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An aptamer-based fluorescence bio-sensor for chiral recognition of arginine enantiomers

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ABSTRACT

In this study, a novel aptamer - based fluorescence bio-sensor (aptamer-AuNps) was developed for chiral recognition of arginine (Arg) enantiomers based on aptamer and gold nanoparticles (AuNps). Carboxyfluorescein (FAM) labeled aptamers (Apt) were absorbed on AuNps and their fluorescence intensity could be significantly quenched by AuNps based on fluorescence resonance energy transfer (FRET). Once D-Arg or L-Arg were added into the above solution, the aptamer specifically bind to Arg enantiomers and released from AuNps, so the fluorescence intensity of D-Arg system and L-Arg system were all enhanced. The affinity of Apt to L-Arg is tighter to D-Arg, so the enhanced fluorescence signals of L-Arg system was stronger than D-Arg system. What's more, the enhanced fluorescence were directly proportional to the concentration of D-Arg and L-Arg ranging from 0–300 nM and 0–400 nM with related coefficients of 0.9939 and 0.9952, respectively. Furthermore, the method was successfully applied to detection L-Arg in human urine samples with satisfactory results. Eventually, a simple "OR" logic gate with D-Arg & L-Arg as inputs and AuNps aggregation state as outputs was fabricated, which can help us understand the chiral recognition process deeply.

1. Introduction

Chiral recognition of biomolecules and drugs have attracted tremendous attentions. It's well known that most chiral drugs existed in the form of racemic mixture; however, because of the specific recognition and toxicological activities, sometimes only a single enantiomer is non-poisonous and medicable for human. For example, R-thalidomide has the medicable function while S-thalidomide has the toxic properties [1]. Most natural amino acids exist in the bio-organism are L-amino acids and most carbohydrates are D-carbohydrates, that is to say only L-amino acids and D-carbohydrates are nutritious to human body. Consequently, simultaneous determination of chiral enantiomers is pretty vital in clinical research and pharmacy industry.

Arg is a kind of chiral amino acid, which existed in the form of D-Arg or L-Arg. The ball-and-stick model and subtle structure difference of D/L-Arg were shown in Fig. 1. L-Arg was involved in the ornithine cycle in human body, played a role in turning ammonia into non-toxic urea and reducing the concentration of blood ammonia [2]. For infants, L-Arg counts for much during their growing process because infants are unable to synthesize or create internally, but for most adults, L-Arg is not essential because their body can produce enough. Consequently, L-Arg is defined as essential or nonessential amino acid depending on the healthy conditions of people [3]. A precious research claimed that Arg breakdown will highlight the early stages of dementia disease in mice. Arg is also supplied to correct the acid and alkali balances in hepatic encephalopathy because of its rich hydrogen ions. If infants are severe deficiency of Arg, they will be troubled by cardiovascular, pulmonary, neurological and intestinal dysfunction [4,5]. Thus, establish a simple, rapid, low cost and highly selective method for the detection of Arg enantiomers is significant important. Up to now, many methods have been applied to detection chiral enantiomers, such as high-performance liquid chromatography (HPLC) [6–8], gas/liquid chromatography-mass spectrometry (GC/LC-MS) [9,10], fluorescence spectrometry [11,12], electrochemistry [13,14], and immunoassays [15]. Among these methods, HPLC, electrochemistry and GC/LC-MS need complicated pretreatment and require expensive chiral columns. Therefore, sensitive and simple methods have been strongly required.

Since discovered in 1990 [16], aptamers have attracted much attention. Aptamer is a new type of single-strand DNA (ssDNA) or RNA oligonucleotides, selected in vitro through Systematic Evolution of Ligands by Exponential enrichment (SELEX) [17,18]. In addition, aptamers have high selectivity which derived from their specific hairpin structure, therefore, aptamer can distinguish between similar compounds with

