Talanta 168 (2017) 196–202

Contents lists available at ScienceDirect

Talanta

journal homepage: www.elsevier.com/locate/talanta

Magnetic separate "turn-on" fluorescent biosensor for Bisphenol A based on magnetic oxidation graphene

Liu-Yin Hu[a], Cheng-Gang Niu[a,*], Xiao-yu Wang[a], Da-Wei Huang[b,*], Lei Zhang[a], Guang-Ming Zeng[a]

[a] College of Environmental Science Engineering, Key Laboratory of Environmental Biology Pollution Control, Ministry of Education, Hunan University, Changsha 410082, China
[b] South China Institute of Environmental Sciences, Ministry of Environmental Protection of PRC, Guangzhou 510655, China

ARTICLE INFO

Keywords:
Bisphenol A
Magnetic oxidation graphene
Aptamer
Turn-on fluorescence

ABSTRACT

Bisphenol A (BPA) is commonly considered to cause a health hazard to wildlife and humans, acting as an exogenous estrogen. Herein, a magnetic separate "turn-on" fluorescent method for the detection of BPA was proposed based on fluorescence resonance energy transfer (FRET) between fluorescein-labeled BPA aptamer and magnetic oxidation graphene (MGO). At different concentrations of BPA, the fluorescence intensity of the sensing system was varied. The detection limit of 0.071 ng/mL was obtained with the linear range of 0.2–10 ng/mL. The biosensor exhibited excellent anti-interference ability and selectivity in actual water samples.

1. Introduction

In recent years, lots of epidemiological studies depicting, in some cases, serious interferences of endocrine system of wild animals and human beings have been published [1–4]. Mounting evidence suggests that the normal physiological function of the endocrine system can be significantly interfered by certain environmental pollutants, industrial chemicals, pesticides and natural phytoestrogens [5–7]. It's about a hundred kinds of industrial chemicals not only show their desired chemical properties, but also display estrogenic activity [8]. This class of chemicals, which are released into the environment by human production and living activities, affect the endocrine system of the human body and animals, and are commonly known as "endocrine disrupting chemicals" [9]. Endocrine disrupting chemicals can interference the stability of endocrine system and eliminate the responsibility of natural-born hormones for the regulation of homeostasis, reproductive and developmental processes due to affect hormone synthesis or degradation, hormone transport, receptor binding and gene transcription [2–7]. Most of endocrine disrupting chemicals are persistent organic compounds and widely used, which are universally existed in the environment and organisms [1]. Bisphenol A (BPA) is a recognized endocrine disrupting chemical , which can disturb endocrine system by interfering with hormones synthesis, transport, release and metabolism [10]. And, BPA is a high-yield, widely used industrial compound, mainly used in the production of polycarbonate, epoxy resin, polysulfone resin, polyphenylene ether resin, unsaturated polyester resin and other polymer materials [11–14]. BPA-based polymers are important raw materials for the production of various consumer goods such as water bottles, food container coatings, sports equipment, medical devices, baby bottles, toys and so on [12–15]. The widespread use of BPA makes it very likely to be released into the natural environment. The security issues of BPA have become the focus of public attention. BPA exposure can cause various adverse health effects such as male sexual dysfunction [16], heart disease [17], prostate and mammary gland cancers, diabetes, and immune system alterations [18]. Because of the serious harmfulness and universal existence of BPA, the effective detection of BPA is very necessary.

To assess the risk and safety of BPA exposure, an accurate data is essential. Thus, a variety of methods for detecting BPA have been reported, including UV spectrometry [19,20], high-performance liquid chromatography (HPLC) [20], gas chromatography–mass spectrometry (GC–MS) [21], liquid chromatography-tandem mass spectrometry (LC-MS/MS) [22,23], immunoassays [24,25], electrochemical sensors [26,27], fluorescence analysis [28–30] etc. Although a variety of methods are available for the detection of BPA, searching new BPA monitoring methods are of interesting and necessary. Fluorescence monitoring is attractive as it is a rapid, sensitive and specific technique [31]. A new method for detection of BPA based on fluorescence monitoring is also acceptable. In particular, FRET methods between a fluorescent donor and an acceptor are extremely attractive and arouse the interest of researchers [32]. The magnetic oxide graphene (MGO) is a composite material formed by compounding magnetic Fe_3O_4 on the

* Corresponding authors.
E-mail addresses: cgniu@hnu.edu.cn, cgniu@hotmail.com (C.-G. Niu), huangdawei@scies.org (D.-W. Huang).

