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Article

Photoelectroanalytical Detection of Adrenaline Based on DNA and TiO_2 Nanoparticles Sensitized with Bis(ethylenedithio)tetrathiafulvalene Exploiting LED Light

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In this study, a photoelectroanalytical sensor for determination of adrenaline based on deoxyribonucleic acid (DNA) and anatase titanium dioxide (TiO_2) nanoparticles sensitized with bis(ethylenedithio)tetrathiafulvalene (BEDT-TTF) was developed, which we henceforward call BEDT-TTF/DNA/TiO_2/ITO. The photoelectroanalytical sensor showed high photocurrent to adrenaline under visible light emitting diode (LED) light irradiation in comparison to each component of the composite material. Under optimized conditions, the BEDT-TTF/DNA/TiO_2/ITO sensor shows a linear response range from 10 nmol L^{-1} up to 100 μmol L^{-1} with a sensitivity of 8.1 nA L μmol^{-1} and limit of detection of 1 nmol L^{-1} for the detection of adrenaline. The photoelectrochemical sensor showed high photocurrent to adrenaline in comparison to photocurrent response to ascorbic acid and uric acid. The BEDT-TTF/DNA/TiO_2/ITO photoelectrochemical sensor was successfully applied to urine samples, with recovery values between 96 and 106%.

Keywords: adrenaline, photoelectrochemical sensor, visible LED light, deoxyribonucleic acid

Introduction

Adrenaline, also known as epinephrine, is one of the most important message transfer compound in the mammalian central nervous system, which exist as an organic cation in the nervous tissue and the biological body fluid.[1] The level of adrenaline in the body affects a series of actions of the nervous system including the regulation of blood pressure, heart rate, lipolysis, immune response and glycogen metabolism.[2] In addition, adrenaline has been advocated during early cardiopulmonary resuscitation, early defibrillation and early advanced care in cardiac arrest for decades.[3]

Therefore, the quantification of adrenaline in biological samples is of high interest nowadays. Urine represents one of the most easily attainable and, consequently, very common samples in adrenaline clinical analysis and diagnostics. The levels of adrenaline in biological fluids such as urine depends on the age and condition of the patient.[4] For healthy people, for example, the physiological concentration of adrenaline found in urine samples are in nanomolar level (22-109 nmol L^{-1}).[5]

A number of analytical methodologies have been proposed for determination of adrenaline such as fluorimetric,[6] spectrophotometric,[7] enzymatic radio-immunoassay,[8] gas chromatography,[9] high performance liquid chromatography,[10] capillary electrophoresis[11] and electrochemical methods.[12-15] Despite the high number of analytical methods for adrenaline determination, most of them suffer from some disadvantages such as high cost, long analysis time, extensive sample pretreatment based on derivatization, extraction and purification as well as demands for highly trained users. The fluorometric and radioenzymatic assays are presently the most widely used techniques for the estimation of plasma, urine and tissue adrenaline. The fluorometric assay lacks specificity and sensitivity. The radioenzymatic assay is significantly more sensitive and specific but is technically very complex, time consuming and expensive.[12]

On the other hand, the electrochemical methods are cheaper, simple and fast in comparison to several analytical methods. However, the most of electrochemical sensors for adrenaline show low linear response range or lack with the limit of detection and sensitivity necessary to adrenaline detection in biological samples.[13-15]

Nowadays, the photoelectroanalytical devices have emerged as a potentially useful and sensitive system with advantage of high linear response range.[16-18] The photoelectrochemical transduction is based on photocurrent detection following light excitation of a photoactive

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material. Since the excitation source and detection apparatus are from distinct nature, the photoelectroanalytical devices show high signal-to-noise ratio.[18,19]

The anatase titanium dioxide (TiO_2) has attracted high attention in the development of photocatalytic and photoelectrochemical areas due to its nontoxicity, hydrophilicity, low cost and stability against photocorrosion.[19] In addition, the anatase TiO_2 shows a band gap with a quite deep valence band allowing that generated holes tend to locates on the surface of the particle, which makes it active to be harvested by free electrons from molecules.[19]

However, anatase TiO_2 shows some limitations as photocatalyst including the recombination of photo-generated charge carriers and wide bandgap (3.22 eV) limiting anatase TiO_2 to almost only ultraviolet (UV) light absorption.[20] The wide bandgap of anatase TiO_2 limits their potential applications in photoelectroanalytical fields because UV light may damage the biologic samples.[21]

A number of strategies have been proposed to improve the photoelectrochemical performance of TiO_2 under visible light excitation including the doping with transition-metal ions or oxygen defects into TiO_2 lattice as well as dye sensitization.[22,23] Thus, the anatase TiO_2 has been sensitized with several compounds in order to make the titanium oxide properties more attractive to development of photoelectroanalytical devices including phthlocyanines,[24,25] conducting polymers,[26] porphyrins,[27] lithium tetracyanoethylenide,[28] quantum dots,[29] among others.

