Sensitive detection of dopamine via leucodopaminechrome on polyacrylic acid-coated ceria nanorods

Sensitive detection of dopamine via leucodopaminechrome on polyacrylic acid-coated ceria nanorods

Weiqin Sheng[a,b], Liang Zheng[a], Yan Liu[c], Xueqin Zhao[d], Jian Weng[b]*, and Yang Zhang[a]*

[a]Laboratory for Nanoelectronics and Nano Devices, School of Electronic Information, Hangzhou Dianzi University, Hangzhou 310018, P. R. China

[b]Department of Biomaterials, College of Materials, Xiamen University, Xiamen 361005, P. R. China

[c]Department of Chemistry and Biochemistry, California State Polytechnic University-Pomona, CA 91768, USA

[d]College of Life Sciences, Zhejiang Sci-Tech University, Hangzhou 310018,P. R. China

* Corresponding authors.

E-mail addresses: jweng@xmu.edu.cn (J. Weng); yzhang09@hdu.edu.cn (Y. Zhang).

Abstract

The major hurdle in detection of dopamine (DA) by electro-analysis is the presence of physiological interferents with a similar oxidation potential of DA. The conventional methods are to enlarge the difference of their oxidation potentials. Here, we report an unconventional method to detect DA via leucodopaminechrome on CeO_2nanorods. Leucodopaminechrome is produced from the cyclization of dopamine-quinone, a product of two-electron oxidation of DA. Thus, its concentration is proportional to the DA concentration. Determining DA is demonstrated by measuring the reduction current of leucodopaminechrome on CeO_2 nanorods. CeO_2nanorods demonstrate high electro-catalytic activity for reduction of leucodopaminechrome with a low potential at -0.27V. The low detection potential of leucodopaminechrome can avoid the interference from ascorbic acid (AA) and uric acid (UA).Therefore, detecting DA via leucodopaminechrome is an effective method to avoid the interference from AA and UA, and the suggested biosensor also displays a good reproducibility and stability.

Keywords: ceria nanorods, dopamine, electrodes, biosensors, leucodopaminechrome

1. Introduction

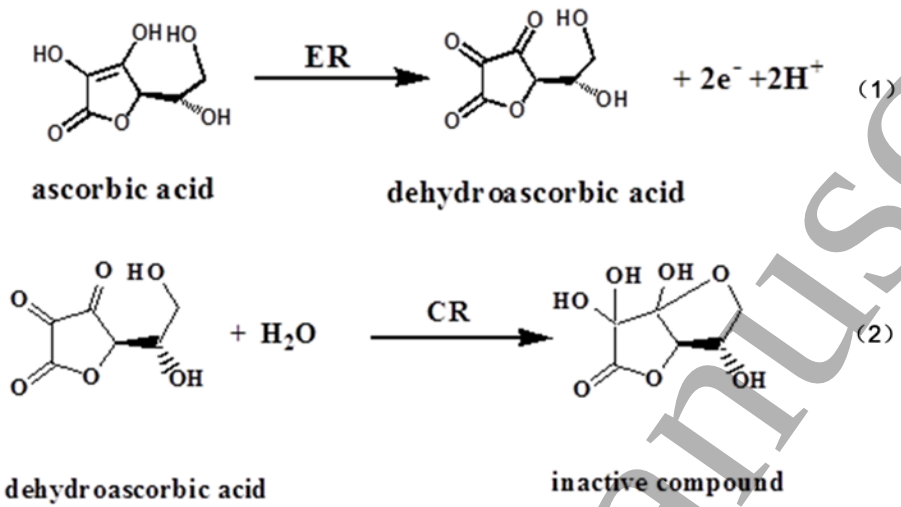
Dopamine (DA) is one of the most significant neurotransmitter, which has a big business with the function of the central nervous, renal, hormonal, and cardiovascular systems[1]. Also, the relative amounts of neurotransmitters are known to be related to a variety of neurological conditions and diseases. Therefore, there are urgent needs for quantification of DA in extra-cellular fluid to monitor neurotransmission processes and diagnose Parkinson's disease[2-4]. So far, there have been several methods to detect DA, such as chemical luminescence, ion chromatography, high performance liquid chromatography, electrochemical, and so on. Above all, electrochemical method is the most popular, because it is rapid, simple, and sensitive in the determination of neurotransmitters, and also the electrodes will be suitable to sense the neurotransmitters in the living organisms. Several methods about electrode pretreatment and electrode modification have been reported to increase selectivity for DA oxidation. For example,

DA can be detected in the presence of ascorbic acid (AA) at Au nanoparticles/polyaniline composite electrodes[5], graphene/MWCNT nanocomposite loaded Au nanoclusters electrodes[6], boron-doped diamond electrode (BDE) electrodes[4,7]. Some negatively charged films, for instance, Nafion, clay, and nanoparticle films, have been reported to attract the cationic DA while effectively rejecting the negatively charged AA and other anionic interfering agents at a physiological pH of 7.4[8-12].

