good reproducibility and rapid response time. Additionally, the use of fullerene provided a great enhancement at Rct value and thus led to a significant improvement in sensitivity of fullerene modified electrode. Easy preparation and rapid response are the main features of our biosensor. Moreover, the single-use fullerene modified PGE based biosensor bring herein the following important advantages: easy to use, cost effective per measurement, reproducible results, able to be prepared in a short time (i.e. 65 min; 30 min fullerene modification, 5 min air drying, 30 min dsDNA immobilization) compared to earlier works [25,27,32,35-38]. Therefore, the presented biosensor can be considered as a potential working electrode for the fast and sensitive impedimetric assay that could be applied for monitoring of interaction between pharmaceutical formulations and DNA. Besides, the proposed assay based on single-use biosensor technology, can be used as a very practical alternative to existing classical methods for monitoring not only drug-DNA interactions, but also to analyze various biomolecular interactions. In the near future, fullerene-based biosensors will appear as effective devices in electrochemical biosensing and be available commercial POC devices.

4. MATERIALS AND METHODS

4.1. Instrument

All electrochemical measurements were carried out in a Faraday cage using a three-electrode system and AUTOLAB-30 with NOVA 1.11 software (Eco Chemie, The Netherlands). Three electrode system was constructed with pencil graphite electrode, Ag/AgCl/3M KCl and Pt wire, as working, reference and counter electrode, respectively.

4.2. Chemicals

Fullerene ((1,2-Methanofullerene C60)-61-carboxylic acid), calf thymus double stranded DNA (dsDNA), Lumazine and all other chemicals were acquired from Sigma-Aldrich.

The stock solution of dsDNA was prepared as 1 mg/mL with Tris-EDTA buffer (10 mM Tris-HCl and 1 mM EDTA, pH 8.00). dsDNA aliquots stored at -20°C. Acetate buffer (0.50 M acetic acid and 20 mM NaCl, ABS, pH 4.80) was used for the preparation of the diluted dsDNA samples. The LMZ stock solution was prepared with Tris buffer (TBS; 50 mM Tris-HCl, 20 mM NaCl, pH 7.00) as reported in our previous work [16].

4.3. Preparation of nanomaterial-based biosensor

Fullerene was prepared in dimethyl sulfoxide (DMSO) by ultrasonication during 1h. PGEs were electrochemically activated by applying +1.40 V for 30s in ABS (pH 4.80) with differential pulse voltammetry (DPV). These PGEs were dipped into 40 µL of fullerene solution and kept for 30 min to achieve the surface modification. Then, f-PGEs were air dried for 5 min. For the immobilization of the dsDNA onto electrode surface, f-PGEs were dipped into 100 µL of 10 µg/mL dsDNA during 30 min. Then, each electrode treated with washing buffer ABS (pH 4.80) for 5s.

4.4. Drug-DNA interaction

To test the suitability of the constructed biosensors as a sensing platform for drug-DNA interaction, lumazine was chosen as a model drug molecule. dsDNA immobilized f-PGEs were dipped in 100 µL of 2 µg/mL LMZ solution at various concentrations and let to interact during various interaction time (15, 30, 60 min). Then, each electrode treated with washing buffer TBS (pH, 7.00) for 5s.

The detailed assay protocol is depicted in Figure 5.

