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Point-of-care diagnostics for therapeutic monitoring of levofloxacin in human plasma utilizing electrochemical sensor mussel-inspired molecularly imprinted copolymer

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ABSTRACT

Therapeutic drug monitoring is mandatory for drugs with narrow therapeutic index and is an integral part of the patient care standards, where drug concentration is measured in biological fluids to "*personalize*" patient's dosage. In this work a disposable electrochemical sensor has been developed for Levofloxacin (LEV) determination in human plasma. The selected substrate was pencil graphite electrode (PGE). To enhance the sensor performance, the PGE has been modified with Au-NPs via electrochemical deposition. To achieve high selectivity towards levofloxacin, the PGE/Au-NPs electrode has been further modified with molecularly imprinted copolymer; poly(L-dopa)/poly(*o*-phenylenediamine), by anodic electropolymerization of the corresponding monomers. The Levodopa not only acts as a functional monomer but moreover, a substrate for *mussel-inspired* polymer. The sensor surface has been characterized using both scanning electron microscopy (SEM) imaging and X-ray photoelectron spectroscopy (XPS) to investigate the morphology and elemental composition of the modified PGE, respectively. To optimize the sensor performance, experimental variables were studied and tuned to improve the outcomes. The sensor has a linear response in two concentration windows (1.0×10^{-6}–1.0×10^{-4} mol/L) and (1.0×10^{-4}–1.0×10^{-2} mol/L) Levofloxacin, with a limit of detection of 4.62×10^{-7} mol/L. Selectivity, repeatability, and low manufacturing cost are some benefits of the proposed sensor. The sensor was successfully used to determine Levofloxacin in Tavanic® tablets and spiked plasma samples.

1. Introduction

Personalized medicine, where the drug dosage is tailored for each individual patient, ensures drug efficacy and safety. Pharmacogenetic information and therapeutic drug monitoring (TDM) are the major tools for personalized medicine. The pharmacogenetic data is based on patient's genome sequence and collected prior to drug administration to anticipate drug efficacy and safety, while TDM is performed once the patient has started the treatment regimen to "*individualize*" the dosing based on drug level in blood. Therapeutic drug monitoring is not only employed for the proper medical care of each patient but, can be applied to monitor patient's compliance as well. Moreover, some antibiotics treatment protocols require frequent sampling to assure that drug level is maintained within the desired therapeutic window and has maximum efficacy, as higher dose increases toxic side effects, while sub-therapeutic antibiotic level potentially causes both treatment failure and emergence of antibiotic bacterial resistance. The broad-spectrum antibiotics; fluoroquinolones class, are very effective and used to treat severe and resistant bacterial infections in medical practices since the late 1980s [1]. Levofloxacin (LEV), whose chemical structure is presented in (Fig. 1(A)) with its closely related interferants, is a third-generation fluoroquinolone antibiotic that is used to treat bacterial infections of the prostate, kidneys, sinuses, skin, and bladder [2]. For individuals with acute sinusitis, acute bronchitis and uncomplicated urinary tract infections who can undergo other treatment regimens, the substantial adverse effects associated with fluoroquinolones often outweigh the benefits [3]. As a result, assessment of LEV in biological fluids and pharmaceutical formulations is crucial.

A. Levofloxacin, B. Gemifloxacin, C. Ciprofloxacin & D. Flucloxacillin.

Several analytical techniques have been reported for LEV analysis in biological fluids including capillary electrophoresis [4], high-perfor-

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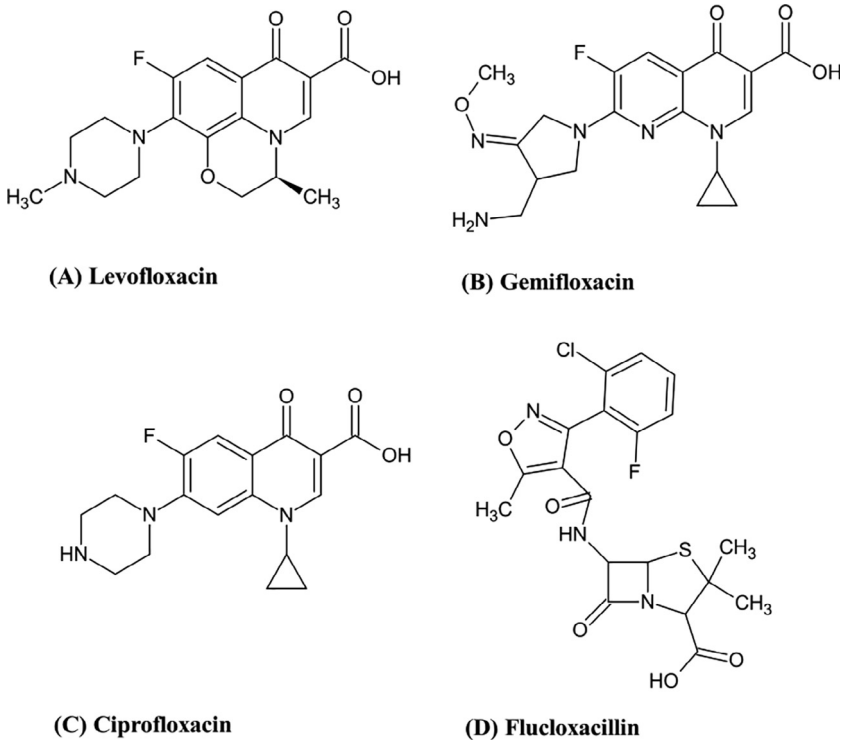

Fig. 1. Chemical structures of Levofloxacin and its interferants.

mance liquid chromatography [5], flow injection [6], electrochemiluminescence [7], spectrophotometric [8], and potentiometric [9] methods. Most of these methods are expensive, time consuming, and require trained personnel, sample manipulations or derivatization steps. Currently, there is an increasing interest to develop point-of-care diagnostics electrochemical sensors for TDM applications due to several advantages over the aforementioned methods such as simplicity, low cost, and speed; recent progress in the electrochemical sensors design for TDM applications has been recently reviewed [10–13]. Several voltammetric methods for LEV determination have been reported using bare or modified glassy carbon electrodes [14–19], multiwalled carbon nanotubes [20,21], carbon nanotubes [22–24], molecularly imprinted polymer (MIP) modified with gold nanoparticles electrode [25], gold nanoparticles modified electrodes [26–28], molecularly imprinted polymer (MIP) based electrodes [29], silver nanoparticles modified electrode [30], boron doped diamond electrode [31,32], pencil graphite electrode [33,34], reduced graphene oxide (rGO) modified electrodes [35–39], screen printed sensor [40], and moreover, voltammetric techniques have been used for studying levofloxacin electrochemical behavior [41].

A great attention is being paid to the development of affinity sensors based on molecularly imprinted polymers (MIPs) nowadays [42]. Molecularly imprinting polymerization is a technique of creating three-dimensional recognition sites for a specific molecule on a synthetic polymer. The recognition sites are designed to be complementary to the target molecule in terms of size, shape, and chemical activities, making them extremely specific and selective for the target analyte [43]. Electropolymerization has several merits over traditional polymerization methods, including: electropolymerization does not involve free radical initiators, light or oxidants, to initiate polymerization; electropolymerization is carried out at room temperature. The fabricated polymer produces adherent, uniform, dense, and conformal films on the surface of electrode; the film characteristics, such as thickness, can be controlled precisely and easily reproduced by optimizing the electrochemical deposition conditions (such as voltage, number of cycles, current, and total polymerization time). Furthermore, polymerization and detection are performed in aqueous media [44]. Finally, the electropolymerization procedure is quick, and the electropolymerized molecularly imprinted polymer can be generated in a matter of minutes [45].