Tetrathiafulvalene is a strong π-electron donor which has attracted particular attention in the development of chemical sensors,[30] superconducting materials,[31] ferromagnets,[32] non-linear optic devices,[33] biofuel cell,[34] and recently in development of dye sensitized solar cells.[35]

The aim of the present work is the development of a novel photoelectrochemical sensor based on indium tin oxide modified with anatase TiO_2 nanoparticles sensitized with bis(ethylenedithio)tetrathiafulvalene (BEDT-TTF/TiO_2) for adrenaline detection with visible light emitting diode (LED) light. The photoelectroanalytical sensor showed a wide linear range, good stability and selectivity to adrenaline. To the best of our knowledge, this is the first photoelectrochemical sensor for adrenaline determination exploiting the interaction between BEDT-TTF and anatase TiO_2 nanoparticles under visible LED light.

Experimental

Materials

All chemicals were of analytical grade and used as received without any further purification steps. Bis(ethylenedithio)tetrathiafulvalene (BEDT-TTF), double-stranded deoxyribonucleic acid (ds-DNA), adrenaline and indium tin oxide coated glass slides (ITO) were purchased from Sigma-Aldrich (Saint Louis, USA). 2-[4-(2-Hydroxyethyl)piperazin-1-yl]ethanesulfonic acid (HEPES), boric acid, citric acid, phosphoric acid, disodium and monosodium phosphates (Na_2HPO_4 and NaH_2PO_4), were acquired from Synth, São Paulo, Brazil. All solutions were prepared with water purified in an OS100LXE system from GEHAKA Company (Gehaka Ltd., São Paulo, SP, Brazil). The actual pH of the buffer solutions was determined with a Quimis pH/Ion Analyser Q400AS model. The anatase TiO_2 nanopowder with nominal particle size of 25 nm were acquired from Sigma-Aldrich (Saint Louis, USA). The double-stranded template deoxyribonucleic acid with UV absorbance ratio (A_{260nm}/A_{280nm}) of 1.9 were isolated from the calf thymus. The double strand DNA used in present work is a double helix of a chain of nucleotides constituted of about 41.9 mole% G-C (guanine-cytidine) and 58.1 mole% A-T (adenosine-thymine).

Apparatus

Photoelectroanalytical measurements were carried out with an Autolab PGSTAT 128N potentiostat/galvanostat from Metrohm Autolab B.V., Utrecht, the Netherlands controlled by GPES software. All photoelectrochemical measurements were carried out in a three-electrode system positioned in a box, which was used for control of the light incidence in the photoelectrochemical cell. The photoelectrochemical measurements were performed with a cheap commercial 20 W white LED light as the source of irradiation energy with emission between 380 and 680 nm. The bare or modified SnO_2/In_2O_3 coated glass slide (ITO) with surface resistivity of 8-12 $\Omega\ sq^{-1}$ was used as the working electrode. The ITO photoactive area was 0.5 cm^2. The ITO glass slides were of 1.1 mm of thickness and nominal transmittance of 84% (nominal at 550 nm). The photoelectrochemical measurements were performed by front side illumination. A Pt wire was used as counter electrode and $Ag/AgCl_{(saturated)}$ was used as reference electrode.

Construction of the BEDT-TTF/DNA/TiO_2 photoelectrochemical sensor

First, an ITO coated glass slide was sonicated and copiously washed with ethanol and water to remove any adsorbed species. After that, a suspension was prepared by mixing 50 mg of anatase TiO_2 nanoparticles and 5 mg BEDT-TTF in 2.5 mL of dimethylformamide (DMF) with the aid of sonication. The suspension was filtered and the

solid washed with water and it was let to dry at 70 ºC for 2 h to give BEDT-TTF/TiO_2 composite.

Then, 5 mg of the BEDT-TTF/TiO_2 composite was dispersed in aqueous solution of single-stranded DNA (ss-DNA), and the resultant mixture was stirred for 1 h. The ss-DNA solution was prepared heating ds-DNA solution at 90 °C for 2 h. After cooling to room temperature, the resulting materials were then centrifuged and washed three times with distilled water to remove excess ss-DNA. The as-prepared BEDT-TTF/DNA/TiO_2 composite was obtained.

Then, 1.0 mg of the BEDT-TTF/DNA/TiO_2 composite was mixed with 50 µL of water with the aid of sonication for 10 min. Finally, 10 µL of this suspension was placed directly onto the photoelectrode substrate and allowed to dry at 50 ºC for 10 min to form BEDT-TTF/ds-DNA/TiO_2/ITO photoelectrochemical sensor. The amount of BEDT-TFF/DNA/TiO_2 dissolved in water was chosen taking into account the capability of the paste to cover ITO surface and produce more stable films. Films prepared with amounts of BEDT-TFF/DNA/TiO_2 composite higher than 1 mg dissolved in water produced surfaces that are more fragile. On the other hand, films prepared with amounts of composite lower than 1 mg did not produce films with homogenous surfaces.

Preparation and analysis of urine samples

Urine samples were collected into the plastic tubes and 6 mol L^{-1} HCl was added to each one to give solutions with 1% of HCl.[36] The acidified samples were centrifuged for 30 min at 2500 rpm.[37] The supernatant was filtered and then diluted 10-times with the phosphate buffer solution (pH 7.0). The solution was transferred into the voltammetric cell to be analyzed with the photoelectroanalytical sensor in three replicates. The standard addition method was used for the determination of adrenaline in real samples.