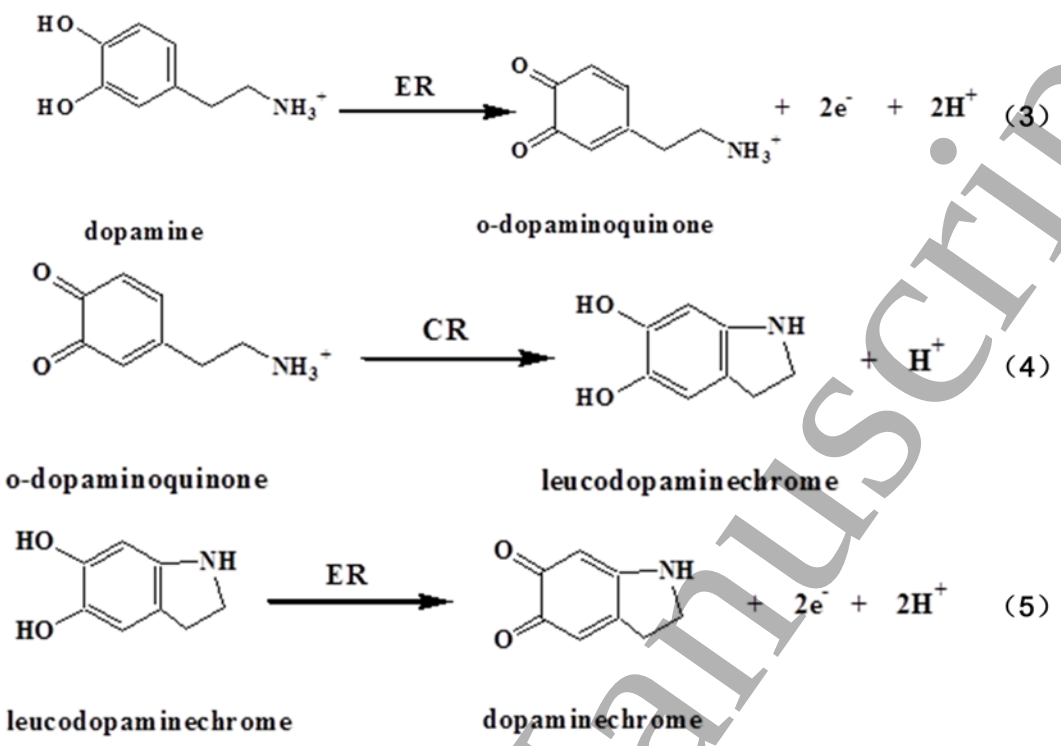
However, DA and AA have a similar oxidation potential at classical electrodes, such as 0.16V and 0.22V on the bare GCE, respectively [4].Usually, different electrodes have been fabricated and modified to determine DA by enlarging the difference of their oxidation potentials[5-12].Although some progresses have been made, the difference in oxidation potential between DA and AA is still small. The potential range of DA and AA would overlap each other. Therefore, it is of great interest to explore a new method to detect DA from AA and other physiological interferents.

As the Equation 1 and Equation2 in scheme 1 depicted, AA is oxidized to dehydro-ascorbic acid which formed an electrochemically inactive compound in water via a ring-closure chemical reaction (CR). For DA, it is first oxidized into o-dopaminoquinone (DOQ) (Equation 3), which then forms leucodopaminechrome via CR (Equation 4), which has been observed at carbon black modified glassy carbon electrode, multi-walled carbon nanotube-poly electrode and so on [4,13-16]. The produced amount of leucodopaminechrome is proportional to the DA concentration. Therefore, it is possible to determine DA indirectly by monitoring the reduction of leucodopaminechrome. Leucodopaminechrome can turn into dopaminechrome (Equation5) at a lower oxidation potential [17-20].The low reduction potential of leucodompaminchrome can avoid the interference from AA and other physiological interferents. However, to date, very few sensor is designed to determine DA through leucodopaminechrome even though there have been only a few researches about the redox reaction of leucodopaminechrome. The possible reason may be the quickly decayed peak current of leucodopaminechrome in continuous voltammetric

scans and weak electrochemical response in neutral solution. Therefore, it remains a challenge to look for new material with high electro-catalytic activity for reduction of leucodopaminechrome at a low potential.



Scheme1. Electrochemical oxidation of AA to form electrochemically inactive compound. Firstly, AA is oxidized to dehydro-ascorbic acid via electrochemical reaction (ER). Then, dehydro-ascorbic acid transforms an electrochemically inactive compound in water via a ring-closure chemical reaction (CR).



Scheme 2. Two steps electrochemical oxidation of DA. Firstly, DA is oxidized into o-dopaminoquinone (DOQ) via electrochemical reaction (ER). Then, DOQ transforms leucodopaminechrome via chemical reaction (CR). Finally, leucodopaminechrome is oxidized into dopaminechrome via electrochemical reaction (ER) at a lower oxidation potential.

CeO_2 is an important n-type semiconductor with a fluoride structure that has been used in heterogeneous catalysis[21-23]. Under a redox environment, cerium might interchange its oxidation state Ce^{3+}/Ce^{4+} and shift between CeO_2 and Ce_2O_3. We can speculate that the excellent catalytic properties of ceria would enhance the redox of leucodopaminechrome to improve the sensitivity for DA detection. Here, ceria nano-materials with different shapes were prepared and used to modify glassy carbon (GC) electrode for monitoring the reduction of leucodopaminechrome. The results indicate that ceria nanorods (NRs) show a higher electro-catalytic activity for leucodopaminechrome reduction than that of ceria nanoparticles (NPs). The low detection potential of leucodopaminechrome at -0.27V can avoid the interference from AA

and UA. At last, selective detecting DA via leucodopaminechrome is demonstrated, and the suggested biosensor also displays a good reproducibility and stability.

2. Experimental

2.1. Materials

Cerium (III) nitrate and $CeCl_3 \cdot 7H_2O$ were bought from Sinopharm Chemical Reagent Company. DA and AA were purchased from Sigma-Aldrich and were used as received. All other chemicals were of analytical grade and used without further purification. All the solutions were prepared with water purified on a Millipore-Q system.

2.2 Synthesis of CeO_2 NPs

CeO_2 NPs were synthesized by hydrothermal process at 180ºC. In typically, a solution containing 0.5 M $Ce(NO_3)_3$ was added to 30.0 ml of ammonium hydroxide solution under continuous stirring, and then sealed tightly in a stainless-steel autoclave. Hydrothermal treatment was carried out at 180 ºC for 24 h. The product was collected by centrifugation, washed with DI water for two times, and dried in vacuum oven at 70 ºC overnight. The dried yellow powders were calcined in air at 400 ºC for 4 h.

2.3 Synthesis of CeO_2 NRs

CeO_2 NRs were synthesized by the hydrothermal process at 100 ºC. Overall, a mixture of NaOH (6M, 20ml) and $CeCl_3 \cdot 7H_2O$ (1 mmol) was stirred at room temperature for 10 min and then sealed tightly in a stainless-steel autoclave. Hydrothermal treatment was carried out at 100 ºC for 24 h. After cooling, the white precipitates were washed with deionized water, and then dried at 70 ºC overnight. At last, the dried yellow powders were calcined in air at 400 ºC for 4 h.

2.4 Characterizations

Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) measurements were conducted using a JEM-2100 transmission electron microscope (JEOL Co. Ltd.) and Leo-1530 scanning electron microscope (JEOL Co. Ltd.), respectively. An X-ray

powder diffractometer (Philips PANalytical X'Pert) equipped with Cu Kα radiation (λ=1.542Å) over the 2θ range of 10-90° was used to characterize the crystalline structure of the CeO_2.

