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Development of a nano plastic antibody for determination of propranolol using CdTe quantum dots

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ABSTRACT

In this work, a nano plastic antibody has been developed for the determination of an important drug, propranolol. For this purpose, water-soluble thioglycolic acid stabilized CdTe QDs (TGA-stabilized CdTe QDs), as a support for the plastic antibody, was synthesis via a refluxing method. Following, reverse micro emulsion technique was applied to stabilize a thin silica shell on the surface of the QDs. In the next step, molecularly imprinted polymer embedded CdTe QDs were obtained using 3-aminopropyl triethoxysilane (as a monomer) and tetraethoxysilane (as a crosslinker) in the present of propranolol. Finally, the obtained nano plastic antibody was used for propranolol sensing. At the optimized conditions, a linear dynamic range was obtained from 3.0 to 139 μmol L^{-1} propranolol with a detection limit as 0.7 μmol L^{-1}. The precision of the method for 30.0 and 70.0 μmol L^{-1} propranolol was obtained as 6.5% and 4.8% (3 replicate detections), respectively. The proposed method is simple, selective, and cost-efficient for propranolol measurement.

1. Introduction

Propranolol (PROP), 1-(isopropylamino)-3-(1-naphthyloxy)-2-propanol, was discovered in 1964 [1]. The Nobel Prize in physiology or medicine in 1988 was awarded to James W. Black and his colleagues for the discovery of PROP [2]. PROP belongs to the class of beta-receptor blocking (beta antagonists) drugs [3]. Beta antagonists affect the heart and circulation system[3]. The World Health Organization (WHO) has put PROP on the list of essential medicines [4]. PROP most widely used to treat a wide range of different diseases and disorders such as cardiac dysrhythmia, high blood pressure, pheochromocytoma (a neuroendocrine tumor), sinus tachycardia, angina pectoris (sensation of chest pain), heart attack (myocardial infarction), abnormal labor, migraine, essential tremor, performance anxiety, hyperthyroidism, capillary hemangioma and fainting [5,6]. The overdose of PROP causes side effects such as dizziness, fainting, bradycardia (abnormally slow heart action) and uneven heartbeats [6]. On the other hand, the International Olympic Committee has considered PROP in the list of prohibited substances [6]. So sensitive and speed determination of trace amount of PROP is critical. As yet, several methods have been reported for PROP determination, including high-performance liquid chromatography [5,7], chemiluminescence [3,8,9], spectrophotometric determination [10–12], phosphorescent probe [13], and electrochemical methods [14–16].

Natural receptors in living organisms such as antibodies specifically interact with their target biomolecules [17]. When they are used in biosensors, the selectivity of the assay is improved. Nevertheless, the natural receptors are unstable in experimental conditions such as different temperature, pH, and other factors [17]. Therefore, design and preparation of artificial receptor are absorbing for researchers. Molecularly imprinted polymer (MIP) was made as antibody mimics and called *'plastic antibody'* [18]. Stability constants for the formation of complexes of these synthetic receptors with targets in most cases are comparable to those of the biological receptors [19]. In the molecular imprinting process, some cavities were created in a polymer matrix with template target. Therefore, shape, size, and orientation of cavities are corresponding to the used target [20]. Until now, several methods have been applied for the formation of MIPs such as suspension, bulk, precipitation, and two-step or multiple swelling polymerizations [21]. The traditional MIPs have various disadvantages such as incomplete removal template, low binding capacity, and limited mass transfer [20]. More recently, surface imprinting technique has received significant notice as a new method that solves the problems of traditional of MIPs [22]. As the name implies, the imprinted binding sites are located at or very near the surface of the support (flat or spherical) through polymerization [22].

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As yet, different MIPs have been applied for pre-concentration of PROP via solid phase extraction/micro-extraction [23–26] and some MIPs have been used for determination of PROP by electrochemical sensor [27,28], phosphorescent probe [13] and surface enhanced Raman detection [29]. Despite the inherent advantages of fluorescence measurement methods, a combination of the unique photo-properties of quantum dots with the advantages of surface imprinting polymer has not been used for determination of PROP.

Semiconductor quantum dots (QDs) are a good candidate as support in molecular imprinting technology (MIT) because of their higher surface area-to-volume ratios. Also, the template removal can be more compliment occurs and better availability of their cavities for a target molecule, higher binding capacity, faster binding kinetics, and easy preparation of the polymer suspensions [30]. QDs are luminescent nanoparticles that have unique optical and electronic properties such as narrow emission, tunable luminescent emission, and resistance to light bleaching [20]. Despite all the advantages, free label QDs without any modifications suffer from low selectivity in quantitative analysis and may response to many species. For example, in the case of MPA stabilized CdTe QD, many applications with quantitative analysis purposes have been reported. Xia et al. have reported a method for the determination of silver(I) by MPA stabilized CdTe QDs [31]. In a similar report, MPA stabilized CdTe QDs were used, by Duan et al. [32], as a probe for the detection of mercury(II) ions. Finally, in research that has recently been reported, MPA-stabilized CdTe QDs have been used for determination of PROP [33]. Therefore, using of quantum dots without any modifications suffers from low selectivity.