Results and Discussion

Electrochemical characteristics of the BEDT-TTF/DNA/TiO_2 composite photoelectrochemical sensor

Figure 1 shows the amperometric response of 1 mmol L^{-1} of adrenaline (ADR) in 0.1 mol L^{-1} phosphate buffer solution (pH 7.0) on ITO, TiO_2/ITO, BEDT-TTF/TiO_2/ITO, BEDT-TTF/TiO_2/ITO and BEDT-TTF/DNA/TiO_2/ITO under LED light on and off. The values of the photocurrents to each one of photosensors previously presented were 0.0011 ± 0.0002, 0.17 ± 0.01, 1.69 ± 0.05 and 1.91 ± 0.02 µA, respectively.

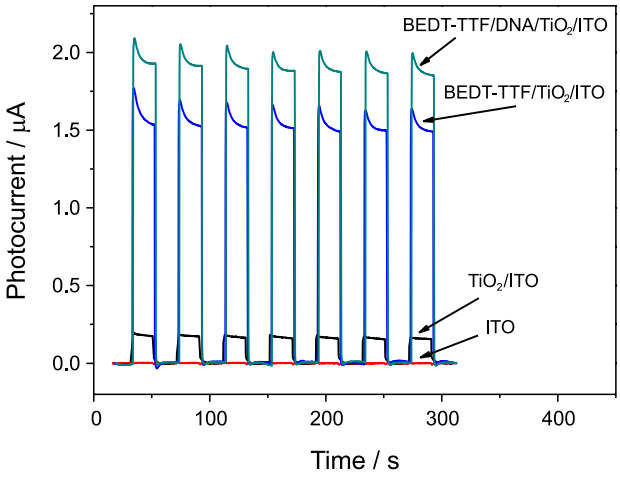

Figure 1. Photocurrent response of BEDT-TTF/DNA/TiO_2/ITO, BEDT-TTF/TiO_2/ITO, TiO_2/ITO, and ITO. Experiments carried in 0.1 phosphate buffer solution (pH 7.0) containing 1 mmol L^{-1} adrenaline. E_{app} = 0.25 V *vs.* Ag/AgCl.

As can be seen, the BEDT-TTF/DNA/TiO_2/ITO shows higher mean value of the photocurrent as well as presented lower standard deviation to seven measurements of photocurrent. The BEDT-TTF/DNA/TiO_2/ITO photosensor presents a photocurrent to adrenaline about 11-fold higher than that to TiO_2/ITO, indicating the high performance of the BEDT-TTF/DNA/TiO_2/ITO photosensor in photo-generate electrons and holes improving the photoelectrochemical efficiency. It is probable that the capability of DNA to form stable biocompatible films can improve the stability and sensitivity of the platform. In addition, the negative character of DNA due to phosphate groups in their chains can favor the interaction between the photocatalyst and adrenaline molecule, since the last is positively charged at physiological pH.

Figure 2 shows schematic diagram for the proposed mechanism to photoelectrochemical oxidation of adrenaline on BEDT-TTF/DNA/TiO_2/ITO. Under white LED light irradiation, the BEDT-TTF complex adsorbed on anatase TiO_2 nanoparticles surface can absorb the LED light such as electrons of the dye are excited from highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO) state since the BEDT-TTF complex shows an absorption band at visible region of the electromagnetic spectrum with maximum at about 460 nm justifying its ability to harvest photons from LED light.[38] The excited electron can then be transferred to the conduction band of the TiO_2 and finally be transferred to ITO electrode to originate the photocurrent.

On the other hand, the addition of adrenaline to photoelectrochemical cell can improve the spatial separation of photogenerated charges such as the holes from TiO_2 can localize on adrenaline and electrons localize within the

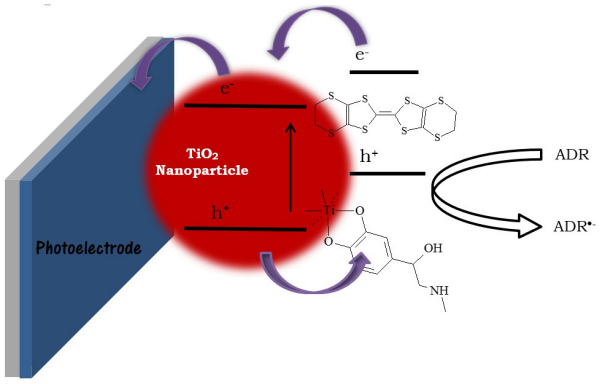

Figure 2. Proposed mechanism for the photoelectrochemical detection of adrenaline.

lattice of TiO_2, which suppress the recombination of charges and consequently improve the photoelectrochemical performance of the composite to adrenaline oxidation. Thus, a higher response to photoelectrochemical adrenaline oxidation is achieved, when more surface complexes are formed between the adrenaline and TiO_2.

After that, the electron in LUMO state of dye is transferred to the conduction band of anatase TiO_2 nanoparticles and the holes in HOMO state promote the adrenaline oxidation. In addition, adrenaline can act as a scavenger of holes generated at TiO_2 nanoparticles improving the spatial separation of charges at valence and conduction bands of TiO_2 nanoparticles. Therefore, the response of the photosensor depends on adrenaline concentration.