Polypyrrole, polythiophene, nanobiocomposite based on poly(1,10-phenanthroline-5,6-dione), poly(9,10-phenanthrenequinone), poly (pyrrole-2-carboxylic acid), carbazole, polyphenanthroline, azobenzene, and other conducting polymers can all be employed for electropolymerization [46]. MIPs-based on (*o*-phenylenediamine) [47] as well as other phenylenediamine-derivatives [48,49] are extensively used in pharmaceutical and analytical applications; for example, molecularly imprinted (*o*-phenylenediamine) was used to determine butyrylcholinesterase [50] and the anticancer Pemetrexed [51]. Furthermore, noncovalent interactions such as stacking, electrostatic interactions, and hydrogen bonding have been described for dopamine as an electropolymerizable monomer with various templates [52]. Liu and coworkers developed a capacitive sensor for nicotine detection in human serum using molecularly imprinted ultrathin electropolymerized polydopamine (ePDA) sheets in 2006 [53]. These (ePDA) films obtained from the electropolymerization method have been used for surface modification of a variety of biomaterials. Poly(levodopa), being dopamine structural analogue, can have extra desired effects due to its two hydroxyl groups and the primary amino group resulting in thicker films which can influence the electrochemical deposition behavior [54]. Poly(levodopa) has only been employed once as a monomer in the development of a molecularly imprinted sensor [55].

One of the most challenging aspects of working with complicated biological fluids is that the concentration of the target molecule in complex biological fluids (such as urine, serum, saliva etc.) is frequently relatively low compared to the enormous number of coexisting background interferents (e.g., proteins, cells) that can non-specifically adsorb onto a sensing interface. This may lead to major operational issues like low signal-to-noise ratios, false positive results, and poor specific recognition/response. A prominent challenge that faces the

design of the electrochemical (bio)sensors for real-life applications is "fouling" which is a key issue that hinders the practical utilization of electrochemical (bio)sensors both *in vitro* and *in vivo* analysis as has been reported in many recent reviews [56–61]. This can be avoided by incorporating non-fouling chemistry into the assaying surface via chemical modifiers that return the interface intensely hydrated with highly polar, hydrated chemical groups/materials, which has been linked to fouling resistance [60]. Recently, polymers derived from catecholamines, such as dopamine and its natural analogues (i.e. levodopa), have received a huge research attention as promising and multifaceted functional materials in many fields such as chemical, biomedical and material sciences. Polymers of catecholamines are characterized with good adherence properties, high biocompatibility, promising antifouling surface and high durability allowing their extensive usage in surface modification and functionalization of several materials. These mussel-inspired polymers possess high hydrophilicity and inherent functional groups in their structure ranging from phenolic hydroxyl, imine to amine [62–64]. In its zwitterionic state, poly (levodopa) may be resistant to nonspecific protein adsorption, allowing it to create stable antifouling surfaces for many biomedical applications.

In the current contribution, a novel electrochemical sensor was developed for fast measurement of LEV in plasma samples. The sensor was designed by depositing gold nanoparticles to modify a pencil graphite electrode (PGE). Since recently, nanoparticles have been assured to be important additives to enhance the performance of electrodes and reduce electrical resistance [65]. The molecularly imprinted copolymer was electropolymerized onto Au-NPs modified PGE by electrochemical co-deposition of *o*-phenylenediamine and Levodopa monomers. The experimental variables (number of electropolymerization cycles, supporting electrolytes, pH, and contact time) were studied and optimized. The sensor surface was characterized by SEM and XPS. The suggested sensor was successfully used for voltammetric assessment of LEV in pharmaceutical tablets and spiked human plasma samples.

2. Experimental

2.1. Chemicals and reagents

Levofloxacin hemihydrate, gemifloxacin mesylate, ciprofloxacin, flucloxacillin sodium and Levodopa were supplied from AMOUN pharmaceuticals (Levofloxacin was labeled to be greater than 99% purity). The monomer, *o*-phenylenediamine (oPD) with purity higher than 99% was purchased from (Oxford laboratory, Mumbai, India), Methanol (Fisher Scientific, UK), Chloroauric acid (Sigma Aldrich, Germany). All other chemicals and the apparatus used were supplied as reported in the Supporting Information (SI).

2.2. Electrodeposition of the gold nanoparticles on PGE

The PGE was modified with Au-NPs as reported previously in the literature [66], briefly, PGE was immersed in an electrolyte of $5x10^{-4}$ mol/L $HAuCl_4$ in 0.1 mol/L KCl as supporting electrolyte, and cyclic voltammetry was performed with a potential scanning started at + 0.2 V, to potential: −1.0 V vs Ag/AgCl reference electrode, for 10 cycles at scan rate of 50 mV/*sec*. For the next copolymer electro-polymerization, the modified PGE was rinsed three times with distilled water and dried under stream of N_2 at ambient temperature.

2.3. Electropolymerzation of the molecularly imprinted copolymer poly (oPD-co-L-Dopa) on PGE/Au-NPs

Au-NPs modified PGE was immersed in 25 mL phosphate buffer (pH 7.0) containing the template; LEV 10 mmol/L, 5 mmol/L *o*-Phenylenediamine, and 5 mmol/L Levodopa after their sonication for 15 min. After a 10-minute Nitrogen purge, cyclic voltammetry was used for the electrochemical polymerization of *o*-phenylenediamine and Levodopa. LEV was encapsulated by a number of consecutive cycles in the potential range of −0.2 to + 0.8 V at a scan rate of 50 mV/s, the effect of number of cycles on sensor's performance was studied. To remove the LEV template, the sensor was rinsed three times (20 min each) with methanol: 1.25% acetic acid (1:1). Finally, for Levofloxacin rebinding and subsequent measurements, the electrode was incubated in LEV sample before measurement; the effect of the incubation time was investigated and optimized.

2.4. Electrochemical detection of levofloxacin and calibrations

The DPV measurements were recorded by scanning potential over range of 0.0 to 1.5 V, scan rate 15.0 mV s^{-1}, pulse amplitude 50 mV, pulse width (modulation time) 50 ms. Measurements of LEV in plasma samples are described in details in the Supporting Information (SI).

3. Results and discussion

3.1. Characterization of PGE/Au-NPs/poly(oPD-co-L-Dopa) sensor – SEM and XPS investigations

The scanning electron microscopy (SEM) images (Fig. S1) show the surface morphology of both PGE/Au-NPs and the modified PGE/Au-NPs/Levofloxacin imprinted copolymer, the images clearly indicate the presence of uniformly distributed Au-NPs on PGE of an average diameter approximately 84 nm as estimated by using the SEM software. Although we can't make a direct comparison, these results are consistent with some extent to the literature where the AuNPs was deposited onto GCE/modified with chitosan where AuNP has range from 30 to 80 nm [66]. It should be noted that GCE is different from PGE and also chitosan provides nucleation sites for Au-NPs formation.

The X-ray photoelectron spectroscopy (XPS) has been employed to investigate the surface elemental composition. The XPS survey spectrum, (Fig. 2A), shows prominent peak of C(1s) around 286 eV, Au (4f) peak around 85 eV, O(1s) peak around 533 eV, and another peak signal around 401 eV for N(1s). Fig. 2B. is a high resolution spectrum of C(1s) region, where deconvolution analysis was performed showing three bands. The deconvoluted bands are around 285.1 eV, 286.8, 288.3 eV corresponding to C—C, C—N, O–C═O bonds, respectively [67] Fig. 2C shows deconvolution of high resolution spectrum of N (1s) region, the devolution shows one deconvoluted band at 400.4 eV corresponding to aromatic N atoms. Fig. 2D represent the deconvolution of the high resolution spectrum of O(1s) region, the two deconvoluted bands at 531.9 eV and 533.2 eV corresponding to O-C═O, C═O respectively [67]. These results indicated the successful modification of the surface with Au-NPs and the copolymer poly(oPD-*co*-L-Dopa) layer.

