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RESEARCH PAPER

A novel fluorescent biosensor for adrenaline detection and tyrosinase inhibitor screening

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Abstract

In this work, a novel simple fluorescent biosensor for the highly sensitive and selective detection of adrenaline was established. Firstly, water-soluble $CuInS_2$ quantum dots (QDs) capped by L-Cys were synthesized via a hydrothermal synthesis method. Then, the positively charged adrenaline was assembled on the surface of $CuInS_2$ QDs due to the electrostatic interactions and hydrogen bonding, which led to the formation of adrenaline-$CuInS_2$ QD (Adr-$CuInS_2$ QD) electrostatic complexes. Tyrosinase (TYR) can catalyze adrenaline to generate H_2O_2, and additionally oxidize the adrenaline to adrenaline quinone. Both the H_2O_2 and the adrenaline quinone can quench the fluorescence of the $CuInS_2$ QDs through the electron transfer (ET) process. Thus, the determination of adrenaline could be facilely achieved by taking advantage of the fluorescence "turn off" feature of $CuInS_2$ QDs. Under the optimum conditions, the fluorescence quenching ratio I_f/I_{f0} (I_f and I_{f0} were the fluorescence intensity of Adr-$CuInS_2$ QDs in the presence and absence of TYR, respectively) was proportional to the logarithm of adrenaline concentration in the range of 1×10^{-8}–1×10^{-4} mol L^{-1} with the detection limit of 3.6 nmol L^{-1}. The feasibility of the proposed biosensor in real sample assay was also studied and satisfactory results were obtained. Significantly, the proposed fluorescent biosensor can also be utilized to screen TYR inhibitors.

Keywords Fluorescence biosensor · Adrenaline · Tyrosinase · Inhibitor screening · Quantum dots

Introduction

Adrenaline, secreted by the adrenal medulla, is an important kind of hormone for the message transfer in the mammalian central nervous system. It plays a significant role in promoting glycogenolysis, elevating blood sugar, increasing lipolysis, and causing rapid heartbeat. It is mainly utilized to treat cardiac arrest, bronchial asthma, and anaphylactic shock in clinical medicine. Meanwhile, it is crucial for alleviating the damnification of arthrosis cartilaginous and the pain of osteoarthritis [1, 2]. It exists as an organic cation in the nervous tissue and biological body fluid [3]. Many diseases are closely related to the change of adrenaline concentration in the body fluid. Low level of adrenaline has been found in patients with Parkinson's disease [4, 5]. Therefore, close monitoring and/or quantification of adrenaline in the body fluid is of crucial significance, which is also vital for developing nerve physiology, making diagnoses, and controlling medicines. Up to now, there are many assays for the determination and/or quantification of adrenaline, such as liquid chromatography (LC) [6, 7], electrochemistry [4, 8, 9], capillary electrophoresis (CE) [10, 11], and chemiluminescence [12, 13]. However, most of these methods are limited due to their high cost, generally tedious operation, and even dependence on the pretreatment of extraction or derivatization. Thus, it is still an urgent need to develop a simple, sensitive, and cost-effective method for quantitative determination of adrenaline, which is important in the investigation of the physiological functions of adrenaline in clinical medicine.

Fluorescence strategies have raised increasing concern for biosensors because they offer attractive advantages over other analytical techniques, including their ease and speed of use and high sensitivity [14]. Semiconductor nanocrystal QDs are among the most promising alternatives for fluorescent materials because of their unique electro-optical properties and

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photophysical features [15], such as high quantum yields, long fluorescence lifetimes, large extinction coefficients, higher brightness and stability against photobleaching, and broad absorption spectra coupled with narrow photoluminescent (PL) emission spectra [16, 17]. However, the applications of QDs have been severely hampered owing to the high toxicity of the QDs. To date, the majority of the reports focused on the cadmium-based QDs that are toxic to biological systems, sensitive to heat and chemical and photochemical disturbances, and eventually would cause serious environmental problems due to the leakage of cadmium [18, 19]. In recent years, the newly emerging I-III-VI $CuInS_2$ QDs are particularly impressive because they do not contain any toxic class A elements (Cd, Pb, and Hg) or class B elements (Se and As) [20–23].

With regard to the above, a novel convenient fluorescent biosensor was fabricated for highly sensitive and selective detection of adrenaline based on the toxic heavy metal-free $CuInS_2$ QDs (capped by L-cysteine). Positively charged adrenaline can absorb onto the surface of $CuInS_2$ QDs via electrostatic interactions and hydrogen bonding, forming Adr-$CuInS_2$ QD electrostatic complexes. Tyrosinase (TYR), a copper-containing enzyme, is a typical polyphenol oxidase [24, 25]. Once TYR was introduced into the Adr-$CuInS_2$ QD system, it can catalyze the adrenaline to generate H_2O_2 [26], and additionally oxidize the adrenaline to adrenaline quinone [27, 28]. Both the H_2O_2 and the adrenaline quinone can quench the fluorescence of the QDs. Thus, the determination of adrenaline can be achieved by monitoring the fluorescence"turn off." In addition, the proposed fluorescent biosensor can be employed for the screening of TYR inhibitors.