http://dx.doi.org/10.1016/j.talanta.2017.03.055
Received 10 December 2016; Received in revised form 15 March 2017; Accepted 17 March 2017
Available online 18 March 2017
0039-9140/

surface of an oxidized graphene (GO). MGO has the characteristics of GO and magnetic Fe_3O_4, which is a strong fluorescence quenching agent [33]. MGO can quench the fluorescence of organic fluorescent dyes and selectively adsorb single-stranded DNA like GO. Additionally, MGO has a magnetic capability to facilitate the separation and enrichment of targets. Thus, MGO may have potential in biosensors using ssDNA probes. Recently, the development of new sensing and biosensing technologies has become the focus of attention [26]. Aptamers are a good type of short single-stranded DNA or RNA sequences which can be screened in vitro and can bind with high affinity and strong specificity of the corresponding ligands, and aptamers have been widely used to detect various targets in place of antibodies [33–38]. In addition to good specificity, aptamers also have many advantages, such as, low cost, simple modification, rapid synthesis, good thermal stability, anti-nuclease degradation, reversible denaturation [39]. Combining the advantages of MGO and aptamer, MGO and aptamer could be used to construct a biosensor to detect BPA.

Herein, a simple, rapid, selective and sensitive biosensor for detection of BPA based on fluorescence resonance energy transfer (FRET) between MGO and fluorescein-labeled BPA aptamer was developed. An anti-BPA aptamer was modified by fluorescein. MGO can adsorb fluorescein-labeled BPA aptamer to form aptamer-MGO complex and can effectively quench the fluorescence of fluorescein due to FRET. In the presence of BPA, the anti-BPA aptamer prefers to switch its configuration to combine with the BPA target, resulting in desorption of the anti-BPA aptamer from the surface of MGO and then the fluorescence recovered by magnetic separation. The fluorescence recovery of the sensing system correlated with the concentration of BPA. Accordingly, the fluorescence intensity of the biosensor is enhanced with an increase of the BPA concentration. This proposed biosensor was of high specificity and selectivity for BPA detection and had a strong capability to resist interference, and it was sensitive. In addition, MGO could be recycled for being reused, which could save costs.

2. Materials and methods

2.1. Materials and reagents

The BPA aptamer was purchased from Sangon Biotech Co., Ltd. (Shanghai, China). The sequence of the BPA aptamer was designed as 5′- CCG GTG GGT GGT CAG GTG GGA TAG CGT TCC GCG TAT GGC CCA GCG CAT CAC GGG TTC GCA CCA-FAM-3′. The MGO was prepared according to the previously published reports [40,41]. The BPA, sym-Diphenylcarbazide (SDC), Catechol (CAT), Benzidine (BZD) and Bisphenol B (BPB) were all obtained from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). Other primary reagents including Na_2HPO_4, KH_2PO_4, KCl, NaCl were also purchased from Sinopharm Chemical Reagent Co., Ltd. Doubly distilled water was used throughout the experiments. Actual blank water samples were taken from the tap water in our laboratory and the river water in Xiangjiang River in Changsha City.

2.2. Instrumentation

All fluorescence measurements were conducted on a Perkin-Elmer LS-55 spectrofluorimeter (United Kingdom) and controlled by a personal computer data processing unit. The parameters of spectrofluorimeter were set as follows: both excitation and emission slits 5.0 nm, and excitation/emission wavelength 494/515 nm. All assays were performed in triplicates and all measurements were performed at room temperature (RT, 25 ± 3 ℃) and atmospheric pressure. To prevent viruses or other organisms, centrifuge tubes, buffer solution, pipettes, pipette tips, beakers and volumetric flasks were all sterilized by High pressure steam in a LDZX-30FBS vertical heating pressure steam sterilizer (Shanghai Shen An Medical Instrument Factory). The centrifugal process were operated on Allegra™ 64 R Centrifuge (Beckman Coulter) and Centrifuge 5415 R (Eppendorf). HY-4 multi-speed oscillator (Jiangsu Jintan Medical Instrument Factory) and QT-1 vortex mixer (Shanghai Qite Analytical Instrument Co., Ltd.) were used throughout oscillating process.

2.3. Preparation of MGO sheets

In this paper, the MGO was accomplished by two steps. The first step was the synthesis of GO, the second step was the MGO synthesized by the reaction of GO and $FeCl_3$ under a certain condition.