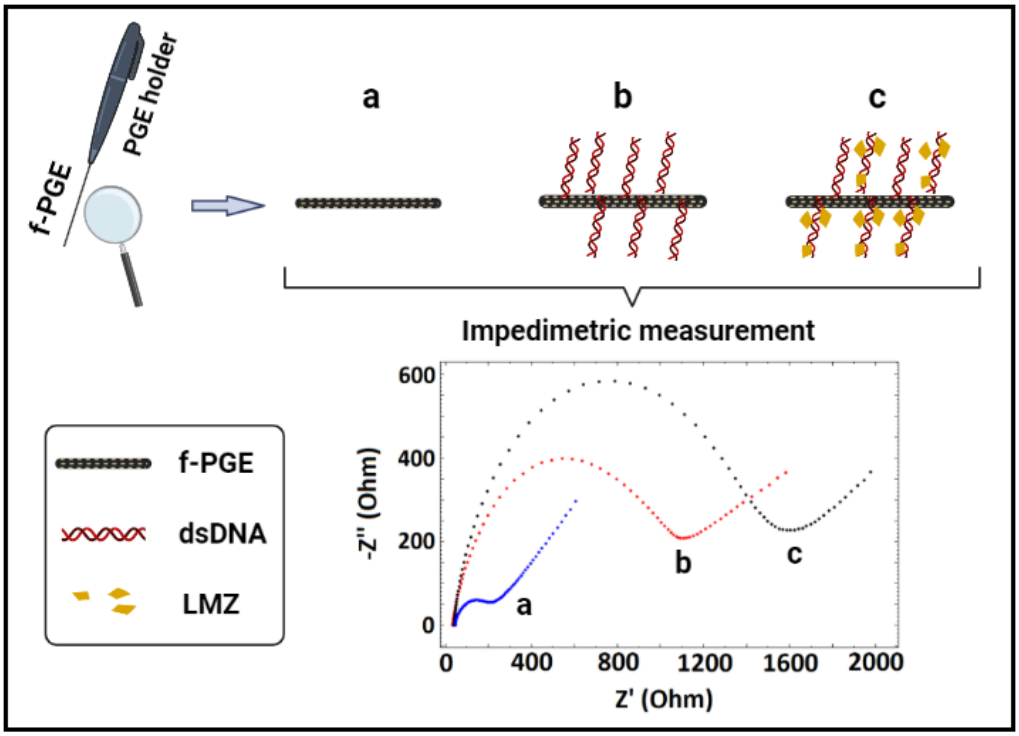

Figure 5. The schematic view of experimental procedure followed for monitoring of drug-DNA interaction by f-PGEs.

4.5. Impedimetric measurement

2.5mM $K_3[Fe(CN)_6]/K_4[Fe(CN)_6]$ (1:1) that prepared in 0.1M KCl was used as redox probe in EIS measurements as reported in previous works [24-27,32,35,39,40]. The frequency range was 100 mHz to 1 kHz at an open circuit potential of +0.23 V vs Ag/AgCl/3M KCl with a 10 mV amplitude. The semicircle diameter of the Nyquist diagram corresponded to the charge-transfer resistance (Rct). The Rct values were determined using the AUTOLAB-30, NOVA 1.11 fitting tool. All impedimetric measurements were performed in a Faraday cage.

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Author contributions: Concept – E.E., A.E.; Design – E.E., A.E.; Supervision – A.E.; Resources A.E.; Materials –A.E.; Data Collection and/or Processing – E.E., A.E.; Analysis and/or Interpretation – E.E., Literature Search – E.E., A.E.; Writing – E.E., A.E.; Critical Reviews – E.E., A.E.

Conflict of interest statement: The authors declared no conflict of interest.

REFERENCES

[1] Tan WT, Bond AM, Ngooi SW, Lim EB, Goh JK. Electrochemical oxidation of l-cysteine mediated by a fullerene-C60-modified carbon electrode. Anal Chim Acta. 2003; 491(2): 181-191. [CrossRef]

[2] Wang S, Chang Q, Zhang G, Li F, Wang X, Yang S, Troyanov S.I. Structural studies of giant empty and endohedral fullerenes. Front Chem. 2020; 8: 607712. [CrossRef]

[3] Csiszár M, Szűcs Á, Tölgyesi M, Mechler Á, Nagy JB, Novák M. Electrochemical reactions of cytochrome c on electrodes modified by fullerene films. J Electroanal Chem. 2001; 497(1-2): 69-74. [CrossRef]

[4] Li G, Han Z, Piao G, Zhao J, Li S, Liu G. To distinguish fullerene C60 nanotubes and C60 nanowhiskers using Raman spectroscopy. Mater Sci Eng B. 2009; 163(3): 161–164. [CrossRef]

[5] Guldi DM, Rahman GMA, Sgobba V, Ehli C. Multifunctional molecular carbon materials-from fullerenes to carbon nanotubes. Chem Soc Rev. 2006; 35: 471-487. [CrossRef]

[6] Chen M, Guan R, Yang S. Hybrids of Fullerenes and 2D Nanomaterials. Adv Sci. 2019; 6: 1800941. [CrossRef]

[7] Zhong X, Yuan R, Chai Y. In situ spontaneous reduction synthesis of spherical Pd@Cys-C 60 nanoparticles and its application in nonenzymatic glucose biosensors. Chem Commun. 2012; 48: 597-599. [CrossRef]