Experimental section

Chemical and apparatus

All chemicals and reagents were of at least analytical reagent grade and used as-received without any further purification. Copper (II) chloride dehydrate ($CuCl_2{\cdot}2H_2O$), indium (III) chloride tetrahydrate ($InCl_3{\cdot}4H_2O$), sulfourea (CS $(NH_2)_2$), L-cysteine (L-Cys), and parathion-methyl (PM) were purchased from Sigma-Aldrich Corporation. Adrenaline was purchased from Aladdin Industrial Corporation. Adrenaline was purchased from J&K Scientific Ltd. (Beijing, China). Human serum albumin (HSA) was obtained from Sino-American Biotechnology Co. Ltd. Glucose, trypsin (Tyr), sodium chloride (NaCl), sodium hydroxide (NaOH), hydrogen peroxide (H_2O_2), sodium dehydrogenized phosphate (NaH_2PO_4), disodium hydrogen phosphate (Na_2HPO_4), sodium phosphate (Na_3PO_4), and the other chemicals used were all purchased from Beijing Dingguo Changsheng Biotechnology Co. Ltd. The water used in all experiments had a resistivity higher than 18 MΩ cm^{-1}.

Fluorescence measurements were all carried out on a RF-5301 PC spectrophotometer equipped with a xenon lamp (Shimadzu Co., Kyoto, Japan) in a 1-cm path-length quartz cuvette. The fluorescence emission intensity was received from the peak value of the emission spectrum. The step size is 1 nm and the interval time is 1 min for each step of the emission scan. pH measurements were all carried out with a PHS-3C pH meter (Tuopu Co., Hangzhou, China). The hydrothermal synthesis processes were completed in a JCZ-JL intelligent digital display drum wind drying oven. The shaking processes were carried out on a HY-2 variable-speed reciprocal shaker (Guo Hua Electric Appliance Co., Changzhou, China). The ultrasonic processes were carried out on a KQ2200 ultrasonic cleaner (Ultrasonic Instrument Co., Kunshan, China). The centrifugation processes were carried out on a TGL-16G (Anke Technology Instrument Co., Shanghai, China).

Synthesis of $CuInS_2$ QDs

$CuInS_2$ QDs capped by L-Cys were directly synthesized in aqueous solution via a hydrothermal synthesis method according to our previous report [29]. In a typical experiment, L-Cys (3.60 mmol) was dissolved in 7.5 mL distilled water. Then, $CuCl_2{\cdot}2H_2O$ (0.15 mmol) and $InCl_3{\cdot}4H_2O$ (0.15 mmol) were injected into the solution. The pH value of the mixture solution was adjusted to 11.3 by adding 4 mol L^{-1} NaOH solution with stirring. Ten minutes later, CS $(NH_2)_2$ (0.30 mmol) was added into the solution. The Cu-to-In-to-S and Cu-to-L-Cys precursor ratios were 1:1:2 and 1:12, respectively. All the abovementioned experimental procedures were performed at room temperature. Then, the solution was transferred into a 15-mL Teflon-lined stainless steel autoclave. The autoclave was kept at 150 °C for 23 h and then cooled down to room temperature. The final concentration of $CuInS_2$ QDs, as measured by the In^{3+} concentration, was 1.36×10^{-4} mol L^{-1}. The luminescence quantum yield of the prepared $CuInS_2$ QDs was 3.4%, which was higher than that synthesized in organic solvent (QY = 3%) [21].

Adrenaline detection

For adrenaline measurement, 200 μL $CuInS_2$ QD solutions were placed in a series of 2.0-mL calibrated test tubes, respectively. Subsequently, different amounts of adrenaline and 5 μg L^{-1} TYR were separately injected into the above mixtures. Then, the mixtures were diluted to 2.0 mL with pH 7.35 phosphate buffered solution (10 mmol L^{-1}) and mixed thoroughly. Thirty minutes later, the fluorescence spectra of Adr-$CuInS_2$ QD-TYR system were recorded in the 610–800-nm emission wavelength range at an excitation wavelength of 590 nm.