The GO was prepared by oxidizing graphite according to the modified Hummer's method [40]. 1.0g of graphite powder and 1.0g of $NaNO_3$ was stirred into 46 mL of concentrated sulfuric acid. The reagents were mixed in a three-necked flask. The mixture was stirred vigorously for 30 min under the condition of cooling to 0 ℃ in an ice-bath. While maintaining vigorous stirring, 6.0g of potassium permanganate was slowly added into the three-necked flask. The rate of addition was controlled slowly to maintaining the solution temperature below 20 ℃. The ice bath was removed after the mixture is completed. The suspension solution was stirred for two hours and the temperature was maintained at 36–37 ℃. Then 92 mL of doubly distilled water was slowly stirred into the three-necked flask and increased the temperature to 98 ℃. The mixture was maintained at this temperature to stirring for 30 min. As the reaction progressed, the mixture was then further diluted with 280 mL of warm water, and then 10 mL of hydrogen peroxide was slowly added into the three-necked flask. Upon treatment with the hydrogen peroxide, the mixture turned yellow. The suspension was filtered while warm, and then a yellow-brown filter cake was obtained. The yellow-brown filter cake was rinsed with warm water and 1:10 hydrochloric acid (5 or 6 times) to effectively remove the solvent and salt impurities, and then dried at 45 ℃ in vacuum drying oven. During each rinsing step, the GO was separated from the suspension by using centrifuge.

For preparation of MGO composites, 0.50g of GO was dispersed in 80 mL of ethylene glycol by ultrasonic dispersion for 4 h. Then, 1.60g of $FeCl_3$ and 3.20*g* of sodium acetate were dissolved into the suspension and stirred vigorously at room temperature for 30 min. As the completion of stirring, the suspension was transferred to a Teflon lined stainless steel autoclave with a reaction of 200 ℃ for 6 h. After being cooled to room temperature, the black precipitate was obtained by centrifugation. The resulting black powder was washed several times with ethyl alcohol and water. During each rinsing step, the black precipitate was separated from the supernatant by using magnetic force. Finally, the black precipitate was dried at 45 ℃ in vacuum drying oven.

2.4. Preparation of BPA aptamer stock solution

According to the oligo DNA storage solution preparation instructions provided by Sangon Biotech Co., Ltd. (Shanghai, China), the centrifuge tube containing oligo DNA powder was placed into the centrifuge and centrifuged at 12,000 rpm for 2 min. And slowly open the lid and add appropriate amount of buffer solution. Then close the lid and the mixture was fully shocked for 5 min to prepare a stock solution of 10 μM. The stock solution was divided into several tubes and stored at −20 ℃ in refrigerator.

2.5. Process for the detection of BPA

For BPA detection, firstly, 750 μL of buffer solution was added into a centrifuge tube. 220 μL of MGO (in buffer solution) was then added into the centrifuge tube and well mixed with buffer solution. Then, 20 μL of BPA aptamer was added into the mixture and mixed well. And, the mixed solution was incubated for 3 min at room temperature and

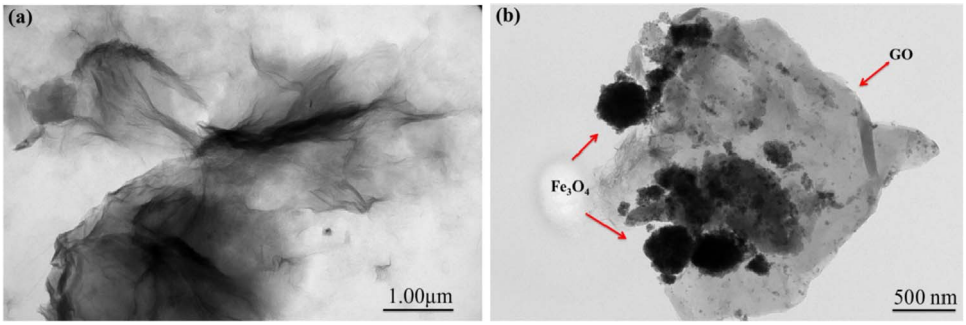


Fig. 1. (a) SEM image of GO; (b) SEM image of MGO.

then magnetic separation by magnet. After that, 10 μL of BPA standard solution was added and incubated at room temperature. At the end of this process, the mixed solution was placed on a magnet to separate the MGO from the mixture. Finally, the fluorescence intensity of the separating solution was measured.