3.2. Effect of supporting electrolyte and contact time

The pH selection is of great importance during the optimization of the MIP sensor response. The fact that pH affects the protonation state of both the monomer and MIP film, and consequently affects the rebinding process *via* the hydrogen bonding and electrostatic interactions. Moreover, the pH has been reported to affect the carbon electrode surface functional groups [68] and can contribute to peak shift. Not only the pH but also the type of buffer supporting electrolyte itself has an effect on stabilization of the analyte molecules in solution and hence electron transfer rate. Therefore, The supporting electrolyte and pH had a marked influence on the modified electrode's response. The optimization of pH and supporting electrolytes were accomplished

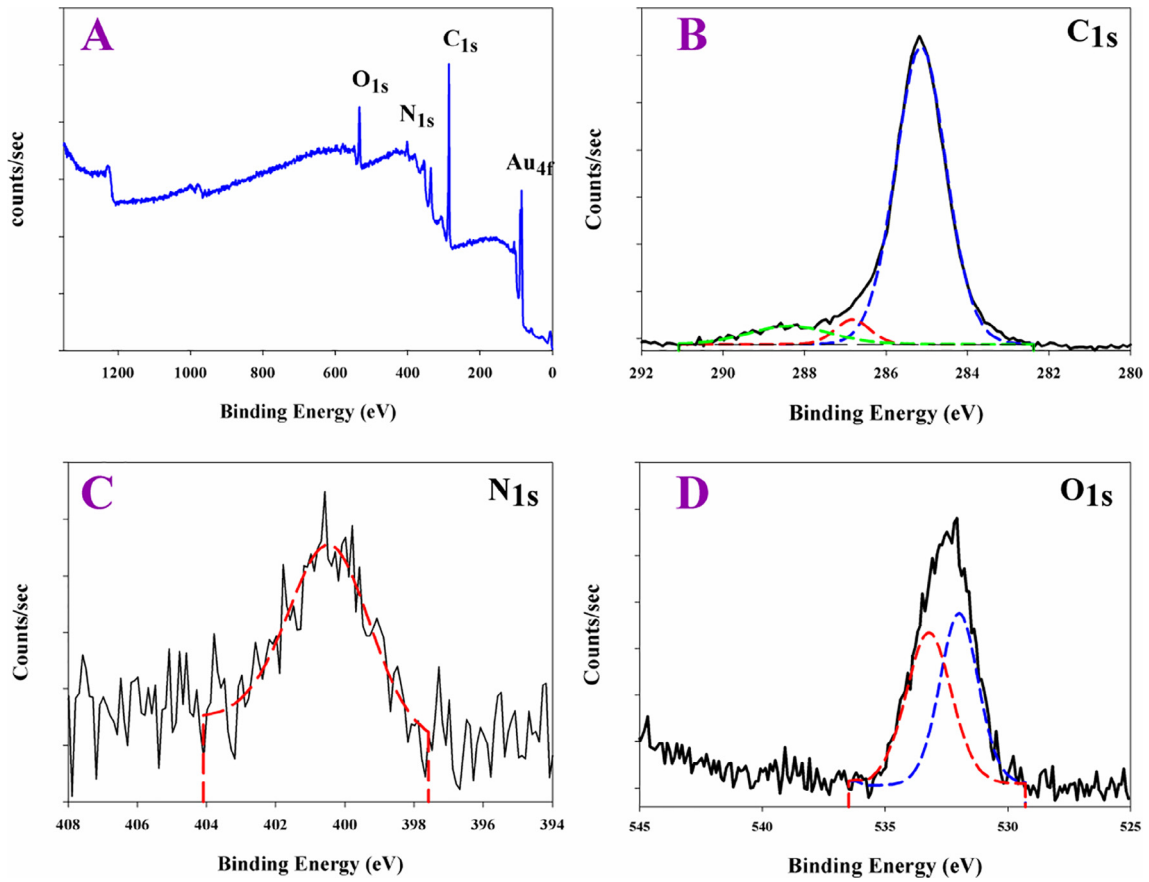

Fig. 2. X-ray photoelectron spectroscopic characterization of PGE/Au-NPs/Poly(*o*-PD-*co*-L-Dopa), (A) a survey spectrum of the modified electrode, (B) high-resolution spectrum in C(1s) region showing peaks that correspond to C—C (blue curve), C—N (red curve), O–C=O (green curve) bonds at 285.1 eV, 286.8, 288.3 eV, respectively, (C) high resolution spectrum of N(1s) region, shows aromatic N atoms band at 400.4 eV, (D) high resolution spectrum of O(1s) region, showing peaks corresponding to O–C=O (blue curve), C=O (red curve) at 531.9 eV and 533.2 eV respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

through two steps. Firstly, different pHs were tested to determine the optimum pH of the supporting electrolyte using phosphate buffer with pH range (2–10), so any difference in peak current can be attributed to pH change only rather than change of supporting electrolyte. As we observed in (Fig. 3), the lower pH has a higher oxidation current peak and pH 2 in phosphate buffer resulted in the highest response. Secondly, various buffers having acidic pH were tried as supporting electrolytes as mentioned in the manuscript (sulphuric acid, phosphate buffer, Britton Robinson buffer, and citrate buffer). Various molar concentrations of sulphuric acid were examined, namely, 0.01, 0.1, 0.2 mol/L and it was observed that 0.2 mol/L produces the highest peak current and more importantly, more reproducible results. Therefore, 0.2 mol/L proved to be the optimum choice for the study.

The diffusion of the Levo template into the ultrathin molecularly imprinted film is a critical factor to ensure re-binding of the redox active template and its accumulation within the 3D cavities to produce optimum response. The optimal incubation time of the sensor immersed in the sample was investigated by measuring the sensor response as a function of time. The contact time has been noticed to influence the sensitivity of the modified electrode, with the peak current increasing as the incubation time was extended until 10 min, and reaches a plateau after that, as shown in (Fig. S2). Therefore, the PGE/Au-NPs/poly(*o*-PDA-*co*-L-Dopa) sensor has be incubated in the sample solution for at least a 10 min period as “accumulation time” prior to initiating the voltammetric measurements, presumably due to slow diffusion and binding kinetics.