Detection of adrenaline in human serum sample

The fresh human blood samples were supplied by the Hospital of Changchun China, Japan Union Hospital. All the blood samples were drug free and obtained through venipuncture. Some pretreatments to remove impurities are necessary before use in further experiment. After storage for 2 h at room temperature, acetonitrile was added to the blood samples (the volume of acetonitrile and blood was 1.5 to 1). Then, the mixture was centrifuged at 10,000 rpm for 5 min. The obtained supernatants were subjected to a 100-fold dilution and a certain concentration of adrenaline was added to prepare spiked samples, which were detected by the method described above.

The inhibition effect of PM

For TYR inhibition screening, the PM standard substance was dissolved in phosphate buffered solution (10 mmol L^{-1}, pH = 7.35) containing 10% ethanol for preparing the standard solution. Various concentrations of PM and TYR (5.0 μg mL^{-1}) were successively added into a series of 2.0-mL calibrated test tubes and incubated for 10 min, respectively. Then, $CuInS_2$ QDs (13.6 μmol L^{-1}) and adrenaline (0.1 mmol L^{-1}) solution were separately added to the reaction mixture; and the mixed solution was diluted to the mark with phosphate buffered solution (10 mmol L^{-1}, pH = 7.35). Thirty minutes later, the fluorescence spectra of Adr-$CuInS_2$ QD-TYR-PM system were recorded in the 610–800-nm emission wavelength range at an excitation wavelength of 590 nm.

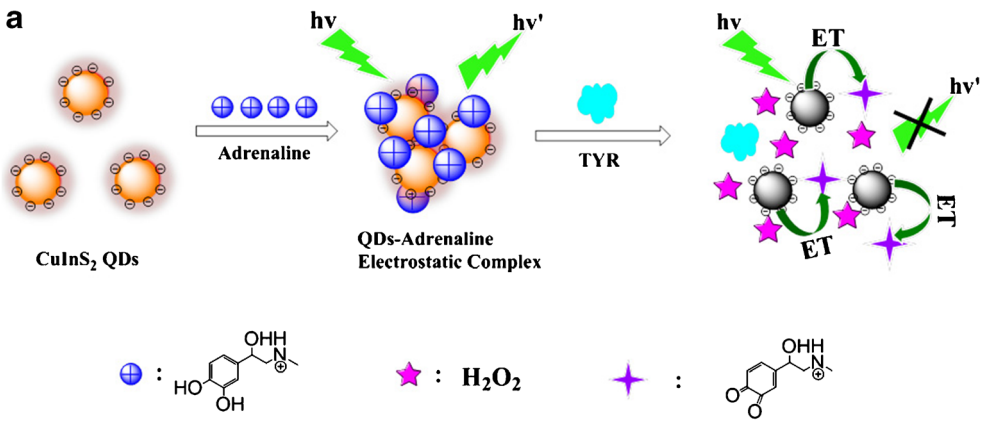
Results and discussion

The strategy for the detection of adrenaline

The basic principle of the present fluorescent biosensor was shown in Scheme 1. As illustrated in Scheme 1, the negatively charged $CuInS_2$ QDs can react with the positively charged adrenaline via the electrostatic interactions, which resulted in the formation of Adr-$CuInS_2$ QD electrostatic complex. Besides electrostatic interaction, hydrogen bonding between -NH_2, -COOH, and -OH groups would be also feasible between $CuInS_2$ QDs and adrenaline [30–32]. Figure 1 was the fluorescence spectra of $CuInS_2$ QDs in the presence of different concentrations of adrenaline in the concentration range of 0–1.0 mmol L^{-1}. It can be seen from Fig. 1 that the fluorescence intensity of Adr-$CuInS_2$ QDs was slightly enhanced with the increasing concentration of adrenaline. Fig. S1 (see Electronic Supplementary Material, ESM) was the TEM of $CuInS_2$ QDs and Adr-$CuInS_2$ QDs complex. From ESM Fig. S1a, it can be observed that the as-prepared $CuInS_2$ QDs were spherical particles with good monodispersity, and the diameter was about 3.23 nm. After adding adrenaline, it can be obviously seen that the spherical particles of $CuInS_2$ QDs aggregated (ESM Fig. S1b). Surface modifications of QDs often change their physicochemical properties [33]. It was supposed that the slight enhancement might be caused by the surface passivation, which increased the resistance of QDs against oxidation or solvent effects in the aqueous media to some extent [30, 34]. In the presence of TYR, the adrenaline was catalyzed by TYR to generate H_2O_2, and additionally oxidized to adrenaline quinone. And, therefore, the fluorescence of the QDs was quenched by both the H_2O_2 and the adrenaline quinone through the electron transfer (ET) from QDs to H_2O_2 and adrenaline quinone. Thus, a novel simple fluorescent biosensor for adrenaline detection could be developed.