2.5 Electrochemical Experiments

Au and GC electrode were first polished on finer sandpaper, followed by alumina slurry (successively 1.0, 0.3, and 0.05 μm particles) on a polishing pad, with intermediate 5 min sonication in double distilled water between each polishing step. 0.1 mg ml^{-1} of CeO_2 (10μL) and 0.5 M of PAA (1μL) solution were casted on GC electrode, and then dried at room temperature overnight. Electrochemical response was measured on an electrochemical workstation (CHI660E, CH Instrument, USA), constituting a conventional three-electrode system: a bare Au, GC or modified GC working electrode, a platinum wire auxiliary electrode, and a 3.0 M KCl-Ag/AgCl reference electrode. All potentials were reported with respect to this reference. Electrochemical surface area of CeO_2 NRs-modified GC electrode was 0.05 cm^2. DA and AA standard solutions were prepared freshly for daily use. All measurements were taken at room temperature in solutions deoxygenated with N_2 for 15 min. Differential pulse voltammetry (DPV) was performed by using the following parameter: 50 mV amplitude and 4 mV step potential. Square-wave voltammetry (SWV) was employed using the following parameters: 25mV amplitude, 4 mV step potential, and frequency of 15 Hz.

3. Results and discussion

3.1 Synthesis of CeO_2 NPs and NRs

CeO_2 NPs were synthesized by the hydrothermal process at 180 ºC. As indicated in the SEM/TEM images of the prepared CeO_2 NPs (Figure1(a, b)), these particles had almost uniform size and the average size of the particles was measured to be 15 nm. For CeO_2 NRs which were synthesized by the hydrothermal process at 100 ºC, the SEM and TEM images of the as-prepared CeO_2 NRs (Figure1(c, d)) indicated that the transverse diameter of CeO_2 NRs was about 21 nm and the average aspect ratio of these nanorods was around12:1 to 16:1.

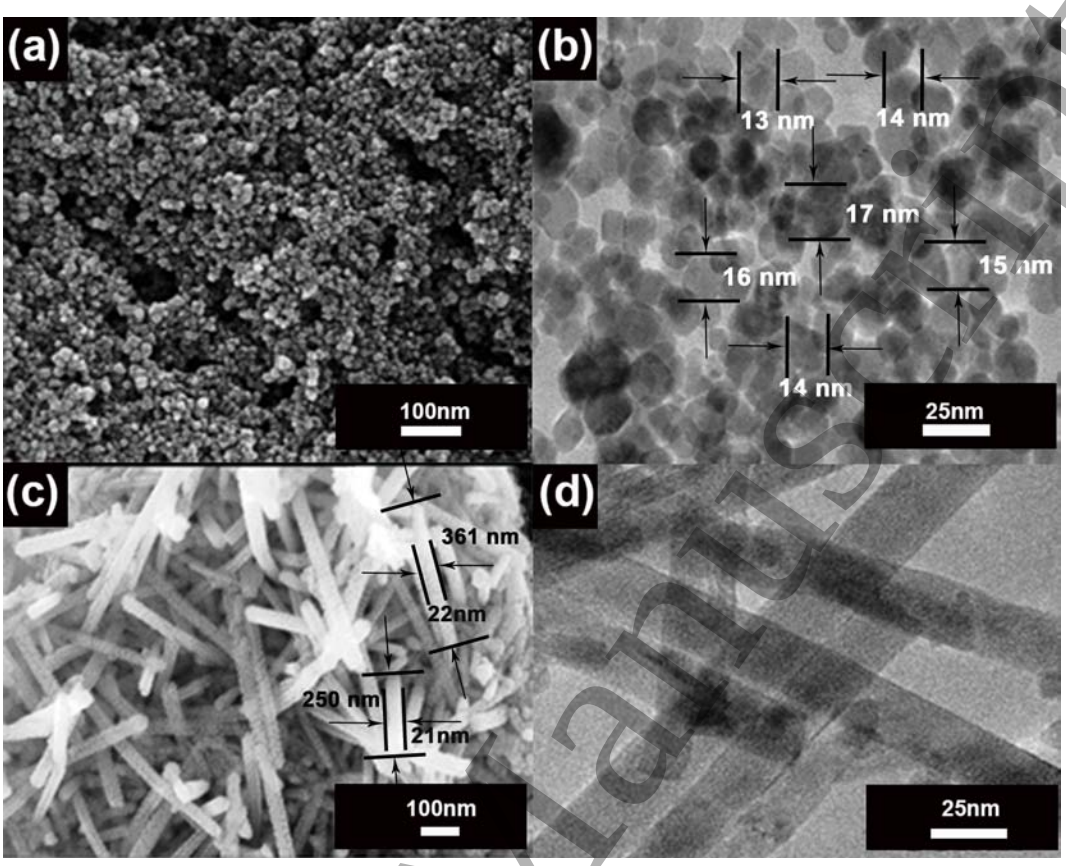


Figure 1. Scanning electron microscopy (SEM) and transmission electron microscopy (TEM)images of the as-prepared CeO_2 NPs (a, b) and CeO_2 NRs (c, d) via hydrothermal method.

Additionally, the X-ray diffraction (XRD) spectroscopy was also used to confirm the structures of as-prepared CeO_2 NPs and NRs (FigureS1 in supporting information). The NPs and NRs had the same XRD patterns, indicating the same crystalline structure of the two products. XRD images showed the presence of (111), (220), (311), and (331) planes, which was an indication of a face-centered-cubic (fcc) crystal[24]. The fcc lattice constant of CeO_2 was calculated to be 5.419 Å, which was in agreement with the value (5.411 Å) tabulated in the JCPD card (NO. 81-0792). Although CeO_2 NPs and NRs had the same size and crystalline structure, different morphologies between the NPs and NRs were observed, resulting in different electro-catalytic activities.

