Poly(3,4-Ethylenedioxythiophene) Derivatives with Electrochemical Chiral Sensor for 3,4-Dihydroxyphenylalanine Discrimination

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Abstract—Two chiral poly(3,4-ethylenedioxythiophene) (PEDOT) derivatives, poly(N-(tert-butoxycarbonyl)-L-phenylalanyl (3,4-ethylenedioxythiophene-2'-yl)methylamidine) (PEDOT-Boc-Leu) and poly(L-phenylalanyl (3,4-ethylenedioxythiophene-2'-yl)methylamidine) (PEDOT-Leu) modified electrodes were used to recognize 3,4-dihydroxyphenylalanine (DOPA) enantiomers by square wave voltammetry (SWV) and cyclic voltammetry (CV) in sulphuric acid solution. It was amazing that the SWV peak currents of enantiomers were found to be quite different and hence the enantiomers could be successfully recognized. However, no obvious difference was observed by the method of CV. Satisfactory results implied that the obtained polymer films could play crucial roles in the development of practical value and analytical application prospects.

Keywords—chiral poly(3,4-ethylenedioxythiophene); dihydroxyphenylalanine enantiomers; recognize; square wave voltammetry

I. INTRODUCTION

3, 4-Dihydroxyphenylalanine (DOPA) is an important neurotransmitter biosynthesized naturally in humans by tyrosinase catalyzed oxidation of tyrosine in a melanin biosynthetic pathway, and by tyrosine hydroxylase in brain for catecholamine neurotransmitter biosynthesis. It also plays an important role in adhesive and cross-linking property of mussel adhesive proteins [1]. On the other hand, DOPA has also been incorporated into proteins by in vitro protein synthesis and solid-phase peptide synthesis [2]. However, DOPA has L- and D- two kinds of configurations due to the particularity of DOPA structure, and the difference for the performance of different configuration is very big. L-DOPA has been widely used in the treatment of Parkinson's disease for more than forty years and it plays a very crucial role in clinic and neurochemistry [3-5]. On the contrary, D-DOPA is inactive and has toxic properties [6, 7]. Owing to different metabolisms of the active and inactive components, using racemic mixtures containing D- and L-DOPA may cause serious side effects [8, 9]. Therefore, the study of chiral recognition of DOPA enantiomers is very necessary. Many methods have been reported to identify enantiomers. These included high-performance liquid chromatography (HPLC) [10-13], capillary electrophoresis (CE) [14-17], electrokinetic chromatography (EKC) [18-19], and microchip electrophoresis (MCE) [20, 21]. Most of these analytical methods deployed ultraviolet (UV) detection that lacked sensitivity and the capability of peak identification. In comparison with these methods, electrochemical methods, which have advantages of low cost, high speed and high sensitivity, are always regarded as the lowest cost effective for the discrimination of DOPA.

poly(3,4-ethylenedioxythiophene) (PEDOT) is one of representatives and highly promising conducting polymers with versatile properties such as high electrical conductivity, low band gap, good redox activity, thermal stability, long-term stability, and excellent transparency in the doped state [22]. Also PEDOT is applied in a variety of areas, such as electrolytic capacitors [23], ITO substitution [24], antistatic coatings [25, 26], organic solar cells [27, 28], electrochromics [29-31], and so on. Chiral PEDOT is a member of PEDOT family, which has attracted considerably widespread interest due to its fascinating properties. Importantly, to the best of our knowledge, the study of using the property of chiral PEDOT for the recognition of chiral drugs still remains blank.

In this work, two PEDOT derivatives, poly(N-(tert-butoxycarbonyl)-L-leucyl(3,4-ethylenedioxythiophene-2'-yl)methylamidine) (PEDOT–Boc–Leu) and poly(L-leucyl(3,4-ethylenedioxythiophene-2'-yl)methylamidine) (PEDOT–Leu), were electropolymerized (Scheme 1). A simple and fast procedure was used for the fabrication of electrodes with chiral PEDOT–Boc–Leu and PEDOT–Leu. The obtained electrodes were used to identify of DOPA enantiomers by methods of cyclic voltammetry (CV) and square wave voltammetry (SWV). The peak currents for the enantiomers were found to be different from each other when D- and L-DOPA were detected by square wave voltammetry (SWV). Hence, the combination of SWV with chiral PEDOT–Boc–Leu and PEDOT–Leu showed the chiral discrimination ability for DOPA.
II. EXPERIMENTAL

A. Materials

Enantiomerically pure 3,4-dihydroxyphenylalanine (DOPA, 99%), L-Leucine (99%), trifluoroacetic acid (TFA, 99%), and sulfuric acid (H₂SO₄, 98%) were purchased from Aladdin Chemistry Co. Ltd. Dichloromethane (CH₂Cl₂, AR; Tianjin Damao Chemical Reagent Factory) was purified by distillation over calcium hydride before use. Tetra-n-butylammonium hexafluorophosphate (Bu₄NPF₆, 99%; Acros Organics) was dried under vacuum at 60 °C for 24 h before use. N-(tert-butoxycarbonyl)-L-leucyl(3,4-ethylenedioxythiophene-2’yl)-methylamide (EDOT–Boc–Leu) and L-leucyl(3,4-ethylenedioxythiophene-2’yl)methylamide (EDOT–Leu) were prepared in accordance with Duan et al. [32].