Optimization for adrenaline detection

Figure 2 was the effect of pH and salt concentration on the fluorescence intensity of the $CuInS_2$ QDs in the presence of adrenaline. It can be observed from Fig. 2(a) that the fluorescence intensity ratio I_a/I_{a0} (I_a and I_{a0} refer to the fluorescence intensity of $CuInS_2$ QDs in the presence and absence of adrenaline) at pH 7.35 was the highest, which indicated that the electrostatic interactions and hydrogen bonding between QDs and adrenaline were much greater in neutral medium than those in acidic or alkaline medium. L-Cys, the stabilizer



Scheme 1 The schematic illustration of the fluorescent biosensor for adrenaline detection

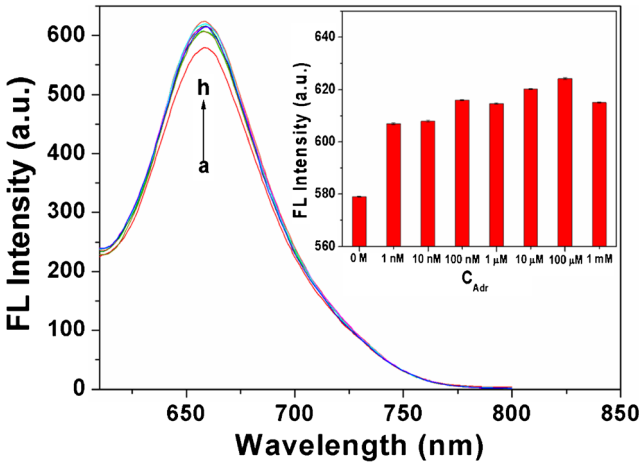


Fig. 1 The fluorescence spectra of $CuInS_2$ QDs [13.6 μmol L^{-1} in phosphate buffered solution (10.0 mmol L^{-1}, pH = 7.35)] in the presence of different concentrations of adrenaline (a to h: 0, 1.0 nmol L^{-1}, 10.0 mmol L^{-1}, 100.0 mmol L^{-1}, 1.0 μmol L^{-1}, 10.0 μmol L^{-1}, 100.0 μmol L^{-1}, and 1.0 mmol L^{-1})

of the $CuInS_2$ QDs used in this study, had a pI of 5.05. Therefore, L-cysteine was protonated and the net charge was positive under acidic conditions (pH < 5.05), which could weaken the electrostatic interactions between $CuInS_2$ QDs and adrenaline. When pH was over 5.05, L-Cys was deprotonated and the net charge was negative, which could enhance the electrostatic interactions between $CuInS_2$ QDs and adrenaline. Adrenaline exists as an organic cation in the biological body fluid with pH about 7.35–7.45. Under alkaline conditions, the amino and hydroxyl groups of adrenaline might be partially deprotonated, which would decrease the electrostatic interactions and hydrogen bonding between $CuInS_2$ QDs and adrenaline. Besides, the most optimal pH for TYR was 6–7. Considering the above results, pH 7.35 was adopted in further experiments. As shown in Fig. 2(b), the salt concentration had no significant effect on the fluorescence intensity of the Adr-$CuInS_2$ QD system. We chose 10 mmol L^{-1} NaCl for further experiment in this work.

Then, the effect of incubation time on the fluorescence intensity of Adr-$CuInS_2$ QD-TYR system was studied [as shown in Fig. 2(c)]. From Fig. 2(c), it can be seen that the fluorescence intensity ratio I_c/I_{c0} (I_c and I_{c0} refer to the fluorescence intensity of the Adr-$CuInS_2$ QD system in the presence and absence of TYR, respectively) decreased gradually with the increase of the incubation time within 30 min. Thirty minutes later, the fluorescence intensity ratio I_c/I_{c0} decreased sharply. The fluorescence spectrum was flatted and the