[8] Anusha T, Bhavani KS, Kumar JVS, Brahman PK. Designing and fabrication of electrochemical nanosensor employing fullerene-C60 and bimetallic nanoparticles composite film for the detection of vitamin D3 in blood samples. Diam Relat Mater. 2020; 104: 107761. [CrossRef]

[9] Zhou L, Wang T, Bai Y, Li Y, Qiu J, Yu W, Zhang S. Dual-amplified strategy for ultrasensitive electrochemical biosensor based on click chemistry-mediated enzyme-assisted target recycling and functionalized fullerene nanoparticles in the detection of microRNA-141. Biosens Bioelectron. 2020; 150: 111964. [CrossRef]

[10] Chuang C-W, Shih J-S. Preparation and application of immobilized C60-glucose oxidase enzyme in fullerene C60-coated piezoelectric quartz crystal glucose sensor. Sens Act B. 2001; 81(1): 1-8. [CrossRef]

[11] Suresh L, Bondili JS, Brahman PK. Development of proof of concept for prostate cancer detection: An electrochemical immunosensor based on fullerene-C60 and copper nanoparticles composite film as diagnostic tool. Mater Today Chem. 2020; 16: 100257. [CrossRef]

[12] Uygun ZO, Şahin Ç, Yılmaz M, Akçay Y, Akdemir A, Sağın F. Fullerene-PAMAM(G5) composite modified impedimetric biosensor to detect Fetuin-A in real blood samples. Anal Biochem. 2018; 542: 11-15. [CrossRef]

[13] Sherigara B.S, Kutner W, D'Souza F. Electrocatalytic properties and sensor applications of fullerenes and carbon nanotubes. Electroanalysis 2003; 15: 753–772.

[14] Yanez-Sedeno P, Campuzano S, Pingarron J.M. Fullerenes in electrochemical catalytic and affinity biosensing: A review. J Carbon Res. 2017; 3: 21. [CrossRef]

[15] Hernandez P, Aguilar-Lira G.Y, Islas G, Rodriguez JA. Development of a new voltammetric methodology for the determination of ciprofloxacin in beef samples using carbon pasta electrode modified with nafion and fullerenes. Electroanalysis 2021; 33(6): 1539-1546. [CrossRef]

[16] Mateon EM, Wong A, Freitas TA, Faria RC, Oliveira Jr ON. A sensitive electrochemical detection of metronidazole in synthetic serum and urine samples using low-cost screen-printed electrodes modified with reduced graphene oxide and C60. J Pharm Anal. 2021; 11(5): 646-652. [CrossRef]

[17] Kong B, Yang X, Dai H, Wu Y, Lu HB, Liu W, Liu X. Sensitive electrochemical determination of baicalein based on D-Ti3C2Tx MXene/fullerene composite modified glassy carbon electrode. Electroanalysis 2022; 34: in press. [CrossRef]

[18] Zhu Y, Huai S, Jiao J, Xu Q, Wu H, Zhang H. Fullerene and platinum composite-based electrochemical sensor for the selective determination of catechol and hydroquinone. J Electroanal Chem. 2020; 878: 114726. [CrossRef]

[19] Sirajuddin M, Ali S, Badshah A. Drug-DNA interactions and their study by UV-Visible, fluorescence spectroscopies and cyclic voltametry. J Photochem Photobiol B. 2013; 124: 1-19. [CrossRef]

[20] Gonzlez-Ruiz VIA, Antonia M, Ribelles P, Teresa M, Carlos J. An overview of analytical techniques employed to evidence drug-DNA interactions. Applications to the design of genosensors. 2011. [CrossRef]

[21] Katz E, Willner I. Probing biomolecular interactions at conductive and semiconductive surfaces by impedance spectroscopy: routes to impedimetric immunosensors, DNA-sensors and enzyme biosensors. Electroanalysis, 2003; 15(11): 913-947. [CrossRef]

[22] Lu Q, Hu H, Wu Y, Chen S, Yuan D, Yuan R. An electrogenerated chemiluminescence sensor based on gold nanoparticles@C60 hybrid for the determination of phenolic compounds. Biosens Bioelectron. 2014; 60: 325–331. [CrossRef]