B. Fabrication of sensor

The glassy carbon electrode (GCE) with a diameter of 3 mm served as the working electrode, and two Pt wires with a diameter of 0.5 mm were used as the counter electrode and the reference electrode. The counter electrode was carefully polished with abrasive paper (1500 mesh). The GCE was polished with alumina (Al₂O₃, 0.05 μm). Then, the counter electrode and the GCE was ultrasonically cleaned in turn with deionized distilled water, ethanol, and deionized distilled water each for 5 min, respectively. Then, they were dried in air before the experiment. Three electrodes in the cell were placed 5 mm apart during electrochemical measurements. To fabricate a sensor, a GCE was used as the working electrode, a platinum wire as an auxiliary electrode and a saturated calomel reference electrode (SCE). The PEDOT–Boc–Leu film was performed by the chronoamperometry (I-t) method at 1.6 V prepared in CH₂Cl₂–Bu₄NPF₆ (0.10 M) containing 0.01 M EDOT–Boc–Leu at room temperature in a one-compartment three-electrode cell. And the PEDOT–Leu film was performed by the I-t method at 0.75 V in CH₂Cl₂–Bu₄NPF₆ (0.10 M) containing 5% TFA and 0.01 M EDOT–Leu in a one-compartment three-electrode cell. The obtained PEDOT–Boc–Leu and PEDOT–Leu modified GCE were washed repeatedly with CH₂Cl₂ to remove the electrolyte and monomer, and dried in air.

III. RESULTS AND DISCUSSION

A. Application of chiral discrimination

The electrochemical behaviours of the enantiomeric pairs (D- and L-DOPA) were studied by CV and SWV, respectively. There is no apparent Faradic response of DOPA at the bare glassy carbon electrode (GCE) in 0.25 mol L⁻¹ H₂SO₄ containing 0.5μmol L⁻¹ L-DOPA (dashed line) or D-DOPA (solid line). This result might due to the concentration of samples too low to be detected for the bare GCE. As shown in Figure 1A, when the GCE was modified by chiral PEDOT–Boc–Leu, a pairs of significant redox peaks were observed in the CV curves owing to two-electron-two-proton oxidation and reduction of DOPA/dopa quinone in this system [9].

Also, the modified of chiral PEDOT–Leu only showed one peak (Figure 1B), and this result might attribute to the amino of PEDOT–Leu. Thus D- and L-DOPA cannot be recognized with the CV technique in the same system. It was presented that the sensitivity of PEDOT–Boc–Leu and PEDOT–Leu modified GCEs is better than bare GCE in the same situation. Theoretically, more modification favours the enantioselective effect. But they may decrease the electrochemical response and had a bad effect on the sensor stability. Frequency was an important parameter to the electrochemical response, and it also was optimized in Figure 2. In addition, different results emerged using the SWV technique in 0.25 mol L⁻¹ H₂SO₄ containing 0.5μmol L⁻¹ L-DOPA (A and C) or D-DOPA (B and D). Square wave voltammetry: step height, 0.004 V; frequency, 5Hz (c), 10Hz (b), 15 Hz (a).
Boc-Leu are -31.5 and -39.1 μA, and the peak currents for PEDOT-Leu are -2.6 and -2.1 μA corresponding to D- and L-DOPA respectively with a reverse scan. The peak current values for PEDOT-Boc-Leu of enantiomers are two times larger than the peak current values for the PEDOT-Phe of enantiomers either in the forward or reverse scanning. So the difference in SWV peak currents may be sufficient to enable an accurate determination of the enantiomeric purity and composition of the DOPA analyte [9].

In 0.25 mol L⁻¹ H₂SO₄ containing 0.5μmol L⁻¹ L-DOPA (dashed line) or D-DOPA (solid line), the DOPA enantiomers showed different SWV behaviours and thus enabled the sensor to convert the enantioselective recognition event into current changes. Basically, DOPA in the solution should exchange electrons with the GCE electrode after passing through the recognition layer. The peak current values for PEDOT-Boc-Leu were larger than PEDOT-Leu’s, and this result may be attributed to the special structure of PEDOT-Boc-Leu, which might accelerate the electron transfer rate between PEDOT-Boc-Leu and DOPA in the solution. The electrochemical activity of DOPA was so good that the enantiomers cannot be distinguished by using common linear sweep voltammetry due to similar peak currents. Consequently, extending the interaction time between the DOPA enantiomers and chiral PEDOT-Boc-Leu and PEDOT-Leu was a key point to success. The waveform of SWV was a staircase scan, each tread of which was superimposed by a symmetrical double pulse, one in the forward direction and the other in the reverse (Figure 3). When SWV was applied in this case, the DOPA enantiomers may pass through the chiral selectivity zone in a manner of oscillation, which would effectively extend the retention time. Each waveform scan made such an interaction time increase a little. After many cycles, the enantioseparation was finally amplified and thus the enantiomers were discriminated. In other words, SWV made limited recognition sites reused, which greatly increased the efficiency of chiral recognition. Meanwhile, PEDOT-Boc-Leu and PEDOT-Leu also acted as bidirectional switches, so the peak currents of D- and L-DOPA were different with different potential scanning directions.

IV. CONCLUSION

In this study, chiral PEDOT–Boc–Leu and PEDOT–Leu modified electrodes were prepared by a simple electrochemical method and used to distinguish DOPA enantiomers with the help of sulphuric acid. DOPA enantiomers were successful identified by chiral PEDOT–Boc–Leu and PEDOT–Leu modified electrodes, and SWV played a significant role in this sensing strategy. The features of the approach were simplicity, rapidity and sensitivity. The method played a vital role for the chiral recognition of various biomolecules.

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