3.2. Electrochemical property of CeO_2 electrode

Electrochemical properties of redox probes such as $[Fe(CN)_6]^{3-}$, $[Ru(NH_3)_6]^{2+}$, and so on, provided a significant information for studying the electrochemical properties of electrode and kinetic barrier of the interface. The extent of kinetic hindrance to the electron-transfer process increased with the increasing thickness and the decreasing defect density of the barrier [25,26]. The electrochemical property of the CeO_2/GC electrode was studied by the cyclic voltammetry (CV) in a phosphate buffer saline (PBS, pH=7.4) containing 5.0 mM $K_3Fe(CN)_6$ and 1M KCl. FigureS2 plotted the CVs for bare GC and CeO_2/GC electrodes in 5.0 mM $K_3Fe(CN)_6$ solution. A symmetric, reversible voltammogram for bare GC with a peak-to-peak separation (ΔEp) of 0.091 V at a scan rate of 100 mV $s^{-1}$was obtained. The similar CVs for CeO_2/GC electrodes were also obtained, but the peak currents decreased and ΔEp increased with the increasing amount of CeO_2, which might result from the fact that CeO_2 was a semiconductor and a large amount of CeO_2 would decrease the conductivity of electrode and hinder electron transfer. However, useful catalytic properties of ceria were attributed to its ability to release or store oxygen in its cubic structure due to a high oxygen mobility at its surface and a large diffusion coefficient of the oxygen vacancy as compared to other metal oxides. Therefore, CeO_2 nanomaterials were good electrode materials and might have a potential application in electrochemical biosensor field.

However, DA and AA have a similar oxidation potential[4], making it difficult to determine DA from AA. Figure2a plotted the DPV curves of DA/AA mixture on the CeO_2 modified GC electrodes and classical electrodes (GC and Au electrodes), showing that the CeO_2 NRs/GC electrode had better oxidation than other electrodes, but the CeO_2 NRs/GC electrode also could not make a difference between DA and AA. However, when the electrodes above were used to determine DA via leucodopaminechrome (Figure2b), the CeO_2 NRs/GC electrode could well different DA from AA with higher catalytic ability than the other electrodes. Above all, ceria nanorods modified electrode would be a better candidate for detecting DA.

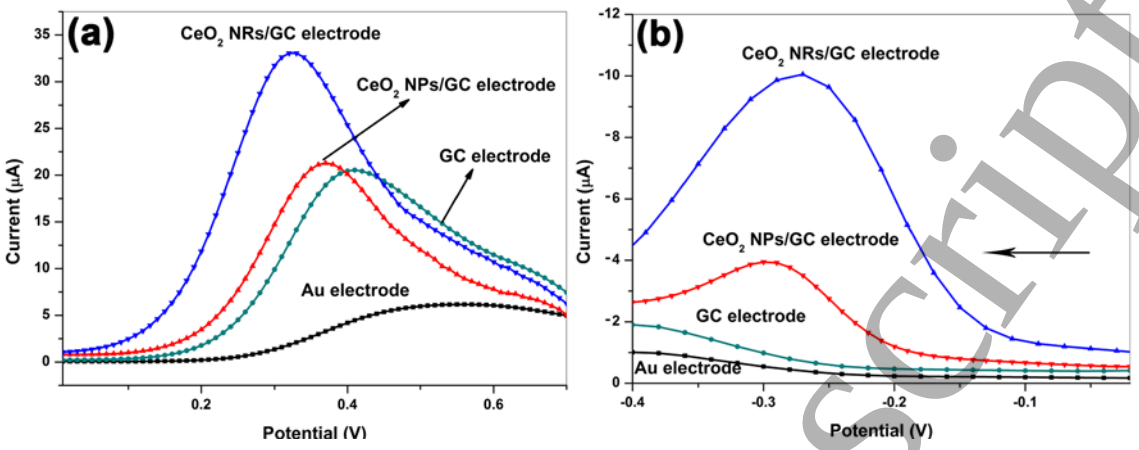


Figure 2.a)DPVs of the mixture of 0.5mM DA and 1mM AA, recorded individually at different electrodes: bare Au electrode, bare GC electrode, CeO_2 NPs/GC electrode and CeO_2 NRs/GC electrode. b) DPVs of leucodopaminechrome, which was produced by prior-oxidation scanning from 0 to 0.6 V for 3 times, recorded individually at different electrodes: bare Au electrode, bare GC electrode, CeO_2 NPs/GC electrode and CeO_2 NRs/GC electrode. Scan rate is 100 mVs^{-1}, the reference electrode is Ag/AgCl and the counter-electrode is platinum wire.

3.3. Determination of DA via leucodopaminechrome on PAA-CeO_2 NRs electrode

3.3.1 The reason of choosing PAA.

In order to further improve the selectivity and sensitivity of CeO_2 NRs/GC electrode for DA determination, PAA was chosen to be casted on the surface of CeO_2 to prepare PAA-CeO_2 NRs/GC electrode. In the pH 7.4 buffer solution, the polyacrylic acid (PAA, pKa 4.75) on the electrode is negatively charged, and able to attract the positively charged DA (pKa 8.9) via electrostatic interactions. When the cycle-voltammetric analysis of DA was carried out, the higher oxidation current of DA was observed at PAA-CeO_2 NRs/GC electrode than that at CeO_2 NRs/GC, shown as FigureS3.

3.3.2 The reason of determining DA via leucodopaminechrome

To minimize the interference from the AA oxidation in the DA analysis, a second-step redox potential was applied to the PAA-CeO_2 NRs/GC electrode. As the Equation 1 and 2 depicted, AA was oxidized to dehydroascorbic acid which formed an electrochemically inactive compound in water via a ring-closure chemical reaction (CR). For DA, it was firstly oxidized into o-dopaminoquinone (DOQ) (Equation 3) which formed leucodopaminechrome via CR (Equation 4). Leucodompaminchrome then turned into dopaminechrome(Equation 5) at a lower potential [17-20,27]. Therefore, the analysis of DA can be differentiated from AA via leucodopaminechrome.

Leucodopaminechrome's oxidation peak was not observed when the electrochemical scan started from -0.4 to 0.4 V (Figure3a), but a new peak at -0.27 V was present when the scan began negatively (Figure3b), which was attributed to the reduction of leucodopaminechrome. The first-step redox potential of DA/leucodopaminechrome was at near 0.16 V and then the redox of leucodopaminechrome/dopaminechrome occurred at about -0.27 V, and meanwhile, AA/dehydroascorbic acid had a redox potential of 0.22V [4].At this time, an idea about detecting DA via leucodopaminechrome came in my heart. In order to confirm the peak at -0.27 V was due to the leucodopaminechrome, two control experiments were carried out.1) PBS in air. 2) PBS with a stream of pure N_2, which was bubbled into the solution for 10 minutes before testing. There was no peak at -0.27 V for PBS in N_2 except a wide peak from 0.1 to -0.2 V for PBS in air, which was attributed to oxygen's reduction (Figure3b). Therefore, the peak at -0.27 V was resulted from leucodopaminechrome. At the same time, CVs of DA and AA further confirmed that DA had a second-step oxidation at lower potential while AA did not (FigureS4). FigureS4b showed that AA and its oxidation product cannot be oxidized at low potential in the potential range of -0.4 to 0 V.