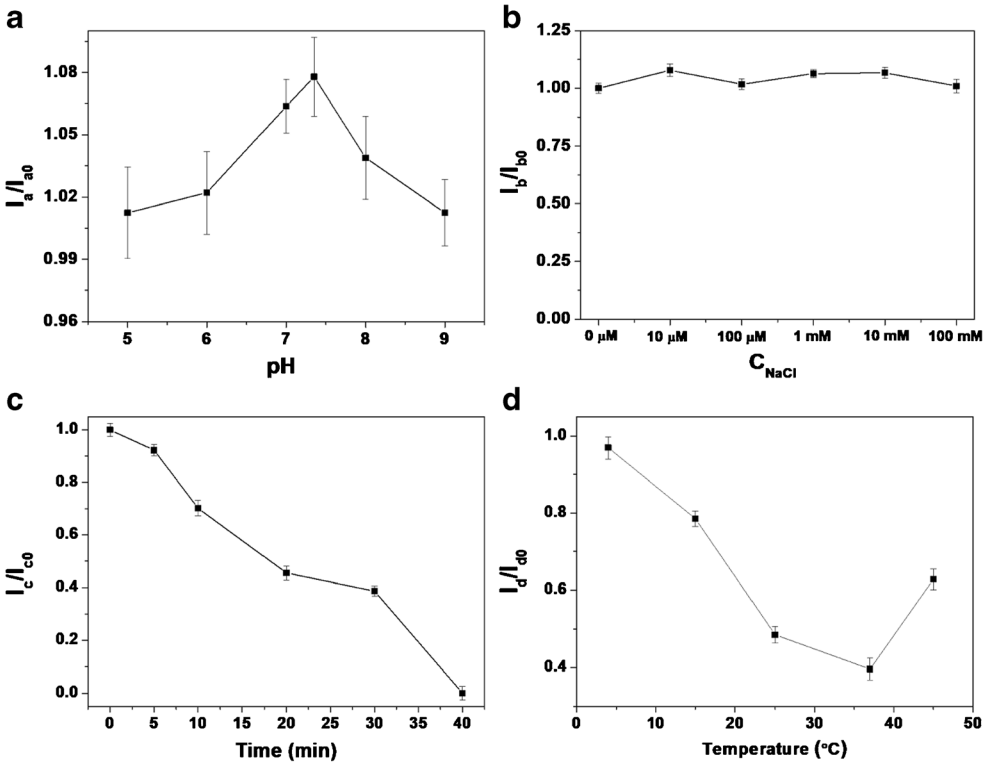


Fig. 2 (a) Effect of pH on the fluorescence intensity of $CuInS_2$ QDs/adrenaline. I_{a0} and I_a represent the fluorescence intensity of $CuInS_2$ QDs in the absence and presence of adrenaline, respectively. (b) Effect of salt concentration on the fluorescence intensity of $CuInS_2$ QDs/adrenaline. I_{b0} and I_b represent the fluorescence intensity of $CuInS_2$ QDs in the absence and presence of adrenaline, respectively. The concentrations of $CuInS_2$ QDs and adrenaline are 13.6 μmol L^{-1} and 0.1 mmol L^{-1}, respectively. (c) Effect of incubation time on the fluorescence intensity of the Adr-$CuInS_2$ QD-TYR system. I_{c0} and I_c represent the fluorescence intensity of the Adr-$CuInS_2$ QD system in the absence and presence of TYR, respectively. (d) Effect of reaction temperature on the fluorescence intensity of the Adr-$CuInS_2$ QD-TYR system. I_{d0} and I_d represent the fluorescence intensity of the Adr-$CuInS_2$ QD system in the absence and presence of TYR, respectively

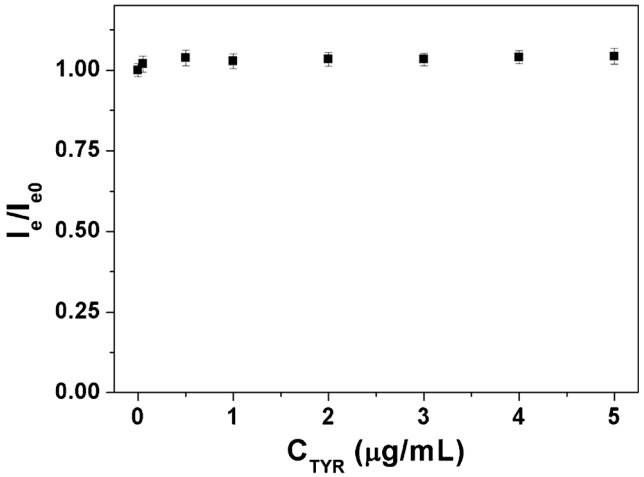


Fig. 3 The effect of various concentration of TYR (from 0 μg mL^{-1} to 5 μg mL^{-1}) on the fluorescence intensity of $CuInS_2$ QDs. I_{e0} and I_e are the fluorescence intensity of $CuInS_2$ QDs in the absence and presence of TYR, respectively

Table 1 The interference of coexisting substances on the determination of adrenaline (1 μmol L^{-1})

Coexisting substance	Tolerable concentration	Molar ratio	$\Delta I_g/I_g$ (%)
Na^+	1.0 mmol L^{-1}	10^3	4.94
K^+	1.0 mmol L^{-1}	10^3	− 1.37
Ca^{2+}	1.0 mmol L^{-1}	10^3	− 2.62
Cl^-	1.0 mmol L^{-1}	10^3	2.82
SO_4^{2-}	0.5 mmol L^{-1}	10^2	3.95
NO_3^-	0.5 mmol L^{-1}	10^2	2.60
DNA	0.1 mmol L^{-1}	10^2	3.82
Glucose	1.0 mmol L^{-1}	10^3	0.85
HSA	0.5 mg mL^{-1}	–	1.25
Tyr	0.1 mg mL^{-1}	–	− 2.23