Optimization of the BEDT-TTF/DNA/TiO_2 photoelectroanalytical sensor response

The influences of buffer solution, solution pH and applied potential on the BEDT-TTF/DNA/TiO_2 sensor response were evaluated in order to found the best experimental conditions for adrenaline determination. In order to evaluate the photocurrent response, the amperometric response was recorded while the LED light was turned on and off. Initially, the effects of solution buffer on the photocurrent of the BEDT-TTF/DNA/TiO_2/ITO obtained for adrenaline was investigated. Figure 3 shows the response of the BEDT-TTF/DNA/TiO_2 modified photoelectrode to adrenaline in different buffer solutions, such as, phosphate, HEPES and Britton-Robinson at 0.1 mol L^{-1} and pH 7.

The values of photocurrents to 100 µmol L^{-1} of adrenaline on BEDT-TTF/DNA/TiO_2 modified photoelectrode in phosphate, HEPES and Britton-Robinson buffers were 0.80 ± 0.04, 0.61 ± 0.02 and 0.45 ± 0.02 µA, respectively. The best response to adrenaline at phosphate buffer solution may be due to the high ionic mobility of the phosphate

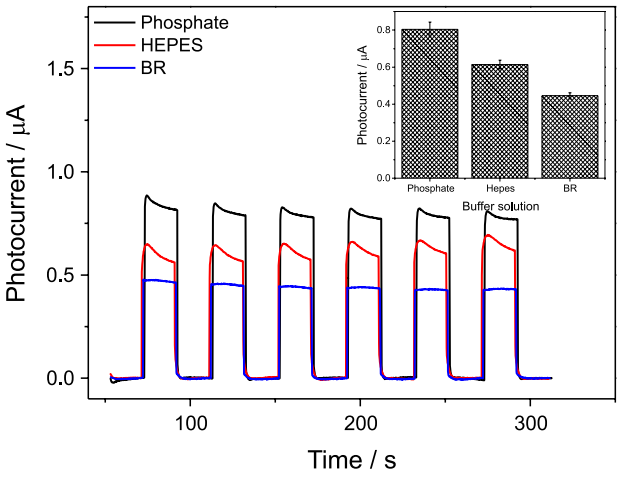

Figure 3. Influence of buffer solution on the photosensor response for 100 µmol L^{-1} of adrenaline. Measurements were carried out in 0.1 mol L^{-1} phosphate buffer solution. E_{app} = 0.25 V *vs.* Ag/AgCl.

and potassium ions making possible a better charge transportation in solution, which may favor the better charge compensating during the adrenaline oxidation. In this sense, the phosphate buffer solution was chosen for further experiments.

After that, the response of the BEDT-TTF/DNA/TiO_2 photoelectrochemical sensor to adrenaline was investigated in phosphate buffer solution with pH ranging from 5.0 up to 8.0 under an applied potential of 0.25 V *vs.* Ag/$AgCl_{(sat)}$ (Figure 4).

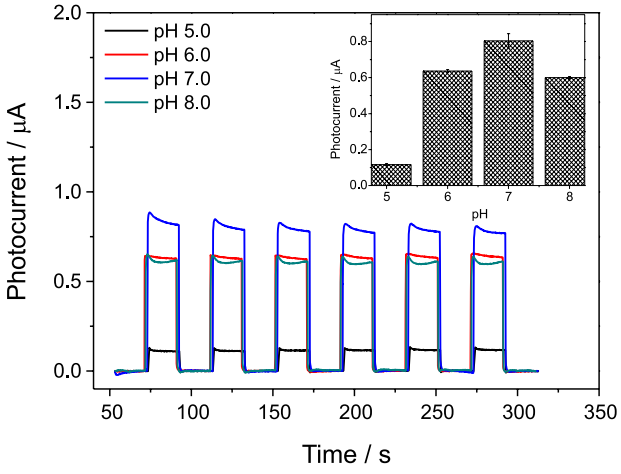

Figure 4. Influence of pH of the solution on the photosensor response for 100 µmol L^{-1} adrenaline. Measurements were carried out in 0.1 mol L^{-1} phosphate buffer solution. E_{app} = 0.25 V *vs.* Ag/AgCl.

The phototocurrent to adrenaline oxidation on BEDT-TTF/DNA/TiO_2/ITO increased from pH 5.0 up to pH 7.0. The changes in the solution pH could significantly affect the relative energies of the sensitizer excited states and the ITO acceptor states, and accordingly sensitized photocurrents. It is possible that the LUMO energy levels

of the dye increase with increasing solution pH, being favorable to the anodic photocurrent generation. After that, the response of the BEDT-TTF/DNA/TiO_2/ITO to adrenaline decreased from pH 7.0 until pH 8.0 (Figure 4), which can be due to the adrenaline decomposition at higher pH values. Therefore, all subsequent measurements were carried out in phosphate buffer solution at pH 7.0.

The applied potential was varied from 0.1 up to 0.6 V in order to evaluate the effect of the electric potential on the photosensor response to adrenaline (Figure 5). The photoelectrochemical response of BEDT-TTF/DNA/TiO_2/ITO to adrenaline were 0.21 ± 0.01, 0.72 ± 0.01, 1.04 ± 0.02, 1.27 ± 0.01, 1.34 ± 0.05 and 1.30 ± 0.03 μA to applied potential of 0.1, 0.2, 0.3, 0.4, 0.5 and 0.6 V, respectively.