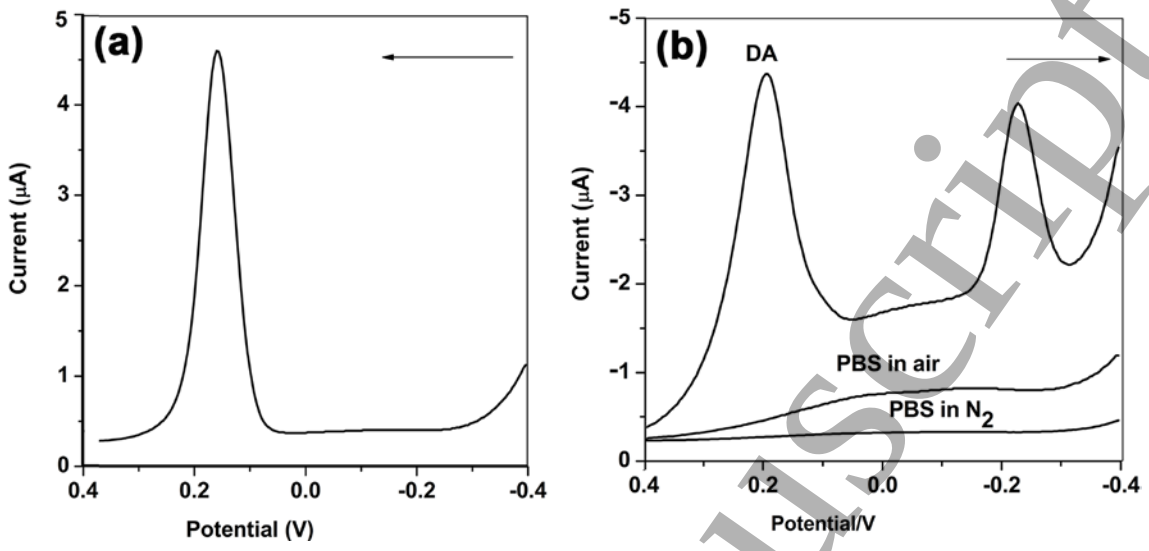


Figure 3.DPVs of 0.1 mM DA at PAA-CeO_2 NR/GC electrode from two different scanning directions: a) scanning from low potential to high potential (-0.4~0.4V); b) scanning from high potential to low potential (0.4~-0.4V).All the scan rate is 100mVs^{-1}, and the reference electrode is Ag/AgCl.

In addition to that, the first cycle of CV curves showed no oxidation peak of leucodopaminechrome, indicating that the fresh DA solution did not contain leucodopaminechrome. Since the original solution did not contain leucodopaminechrome that was produced only by the electrochemical oxidation of DA in the potential range of 0~0.4 V, it was deduced that the leucodopaminechrome's reduction current would increase with the increasing measurements in the potential range of 0 to 0.4 V. Figure4 showed the SWVs of DA by scanning in the different potential ranges for different times. It could be seen that, after only one scan in 0~0.4V (Figure4a), the leucodopaminechrome's reduction current decreased with the increasing scan-times and then the peak completely disappeared (Figure4b). In order to further confirm the fact that the peak at -0.27V was from the redox of leucodopaminechrome/dopaminechrome, the positive scan was carried out for six times (Figure4c), showing the increasing oxidation current of leucodopaminechrome/dopaminechrome. Then, leucodopaminechrome's reduction current decreased gradually again without the first-step

oxidation (Figure4d). The result was expected because DA was oxidized in the potential range of 0~0.4V to form a fixed amount of o-dopaminoquinone after the fifteenth positive scan. The resulted leucodopaminechrome would be reduced at subsequent measurements from 0 to -0.4 V and then result in decreasing reduction current. Therefore, these experiments further confirmed that the peak at -0.27 V was resulted from the leucodopaminechrome's reduction.