$\Delta I_g = I_{g0} - I_g$, where I_{g0} and I_g are the fluorescence intensities of the Adr-$CuInS_2$ QD-TYR system in the absence and presence of coexisting substances

emission peak could not be read out. In view of the above, we chose 30 min as the incubation time in this work. The influence of the reaction temperature on the fluorescence intensity ratio I_d/I_{d0} (I_{d0} and I_d represent the fluorescence intensity of the Adr-$CuInS_2$ QD system in the absence and presence of TYR, respectively) was shown in Fig. 2(d). The results show that the quenching effect reaches the maximum at 37 °C. Thus, we chose 37 °C as the optimal reaction temperature for adrenaline detection in further experiments.

Fluorescence detection of adrenaline

Figure 3 was the effect of TYR concentration on the fluorescence intensity of $CuInS_2$ QDs. It can be seen that the fluorescence intensity of $CuInS_2$ QDs was not influenced by the addition of TYR in the concentration range of 0 μg mL^{-1} to 5 μg mL^{-1}, which indicated that the interaction between TYR and $CuInS_2$ QDs could be negligible. Figure 4(a) was the fluorescence spectra of $CuInS_2$ QDs with different concentrations of adrenaline from 0 nmol L^{-1} to 1.0 mmol L^{-1} in the presence of TYR (5 μg mL^{-1}). It can be observed that the fluorescence intensity of Adr-$CuInS_2$ QD-TYR system gradually decreased with increasing concentration of adrenaline. Figure 4(b) showed that there was good linearity between I_f/I_{f0} (I_{f0} was the fluorescence intensity of $CuInS_2$ QDs; I_f was the fluorescence intensity of Adr-$CuInS_2$ QD-TYR system) and adrenaline concentration in the range of 0.01–100 μmol L^{-1}. The regression equation is $I_f/I_{f0} = 1.048–0.136$ [Adr]. The corresponding regression coefficient is 0.990, and the detection limit (LOD) for adrenaline was 3.6 nmol L^{-1}. The detection limit is defined by the equation LOD = $3\sigma/s$, where σ is the

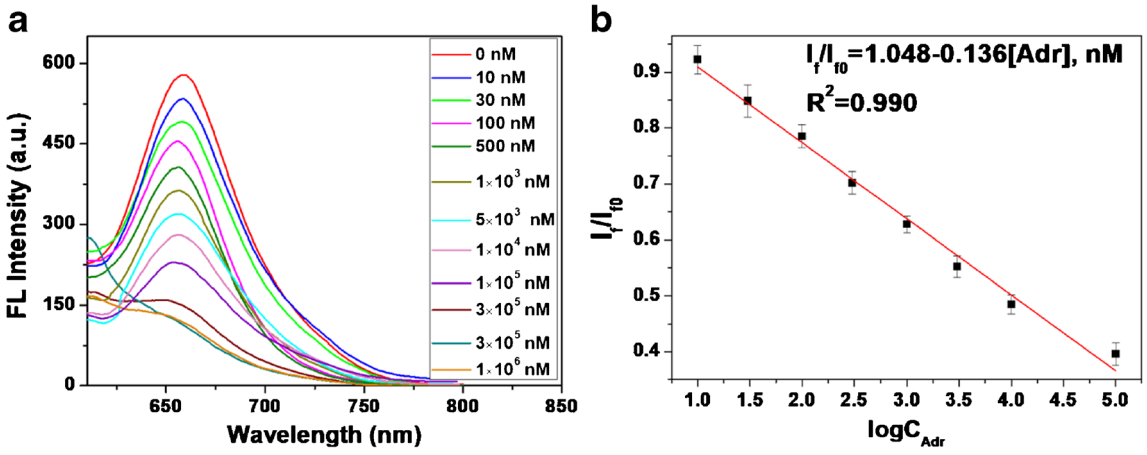


Fig. 4 (a) The fluorescence spectra of $CuInS_2$ QDs [13.6 μmol L^{-1} in phosphate buffered solution (10.0 mmol L^{-1}, pH = 7.35)] with different concentrations of adrenaline in the presence of TYR (5 μg mL^{-1}). (b) The relationship between I_f/I_{f0} and the concentration of adrenaline from 10 nmol L^{-1} to 100.0 μmol L^{-1}. I_{f0} was the fluorescence intensity of $CuInS_2$ QDs. I_f was the fluorescence intensity of Adr-$CuInS_2$ QD system in the presence of TYR (5 μg mL^{-1})

