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Enantioselective recognition of chiral mandelic acid in the presence of Zn(II) ions by L-cysteine-modified electrode

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ABSTRACT

An obviously enantioselective strategy for the recognition of mandelic acid (MA) enantiomers in the presence of Zn(II) ions on a L-cysteine (L-Cys) self-assembled gold electrode is described. The high recognition of MA was evaluated via electrochemical impedance spectroscopy and cyclic voltammetry. After the modified electrode interacted with R- or S-MA solution containing Zn(II) ions for 10 min, larger electrochemical response signals were observed for R-MA. Time dependencies of the enantioselective interaction for the modified electrode with the solitary Zn(II) solution and MA enantiomers solutions containing Zn(II) were also investigated. The results showed that the enantioselective recognition was caused by the selective formation of Zn complex with L-Cys and MA enantiomers. In addition, the enantiomeric composition of R- and S-MA enantiomer mixtures could be monitored by measuring the current responses of the sample.

1. Introduction

Chiral recognition is important in pharmaceutical sciences, drug screening and biological processes because of the high selectivity of chiral molecular species in nature and life [1–6]. Chiral mandelic acid (MA) plays a significant role in the pharmaceutical synthetic industry. For example, R-mandelic acid (R-MA) is used not only as a key intermediate for semisynthetic penicillin and cephalosporin, but also as a chiral resolving agent and chiral synthon for the synthesis of anti-tumor agents [7]. Developing practical, rapid and available methods for the chiral recognition of MA is valuable and fascinating. Various discrimination techniques about MA have been reported, such as diastereomeric crystallization [8,9], high-performance liquid chromatography (HPLC) [10], quartz crystal microbalance (QCM) [11], fluorescence detection [12] and electrochemical detection [13]. And with the advantages of simple operation, rapid detection and low cost, chiral electrochemical sensor have potential applications in pharmaceutical systems and clinic diagnoses [14–17].

Some amino acids were investigated as the selector in chiral electrochemical recognition [11,18]. Owing to amino acids can form metal complexes with metal ions, such as Cu(II), Zn(II) [19,20], the principle of chiral ligand exchange has been used in the recognition and separation of amino acids and their derivatives, especially in chromatography analysis [21–23]. Here we describe a new strategy for highly recognizing target MA enantiomers. The recognition is based on the enantioselective forming metal complexes with MA enantiomers (a chiral α-hydroxy carboxylic acid, which can use as a chiral ligand in the synthesis of chiral drugs [24,25]) and L-cysteine in the presence of Zn(II) ions. Electrochemical impedance spectroscopy (EIS) and cyclic voltammetry (CV) were employed to monitor the enantioselectivity. These stereospecific responses were sensed quickly according to the remarkably different changes in current and impedance responses.

2. Experimental

2.1. Reagent and apparatus

L-Cysteine (L-Cys), R- and S-mandelic acid (R- and S-MA) were purchased from Sigma Chemical Co. (St. Louis, MO, USA). $K_3[Fe(CN)_6]$, $K_4[Fe(CN)_6]$, $Zn(OOCCH_3)_2$ and other chemicals were analytical grade. Double distilled water was used throughout this study.

Electrochemical impedance spectroscopy (EIS) and cyclic voltammetry (CV) measurements were carried out on a CHI 660D electrochemistry workstation (Shanghai Chenhua Instruments Co., China).

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2.2. Preparation of the L-cysteine-modified electrode

First, the gold electrodes ($\Phi = 3$ mm) were polished on microcloth with 1.0, 0.3 and 0.05 μm alumina slurries, and sonicated sequentially in ethanol and water for 5 min each. Subsequently, the electrodes were treated with electrochemical method through three steps [26], (1) applied a positive potential of 2 V to the electrodes for 5 s, and followed by a negative potential of −0.35 V for 10 s, (2) scanned 10 cycles of CV between −0.3 and +1.55 V in 0.5 M H_2SO_4 solution at a scan rate of 1 V s^{-1}, (3) run 10 cycles of CV again in a fresh 0.5 M H_2SO_4 solution with the same potential range at 0.1 V s^{-1}, and rinsed with a copious amount of water. At last, the pretreated electrodes were immediately immersed in the 10 mM L-Cys solution for 12 h at room temperature, and the L-Cys modified gold electrodes (L-Cys-Au) were constructed successfully.

2.3. Experimental measurements

Electrochemical experiments were performed in a three-electrode electrochemical cell containing a working electrode (the modified electrode or bare electrode), a platinum wire auxiliary electrode and a saturated calomel reference electrode (SCE). After the L-Cys-Au electrodes were immersed in 1 ml S-MA or R-MA solution (containing 0.05 mM $Zn(OOCCH_3)_2$, which denoted S-MA + Zn(II) or R-MA + Zn(II), pH 5.5) for a certain time, cleaned carefully with water, then recorded the response signals in 5 mM $[Fe(CN)_6]^{4-/3-}$ solution via CV or EIS techniques. The frequency range of EIS measurements from 0.1 to 10^5 Hz in a given open circuit voltage, amplitude was 0.22 V. The difference of reduction peak current (ΔI) was given by the following equation: $\Delta I = I_0 - I_1$, where I_0 and I_1 were the reduction peak currents before and after the interaction with MA + Zn(II), respectively.