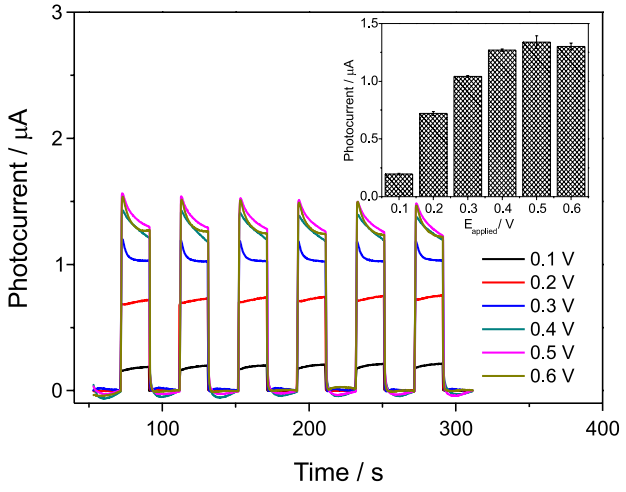

Figure 5. Influence of applied potential on the photocurrent for 100 μmol L^{-1} of adrenaline. Measurements were carried out in 0.1 mol L^{-1} phosphate buffer solution.

As can be seen, the photoelectrochemical response of BEDT-TTF/DNA/TiO_2/ITO to adrenaline showed a high increase until an applied potential of 0.4 V. Therefore, the measurements with the proposed photoelectrochemical sensor were carried out in 0.1 mol L^{-1} phosphate buffer solution at pH 7.0 under an applied potential of 0.4 V *vs.* $Ag/AgCl_{(sat)}$ for all subsequent determinations of adrenaline.

Analytical performance of the BEDT-TTF/DNA/TiO_2/ITO sensor

Figure 6 shows the amperometric response of BEDT-TTF/DNA/TiO_2/ITO sensor under an applied potential of 0.4 V to successive additions of adrenaline into 0.1 mol L^{-1} in phosphate buffer solution (pH 7.0) under light off and on, respectively.

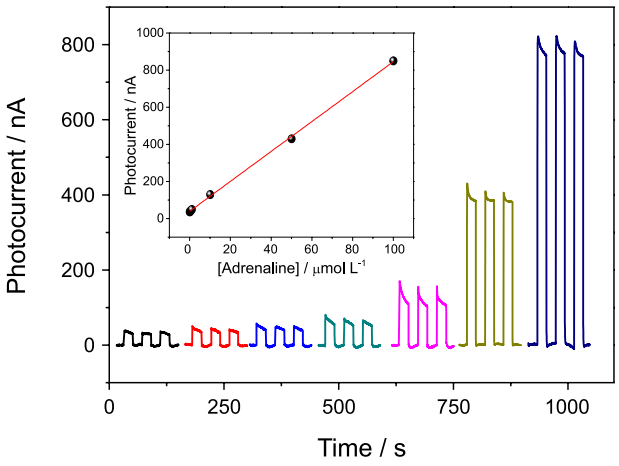

Figure 6. Photocurrent of photoelectrochemical sensor obtained under optimized conditions to adrenaline concentrations between 0.01 and 100 μmol L^{-1}. Inset: analytical curve.

The photoelectrochemical sensor showed a linear response range to adrenaline from 10 nmol L^{-1} to 100 μmol L^{-1}, which can be expressed according to equation 1 (inset of Figure 6):

$$I_{photocurrent}\ (nA) = (25 \pm 3) + (8.1 \pm 0.1)[Adrenaline]\ (\mu mol\ L^{-1})\ (1)$$

with a correlation coefficient of 0.999 (for n = 7).

A detection limit (LOD) of 1 nmol L^{-1} was determined using the equation LOD = 3 σ_{bl}/slope, where σ_{bl} is the standard deviation of the blank response which is obtained from 10 replicate measurements of the blank solution and slope is the sensitivity of the analytical photosensor. The linear range of response and limit of detection were analyzed in comparison to electrochemical sensors to adrenaline reported in the literature (Table 1).[39-51]

As can be seen, the BEDT-TTF/DNA/TiO_2/ITO photoelectroanalytical sensor shows a linear range of response of four orders of magnitude and a limit of detection of 1 nmol L^{-1}, which were as good as the best electrochemical sensors to adrenaline. The precision of measurements using the BEDT-TTF/DNA/TiO_2/ITO photoelectroanalytical sensor was investigated from intra-day and inter-day repeatability studies. The relative standard deviation for 10 determinations of 100 μmol L^{-1} adrenaline carried out in the same working day was 3.0%. The inter-day reproducibility was performed by comparing the analytical response of the photosensor for 10 determinations of 100 μmol L^{-1} adrenaline. The relative standard deviation of photosensor response for adrenaline at ten different days was 5.3%. This set of results indicates a high precision in terms of repeatability and reproducibility of the measurements obtained using the BEDT-TTF/DNA/TiO_2/ITO photoelectroanalytical sensor.