Table 2 Results of adrenaline determination in human serum samples

Sample	Added (nmol L^{-1})	Found (nmol L^{-1})	Recovery (%)	RSD ($n = 3$, %)
1	10.00	9.75	97.5	3.00
2	50.00	51.32	102.6	1.02
3	100.00	96.64	96.7	3.84

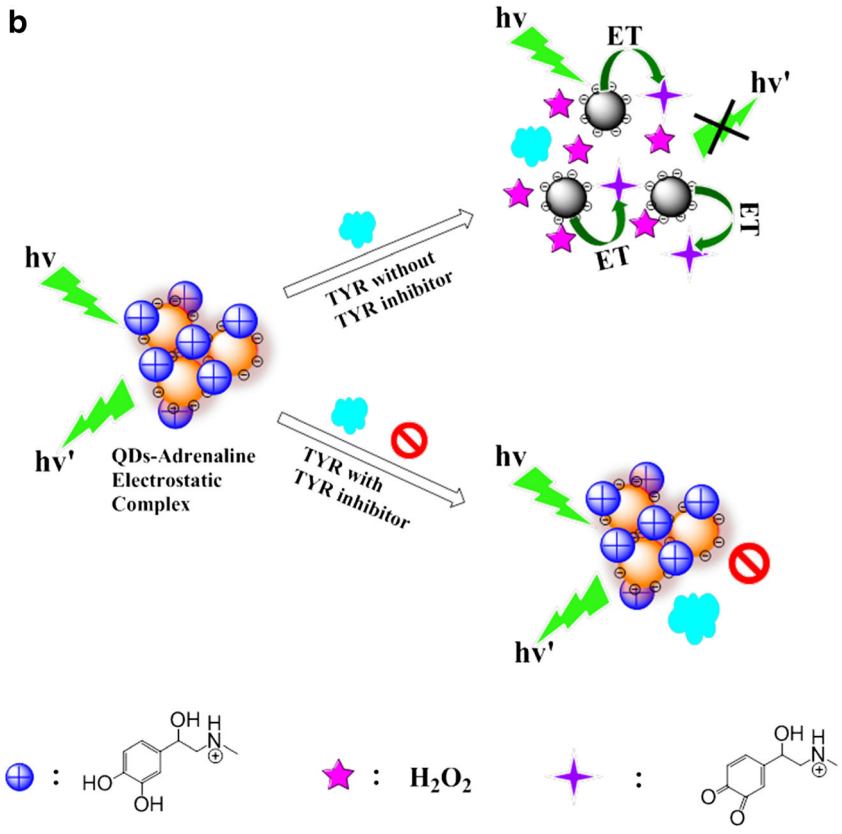
standard deviation of the corrected blank signals of the $CuInS_2$ QDs and s is the slope of the calibration curve. A comparison between the present method and other reported methods for adrenaline determination with regard to detection limit and linear range was summed up in Table S1 in the ESM. It could be seen from ESM Table S1 that the sensitivity of this proposed method was better than that of most of the well-known methods.

Interference study

Selectivity is a very important parameter to evaluate the performance of a new sensor, especially for a biosensor with potential application in biological sample, a highly selective response to the target over other potentially competing species is necessary. Therefore, we further investigated the selectivity of the proposed biosensor with various coexisting substances added. Table 1 showed the interference effect of some common inorganic ions and biological molecules on the determination of adrenaline, where a relative error of ± 5.0% was considered to be tolerable. As shown in Table 1, the tolerable concentration ratios of coexisting substances to 1 μmol L^{-1} adrenaline was over 1000-fold for that of Na^+, K^+, Ca^{2+}, Cl^-, and glucose, 500-fold for $SO_4^{2-}$and NO_3^-, and 100-fold for DNA. The concentration of HSA was 0.5 mg mL^{-1} and the concentration of Tyr was 0.1 mg mL^{-1}. The results showed that there was little interference from commonly existing substances. Thus, the present method was suitable for selective detection of adrenaline.

Real sample assay

In order to demonstrate the applicability of the proposed sensor in real sample detection, the developed fluorescence biosensor was applied for the determination of adrenaline in human serum samples. The results were listed in Table 2. The average recovery test was made by using the standard addition method and the RSD was generally obtained from a series of three samples. The adrenaline content in the samples was derived from the standard curve and the regression equation. From Table 2, it can be seen that the RSD was lower than 5.0% and the average recoveries of adrenaline in the real samples were in the range of 96–103%, indicating that the accuracy and precision of the proposed method were satisfactory.