3.3. Electrochemical behavior of Levofloxacin at the modified PGE

The sp^2 hybridized pencil graphite electrodes (PGEs) have recently gained a lot of attention due to high conductivity, adsorption,

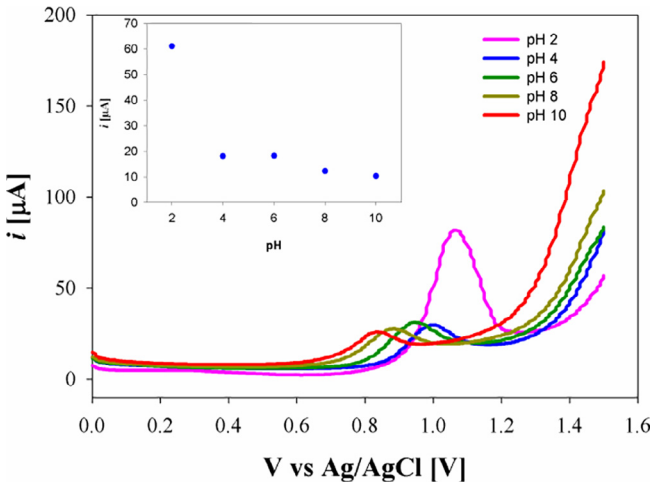

Fig. 3. DPV voltammograms of 100 μmol/L Levofloxacin at pH 2, 4, 6, 8 and 10. The inset is a plot for the oxidation peak current of Levofloxacin at various pH.

improved sensitivity, low background current, ease of surface modification, and commercial availability. Different PGEs were tested as substrates such as (2B, HB, B). It was observed that 2B exhibited the highest response and thus was used in this study. Cyclic voltammetry was utilized to characterize the electrochemical behavior of LEV on bare and modified PGE. Cyclic voltammograms were measured with a potential range of 0 to 1.5 V and scan rate (ν) = 50 mV/s. The results show an oxidation peak at 0.966 V vs Ag/AgCl reference electrode at forward scan and no reduction peak at reverse scan, indicating that the LEV oxidation process is irreversible. The electrochemical behavior of LEV was then assessed using differential pulse voltammetry on a variety of working electrodes, including glassy carbon, screen printed, and pencil graphite electrodes, in the presence of 1.0×10^{-4} mol/L LEV in 0.2 mol/L H_2SO_4, with the pencil electrode demonstrating higher current response and thus being used for this study. Levofloxacin was determined electrochemically by oxidation (at 0.966 V) at the surface of PGE in 0.2 mol/L H_2SO_4. Fig. 4 shows differential pulse voltammograms of 1.0×10^{-4} mol/L LEV on bare PGE, PGE/*o*-PD, PGE/poly(*o*-PDA-*co*-L-Dopa), and PGE/Au-NPs/poly(*o*-PDA-*co*-L-Dopa) in 0.2 mol/L H_2SO_4 (curves a, b, c, and d, respectively). The LEV oxidation peak at the PGE was substantially improved by gold electrodeposition and copolymer surface modification, as shown in Fig. 5. The results indicate the beneficial effect of nanocomposite on the peak current enhancement where the measured current for 1.0×10^{-4} mol/L LEV on the bare PGE was 4.43 μA, 12.87 μA on PGE/*o*-PD, 16.52 μA on PGE/poly(*o*-PDA-*co*-L-Dopa), and 18.90 μA on PGE/Au-NPs/poly(*o*-PDA-*co*-L-Dopa). The increase of current peak upon PGE modification with Au-NPS from 16.52 μA to 18.90 μA is attributed to the catalytic activity of Au-NPs and increasing electrode surface area.

3.4. Optimization of electropolymerization conditions

For electropolymerization, *o*-phenylenediamine was utilized as the monomer. Since the profusion of (bio)molecules in biological fluids can remarkably hinder performance at the transducing interface, where unspecified adsorption (fouling) can both obstruct specific signal (reducing sensitivity) and considerably decrease assay specificity [60], as dopamine analog; Levodopa has been suggested in many reports in the literature as antifouling and bio-compatible coating [69–71] and hence was added in the current study to exploit its antifouling characteristics. The ratio of monomer to template and the ratio of the two monomers to each other were investigated. Two

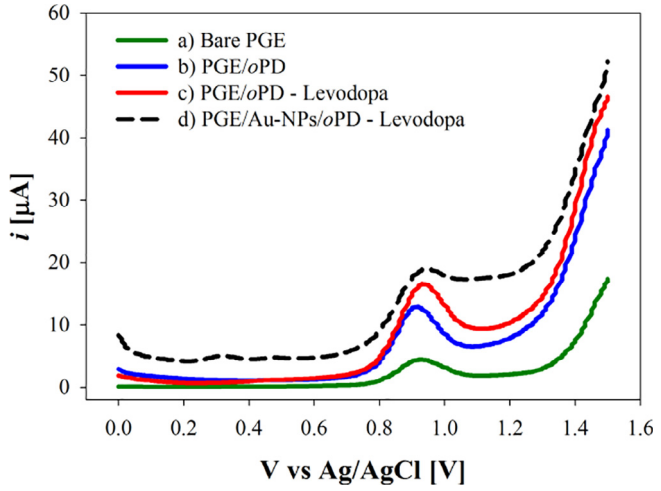

Fig. 4. DPV voltammograms of 100 μM Levofloxacin in 0.2 mol/L sulphuric acid using: (A) Bare PGE, (B) PGE/Levofloxacin imprinted *o*-PD only, (C) PGE/Levofloxacin imprinted *o*-PD and (poly)levodopa, (D) PGE/Au-NPs/Levofloxacin imprinted *o*-PD and (poly)levodopa.

ratios of both monomers *o*PD: L-dopa (1:0) and (1:1) (i.e with *o*PD alone and both monomers in the ratio 1:1) were investigated. It was observed that the *o*PD: L-dopa ratio of 1:1 had a "better" response than *o*PD alone. Therefore, both *o*PD and Levodopa were mixed in the same ratio (1:1) (5 mmol/L each), with the template (10 mmol/L) forming acceptable recognition sites number. The number of electropolymerization cycles was observed to alter polymer thickness and alter the sensor response, with the response increasing with raising cycles number up to 5 cycles, which was chosen for the study as indicated in (Fig. S3) and was in coincidence with [25] which prepared a MIP for Levofloxacin using Pyrrole-Au nanoparticles and 6 cycles were the optimum for polymerization. A potential explanation of difference between 4 and 5 cycles with respect to the sensors response, might stem from the fact that as we increase the number of electropolymerization cycles the thickness of MIP increases, hence increase vacant imprinted cavity recognition sites for the template; levofloxacin, but there is a limit where increasing the thickness further, film thickness might hinder diffusion of the levofloxacin to the electrode surface and limit the electrochemical oxidation of levofloxacin and therefore, decline the electrochemical response, as the excessive thickness with less imprinted sites could arise thus, can hinder the diffusion of the template to the electrode surface [72,73]. Hence 5 cycles were chosen as the optimum number of cycles.

3.5. Quantitative determination of LEV under optimal conditions

The calibration curve was constructed by plotting the current peak height vs LEV molar concentration as shown in (Fig. 5a). The response of Levofloxacin was linear in two concentration ranges (1.0×10^{-6}–1.0×10^{-4} mol/L) and (1.0×10^{-4}–1.0×10^{-2} mol/L) utilizing the modified electrode where current peak height is proportional to LEV concentration under optimum conditions, as shown in (Fig. 5b), with two linear regression equations. The first linear regression was i_c (μA) = 356955C (mol/L) + 2.7441 and a correlation coefficient r = 0.9989, and the second was i_c (μA) = 61130C (mol/L) + 42.362 with a correlation coefficient r = 0.9999. It should be noted that in Fig. 5a there are two peaks, those peaks probably form the supporting electrolyte "sulphuric acid", which appear also if DPV was performed for the supporting electrolyte alone. The LOD was calculated to be 4.62×10^{-7} mol/L (3 σ/S), while, the LOQ was estimated to be 1.38×10^{-6} mol/L (10 σ/S), where S is the calibration curve slope and σ is the standard deviation of the blank [74,75]. Different validation parameters including accuracy, intraday and interday precision were calculated as RSD% to be 5.92, 4.33 and 4.04%, respectively.