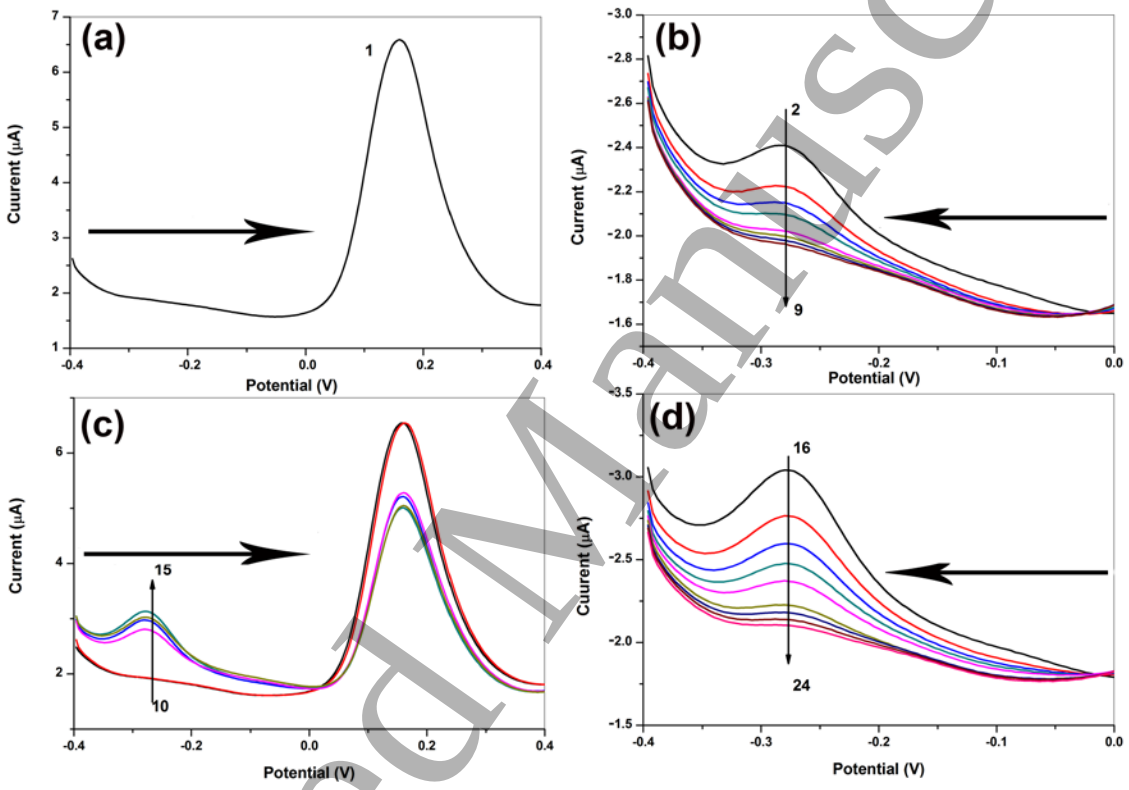


Figure 4.SWVs of 0.1 mM DA at PAA-CeO_2 NRs/GC electrode at different scanning potentials: a) from -0.4 to 0.4 V for 1 time, b) from 0 to -0.4V for 8 times, c) from -0.4 to 0.4V for 6times,and then d) from 0 to -0.4 V for 9 times.All those scan rate is 100mVs^{-1}, and the reference electrode is Ag/AgCl.

3.3.3Confirm the possibility of determining DA according to leucodopaminechrome

In order to further investigate the selectivity of the electrode and the effect of AA on the detection of DA in low concentration, the DPVs of DA with various concentrations (containing 5.0×10^{-5} M AA) were firstly performed from 0 to 0.4V, then the DPV of a mixture of 10^{-4} M DA

and 5.0×10^{-5} M AA was performed at PAA-CeO_2 NRs/GC electrode from 0 to -0.4V, indicating that AA and its oxidation product cannot further undergo redox reaction at lower potential (Figure5). The peak current of the mixture at -0.27V was equal to that of 10^{-4} M DA, indicating that the PAA-CeO_2 NRs/GC electrode could selectively determine DA in the presence of AA.

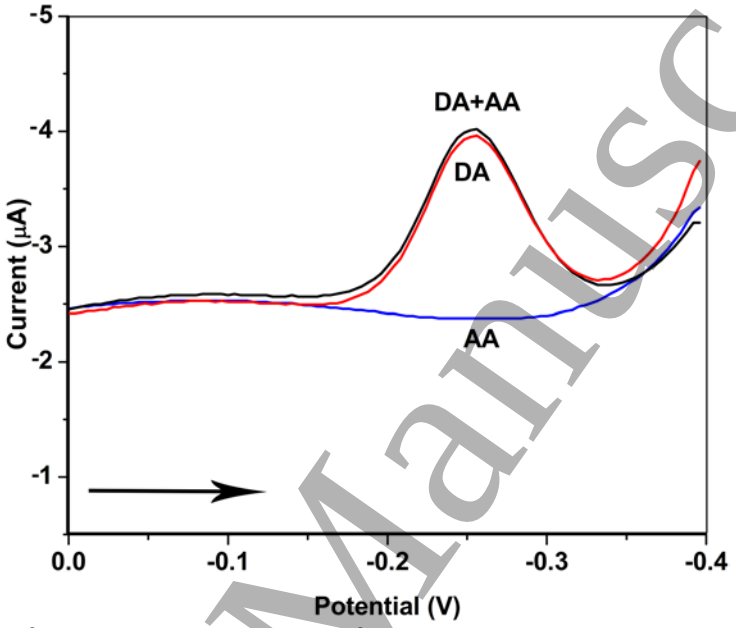


Figure 5.DPVs of DA, AA andmixture of DA/AA at PAA-CeO_2 NRs/GC electrodes after the three pre-oxidations from 0 to 0.4 V. $C_{DA}=1\times10^{-4}$ M, $C_{AA}=5.0\times10^{-5}$M. All the scan rate is 100mVs^{-1}, and the reference electrode is Ag/AgCl.

3.3.4Optimization of PAA-CeO_2 NRs electrode for better detection DA.

As we all know, CeO_2 was a semiconductor and a large amount of CeO_2 would hinder electron transfer and then decrease the electrode's conductivity. So, one of the important keys was to choose the appropriate amount of ceria. According to FigureS5, the optimal concentration of CeO_2 NRs was 0.1 mg ml^{-1}. As a result, the following experiments were carried out with 0.1 mg ml^{-1} CeO_2 NRs on GC electrode.

Determination of DA could be carried out via leucodopaminechrome, which was resulted from the oxidation of DA in the potential range of 0~0.4V. The amount of leucodopaminechrome gradually increased with the increase of scanning times from 0 to 0.4 V. So, the maximum

reduction current of leucodopaminechrome had a big relationship with the number of dopamine's first-step oxidation. FigureS6 showed the reduction current of leucodopaminechrome gradually increased during the first three oxidations (from 0 to 0.4 V),and then the reduction current gradually decreased, which might be the oxidation of leucodopaminechrome (high concentration) by the trace of O_2 in solution even though deoxygenated with N_2. Therefore, the determination of DA via leucodopaminechrome in following experiments was carried out after the oxidation of DA at 0~0.4V for 3 times.

Based on the above results, determination of DA via leucodopaminechrome was carried out with the pre-oxidation at 0~0.4V on the 0.1mg ml^{-1}PAA-CeO_2 NRs/GC working electrode for 3 times. FigureS7 showed the calibration plot of leucodopaminechrome's reduction current as the function of dopamine's concentration in PBS (pH7.4). The calibration curve indicated that the linear relationship between the reduction current and the concentration of DA in the range of 0.01-100 μM with a standard deviation of 4% (linear equation: $y = -0.09 + 0.036\ x$,$R^2 = 0.98$, S/N=2).Furthermore, dopamine and its oxidative products can be adsorbed at many substrates, which is a critical influence for electrode's performance. So, the study about the adsorption of leucodopaminechrome on $CeO_2$was carried out as followed. Firstly, the PAA-CeO_2 /GC working electrode was used to perform DPV in 1mM DA solution from 0~0.4Vfor 3 times; Secondly, the same electrode was used to perform DPV again in PBS solution (pH=7.4) from 0~-0.4V. The corresponding DPV result (Figure S8) did not show any reduction peak, indicating that the leucodopaminechrome was not adsorbed on CeO_2.

