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Chirality detection of amino acid enantiomers by organic electrochemical transistor

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ABSTRACT

Chiral recognition of α-amino acids is attracting increasing interest due to the importance of α-amino acids in protein metabolism as well as in food products and pharmaceuticals. Organic electrochemical transistors (OECTs) with gate electrodes modified with molecularly imprinted polymer (MIP) films were fabricated and successfully used as highly selective and sensitive chiral recognition biosensors for D/L-tryptophan (D/L-Trp) and D/L-tyrosine (D/L-Tyr). The MIP films, which can specifically recognize and has an electrocatalytic effect on the oxidation of Trp and Tyr, together with the amplification function of an OECT, provide a highly sensitive and selective OECT biosensor. The sensor showed a linear response range for L-Trp and L-Tyr from 300 nM to 10 μM with a sensitivity of 3.19 and 3.64 μA/μM, respectivity. And the detection limit for L-Trp and L-Tyr is of 2 nM and 30 nM (S/N > 3). The selectivity factors of L-Trp, D-Trp, L-Tyr and D-Tyr to their enantiomers are 11.6, 3.5, 14.5 and 2.6, respectively. This method can pave the way for widespread applications of OECT-based sensors in chiral material identification.

1. Introduction

Amino acids are important components in the chemical and biological system. However, only L-amino acids have biological activity and are allowed to as foods and pharmaceutical supplement, whilst the related D-forms may have different biological or physiological properties and they may not be metabolized efficiently or can even result in untoward effects on living. So the presence of D-amino acids in food and pharmaceutical can lead to nutritionally poorer and less safe products. Therefore, chiral recognition of α-amino acids is very important (Liu et al., 2015; Sanchez-Hernandez et al., 2016; Zhao et al., 2016). Many techniques have been developed for recognition and analysis of α-amino acid enantiomers, such as high-performance liquid chromatography (HPLC) (Alajmi et al., 2016), nuclear magnetic resonance (NMR) (Li et al., 2006; Nieto et al., 2012), ultraviolet visible spectroscopy (UV–vis) (Ingole et al., 2016),circular dichroism (CD) (Zhao et al., 2016), fluorescence spectroscopy (Peng et al., 2015) and electrochemical sensors (Liu et al., 2015; Zor et al., 2013; Wang et al., 2016; Gu et al., 2016). However, these methods have several drawbacks such as the requirement for corresponding chiral selection agents, long analysis times, high cost of analysis, low sensitivity and selectivity, higher detection limits and lack of portability. Therefore, it is necessary to explore a simple, rapid, low cost, user-friendly, and high selectivity method.

Organic thin film transistors (OTFTs) have shown huge potential for biological and chemical sensing applications due to their advantages such as high sensitivity, low cost, flexibility and simple fabrication processes (Bernards and Malliaras, 2007; Choi et al., 2011). Organic electrochemical transistors (OECTs) as a type of organic thin film transistors (OTFTs), have demonstrated great potential in bio-sensing applications because of their unique properties such as biocompatibility, simple structures, low cost, and low operation voltages of less than 1 V, which allow them to be operated in an aqueous environment (Tarabella et al., 2012; Liao et al., 2013, 2015b; White et al., 1984). OECTs based on poly(3,4-ethylenedioxythiophene) poly(styrenesulfonate) (PEDOT/PSS) have been applied for sensing of pH

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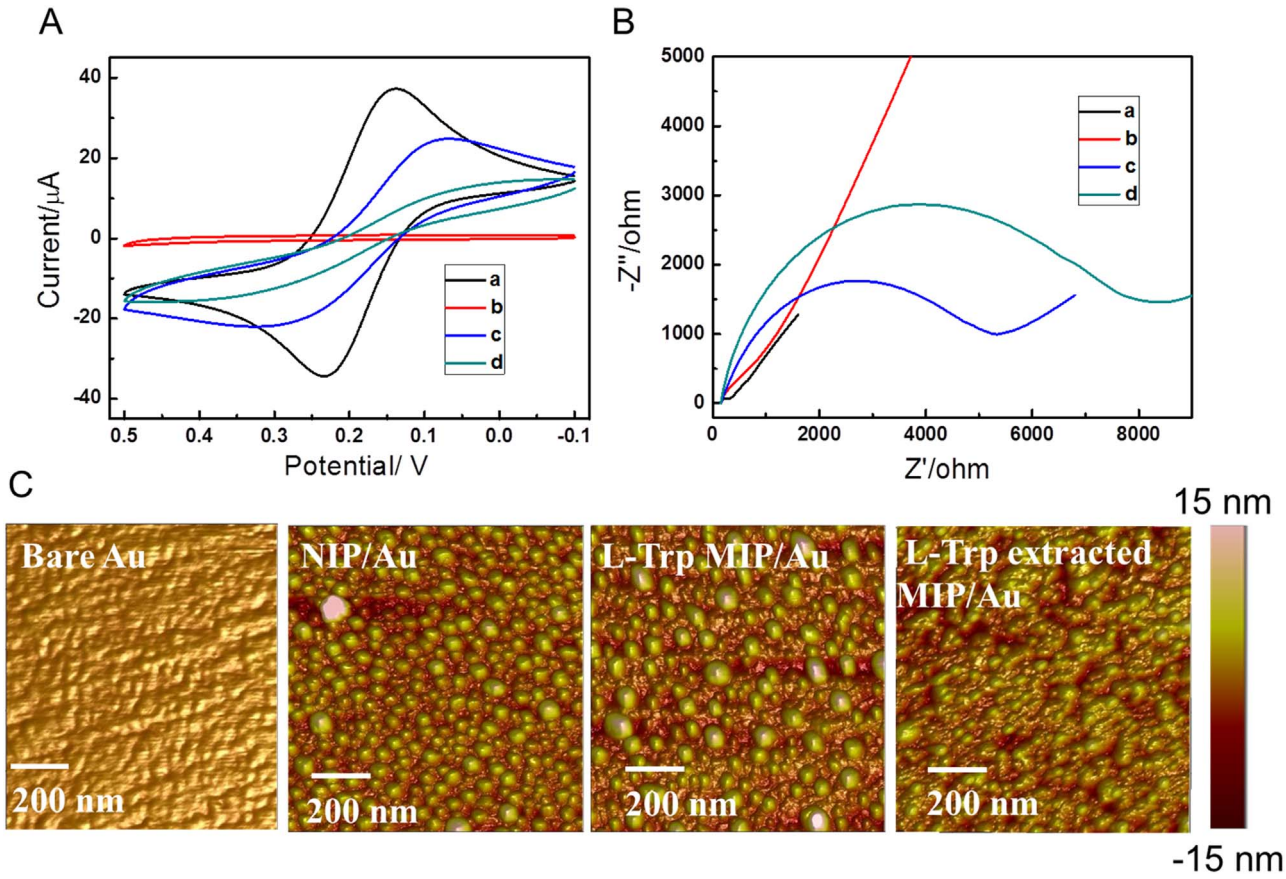