3.6. Reproducibility, selectivity, and stability of the sensor

To test the reproducibility, ten independently fabricated PGE modified electrodes were tested in a 1.0×10^{-4} mol/L Levofloxacin solution. RSD was calculated to be 2.09%, indicating acceptable reproducibility. The responses of LEV in the presence of interferants such as Gemifloxacin Mesylate (chemical structure Fig. 1(B)), Ciprofloxacin (chemical structure Fig. 1(C)), and Flucloxacillin sodium (chemical structure Fig. 1(D)) were tested to investigate the selectivity of the molecularly imprinted copolymer where they were measured at concentration of 1×10^{-4} mol/L, each one alone without Levofloxacin. Oxidation peaks were at 1.225 V for both Ciprofloxacin and Gemifloxacin and 1.219 V for Flucloxacillin. Structurally similar compounds such as Ciprofloxacin, Gemifloxacin and Flucloxacillin exhibited oxidation with peak currents of 28.77%, 20.84%, and 4.0% respectively compared to that of LEV peaks, the results are summarized in Table 1. Consequently, none of these analogues interfered with the voltammetric detection of LEV, showing the sensor's high selectivity. The modified PGE's response was tested in a 1.0×10^{-4} mol/L LEV solution

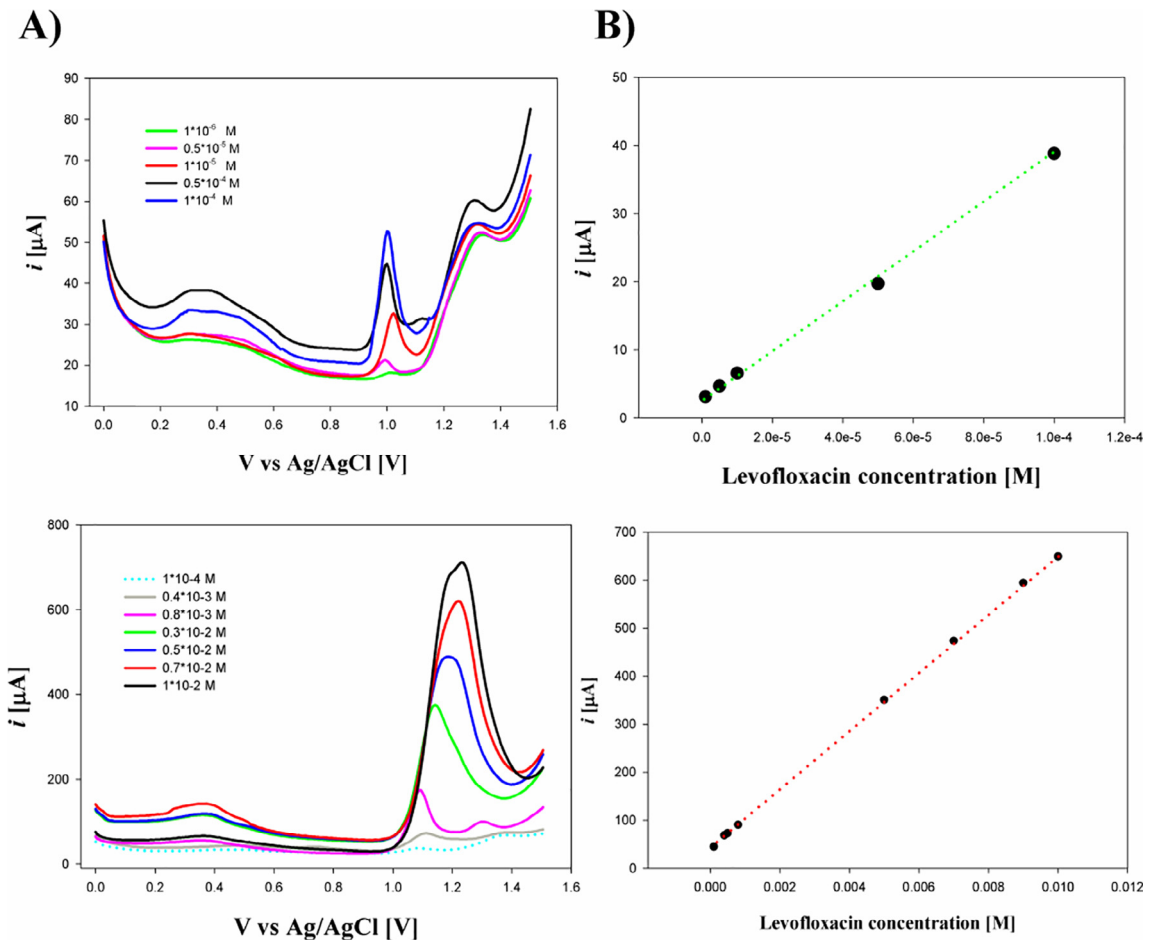

Fig. 5. a. DPV voltammograms of Levofloxacin in two concentration ranges (1.0×10^{-6}–1.0×10^{-4} mol/L) and (1.0×10^{-4}–1.0×10^{-2} mol/L) by modified electrode. 5b. Respective linear regression plot.

Table 1
Effect of various interferences on the oxidation peak current signals of 100 µM Levofloxacin in 0.1 mol/L Phosphate buffer (pH 7.0) at PGE /AuNPs/o-PD/L-DOPA.

Interferant	Ratio of interferant oxidation peak (%) compared to LEV peak
Ciprofloxacin	28.77%
Gemifloxacin	20.44%
Flucloxacillin	4%

where Levofloxacin's peak intensity did not change within one month indicating its stability throughout this period.

3.7. Analysis of LEV in Tavanic® tablets and real human plasma samples

Table 2 shows that the modified PGE was used to analyze LEV content in Tavanic® tablets, with recoveries ranging from 90.37 to 105.63%. The approach was further tested on spiked blank human plasma samples utilizing protein precipitation with acetonitrile, as shown in (Table 2), the results ranging from 86.54 to 120.72% were obtained. These results mean that the suggested sensor is suitable for the selective and rapid determination of LEV in plasma sample.

In literature, the reported voltammetric approaches incorporating gold nanoparticles and/or MIP have been proposed; these are outlined in Table S1. In comparison to screen printed electrodes (SPE) or glassy carbon electrodes (GCE), our sensor has the benefit of being cost-effective, commercially available (a simple pencil graphite), as well as having antifouling capabilities due to the usage of Levodopa, which has highly polar chemical groups linked with fouling resistance. The use of gold nanoparticles raised the effective electrode surface area and accelerated electron transfer, as demonstrated by a small increase in LEV voltammetric responses when compared to the bare electrode.

3.8. Compliance of the LEV point-of-care (POC) diagnostic sensor with WHO ASSURED criteria

Following the WHO guidelines [76], our suggested sensor virtually meets the "ASSURED" criteria for ultimate POC diagnostics as being: (a) low-cost: the proposed working electrode was pencil graphite electrode. The PGE as a substrate is a cost-effective platform, with low capital costs (only 1 $ can be spent to create 10 sensing electrodes). (b) sensitive: the LOD found was 4.62×10^{-7} mol/L, which could reach c max easily in plasma samples. (c) selective: the sensor can detect LEV quantitatively in the presence of its interferants, which will reduce false positives. c) It is user-friendly: non-medical people can use the sensor to detect LEV; (e) quick: the electrode has relatively quick response in comparison to other analytical procedures; (f) Low-cost equipment: On-site data analysis requires only a small amount of portable equipment. In contrast to other commonly used procedures that necessitate complex equipment, (g) delivery is simple to end users.

Table 2
The analytical results of Levofloxacin in tablets and human plasma samples (n = 3).