Table 1. Comparison of some analytical parameters of sensors for determination of adrenaline

Electrode	Technique	Linear range / (μmol L^{-1})	LOD / (μmol L^{-1})	Reference
DTT-DDT/AuNP/AuE	CV	0.1-8	0.06	39
Pt-AuNPs/GCE	DPV	63-400	57	40
PtNP/BMI.PF_6/LAC/CPE	SWV	0.99-210	0.29	41
Poly(methyl-Py)/GCE	SWV	0.75-200	0.17	42
P(tau)/GCE	DPV	2-600	0.3	43
PR/PIGE	DPV	3-90	0.8	44
Au/PP/GCE	DPV	0.3-21	0.03	45
PP/MWCNT/GCE	DPV	0.1-8	0.04	46
CHIT/IL/SWCNT/GCE	DPV	1-580	0.09	47
IL/CNT/CPE	DPV	0.3-450	0.09	48
HT/MWCNT/GCE	DPV	0.078-0.2	0.02	49
$CuFe_2O_4$/ILs/CPE	SWV	0.1-400	0.07	50
BDDFE	SWV	0.7-60	0.21	51
BEDT-TTF/DNA/TiO_2/ITO	PEC	0.01-100	0.001	this work

LOD: limit of detection; DTT: dithiothreitol; DDT: dodecanethiol; AuNP: gold nanoparticle; CV: cyclic voltammetry; GCE: glassy carbon electrode; DPV: differential pulse voltammetry; PtNP: platinum nanoparticle; BMI.PF_6: ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphate; LAC: laccase; CPE: carbon paste electrode; SWV: square-wave voltammetry; Poly(methyl-Py): polymethoxyphenol; P(tau): polytaurine; PR: polyrutin; PIGE: paraffin-impregnated graphite electrode; PP: polypyrrole; ; MWCNT: multi-walled carbon nanotube; CHIT: chitosan; ; IL: ionic liquid; SWCNT: single-walled carbon nanotube; HT: hematoxylin; BEDT-TTF: bis(ethylenedithio)tetrathiafulvalene.

In order to evaluate the selectivity of proposed photosensor, the influence of potential interfering agents commonly existing in the human urine was investigated (Figure 7).

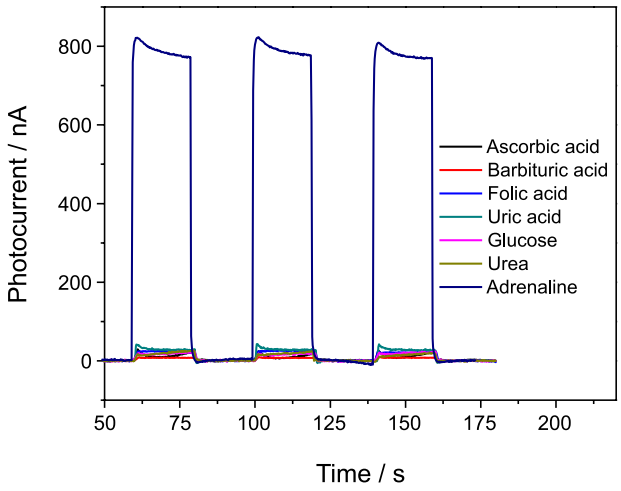

Figure 7. Photocurrent obtained for proposed photoelectrochemical sensor toward several foreign species in comparison to that obtained for adrenaline under optimized conditions at an applied potential of 0.4 V *vs.* Ag/AgCl. The concentration of all species was fixed at 100 μmol L^{-1}.

Thus, the effects of substances frequently found in urine samples, such as ascorbic acid, uric acid, urea, glucose, folic acid and barbituric acid on the response of BEDT-TTF/DNA/TiO_2/ITO photoelectroanalytical sensor were investigated. Solutions of 100 μmol L^{-1} of these compounds were freshly prepared under the same conditions of adrenaline (0.1 mol L^{-1} phosphate buffer solution, pH 7.0) at four different concentrations. The photocurrent response of foreign species was monitored and compared with the signal obtained to adrenaline. The variation in the photosensor response was evaluated by amperometry under dark/light conditions at +0.4 V *vs.* Ag/AgCl. It was interesting to note that high concentrations of these foreign compounds showed very low photoelectrochemical response under the same conditions of adrenaline (Figure 7).

The stability of the photoelectrochemical sensor evaluated by successive measurements of the photocurrent of the BEDT-TTF/DNA/TiO_2/ITO sensor to 100 μmol L^{-1} adrenaline in 0.1 mol L^{-1} phosphate buffer solution at pH 7.0. After 100 measurements the photocurrent shows a decrease of only 6% in respect to the first measurement of the photocurrent.

Application of BEDT-TTF/DNA/TiO_2/ITO photoelectroanalytical sensor in urine samples

The standard addition method was applied for analysis of human urine samples spiked with adrenaline for evaluation of the practical usefulness of proposed photoelectrochemical sensor. The average results of three replicate measurements of adrenaline with the BEDT-TTF/DNA/TiO_2/ITO photoelectroanalytical sensor are summarized in Table 2.

