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Sensitive and selective electrochemical detection of artemisinin based on its reaction with *p*-aminophenylboronic acid

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HIGHLIGHTS

- Reaction of artemisinin with aromatic boronic acid has been first reported.
- Reaction of artemisinin with *p*-aminophenylboronic acid generates aminophenol.
- Artemisinin is detected by determining aminophenol with higher sensitivity.
- The method is selective and can detect real samples.
- The method may be extended to detect artemisinin derivatives.

GRAPHICAL ABSTRACT

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ABSTRACT

The electrochemical detection of artemisinin generally requires high oxidation potential or the use of complex electrode modification. We find that artemisinin can react with *p*-aminophenylboronic acid to produce easily electrochemically detectable aminophenol for the first time. By making use of the new reaction, we report an alternative method to detect artemisinin through the determination of *p*-aminophenol. The calibration curve for the determination of artemisinin is linear in the range of 2 μmol L^{-1} to 200 μmol L^{-1} with the detection limit of 0.8 μmol L^{-1}, which is more sensitive than other reported electrochemical methods. The relative standard deviation is 4.83% for the determination of 10 μM artemisinin. Because the oxidation potential of *p*-aminophenol is around 0 V, the present method is high selective. When 40 μM, 90 μM and 140 μM of artemisinin were spiked to compound naphthoquine phosphate tablet samples, the recoveries are 107.6%, 105.4% and 101.7%, respectively. This detection strategy is attractive for the detection of artemisinin and its derivatives. The finding that artemisinin can react with aromatic boronic acid has the potential to be exploited for the development of other sensors, such as fluorescence artemisinin sensors.

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1. Introduction

Malaria is a mosquito-borne infectious disease [1]. It can cause fever, fatigue, vomiting, headaches, yellow skin, seizures, coma, or death [2]. It is widespread in Sub-Saharan Africa, Asia, and Latin America [3,4]. In 2015, there were 214 million cases of malaria and an estimated 438,000 deaths worldwide. Artemisinin and its derivatives possess rapid action against plasmodium falciparum malaria [5–7]. Artemisinin and its derivative (artemisinin-combination therapies, ACTs) are now standard treatment worldwide for plasmodium falciparum malaria and save millions of lives [8,9]. As a result, its discoverer, Youyou Tu, was awarded half of the 2015 Nobel Prize in Medicine.

Several methods have been developed for the determination of artemisinin, such as chemiluminescence [10,11], molecular imprinting sensor [12], and electrochemistry [13–15]. Compared with other methods, the electrochemical method is an especially promising approach due to its high sensitivity, low cost, operational convenient, rapid response, and suitability for real-time detection. However, current electrochemical methods for measuring artemisinin need either complex electrode modification or high positive potentials and have low sensitivity.

In this study, we report a new method for the detection of artemisinin based on the selective oxidation of *p*-aminophenylboronic acid by artemisinin to generate *p*-aminophenol and subsequent detection of as-generated *p*-aminophenol (Fig. 1). Aminophenol is measured at a low potential of 0.045 V [16]. The proposed method shows high sensitivity and selectivity, and thus holds great promise for the determination of artemisinin and its derivatives.

2. Experimental

2.1. Apparatus

Square wave voltammetry was carried out with a CHI 660C electrochemical workstation (Shanghai, China) and CV with CHI 800B electrochemical workstation (Shanghai, China). Three-electrode cell is composed of a glassy carbon (GC) working electrode, a gold wire counter electrode, and an Ag/AgCl (saturated KCl) reference electrode. The working electrode was polished with alumina powder (Al_2O_3, 0.05 μm), ultrasonicated in water bath and rinsed with bidistilled water before measurements.

Fig. 1. Schematic of electrochemical determination of artemisinin based on reaction between artemisinin and *p*-aminophenylboronic acid.

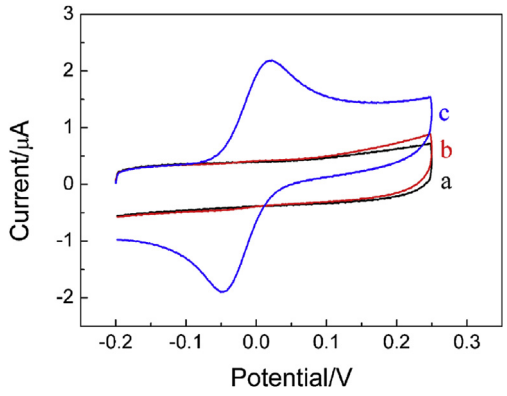
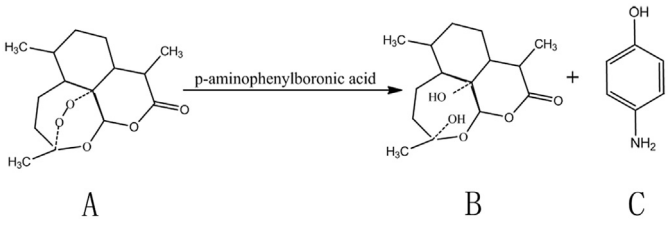


Fig. 2. The cyclic voltammograms of (a) 1 mM artemisinin, (b) 1 mM *p*-aminophenylboronic acid, as well as (c) 5.0 min reaction solution of 1 mM artemisinin and 1 mM *p*-aminophenylboronic acid in 50 mM sodium hydroxide ethanol/water (9/1, v/v) solution mixed with equal volume of pH 7.1 tris-HCl buffer solution. Scan rate: 100 mV/s.



Scheme 1. Reaction equation for the reaction between artemisinin and *p*-aminophenylboronic acid.

2.2. Chemicals and reagents

Artemisinin was purchased from Shanghai TCI Company, and *p*-aminophenylboronic acid was obtained from Beijing Ouhe Technology Company. The compound naphthoquine phosphate tablets were bought from Kunming Pharmaceutical Company, China. The pH of tris buffer solutions (50 mM) was adjusted to 7.1 by adding HCl solution. All other chemicals were of analytical grade and were used as received. The double distilled water was employed for all the electrochemical experiments. The stock solution of artemisinin (5 mM) was prepared in ethanol and the stock solution of *p*-

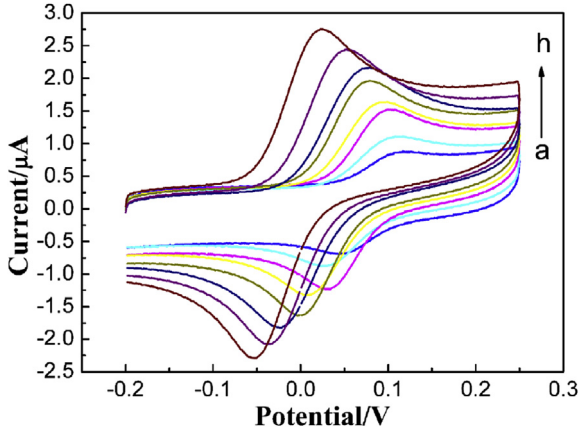


Fig. 3. Cyclic voltammograms at a GC electrode of reaction solutions of 1 mM artemisinin and 1 mM *p*-aminophenylboronic acid mixed with equal volume of pH = 7.1 tris-HCl buffer solution in different concentrations of sodium hydroxide, a) 10, b) 15, c) 20, d) 25, e) 30, f) 40, g) 50, h) 60 mM. Reaction time: 5.0 min. Scan rate: 100 mV/s.