Sample	Added (mol/L)	Found (mol/L) *	Recovery	RSD%**
Tavanic® tablets	1.0×10^{-6}	9.69×10^{-7}	96.90	2.34
	1.0×10^{-5}	1.0×10^{-5}	100.00	1.98
	1.0×10^{-4}	1.05×10^{-4}	105.00	0.68
	1.0×10^{-3}	1.01×10^{-3}	101.00	1.79
	1.0×10^{-2}	0.9×10^{-2}	90.00	2.05
Human plasma	1.0×10^{-6}	1.20×10^{-6}	120.00	3.45
	1.0×10^{-5}	8.65×10^{-5}	86.50	2.71
	1.0×10^{-4}	9.19×10^{-5}	91.90	1.49
	1.0×10^{-3}	1.22×10^{-3}	122.00	1.73
	1.0×10^{-2}	9.5×10^{-3}	95.00	1.25

* Average of 3 determinations.
**Average of 3 determinations.

4. Conclusion

A unique selective sensor based on mussel-inspired poly(L-dopa) polymer was established for the voltammetric determination of LEV that is capable of LEV detection in complicated matrices. The sensor used gold nanoparticles for enhanced electron transfer kinetics and selectivity was based on molecular imprinting copolymerization with *o*-phenylenediamine and levodopa as the functional monomers. In this work, ***mussel-inspired "Levodopa"*** (a dopamine analogue) has been copolymerized with *o*PD for the first time to fabricate a selective levofloxacin MIP sensor. Levodopa as a functional monomer offers many advantages such as levodopa monomer has both phenolic and carboxylic functional groups that permit various interactions with the template molecule. In accordance with the polymer's strong affinity for LEV, the modified electrode showed a high selectivity. Over two concentration ranges of (1.0×10^{-6}–1.0×10^{-4} mol/L) and (1.0×10^{-4}–1.0×10^{-2} mol/L) LEV, a linear response was observed. The electrode was used to determine LEV in Tavanic® tablets as well as genuine human plasma samples with excellent results.

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CRediT authorship contribution statement

Noha F. El Azab: Conceptualization, Methodology, Validation, Investigation, Writing – original draft, Visualization. **Amr M. Mahmoud:** Conceptualization, Methodology, Validation, Investigation, Writing – original draft, Visualization. **Yossra A. Trabik:** Conceptualization, Methodology, Validation, Investigation, Writing – original draft, Visualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jelechem.2022.116504.

References

[1] S. Buffet-Bataillon, P. Tattevin, J.-Y. Maillard, M. Bonnaure-Mallet, A. Jolivet-Gougeon, Efflux pump induction by quaternary ammonium compounds and fluoroquinolone resistance in bacteria, Future Microbiol. 11 (1) (2016) 81–92.
[2] W. Yi, C. Han, Z. Li, Y. Guo, M. Liu, C. Dong, A strategy of electrochemical simultaneous detection of acetaminophen and levofloxacin in water based on gC 3 N 4 nanosheet-doped graphene oxide, Environ. Sci. Nano 8 (1) (2021) 258–268.
[3] T. Chan, P.E. Bunce, Fluoroquinolone antimicrobial drugs, CMAJ 189 (17) (2017) E638.
[4] Y.H. Tsai, M.J. Bair, C.C. Hu, Determination of levofloxacin in human urine with capillary electrophoresis and fluorescence detector, J. Chin. Chem. Soc. 54 (4) (2007) 991–995.
[5] O. Szerkus, J. Jacyna, P. Wiczling, A. Gibas, M. Sieczkowski, D. Siluk, M. Matuszewski, R. Kaliszan, M.J. Markuszewski, Ultra-high performance liquid chromatographic determination of levofloxacin in human plasma and prostate tissue with use of experimental design optimization procedures, J. Chromatogr. B 1029 (2016) 48–59.
[6] G. Altiokka, Z. Atkosar, N.O. Can, The determination of levofloxacin by flow injection analysis using UV detection, potentiometry, and conductometry in pharmaceutical preparations, J. Pharm. Biomed. Anal. 30 (3) (2002) 881–885.
[7] Y.M. Liu, J.T. Cao, W. Tian, Y.L. Zheng, Determination of levofloxacin and norfloxacin by capillary electrophoresis with electrochemiluminescence detection and applications in human urine, Electrophoresis 29 (15) (2008) 3207–3212.
[8] M. Maleque, M.R. Hasan, F. Hossen, S. Safi, Development and validation of a simple UV spectrophotometric method for the determination of levofloxacin both in bulk and marketed dosage formulations, J. Pharm. Anal. 2 (6) (2012) 454–457.
[9] N.E.T.A. Ghani, F.M. Abdel-Haleem, S. Mahmoud, R.M. El Nashar, Electrochemical detection of the different species of levofloxacin using PVC, carbon paste and screen-printed electrodes: Effect of pH, J. Anal. Test. 2 (2) (2018) 175–183.
[10] S. Bian, B. Zhu, G. Rong, M. Sawan, Towards wearable and implantable continuous drug monitoring: A review, J. Pharm. Anal. 11 (1) (2021) 1–14.
[11] H. Teymourian, M. Parrilla, J.R. Sempionatto, N.F. Montiel, A. Barfidokht, R. Van Echelpoel, K. De Wael, J. Wang, Wearable electrochemical sensors for the monitoring and screening of drugs, ACS Sensors 5 (9) (2020) 2679–2700.
[12] H.C. Ates, J.A. Roberts, J. Lipman, A.E. Cass, G.A. Urban, C. Dincer, On-site therapeutic drug monitoring, Trends Biotechnol. 38(11) (2020) 1262-127.
[13] A. Mahmoud, E. Moaaz, M. Rezk, E. Abdel-Moety, A. Fayed, Microfabricated Solid-Contact Potentiometric Sensor for Determination of Tedizolid Phosphate, Application to Content Uniformity Testing, Electroanalysis.
[14] A. Radi, Z. El-Sherif, Determination of levofloxacin in human urine by adsorptive square-wave anodic stripping voltammetry on a glassy carbon electrode, Talanta 58 (2) (2002) 319–324.
[15] U. Bilibio, L.H. de Oliveira, V.S. Ferreira, M.A.G.a. Trindade, Enhanced simultaneous electroanalytical determination of two fluoroquinolones by using surfactant media and a peak deconvolution procedure, Microchem. J. 116 (2014) 47–54.
[16] A. Wong, A.M. Santos, O. Fatibello-Filho, Simultaneous determination of paracetamol and levofloxacin using a glassy carbon electrode modified with carbon black, silver nanoparticles and PEDOT: PSS film, Sens. Actuators B 255 (2018) 2264–2273.
[17] H.R. Lotfi Zadeh Zhad, R.Y. Lai, Iron (III)-mediated Electrochemical Detection of Levofloxacin in Complex Biological Samples, Electroanalysis 29 (11) (2017) 2672–2677.
[18] A.A. Özcan, M. Gürbüz, A. Özcan, Preparation of a modified electrode for the determination of levofloxacin, Anadolu Univ. J. Sci. Technol. A 18(5), 962–972.
[19] Y. Jin, G. Xu, X. Li, J. Ma, L. Yang, Y. Li, H. Zhang, Z. Zhang, D. Yao, D. Li, Fast cathodic reduction electrodeposition of a binder-free cobalt-doped Ni-MOF film for directly sensing of levofloxacin, J. Alloy. Compd. 851 (2021) 156823.
[20] Y. Chi, J. Li, Determination of levofloxacin hydrochloride with multiwalled carbon nanotubes-polymeric alizarin film modified electrode, Russ. J. Electrochem. 46 (2) (2010) 155–160.
[21] W. Wen, D.-M. Zhao, X.-H. Zhang, H.-Y. Xiong, S.-F. Wang, W. Chen, Y.-D. Zhao, One-step fabrication of poly (o-aminophenol)/multi-walled carbon nanotubes