Table 2. Recovery values of adrenaline (ADR) obtained for two urine samples (n = 5)

Sample	[ADR] added / (μmol L^{-1})	[ADR] found[a] / (μmol L^{-1})	Recovery / %
	0	0.032 ± 0.005	–
A	0.5	0.48 ± 0.2	96 ± 0.10
	5	5.30 ± 0.1	106 ± 0.40
	0	0.045 ± 0.009	–
B	10	10.4 ± 0.10	104 ± 0.20
	50	49.2 ± 0.3	98 ± 0.10

[a]ADR found means the total measured ADR minus the founded ADR in non-spiked urine samples.

The recovery values between 96 and 106% using the BEDT-TTF/DNA/TiO_2/ITO photoelectroanalytical sensor indicate that there are no significant interferences of matrix of the human urine as well as that the method is sufficiently accurate and suitable for quantification of adrenaline. Taking into account that the proposed sensor exhibited wider linear response range and lower LOD compared to previously reported electrochemical sensors, it is cost effective and exhibits satisfactory applicability for adrenaline determination. In this sense, the proposed sensor could be directly applied to the determination of adrenaline in urine samples without prior complex sample preparation or separation.

Conclusions

To the best of our knowledge, the present work describes the first photoelectrochemical sensor for determination of adrenaline based on BEDT-TTF/DNA/TiO_2/ITO composite material exploiting visible LED light. The proposed sensor exhibited low limit of detection, wide linear range, high stability and repeatability for the determination of adrenaline. The BEDT-TTF/DNA/TiO_2/ITO photoelectrochemical sensor was able to detect adrenaline at 0.4 V *vs.* Ag/AgCl without the interference of ascorbic acid, uric acid, urea, glucose, folic acid and barbituric acid. In this sense, the BEDT-TTF/DNA/TiO_2/ITO photoelectrochemical sensor is a sensitive, precise, robust and stable sensor for adrenaline determination in urine samples.

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References

1. Zare, H. R.; Ghanbari, Z.; Nasirizadeh, N.; Benvidi, A.; *C. R. Chim.* **2013**, *16*, 287.
2. Tavana, T.; Khalilzadeh, M. A.; Karimi-Maleh, H.; Ensafi, A. A.; Beitollahi, H.; Zareyee, D.; *J. Mol. Liq*. **2012**, *168*, 69.
3. Machida, M.; Miura, S.; Matsuo, K.; Ishikura, H.; Saku, K.; *J. Cardiol.* **2012**, *60*, 503.
4. Goodall, McC.; Stone, C.; Haytens Jr., B. W.; *Ann. Surg*. **1957**, *145*, 479.
5. Szeponik, J.; Moller, B.; Pfeiffer, D.; Lisdat, F.; Wollenberger, U.; Makower, A.; Scheller, F. W.; *Biosens. Bioelectron*. **1997**, *9-10*, 947.
6. Adeniyi, W. K.; Wright, A. R.; *Spectrochim. Acta, Part A* **2009**, *74*, 1001.
7. Bulatov, A. V.; Petrova, A. V.; Vishnikin, A. B.; Moskvin, A. L.; Moskvin, L. N.; *Talanta* **2012**, *96*, 62.
8. Raum, W. J.; *Methods Enzymol.* **1987**, *142*, 550.
9. Gyllenhaal, O.; Johansson, L.; Vessman, J.; *J. Chromatogr. A* **1980**, *190*, 347.
10. Carrera, V.; Sabater, E.; Vilanova, E.; Sogorb, M. A.; *J. Chromatogr. B: Anal. Technol. Biomed. Life Sci.* **2007**, *847*, 88.
11. Li, T.; Wang, Z.; Xie, H.; Fu, Z.; *J. Chromatogr. B: Anal. Technol. Biomed. Life Sci.* **2012**, *911*, 1.
12. Raum, W. J.; *Am. J. Physiol.* **1984**, *247*, E4.
13. Ding, M.; Zhou, Y.; Liang, X.; Zou, H.; Wang, Z.; Wang, M.; Ma, J.; *J. Electroanal. Chem.* **2016**, *763*, 25.
14. Dorraji, P. S.; Jalali, F.; *Sens. Actuators, B* **2014**, *200*, 251.
15. Thomas, T.; Mascarenhas, R. J.; D'Souza, O. J.; Detriche, S.; Mekhalif, Z.; Martis, P.; *Talanta* **2014**, *125*, 352.
16. Zhang, X.; Xu, F.; Zhao, B.; Ji, X.; Yao, Y.; Wu, D.; Gao, Z.; Jiang, K.; *Electrochim. Acta* **2014**, *133*, 615.
17. Shen, Q.; Jiang, J.; Liu, S.; Han, L.; Fan, X.; Fan, M.; Fan, Q.; Wang, L.; Huang, W.; *Nanoscale* **2014**, *6*, 6315.
18. Devadoss, A.; Sudhagar, P.; Terashima, C.; Nakata, K.; Fujishima, A.; *J. Photochem. Photobiol., C* **2015**, *24*, 43.
19. Zhao, W.-W.; Xu, J.-J.; Chen, H.-Y.; *TrAC, Trends Anal. Chem.* **2016**, *82*, 307.
20. Etacheri, V.; di Valentin, C.; Schneider, J.; Bahnemann, D.; Pillai, S. C.; *J. Photochem. Photobiol., C* **2015**, *25*, 1.
21. Okoth, O. K.; Yan, K.; Liu, Y.; Zhang, J.; *Biosens. Bioelectron*. **2016**, *86*, 636.
22. Dahl, M.; Liu, Y.; Yin, Y.; *Chem. Rev.* **2014**, *114*, 9853.
23. Asahi, R.; Morikawa, T.; Irie, H.; Ohwaki, T.; *Chem. Rev*. **2014**, *114*, 9824.
24. Yotsumoto Neto, S.; Luz, R. C. S.; Damos, F. S.; *Electrochem. Commun*. **2016**, *62*, 1.
25. Yotsumoto Neto, S.; Luz, R. C. S.; Damos, F. S.; *Electroanalysis* **2016**, *28*, 1.
26. Wang, Y.; Wang, W.; Wang, S.; Chu, W.; Wei, T.; Tao, H.; Zhang, C.; Sun, Y.; *Sens. Actuators, B* **2016**, *232*, 448.

