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A simple and sensitive colorimetric method for the determination of propafenone by silver nanoprobe

Ji-chun Qu[a,b], Yan-ping Chang[a,b], Yan-hua Ma[a,b], Jin-min Zheng[a,b], Hong-hong Li[a,b], Qian-qian Ou[a,b], Cuiling Ren[a,b], Xing-guo Chen[a,b,c,*]

[a] *National Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, China*
[b] *Department of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000, China*
[c] *Key Laboratory of Nonferrous Metal Chemistry and Resources Utilization of Gansu Province, Lanzhou 730000, China*

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ABSTRACT

A simple, rapid and ultrasensitive colorimetric method for the determination of propafenone, based on the specific recognition property of propafenone with the unique optical properties of AgNPs, has been developed. The addition of propafenone induced the citrate to be desorbed from the surface of the AgNPs, leading to the aggregation of the AgNPs, accompanied by a dramatic surface plasmon absorption band shift and thereby results in their yellow-to-red even purple color change. The concentration of propafenone can be determined by monitoring with the naked eyes or a UV–Vis spectrophotometer. The detection limit of the present method for propafenone was 2.4 μM. The proposed method is a promising mean for on-site detection of propafenone in actual samples without costly instruments.

1. Introduction

Propafenone (PPF) is one of the most important anti-arrhythmic drugs for ventricular and supraventricular arrhythmias. It is a class Ic antiarrhythmic drug that acts on the Nav 1.5 and KCNH2 (hERG) ion channels and has weak β-blocking effects [1]. The overdose of PPF has been reported to be associated with features of severe seizures [2], cardiovascular and CNS toxicity [3], even with similar life-threatening symptoms in which cardiac features predominate with QRS/QTc prolongation and ventricular arrhythmias [4]. Therefore, the quantification of PPF is usually required in clinical assay. Some analytical methods for the detection of PPF have been established, including LC [5–8], HPLC [9–11] and so on. These methods have the advantages of high sensitivity and good selectivity. However, these protocols, which usually require specialized equipment or complicated procedures, are somewhat laborious, time-consuming, expensive, and unsuitable for real-time detection. Therefore, it is still a challenge to develop a method for expedient, rapid and real-time detection of PPF. Colorimetric sensors, which require minimal instrumentations and make on-site real-time sensing even easier, are free of the above problems.

Metal nanomaterials such as silver nanoparticles (AgNPs) and Au nanoparticles (AuNPs) have been found wide applications as ideal reporters for colorimetric detection owing to their unique optical and electric properties [12–15]. The major advantage of Au/AgNPs-based assays is that the molecular recognition events can be transformed into color changes, which can be observed by the naked eye. Moreover, the extraordinarily high absorption coefficient of Au/AgNPs enables the colorimetric assay to be sensitive. Additionally, AgNPs have shown some unique characteristics and advantages over AuNPs to a certain degree since they possess much higher absorption coefficients than AuNPs of the same size [16,17], which can achieve approximately 100-fold [18,19]. This allows sensitive colorimetric detection with minimal material consumption. More importantly, the cost of the preparation of AgNPs is much lower when compared with AuNPs. On this account, AgNPs have gained more popularity than AuNPs. The dispersed solution of AgNPs is yellow in color, while it will change to red or even purple because of aggregation. Contrary to previous reports, in which citrate is considered to be a “magic” component critically required for the formation of silver nanoparticles, Zhang et al. have determined that the ligands which can selectively adhere to Ag (1 1 1) facets can be expanded to many di- and tricarboxylate compounds whose two nearest carboxylate groups are separated by two or three carbon atoms. They have also found that the widely used secondary ligand can be replaced by many hydroxyl and thiol [20] groups-containing compounds or even removed entirely while still producing nanoparticles of excellent uniformity and

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* Corresponding author at: National Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, China. Tel.: +86 931 8912763; fax: +86 931 8912582.
E-mail address: chenxg@lzu.edu.cn (X.-g. Chen).

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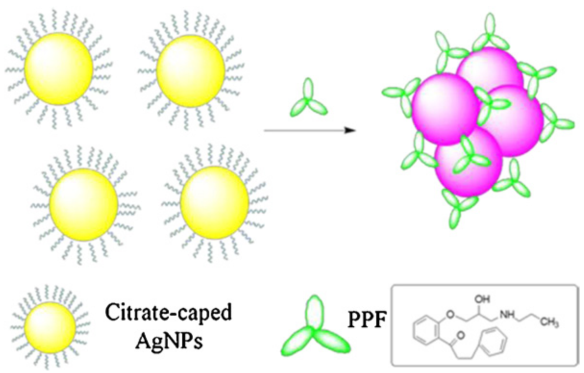

Scheme 1. Schematic illustration of the colorimetric assay for PPF induced the non-crosslinking AgNPs aggregation.

stability [20,21]. Lin et al. have fabricated a facile colorimetric DA (dopamine) biosensor based on the special interaction between DA and AgNPs, in which the stabilizing citrate ions were displaced by the chemisorbed DA and the surface charges were partly neutralized [22]. It is well known that colloidal stability can be adjusted by modifying surface charges and aggregation can be induced due to the loss of surface charges [22–24]. Our strategy was inspired by the probability that the PPF ligands could displace the citrate ions on the AgNPs and the surface charges of the AgNPs would be reduced significantly. As a result, the AgNPs aggregated and the color of the solution changed from bright yellow to red and then purple. Based on this phenomenon, a simple colorimetric assay for PPF was established (Scheme 1). To the best of our knowledge, this method is the first example of using the special interaction between PPF and AgNPs to fabricate a facile colorimetric PPF biosensor with high sensitivity and good selectivity.