3. Results and discussion

3.1. Determination of the surface roughness

The surface roughness factor (R_f) of the gold electrode plays an important role in the reproducible formation of high-quality self-assembled monolayer on gold electrode [27,28]. R_f is the ratio of real surface area, A_{real} and geometrical surface area, A_{geom} ($R_f = A_{real}/A_{geom}$). Before immersed in the L-Cys solution, the surface roughness of the pretreated electrode was determined by CV using 5 mM $[Fe(CN)_6]^{4-/3-}$ (0.1 M KCl) probe at different scan rates as the redox according to the Randles–Sevcik equation [29,30]

$$I_P = 2.69 \times 10^5 A D^{1/2} n^{3/2} \nu^{1/2} c_0$$

where I_P represents the peak current, n and c_0 refer to the transferring electron number and the concentration of the ferricyanide, D is the diffusion coefficient of the molecule in solution, ν is the scan rate. From the slope of the $I_P \sim \nu^{1/2}$ relation, the average value of the active surface area (average of 3 measurements) for the pretreated gold electrode was 0.0895 cm^2, and R_f was 1.27.

3.2. Characteristics of the L-cysteine-modified electrode

Compared the cyclic voltammograms (CVs) of the L-Cys-Au with bare gold electrode, a little decrease of peak current and minute migration of peak potential were observed. Based on the electrical charge associated with the reductive desorption of L-Cys by CV scanned in 0.5 M KOH, the molecular density of L-Cys on the gold electrode could be calculated as 9.10×10^{-10} mol cm^{-2} according to the literature [31].

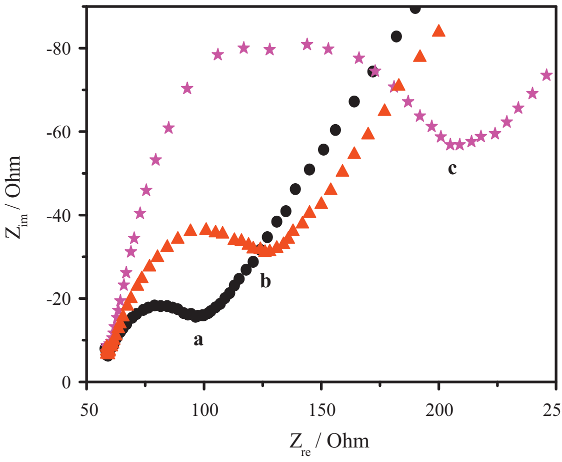

Fig. 1. The electrochemical impedance spectroscopy (EIS) of different electrodes in 5 mM $[Fe(CN)_6]^{4-/3-}$ solution: (a) L-Cys-Au and after L-Cys-Au interacted with (b) 1 ml S-MA + Zn(II) or (c) 1 ml R-MA + Zn(II) solution for 10 min. The concentration of MA was 10 mM, Zn(II) was 0.05 mM.

3.3. Enantioselective recognition of MA in the presence of Zn(II)

EIS is considered to be an effective tool for probing the interface properties of surface-modified electrodes, and widely used to understand chemical transformations and processes associated with the conductive supports [32]. In EIS, the semicircle diameter in the impedance spectrum equals to the electron-transfer resistance, R_{et} [33,34]. This resistance controls the electron transfer kinetics of the redox-probe at electrode interface. Its value changes when different substances are adsorbed onto the electrode surface [35]. Fig. 1 showed the EIS of the enantioselective interaction of L-Cys-Au with MA in the presence of Zn(II). The R_{et} of L-Cys-Au (96.4 Ω) was a little larger than the R_{et} of bare electrode (85.7 Ω), indicating the formation of L-Cys monolayer slightly hindered the electron transfer of $[Fe(CN)_6]^{4-/3-}$ on electrode surface. But the obvious increasing impedance were both exhibited in S-MA + Zn(II) and R-MA + Zn II) (Fig. 1b and c), confirming the occurrence of the interaction between L-Cys-Au and MA enantiomers solutions. More interesting, the impedance of R-MA + Zn(II) ($R_{et} = 209$ Ω) was larger than S-MA + Zn(II) ($R_{et} = 128$ Ω), hinting that the interaction between the modified electrode and R-MA + Zn(II) was stronger, and inducing a larger interfacial resistance on the electrode. It clarified that L-Cys-Au showed highly enantioselective recognition to MA enantiomers in the presence of Zn(II), especially to R-MA.

In the meantime, CV detection was measured. As shown in Fig. 2A, after interacted with S- or R-MA + Zn(II) for 10 min, the peak current of the modified electrode decreased, suggesting that the interaction between L-Cys-Au and S- or R-MA + Zn(II) solution had been introduced a barrier on the electrode surface for electron transfer. And ΔI of R-MA + Zn(II) (ΔI_R) was larger than the ΔI of S-MA + Zn(II) (ΔI_S) too (curves b and c). The average difference of ΔI_R and ΔI_S was 32 μA, and the relative standard deviation (*RSD*) was 3.71%, $n = 6$. The result was consistent with EIS measurements.

In order to explore the effect of Zn(II) in the chiral recognition, the interaction of L-Cys-Au with MA in the absence of Zn(II) was performed as a contrast experiment. From the curves b and c in Fig. 2B, the similar CVs and a little decrease of peak currents for R-MA and S-MA were observed after interacting for 10 min, but the changes of current were less than S-MA + Zn(II). The result emphasized that chiral recognition was not obtained for MA in the absence of Zn(II). Zn(II) was a crucial factor in the enantioselective recognition.