27. Wei, M.; Wan, J.; Hu, Z.; Peng, Z.; Wang, B.; *Appl. Surf. Sci*. **2016**, *377*, 149.
28. Monteiro, T. O.; Yotsumoto Neto, S.; Damos, F. S.; Luz, R. C. S.; *J. Electroanal. Chem*. **2016**, *774*, 36.
29. Pang, X.; Pan, J.; Wang, L.; Ren, W.; Gao, P.; Wei, Q.; Du, B.; *Biosens. Bioelectron.* **2015**, *71*, 88.
30. Zamfira, L.-G.; Rotariua, L.; Bala, C.; *Biosens. Bioelectron.* **2013**, *46*, 61.
31. Nishida, Y.; Isono, T.; Ueda, A.; Mori, H.; *Eur. J. Inorg. Chem.* **2014**, *24*, 3845.
32. Nishijo, J.; Enomoto, M.; *Inorg. Chem.* **2013**, *52*, 13263.
33. Konuma, T.; Akutagawa, T.; Yumoto, T.; Nakamura, T.; Kawamata, J.; Inoue, K.; Nakamura, T.; Tachibana, H.; Matsumoto, M.; Ikegami, H.; Horiuchi, S.; Yamochi, H.; Saito, G.; *Thin Solid Films* **1998**, *327-329*, 348.
34. Koo, M. H.; Yoon, H. H.; *J. Nanosci. Nanotechnol*. **2013**, *13*, 7434.
35. Wenger, S.; Bouit, P.-A.; Chen, Q.; Teuscher, J.; di Censo, D.; Humphry-Baker, R.; Moser, J. E.; Delgado, J. L.; Martín, N.; Zakeeruddin, S. M.; Gratzel, M.; *J. Am. Chem. Soc.* **2010**, *132*, 5164.
36. Davletbaeva, P.; Falkova, M.; Safonova, E.; Moskvin, L.; Bulatov, A.; *Anal. Chim. Acta* **2016**, *911*, 69.
37. Bavandpour, R.; Karimi-Maleh, H.; Asif, M.; Gupta, V. K.; Atare, N.; Abbasghorbanif, M.; *J. Mol. Liq*. **2016**, *213*, 369.
38. Shen, Y.; Cosquer, G.; Breedlove, B. K.; Yamashita, M.; *Magnetochemistry* **2016**, *44*, 1.
39. Wang, L.; Bai, J.; Huang, P.; Wang, H.; Zhang, L.; Zhao, Y.; *Electrochem. Commun.* **2006**, *8*, 1035.
40. Thiagarajan, S.; Chen, S. M.; *J. Solid State Electrochem*. **2009**, *13*, 445.
41. Brondani, D.; Scheeren, C. W.; Dupont, J.; Vieira, I. C.; *Sens. Actuators, B* **2009**, *140*, 252.
42. Aslanoglu, M.; Kutluay, A.; Karabulut, S.; Abbasoglu, S.; *J. Chin. Chem. Soc*. **2008**, *55*, 794.
43. Wang, Y.; Chen, Z. Z.; *Colloids Surf., B* **2009**, *74*, 322.
44. Jin, G. P.; Chen, Q. Z.; Ding, Y. F.; He, J. B.; *Electrochim. Acta* **2007**, *52*, 2535.
45. Li, J.; Lin, X. Q.; *Anal. Chim. Acta* **2007**, *596*, 222.
46. Shahrokhian, S.; Saberi, R. S.; *Electrochim. Acta* **2011**, *57*, 132.
47. Babaei, A.; Babazadeh, M.; Afrasiabi, M.; *Chin. J. Chem.* **2011**, *29*, 2157.
48. Tavana, T.; Khalilzadeh, M. A.; Karimi-Maleh, H.; Ensafi, A. A.; Beitollahi, H.; Zareyee, D.; *J. Mol. Liq.* **2012**, *168*, 69.
49. Zare, H. R.; Nasirizadeh, N.; *Sens. Actuators, B* **2010**, *143*, 666.
50. Bavandpour, R.; Karimi-Maleh, H.; Asif, M.; Gupta, V. K.; Atar, N.; Abbasghorbani, M.; *J. Mol. Liq*. **2016**, *213*, 369.
51. Sochr, J.; Švorc, L.; Rievaj, M.; Bustin, D.; *Diamond Relat. Mater*. **2014**, *43*, 5.

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