Fig. 1. (A) The CV curves and (B) EIS in 10 mM [Fe(CN)6]; of (a) bare Au, (b) MIP/Au before removal of L-Trp, (c) MIP/Au after removal of L-Trp, (d) MIP/Au after incubation in 10 μM of L-Trp. And C) AFM images of the surfaces of bare Au, NIP/Au, MIP/Au before removal of L-Trp, MIP/Au after removal of L-Trp.

(Thackeray and Wrighton, 1986), humidity (Chao and Wrighton, 1987), ions (Lin et al., 2010a; Sessolo et al., 2014; Isaksson et al., 2007), glucose (Liao et al., 2013; Zhu et al., 2004; Macaya et al., 2007; Kim et al., 2010; J.J. Liao et al., 2015), DNA This method is often used for detecting glucose (Lin et al., 2011), uric acid (Liao et al., 2015a), dopamine (Tang et al., 2011; Liao et al., 2014; Gualandi et al., 2016), bacteria (He et al., 2012), cells (Lin et al., 2010b), epinephrine (Mak et al., 2015), etc. Most of these studies show that the sensitivities of OECT sensors are much higher than those of traditional sensors. Selectivity is another important parameter for OECTs based sensors. Generally, there are three main strategies to realize high selectivity of OECT sensors. The first method is to modify the gate or channel of OECTs by one or more specific enzymes. This method is often used for detecting glucose (Zhu et al., 2004; Macaya et al., 2007; Kim et al., 2010; J.J. Liao et al., 2015), dopamine (Tang et al., 2011; Liao et al., 2014; Gualandi et al., 2016), uric acid (Liao et al., 2015a) and substances which have corresponding oxidases. The second method is to modify the transistor by using selective membranes. For example, K^+-selective sensor was fabricated by integrating a K^+-selective membrane with an OECT (Sessolo et al., 2014). The third method is to use special interactions between the analyte and the modified substances. For example, Yan's group immobilized antibodies on the PEDOT/PSS active layer surface of the OECT to detect E. coli bacteria O157:H7 and modified gate electrodes by single stranded DNA to detect DNA (Lin et al., 2011). However, there are obvious disadvantages to these methods, such as the limited categories of enzymes and selective membranes that can be immobilized and the facile deactivation of enzymes, indicating that the selectivity of OECT is unsatisfactory for widespread applications, especially chiral recognition. Therefore, it is of practical significance to explore new highly selective sensors based on OECT.

Molecularly imprinted polymers (MIPs) are obtained by polymerizing template molecules with functional monomers through non-covalent or covalent bonds and eluting the template molecules. MIPs provide high selectivity for the empty cavities in the polymer structures, which are complementary to the template molecule in size, shape and functionality (Granot et al., 2008; Lautner et al., 2011; Linares et al., 2009). Furthermore, they have many advantages such as durability, low cost, ease of preparation, and stability under harsh conditions. Therefore, MIPs have been used in sensing devices for various applications, such as detection of protein (Linares et al., 2009; Abbas et al., 2013; Dechtrirat et al., 2014), small biological molecules (Fuchs et al., 2014; Jetzschmann et al., 2015), stereo-selective and enantio-selective (Granot et al., 2008; Ouyang et al., 2007), detection of chemical substances (Tiu et al., 2016), and electro-analysis (Qin et al., 2011). We have found that the integration of MIP in OECT was an effective way to improve the selectivity of OECT in ascorbic acid detection (Zhang et al., 2018). But the selectivity of OECT in weak oxidation substance and enantio-selective has not been reported.

In this study, a novel OECT with MIP-modified gate electrode was successfully prepared and used as a sensor for the chiral detection of α-amino acids for the first time. A variety of test methods were used to investigate the selectivity and sensitivity of the modified OECTs, as well as their ability to serve as a sensor for chiral recognition of Trp and Tyr. The electro-catalytic effect of MIP films on the oxidation of L-Trp was also investigated.

2. Experimental

2.1. Chemicals and Reagents

Tryptophan (Trp), tyrosine (Tyr), phenylalanine (Phe), histidine