2. Materials and methods

2.1. Chemicals

Propafenone hydrochloride was purchased from Sigma–Aldrich. Sodium citrate, silver nitrate ($AgNO_3$, 99%), sodium borohydride ($NaBH_4$, 98%), KCl, NaCl, glucose, lactose and starch were received from Tianjin Guangfu Institute (China). Propafenone hydrochloride tablets were obtained from Shandong Junan Pharmaceutical Ltd. (Shandong, China). All the reagents were of analytical grade and used as received without further purification. The ultra-water prepared using Milli-XQ equipment was used throughout the experiment.

2.2. Apparatus

TEM analysis was performed on a Hitachi-6000 transmission electron microscope (TEM, Japan). UV–Vis absorption spectra were measured on a TU-1901 double beams UV–Vis spectrophotometer (Purkinje General Instrument Co. Ltd., China) with a 1.0 cm path length quartz cuvette. Photographs of the AgNPs suspension used for visual colorimetric detection were captured by a Nikon 4500 digital camera. A pH-3C digital pH meter (Xiaoshan Scientific Instrument Plant, Zhejiang, China) was used to measure the pH values.

2.3. Synthesis of AgNPs

The citrate modified AgNPs (cit-AgNPs) were prepared with modified Creighton method [25,26], which employed sodium citrate as a stabilizer [23]. Briefly, 1.00 mL 50 mM sodium citrate aqueous solution was added into 39 mL 0.64 mM $AgNO_3$ aqueous solution under vigorous stirring. After stirring for 20 min, 0.01 g sodium borohydride (freshly prepared) in 10 mL water was added at room temperature (25 °C) and the dark colloidal silver nanoparticles were produced. During the reaction, the dark colloidal solution changed to bright yellow and the stirring was stopped after 1 h. The prepared AgNPs suspension could be used after 2 h. The AgNPs suspension was stored in the dark under $4.0 \pm 2.0\,^{\circ}C$ to remain stable for several weeks.

2.4. Procedures for the detection of PPF

In a typical experiment for detecting PPF, 20.0 mL of cit-AgNPs was placed in a 100.00 mL volumetric flask and the solution was diluted to 100.00 mL with water and mixed thoroughly. To investigate the effect of pH of the buffer solutions on PPF detection, 0.05 M HCl or NaOH solution was used to adjust the pH. Then, 3.0 mL of the prepared cit-AgNPs aqueous solution and 30.0 μL different amount of PPF were sequentially added into 5.0 mL calibrated test tube to incubate for a certain time, and the absorption spectra of the sensing system with varying concentration of PPF were collected by UV–Vis spectrophotometer.

2.5. Influence of the ionic strength on AgNPs

30 μL PPF (1 mM) with different amount of NaCl (1.0 M) making the ionic strength ranging from 3.66×10^{-3} M to 7.49×10^{-3} M were added into the solution including 600 μL AgNPs (0.5 mM), 2.4 mL distilled water (pH 9.0). The reactions were performed for 20 min at 25 °C, and then the absorbance was measured.

2.6. Detection of the PPF in actual samples

Firstly, three pieces of propafenone hydrochloride tablet were ground to powder and weighed. Secondly, the obtained powder (approximately 210 mg) was immersed in a suitable amount of methanol. Thirdly, the mixture was dispersed under ultrasonication for 30 min and kept for a few hours to ensure that the PPF was extracted completely from the sample. Then, the mixture was centrifuged and the supernatant containing PPF was collected, which was spined to dryness by a rotary evaporator. Finally, the obtained PPF powder was further dissolved with water, making sure the final concentration of PPF in the solution was within the working range. In order to further explore the practicality of the proposed colorimetric method, standard addition method was applied to detect PPF. To confirm the accuracy of the present procedure, recovery test was also investigated.

This method was also applied to urine samples for the determination of PPF. For this purpose the urine of a healthy female volunteer was precipitated to obtain the clear yellowish urine sample after centrifuging at 3000 rpm for 15 min. The recovery of PPF was determined by standard addition method. Three different levels of PPF concentration (10, 20, 25 μM) were added into the sample, respectively, and three replicates were performed at each level for measurement. These samples were diluted with a ratio of urine to distilled water of 1:6. Then 30 μL of the diluted urine was added into the solution containing 600 μL AgNPs (0.5 mM), and 2.37 mL distilled water (pH 9.0). The reactions were carried out at 25 °C for 20 min. After the reactions, we measured the absorbance of the solution by using a TU-1901 double beams UV–Vis spectrophotometer.