[23] Shahdost-fard F, Roushani M. Impedimetric detection of trinitrotoluene by using a glassy carbon electrode modified with a gold nanoparticle@fullerene composite and an aptamer-imprinted polydopamine. Microchim Acta 2017; 184: 3997–4006. [CrossRef]

[24] Karadeniz H, Eksin E, Erdem A. Electrochemical detection of anticancer drug lumazine and DNA interaction by using carbon nanotube modified electrodes. J Res Pharm. 2019; 23(4): 682-688. [CrossRef]

[25] Eksin E, Polat D, Erdem A. Voltammetric and impedimetric detection of interaction between dacarbazine and nucleic acids. Electroanalysis, 2019; 31(10): 2012-2019. [CrossRef]

[26] Erdem A, Congur G. Impedimetric detection of in situ interaction between anti-cancer drug bleomycin and DNA. Int J Bol Macromol. 2013; 61: 295-301. [CrossRef]

[27] Eksin E, Zor E, Erdem A, Bingol H. Electrochemical monitoring of biointeraction by graphene-based material modified pencil graphite electrode. Biosens Bioelectron. 2017; 92: 207-214. [CrossRef]

[28] Ensafi AA, Heydari-Bafrooei H, Rezaei B. DNA-Based biosensor for comparative study of catalytic effect of transition metals on autoxidation of sulfite. Anal Chem. 2013; 85(2): 991. [CrossRef]

[29] Ensafi AA, Heydari-Bafrooei E, Dinari M, Mallakpour S. Improved immobilization of DNA to graphite surfaces, using amino acid modified clays. J Mater Chem B 2014; 2: 3022. [CrossRef]

[30] Janek RP, Fawcett WR, Ulman A. Impedance spectroscopy of self-assembled monolayers on Au(111): Sodium Ferrocyanide charge transfer at modified electrodes. J Phys Chem B 1997; 101 (42): 8550-8558. [CrossRef]

[31] Miller JN, Miller JC. Statistics and Chemometrics for Analytical Chemistry, Pearson: Harlow, London, UK, 2005, 121–123 pp

[32] Unal DN, Eksin E, Erdem A. Electrochemical determination of 6-thioguanine and its interaction with DNA oligonucleotides using disposable graphite pencil electrodes. Anal Lett. 2018; 51(1-2): 265–278. [CrossRef]

[33] Li C-Z, Liu Y, Luong JHT. Impedance sensing of dna binding drugs using gold substrates modified with gold nanoparticles. Anal Chem. 2005; 77(2): 478-485. [CrossRef]

[34] Coury JE, McFail-Isom L, Dean-Williams L, Bottomley LA. A novel assay for drug-DNA binding mode, affinity, and exclusion number: scanning force microscopy. Proc Natl Acad Sci. U.S.A. 1996; 93(22): 12283-12286. [CrossRef]

[35] Kanat E, Eksin E, Karacicek B, Erac Y, Erdem A. Electrochemical detection of interaction between dacarbazine and nucleic acids in comparison to agarose gel electrophoresis. Electroanalysis 2018; 30(7): 1566–1574. [CrossRef]

[36] Satyanarayana M, Goud KY, Reddy KK, Gobi KV. Conducting polymer-layered carbon nanotube as sensor interface for electrochemical detection of dacarbazine in-vitro. Electrocatalysis 2017; 8: 214–223. [CrossRef]

[37] Prasad BB, Pathak PK. Development of surface imprinted nanospheres using the inverse suspension polymerization method for electrochemical ultra-sensing of dacarbazine. Anal Chim Acta 2017; 974: 75–86. [CrossRef]

[38] Ibrahim MS. Phase-selective a.c. adsorptive stripping voltammetry of lumazine on a hanging mercury drop electrode. Fresenius' J Anal Chem. 2000; 367: 189-194. [CrossRef]

[39] Shah AK, Hill MM, Shiddiky JA, Trau M. Electrochemical detection of glycan and protein epitopes of glycoproteins in serum. Analyst 2014; 139: 5970. [CrossRef]

[40] Li Z, Hu J, Lou Z, Zeng L, Zhu M. Molecularly imprinted photoelectrochemical sensor for detecting tetrabromobisphenol A in indoor dust and water. Microchim Acta 2021; 188: 320. [CrossRef]