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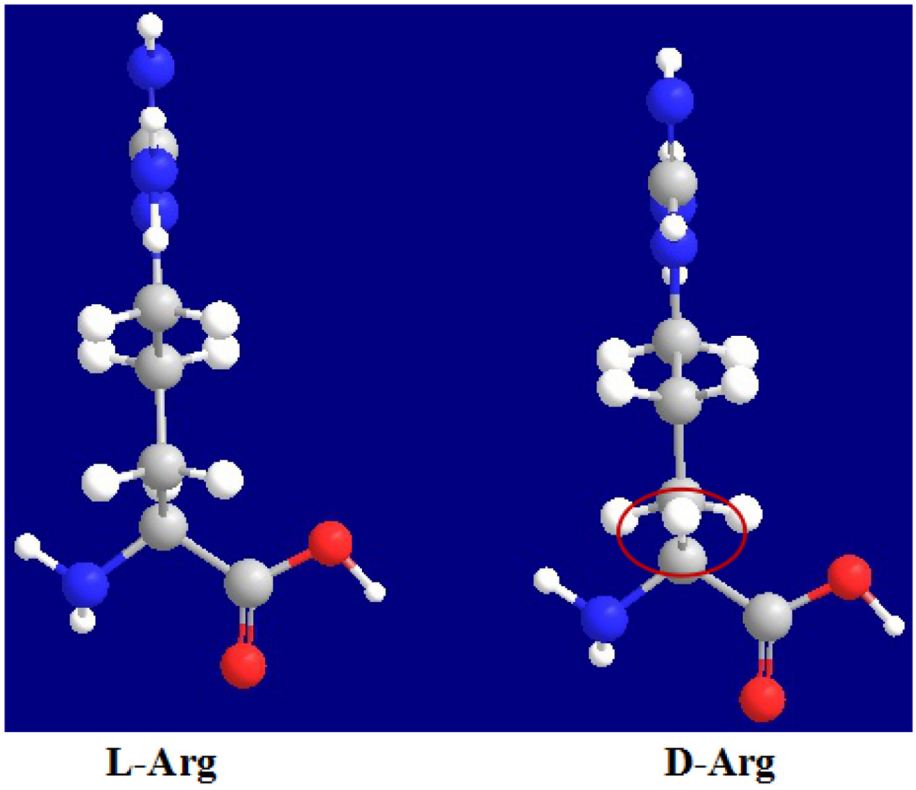

Fig. 1. The ball-and-stick model of Arg.

only subtle structure difference [19,20]. For example, Michael Famulok et al. [21] reported that the RNA aptamer had an affinity to L-Arg and bound 12,000 bold tighter than to its enantiomer, D-Arg. The recognizing process of aptamer is similar to the antibodies but in terms of high stability, low-cost, easy synthesis and flexible chemical labeling, aptamers are better than antibodies. Aptamer are utilized as various sensors, according to the differences of signals obtained, aptasensors are divided into eletrochemical [22,23] optical [24] and mass-sensitive [25]. For example, Citartan Marimuthu and their workers used electrochemical aptasensor for chiral recognition of S-naproxen from R-naproxen. Yuan Huo, Xin Lv had established fluorescence and colorimetry methods based on optical aptasensors [26,27]. Zhi-Qi Zhang et al. [28], Shulin Yang et al. [29] developed a DNA aptasensor for the colorimetric detection of adenosine triphosphate, arginine vasopressin and omethoate, respectively. Shuhao Wang et al. [30] reported a florescence signals off-on aptasensor for fluorescent detection of ochratoxin A based on the quenching effect of gold nanoparticles and showed a linear range from 25 nM to 300 nM. Erkang Wang [31] and their workers developed a fluorescent indicator for D-arginine vasopressin detection. In 2005, Arg - specific aptamer was first screened out through SELEX [32]. To the best of our knowledge, there almost no research reported about simultaneous detection of chiral Arg enantiomers based on aptamer-AuNps biosensor.

Gold nanoparticles (AuNps) were widely used in chemical and biological detection because of their outstanding advantages, including extremely high extinction coefficients, strong size, distance-dependent

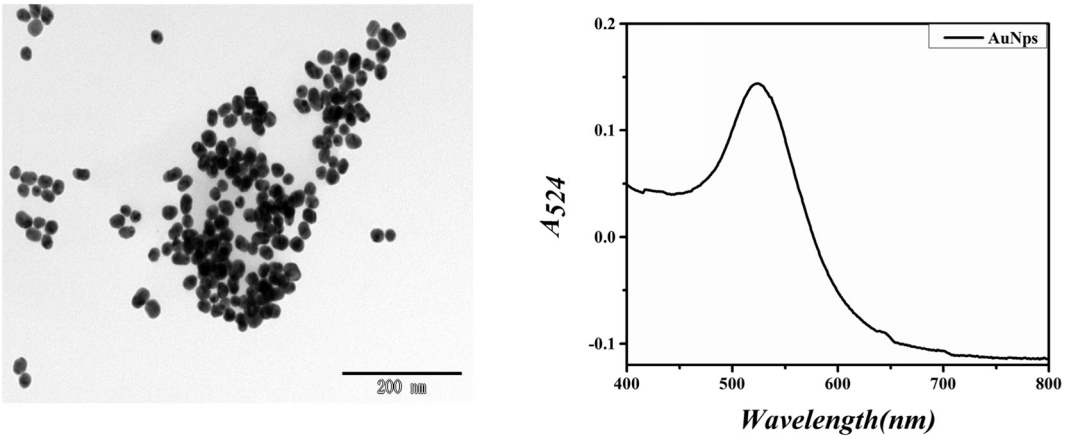

Fig. 2. (A) The TEM image and (B) UV–vis absorption spectra of AuNps in 50 μL Tris-HCl buffer solution at pH = 7.2.