3.3.5Reusability and regeneration of PAA-CeO_2 NRs electrode

The reusability of PAA-CeO_2 NRs-modified solid phases in electrochemical analysis was also critical for the evaluation of the biosensor. The consistent value of the peak current for 10 consecutive measurements proved the stability of the PAA-modified CeO_2 NRs electrode (FigureS9). PAA could improve the sensitivity and provided an antifouling effect. The negative -CO_2^- groups of PAA pre-concentrated the cationic DA and excluded anionic AA; this was similar

to the effect observed for Nafion-coated electrodes, which had been used for many years because Nafion enhanced sensitivity and selectivity. PAA was easier to prepare or commercially available in lower costs than Nafion. The peak current decreased after 10 measurements, which might be due to desorption of PAA or CeO_2 NRs from the electrode surface.

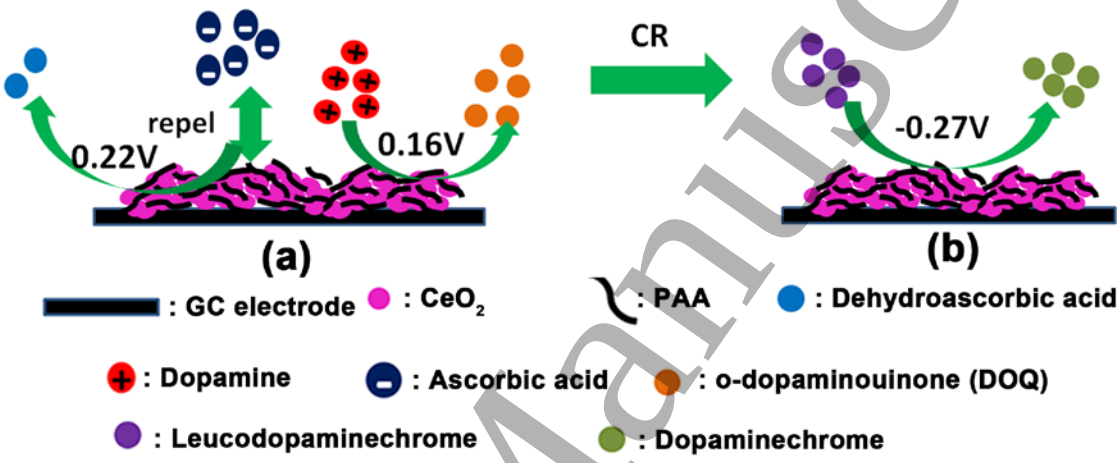
Furthermore, regeneration of the electrode was also studied by the procedures as followed. Firstly, PAA-CeO_2 NRs were removed and cleaned from the GC electrode surface by polishing with 0.3 and 0.05 μm alumina slurry on a Buehler polishing cloth. Secondly, the electrode was sonicated in a water bath for 15 min, and coated with PAA-CeO_2 NRs again. Lastly, the modified electrode was used to determine DA again. As shown in FigureS10, the electrode-to-electrode reproducibility of sensor response with RSDs < 5% variability, and the repeated runs on the same electrode were reproducible with relative standard deviations (RSDs) < 4%.Good regeneration of the PAA-CeO_2 electrode could decrease the cost of electrode fabrication, which was an advantage over those microelectrodes.

In addition to that, the pH effect for the reduction of leucodopaminechrome at PAA-CeO_2 NR/GC electrode was also studied. Figure S11 showed the DPVs of 1 mM DA with different pH in the potential range of 0 ~ -0.4V after scanning from 0 to 0.4V for 3 times at PAA-CeO_2 NRs/GC electrode. Although pH 8.15 was better for the oxidation of leucodopaminechrome at PAA-CeO_2 NR/GC electrode, we still chose pH 7.4, because pH 7.4 was more nearly with the real sample environment and the detecting result was not too worse than that at pH 8.15.

3.4. Possible mechanism for determination of DA via leucodopaminechrome

As illustrated in scheme 3, the possible mechanism for determination of DA via leucodopaminechrome on PAA-CeO_2 NRs was as followed. Firstly, in buffer solution (pH 7.4), the PAA on the electrode was negatively charged, and able to attract the positively charged DA via electrostatic interactions, and simultaneously, AA with negative charge was repelled by electrostatic repulsion, resulting more DA molecular adsorbed on PAA-CeO_2 NRs electrode. Secondly, in the potential range of 0~0.4V, the adsorbed DA on PAA-CeO_2 NRs electrode was

electrochemically oxidized into DOQ (as depicted in Equation 3), which then formed leucodopaminechrome via CR. The formed leucodopaminechrome then underwent further electrochemical reduction at -0.27V. Meanwhile, AA only had one oxidation at 0.22V, as depicted in Equation1 and Equation 2. Finally, the determination of DA from AA via leucodopaminechrome on PAA-CeO_2 NRs electrode was successfully achieved.



Scheme 3. Scheme model of DA attraction and first-step oxidation on a negative PAA-CeO_2 NRs electrode from 0 to 0.4 V (a) and indirect detection of DA by measuring the reduction of leucodopaminechrome from 0 to -0.4 V (b).

3.5Interference of uric acid (UA)

Except AA, another physiological interferent, UA, also have similar potential, resulting in overlap of voltammetric responses [28-30]. When the volume ratio of DA:UA is 5:5 ([DA]=1 mM, [UA]= 4 mM), the corresponding DPV (Figure6a) showed that traditional detecting methods could not detect DA and UA together with only one single oxidation wave. However, when the DA detecting was carried out via leucodopaminechrome, PAA-CeO_2 NRs/GC electrode showed high sensitive detection of DA. According to Figure 6b, the reduction current of leucodopaminechrome increased with the increasing volume ratio of DA/UA from 0/10 to 10/0.