In this work, a nano plastic antibody has been developed for the determination of an important drug, PROP. This artificial antibody is an optical sensor, based on molecularly imprinted polymer on CdTe quantum dots. For the formation of the polymer via reverse micro-emulsion technique, 3-aminopropyltriethoxysilane (APTES) was used as a functional monomer, and tetraethoxysilane (TEOS) was consumed as a cross-linker. The synergic advantages of MIT and QDs caused a PROP optical sensor with excellent properties such as fast response and high selectivity.

2. Experimental

2.1. Chemicals

PROP and other chemicals such as TGA, $CdCl_2$, Na_2TeO_3, $NaBH_4$, cyclohexane, Triton X-100, TEOS, ammonium hydroxide solution (25–28%), APTES, trichloroacetic acid, acetone, ethanol, and acetonitrile were purchased from Aldrich (London, UK). Universal buffer solution (pH 6.5) was prepared by mixing of boric acid, acetic acid and phosphoric acid (each 0.04 mol L^{-1}) and 0.2 mol L^{-1} NaOH solution for pH adjusting to desired values.

2.2. Apparatus

The luminescence spectra were obtained using a Jasco FP–750 spectrofluorometer (Tokyo, Japan). UV/Vis absorption spectra were performed on a double beam Jasco V–570 UV/Vis/NIR spectrophotometer (Tokyo, Japan) with a 1.0-cm quartz cell. Fourier transform infrared (FT-IR) spectra were carried out (at 4000–400 cm^{-1}, KBr plate) on a Jasco 680-plus spectrophotometer (Tokyo, Japan).

Dynamic light scattering instrument, Malvern ZEN3600A (UK) was used to measure the size of the prepared QDs and their distribution.

X-ray diffraction (XRD, D8-Advance Bruker using Cu-Ka radiation, Germany), transmission electron microscopy (TEM) (Philips CM30 300 kV, Netherlands) was used for characterization of the QDs and the prepared nanocomposites.

A Malvern Zetasizer Nano-ZS measured zeta potential instrument (Model ZEN3600, UK) was used to evaluate the QDs.

2.3. Preparation of TGA-stabilized CdTe QDs

Synthesis of aqueous soluble TGA-stabilized CdTe QDs was done according to the method described in the literature [34]. Briefly, first TGA (0.3 mL) was added to water (110 mL), and the mixture was stirred (5 min). Then, $CdCl_2{\cdot}H_2O$ (0.508 g) was added to the solution and stirred for 30 min at room temperature. Following, $NaBH_4$ (1.25 g) was added to the above mixture then Na_2TeO_3 (10 mL 0.1 mol L^{-1} mL) was slowly added to the above mixture and it was heated to 95 °C. The mixture was refluxed for 13 h at 95 °C. The obtained TGA-stabilized CdTe QDs was filtered (using centrifugal filter unit with 10 kDa MW cut-off) and kept in a dark glass container at 4 °C. For XRD and FT-IR spectroscopic analysis, the QDs were precipitated with acetone and dried under vacuum at room temperature.

2.4. Synthesis of CdTe@SiO_2@MIPs and CdTe@SiO_2@NIPs nanocomposites

In this work, silica coating was performed through the formation of water/cyclohexane reverse microemulsion, according to the previously described process [35].

Typically, 1.8 mL of a surfactant (Triton X-100) was dispersed into 7.5 mL oily solvent (cyclohexane) at room temperature with stirring. After 15 min, 400 μL as-prepared CdTe QDs, 50 μL of TEOS and 100 μL ammonium hydroxide (25–28% v/v in water) were added to the above mixture and letting the mixture reacts for 2 h. Next, 20 μL of APTES and 5 mg of PROP were added to the above mixture, and the reaction system was sealed for overnight at room temperature under continuous stirring. During this time CdTe@SiO_2@MIPs nanocomposites were obtained. Finally, acetone (20 mL) was used as a microemulsion broker agent. Then, the nanocomposites were collected by centrifugation (10,000 rpm for 5 min) and washed with a mixture solvent of ethanol/acetonitrile (v/v, 8:2) to template removal until no PROP was detected by UV–vis spectrometry. The washed CdTe@SiO_2@MIPs nanocomposite was dried under vacuum at room temperature. For comparison and evaluate the CdTe@SiO_2@MIPs, non-imprinted polymers (NIPs), CdTe@SiO_2@NIPs were prepared and treated via the same procedure without the addition of PROP through the polymerization procedure.

2.5. Measurement procedure

For determination of PROP, the mixture contains 250 mg L^{-1} of the nano plastic antibody (CdTe@SiO_2@MIPs composite) in the universal buffer (pH 6.5) was dispersed using an ultrasonic bath (for 6 min). The fluorescence spectrum of this mixture, in the range of 500–650 nm (at λ_{ex} 400 nm), was recorded before and after addition of PROP in different concentrations. The fluorescence intensities (at λ_{max} = 550 nm) in the absence and presence of PROP were named as F_0 and F, respectively. The amount quenching of the fluorescence (F_0-F) signal exhibited the PROP concentration.

2.6. Sample preparation

Human plasma samples were prepared from the Health Center of Isfahan University. A same volume of the plasma and trichloroacetic acid 10% (w/v) were added to a centrifugal tube to precipitate the presence proteins. After collecting of the proteins by centrifugation (20 min at 5000 rpm), the upper phase was filtered (0.45-μm Millipore filter) and diluted (10-fold) with the universal buffer (pH 6.5). Certain volumes of the standard PROP