composite film modified electrode and its application for levofloxacin determination in pharmaceuticals, Sens. Actuators B 174 (2012) 202–209.
[22] F.C. Moraes, T.A. Silva, I. Cesarino, M.R.V. Lanza, S.A.S. Machado, Antibiotic detection in urine using electrochemical sensors based on vertically aligned carbon nanotubes, Electroanalysis 25 (9) (2013) 2092–2099.
[23] V. Cesarino, I. Cesarino, F.C. Moraes, S.A.S. Machado, L.H. Mascaro, Carbon nanotubes modified with SnO2 rods for levofloxacin detection, J. Braz. Chem. Soc. 25 (2014) 502–508.
[24] Ç.C. Koçak, Poly (Taurine-Glutathione)/Carbon Nanotube Modified Glassy Carbon Electrode as a New Levofloxacin Sensor, Electroanalysis 31 (8) (2019) 1535–1544.
[25] F. Wang, L. Zhu, J. Zhang, Electrochemical sensor for levofloxacin based on molecularly imprinted polypyrrole–graphene–gold nanoparticles modified electrode, Sens. Actuators B 192 (2014) 642–647.
[26] L. Tang, Y. Tong, R. Zheng, W. Liu, Y. Gu, C. Li, R. Chen, Z. Zhang, Ag nanoparticles and electrospun CeO2-Au composite nanofibers modified glassy carbon electrode for determination of levofloxacin, Sens. Actuators B 203 (2014) 95–101.
[27] J. Borowiec, K. Yan, C.-C. Tin, J. Zhang, Synthesis of PDDA functionalized reduced graphene oxide decorated with gold nanoparticles and its electrochemical response toward levofloxacin, J. Electrochem. Soc. 162 (3) (2015) H164–H169.
[28] M.H. Ghanbari, A. Khoshroo, H. Sobati, M.R. Ganjali, M. Rahimi-Nasrabadi, F. Ahmadi, An electrochemical sensor based on poly (L-Cysteine)@ AuNPs@ reduced graphene oxide nanocomposite for determination of levofloxacin, Microchem. J. 147 (2019) 198–206.
[29] H. Khoshsafar, H. Bagheri, M. Rezaei, A. Shirzadmehr, A. Hajian, Z. Sepehri, Magnetic carbon paste electrode modified with a high performance composite based on molecularly imprinted carbon nanotubes for sensitive determination of levofloxacin, J. Electrochem. Soc. 163 (8) (2016) B422–B427.
[30] C. Liu, D. Xie, P. Liu, S. Xie, S. Wang, F. Cheng, M. Zhang, L. Wang, Voltammetric determination of levofloxacin using silver nanoparticles deposited on a thin nickel oxide porous film, Microchim. Acta 186 (1) (2019) 1–10.
[31] L.M. Alencar, L.H. de Oliveira, R. Backes, T.M. Rosa, P.R. de Oliveira, R.A.B. da Silva, M.A.G. Trindade, Liquid-liquid Extraction Coupled to Batch Injection Analysis for Electroanalysis of Levofloxacin at Low Concentration Level, Electroanalysis 29 (11) (2017) 2559–2564.
[32] M. Rkik, M.B. Brahim, Y. Samet, Electrochemical determination of levofloxacin antibiotic in biological samples using boron doped diamond electrode, J. Electroanal. Chem. 794 (2017) 175–181.
[33] M. Gurbuz, A.A. Ozcan, A. Ozcan, Preparation of activated disposable pencil graphite electrode for the selective and sensitive determination of a fluoroquinolone antibiotic: levofloxacin, Curr. Pharm. Anal. 14 (3) (2018) 247–254.
[34] M.M. Vinay, Y.A. Nayaka, R.O. Yatisha, K.V. Basavarajappa, P. Manjunatha, H.T. Purushothama, Development of Azure-B modified pencil graphite electrode as an electrochemical sensor for the investigation of Levofloxacin in pharmaceutical and biological samples, Chem. Data Collect. 28 (2020) 100441.
[35] L. Han, Y. Zhao, C. Chang, F. Li, A novel electrochemical sensor based on poly (p-aminobenzene sulfonic acid)-reduced graphene oxide composite film for the sensitive and selective detection of levofloxacin in human urine, J. Electroanal. Chem. 817 (2018) 141–148.
[36] M.K.L. Da Silva, R. Plana SimÃµes, I. Cesarino, Evaluation of reduced graphene oxide modified with antimony and copper nanoparticles for levofloxacin oxidation, Electroanalysis 30 (9) (2018) 2066–2076.
[37] M.H. Ghanbari, M. Rahimi-Nasrabadi, H. Sobati, Modifying a glassy carbon electrode with reduced graphene oxide for the determination of levofloxacin with a glassy, Analytical & Bioanalytical Electrochemistry 11 (2) (2019) 189–200.
[38] M.H. Ghanbari, F. Shahdost-Fard, A. Khoshroo, M. Rahimi-Nasrabadi, M.R. Ganjali, M. Wysokowski, T. Rębiś, S. Żółtowska-Aksamitowska, T. Jesionowski, P. Rahimi, A nanocomposite consisting of reduced graphene oxide and electropolymerized β-cyclodextrin for voltammetric sensing of levofloxacin, Microchim. Acta 186 (7) (2019) 1–11.
[39] D.M. de Farias, L.V. de Faria, T.P. Lisboa, M.A.C. Matos, R.A.A. Muñoz, R.C. Matos, Determination of levofloxacin in pharmaceutical formulations and urine at reduced graphene oxide and carbon nanotube-modified electrodes, J. Solid State Electrochem. 24 (5) (2020) 1165–1173.
[40] P.B. Deroco, O. Fatibello-Filho, F. Arduini, D. Moscone, Effect of Different Carbon Blacks on the Simultaneous Electroanalysis of Drugs as Water Contaminants Based on Screen-printed Sensors, Electroanalysis 31 (11) (2019) 2145–2154.
[41] V.M. Wagh, Study of variation in electrochemical behavior of Ornidazole and levofloxacin simultaneously by differential pulse voltammetry, Pharma Innov. J. 8 (6) (2019) 617–620.
[42] M.F. Abdel-Ghany, L.A. Hussein, N.F. El Azab, Novel potentiometric sensors for the determination of the dinotefuran insecticide residue levels in cucumber and soil samples, Talanta 164 (2017) 518–528.
[43] D. Fauzi, F.A. Saputri, Molecularly Imprinted Polymer Nanoparticles (MIP-NPs) Applications in Electrochemical Sensors, Int. J. Appl. Pharm. (2019) 1–6.
[44] I.F. Abo-Elmagd, A.M. Mahmoud, M.A. Al-Ghobashy, M. Nebsen, N.S. El Sayed, S. Nofal, S.H. Soror, R. Todd, S.A. Elgebaly, Impedimetric Sensors for Cyclocreatine Phosphate Determination in Plasma Based on Electropolymerized Poly (o-phenylenediamine) Molecularly Imprinted Polymers, ACS Omega 6 (46) (2021) 31282–31291.
[45] A. Lamaoui, J.J. García-Guzmán, A. Amine, J.M. Palacios-Santander, L. Cubillana-Aguilera, Synthesis techniques of molecularly imprinted polymer composites, in: Sooraj M.P., Archana Nair, Beena Mathew, S. Thomas (Eds.), Molecularly Imprinted Polymer Composites, Elsevier, 2021, pp. 49-91.
[46] S. Ramanavicius, A. Jagminas, A. Ramanavicius, Advances in molecularly imprinted polymers based affinity sensors, Polymers 13 (6) (2021) 974.