Scheme 2 Schematic illustration of the fluorescent biosensor for TYR inhibitor screening

Inhibitor screening

The activity of TYR will be retarded when the corresponding TYR inhibitors are present in the solution. Therefore, the proposed fluorescent biosensor could also be utilized to screen potential inhibitors of TYR. According to the previous studies, the inhibitors of TYR are becoming more and more important in clinical treatment, cosmetic industry, and food industry [35]. Meanwhile, it has been reported that the organophosphorus pesticides (OPs) have displayed their great inhibition effects on TYR [36–38]. In this work, as a model of OPs, parathion-methyl (PM) was selected as the TYR inhibitor to demonstrate the ability of the optical sensor for screening the inhibitors of TYR. As shown in Scheme 2, when TYR inhibitor (PM) existed in the Adr-$CuInS_2$ QD-TYR system, the enzymatic reaction was inhibited and less H_2O_2 and adrenaline quinone were generated, thus decreasing the fluorescence quenching rate. Figure 5 showed the fluorescence intensity changes of the biosensor with various concentrations of PM in the range of 0–10 μg mL^{-1}. It could be observed that the fluorescence intensity of Adr-$CuInS_2$ QD-TYR system increased significantly when PM existed. The inset in Fig. 5 displayed the plot of the inhibition efficiency $I(\%)$ of PM toward TYR versus the concentration of PM. $I(\%)$ was analyzed by the following equation:

$$I(\%) = \frac{I_{\text{Inhibitor}} - I_{\text{No inhibitor}}}{I_0 - I_{\text{No inhibitor}}} \times 100$$

Where $I_{\text{Inhibitor}}$ and $I_{\text{No inhibitor}}$ refer to the fluorescence intensities of the Adr-$CuInS_2$ QD-TYR system in the presence and absence of the PM inhibitor, respectively; I_0 refers to the fluorescence intensity of the Adr-$CuInS_2$ QDs in the absence of TYR and PM. It can be seen that the inhibition percentage was proportional to the concentration of PM in the range of 2.0–10.0 μg mL^{-1}. The corresponding IC_{50} value (the concentration of the inhibitor that led to 50% inhibition of the enzyme activity) of PM toward TYR was estimated to be 5.79 μg mL^{-1} (21.9 mM), which was consistent with the reported methods [39]. The results demonstrated that the proposed method is indeed suitable for screening the inhibitors of TYR.

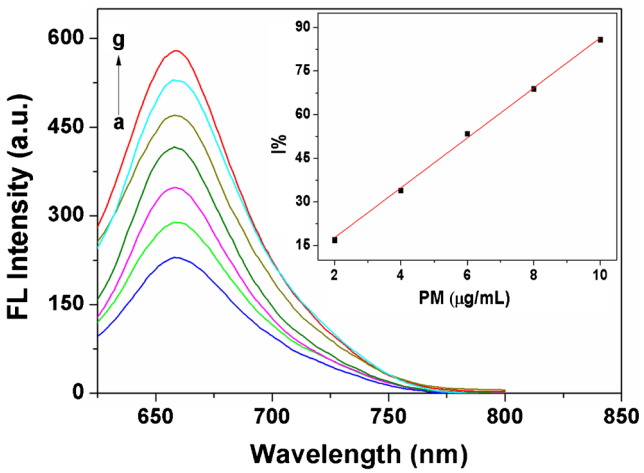


Fig. 5 Fluorescence spectra of Adr-$CuInS_2$ QD-TYR system with different concentrations of PM in the range of 0–10 μg mL^{-1} (a–f: 0, 2, 4, 6, 8, and 10 μg mL^{-1}); g represents the fluorescence intensity of the Adr-$CuInS_2$ QDs in the absence of TYR and PM. The inset shows the plot of the inhibition efficiency of PM toward TYR versus the concentration of PM

Conclusion

In summary, a novel simple fluorescent biosensor has been successfully developed for the highly sensitive and selective detection of adrenaline. The fluorescent biosensor is significant for the following features: (i) It is based on the water-soluble $CuInS_2$ QDs that have unique electro-optical properties and low toxicity in comparison with traditional semiconductor nanoparticles; (ii) It is straightforward and economical, just utilizing the electrostatic interactions and hydrogen bonding between the QDs and adrenaline and specially catalytic oxidation of TYR to trigger the optical response, avoiding complex chemical reactions. The proposed biosensor has been employed for the determination of adrenaline in human serum samples with good accuracy and satisfactory recovery. Particularly worth mentioning is that the proposed fluorescent biosensor can also be utilized to screen potential TYR inhibitors with good sensitivity.

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Compliance with ethical standards

Ethical committee approval All experiments were performed in compliance with the relevant laws and institutional guidelines and were approved by the Ethics Committee, Hospital of Changchun China, Japan Union Hospital. The writing of informed consent for all samples was obtained from human subjects.

Conflict of interest The authors declare that they have no competing interests.

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