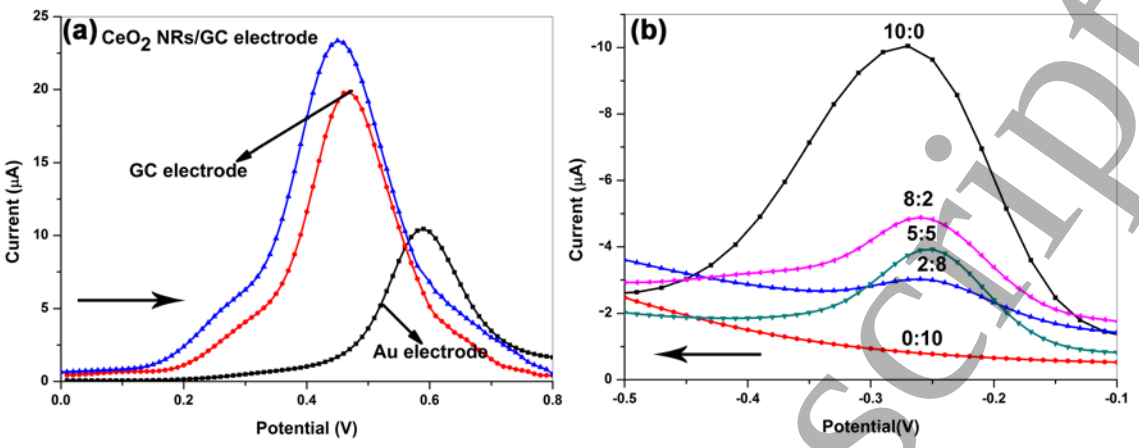


Figure 6.a)DPVs of the mixture of 1mM DA and 4mM UA, recorded individually at different electrodes: bare Au electrode, bare GC electrode and CeO_2 NRs/GC electrode. b) DPVs of leucodopaminechrome, which was produced by prior-oxidation scanning from 0 to 0.4 V for 3 times. The volume ratio of 1 mM DA to 4 mM UA increased from 0:10 to 10:0.All scan rate is 100 mV/s, the reference electrode is Ag/AgCl and the counter-electrode is platinum wire.

4. Conclusions

In this work, CeO_2 NPs and NRs were successfully prepared via hydrothermal process, and then used to modify GC electrode to detect dopamine from the interferents of ascorbic acid and uric acid. Detection of dopamine was carried out by an unconventional method - detection via leucodopaminechrome, effectively avoid the interference of ascorbic acid, uric acid and other bio-molecules. Here, this indirect way of detection works because the redox peaks of leucodopaminechrome are at -0.27V at CeO_2 NRs/GC electrode, significantly lower than that of other bio-molecules. It was also demonstrated that CeO_2 can be used as a potential electrode and CeO_2 NRs showed higher electrochemical activity than CeO_2 NPs. Additionally, the potential biosensor also displayed a good reproducibility and stability. However, this paper only provided us a new insight to detect DA, and later, we would devote our minds to improve the sensitivity of detecting DA via leucodopaminechrome in real samples.

Acknowledgements

The authors thank the fund (ZX150204307002/007) of Hangzhou Dianzi university and Natural Science Foundation of Zhejiang Province (LY17F010021) for support of this work.

References

[1]Wightman RM, May LI and Michael AC1988 *Anal. Chem.***60**7 69A

[2]Patil PG and Turner DA 2008 *Neurotherapeutics* **5** 137

[3]Berger TW, Baudry M, Brinton RD, Liaw JS, Marmarelis V, Park AY, Sheu BJ and Tanguay A 2001 *Proc. IEEE* **89** 993

[4]Jiang LY, Nelson GW, Abda J and Foord JS 2016 *ACS Appl. Mater. Interfaces* **8** 28338

[5]Chu WY, Zhou Q, Li SS, Zhao W, Li N and Zheng JW 2015 *Appl. Surf. Sci.***353** 425

[6]Abdelwahaba AA and Shimb YB 2015 *Sens. Actuators B* **221** 659

[7]Weng J, Xue JM, Wang J, Ye JS, Cui HF, Sheu FS and Zhang QQ 2005 *Adv. Funct.Mater.***15** 639

[8]Kawagoe KT, Zimmerman JB and Wightman RM 1993*J. Neurosci, Methods* **48** 225

[9]Lacroix M, Bianco P and Lojou E1999 *Electroanalysis* **11** 1068.

[10]Zen JM and Chen PJ 1997*Anal. Chem.***69** 5087

[11]Yuan S and Hu S 2004 *Electrochim. Acta.***49** 4287

[12]Poh WC, Loh KP, Zhang WD, Sudhiranjan T, Ye J -S and Sheu F-S 2004 *Langmuir* **20** 5484

[13]Zhao YF, Gao YQ, Zhan DP, Liu H, Zhao Q, Kou Y, Shao YH, Li MX, Zhuang QK and Zhu ZW 2005 *Talanta* **66** 51

[14]Yogeswaran U and Chen SM 2007 *Electrochim.Acta* **52** 5985

[15]Zhou X, Zheng N, Hou SR, Li XJ and Yuan ZB 2010 *J. Electroanal. Chem.***642** 30

[16]Luczak T 2008 *Electrochim.Acta* **53** 5725

[17]Hawley MD, Tatawawadi SV, Piekarski S and Adarns RN 1967 *J. Am. Chem. Soc.***89** 447

[18]Hawley MD and Feldberg SW 1966 *J. Phys. Chem.***70** 3459

[19]Adarns RN, Hawley MD and Feldberg SW 1967*J. Phys. Chem.***71** 851

[20]Forzani ES, Rivas GA and Solís VM 1997 *J.Electroanal. Chem.* **435** 77

[21]Du XJ, Jiang D, Chen SB, Dai LM, Zhou L, Hao N, You TY, Mao HP and Wang K 2017 *Biosens Bioelectron* **89** 681

[22]Carrettin S, Concepción P, Corma A, López Nieto JM and Puntes VF 2004 *Angew. Chem. Int. Ed.***43** 2538

[23]Xu LJ and Wang JL, 2012 *Environ. Sci. Technol.***46** 10145

[24] Si R and Flytzani-Stephanopoulos M 2008 *Angew. Chem. Int. Ed.***47** 2884

[25]Liu AH, Wei MD, Honma I and Zhou HS 2006 *Adv. Funct. Mater.***16** 371

[26]Bard AJ and Faulkner LR 2001 *Electrochemical Methods: Fundamentals and Applications* 2nd ed. (New York:Wiley)

[27]Ismail I, Okajima T, Kawauchi S and Ohsaka T 2016 *ElectrochimicaActa* **211** 777

[28]Ernst H and Knoll M 2001 *Anal Chim Acta* **449** 129

[29]Zhu LD, Tian CY, Zhai JL and Yang RL 2007 *Sens. Actuators B* **125** 254

[30]Huffman ML and Venton BJ 2008 *Electroanalysis* **20** 2422