[47] B. Bozal-Palabiyik, C. Erkmen, B. Uslu, Molecularly imprinted electrochemical sensors: Analytical and pharmaceutical applications based on ortho-phenylenediamine polymerization, Curr. Pharm. Anal. 16 (4) (2020) 350–366.
[48] A. Raziq, A. Kidakova, R. Boroznjak, J. Reut, A. Öpik, V. Syritski, Development of a portable MIP-based electrochemical sensor for detection of SARS-CoV-2 antigen, Biosens. Bioelectron. 178 (2021) 113029.
[49] A.G. Ayankojo, J. Reut, V. Ciocan, A. Öpik, V. Syritski, Molecularly imprinted polymer-based sensor for electrochemical detection of erythromycin, Talanta 209 (2020) 120502.
[50] G. Ozcelikay, S. Kurbanoglu, X. Zhang, C. Kosak Soz, U. Wollenberger, S.A. Ozkan, A. Yarman, F.W. Scheller, Electrochemical MIP sensor for butyrylcholinesterase, Polymers 11(12) (2019) 1970.
[51] G. Ozcelikay, N. Karadas-Bakirhan, T. Taskin-Tok, S.A. Ozkan, A selective and molecular imaging approach for anticancer drug: Pemetrexed by nanoparticle accelerated molecularly imprinting polymer, Electrochim. Acta 354 (2020) 136665.
[52] D.R. Dreyer, D.J. Miller, B.D. Freeman, D.R. Paul, C.W. Bielawski, Perspectives on poly (dopamine), Chem. Sci. 4 (10) (2013) 3796–3802.
[53] K. Liu, W.-Z. Wei, J.-X. Zeng, X.-Y. Liu, Y.-P. Gao, Application of a novel electrosynthesized polydopamine-imprinted film to the capacitive sensing of nicotine, Anal. Bioanal. Chem. 385 (4) (2006) 724–729.
[54] S. Li, H. Wang, M. Young, F. Xu, G. Cheng, H. Cong, Properties of electropolymerized dopamine and its analogues, Langmuir 35 (5) (2018) 1119–1125.
[55] J. Ghodsi, A.A. Rafati, A novel molecularly imprinted sensor for imidacloprid pesticide based on poly(levodopa) electro-polymerized/TiO2 nanoparticles composite, Anal. Bioanal. Chem. 410 (29) (2018) 7621–7633.
[56] M.J. Russo, M. Han, P.E. Desroches, C.S. Manasa, J. Dennaoui, A.F. Quigley, R.M. Kapsa, S.E. Moulton, R.M. Guijt, G.W. Greene, Antifouling strategies for electrochemical biosensing: mechanisms and performance toward point of care based diagnostic applications, ACS Sensors 6 (4) (2021) 1482–1507.
[57] L. Zhou, X. Li, B. Zhu, B. Su, An Overview of Antifouling Strategies for Electrochemical Analysis, Electroanalysis (2021).
[58] B.L. Hanssen, S. Siraj, D.K. Wong, Recent strategies to minimise fouling in electrochemical detection systems, Rev. Anal. Chem. 35 (1) (2016) 1–28.
[59] S. Campuzano, M. Pedrero, P. Yáñez-Sedeño, J.M. Pingarrón, Antifouling (bio) materials for electrochemical (bio) sensing, Int. J. Mol. Sci. 20 (2) (2019) 423.
[60] C. Jiang, G. Wang, R. Hein, N. Liu, X. Luo, J.J. Davis, Antifouling strategies for selective in vitro and in vivo sensing, Chem. Rev. 120 (8) (2020) 3852–3889.
[61] J. Barek, How to improve the performance of electrochemical sensors via minimization of electrode passivation, Chemosensors 9 (1) (2021) 12.
[62] R. Batul, T. Tamanna, A. Khaliq, A. Yu, Recent progress in the biomedical applications of polydopamine nanostructures, Biomater. Sci. 5 (7) (2017) 1204–1229.
[63] W. Cheng, X. Zeng, H. Chen, Z. Li, W. Zeng, L. Mei, Y. Zhao, Versatile polydopamine platforms: synthesis and promising applications for surface modification and advanced nanomedicine, ACS Nano 13 (8) (2019) 8537–8565.
[64] Y. Liu, K. Ai, L. Lu, Polydopamine and its derivative materials: synthesis and promising applications in energy, environmental, and biomedical fields, Chem. Rev. 114 (9) (2014) 5057–5115.
[65] M.F. Ayad, Y.A. Trabik, M.H. Abdelrahman, N.V. Fares, N. Magdy, Potentiometric Carbon Quantum Dots-Based Screen-Printed Arrays for Nano-Tracing Gemifloxacin as a Model Fluoroquinolone Implicated in Antimicrobial Resistance, Chemosensors 9 (1) (2021) 8.
[66] J. Li, H. Xie, L. Chen, A sensitive hydrazine electrochemical sensor based on electrodeposition of gold nanoparticles on choline film modified glassy carbon electrode, Sens. Actuators B 153 (1) (2011) 239–245.
[67] L. Zhang, L.-Y. Tu, Y. Liang, Q. Chen, Z.-S. Li, C.-H. Li, Z.-H. Wang, W. Li, Coconut-based activated carbon fibers for efficient adsorption of various organic dyes, RSC Adv. 8 (74) (2018) 42280–42291.
[68] P.L. Runnels, J.D. Joseph, M.J. Logman, R.M. Wightman, Effect of pH and surface functionalities on the cyclic voltammetric responses of carbon-fiber microelectrodes, Anal. Chem. 71 (14) (1999) 2782–2789.
[69] S. Azari, L. Zou, Using zwitterionic amino acid l-DOPA to modify the surface of thin film composite polyamide reverse osmosis membranes to increase their fouling resistance, J. Membr. Sci. 401 (2012) 68–75.
[70] A. Nguyen, S. Azari, L. Zou, Coating zwitterionic amino acid l-DOPA to increase fouling resistance of forward osmosis membrane, Desalination 312 (2013) 82–87.
[71] X. Tan, P. Gao, Y. Li, P. Qi, J. Liu, R. Shen, L. Wang, N. Huang, K. Xiong, W. Tian, Poly-dopamine, poly-levodopa, and poly-norepinephrine coatings: Comparison of physico-chemical and biological properties with focus on the application for blood-contacting devices, Bioact. Mater. 6 (1) (2021) 285–296.
[72] L. Özcan, Y.c. Şahin, Determination of paracetamol based on electropolymerized-molecularly imprinted polypyrrole modified pencil graphite electrode, Sens. Actuators B 127 (2) (2007) 362–369.
[73] S.P.i. Ozkorucuklu, Y.c. Sahin, G.l. Alsancak, Voltammetric behaviour of sulfamethoxazole on electropolymerized-molecularly imprinted overoxidized polypyrrole, Sensors 8 (12) (2008) 8463–8478.
[74] M.R. Romero, F. Ahumada, F. Garay, A.M. Baruzzi, Amperometric biosensor for direct blood lactate detection, Anal. Chem. 82 (13) (2010) 5568–5572.
[75] M.M. Elhassan, A.M. Mahmoud, M.A. Hegazy, S. Mowaka, Electrochemical determination of ipragliflozin in pure form and in spiked human plasma on a glassy carbon electrode, J. Electrochem. Soc. 168 (3) (2021) 036507.
[76] S.A. Hassan, N.B. ElDin, H.E. Zaazaa, A.A. Moustafa, A.M. Mahmoud, Point-of-care diagnostics for drugs of abuse in biological fluids: application of a microfabricated disposable copper potentiometric sensor, Microchim. Acta 187 (9) (2020) 1–9.