3. Results and discussion

3.1. Principle of the proposed method

A magnetic separate "turn-on" fluorescent biosensor for BPA based on MGO was developed. As shown in Fig. 1, MGO is a kind of composite material formed by compounding magnetic Fe_3O_4 on the surface of GO, and, the MGO has the characteristics of GO and the characteristics of magnetic Fe_3O_4. Therefore, MGO can adsorb single-stranded DNA (ssDNA) to form ssDNA-MGO complex and can effectively quench the fluorescence of fluorescent dyes labeled on ssDNA due to FRET. And, the two magnetic separation process of the sensing system could be achieved. A schematic of the sensing principle is shown in Scheme 1.

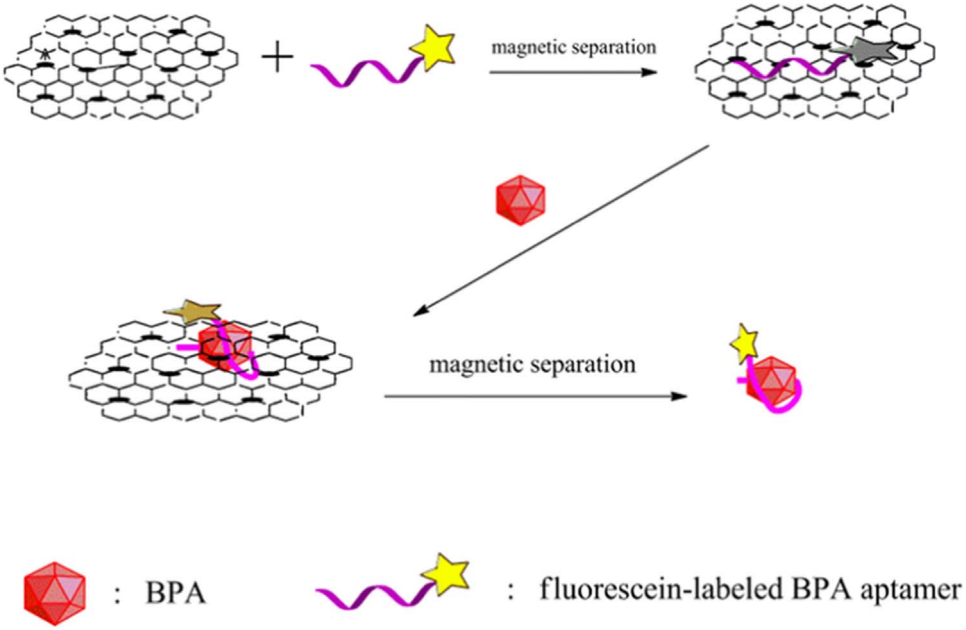
BPA aptamer is a segment of DNA sequence which can be used to ensure the specificity of detecting for BPA. Upon the binding of the BPA aptamer to the BPA, the BPA aptamer can switch its conformation, resulting in desorption of BPA aptamer from the surface of the MGO.

In the absence of BPA, the fluorescein-labeled BPA aptamer was absorbed onto the surface of MGO by strong absorbability of MGO and the fluorescence of the fluorescein was quenched by MGO. In the presence of BPA, aptamer preferentially binds to the BPA because of the strong specific affinity effects, including the spatial matching effect, hydrogen bond effect, and electrostatic effect [40]. And, this specific affinity was stronger than the absorbability of MGO, which desorb the fluorescein-labeled BPA aptamer from the surface of MGO and prevent the aptamer from being adsorbed onto the surface of MGO. And then through a magnetic separation, the fluorescence of this reaction system was recovered. There are two magnetic separations in the process. The first magnetic separation was performed to remove fluorescein-labeled aptamers that were not adsorbed to the surface of the MGO in the detection system, thereby reducing the background interference caused by the non-quenched fluorescein. As shown in Fig. 2, the fluorescence intensity of the sensing system after the second magnetic separation was significantly stronger than the fluorescence intensity of the sensing system without the second magnetic separation. In addition, as shown in Fig. 3, MGO could be separated for reusing, and the recycling of water could save the costs. Therefore, the two magnetic separation processes are necessary.

3.2. Optimization of the experimental conditions

3.2.1. pH optimization

Since, the pH of the buffer had a strong influence on the stable conformation of aptamer and the fluorescence intensity of fluorescein. The effects of the different pH buffer solutions inducing the fluorescent signal changes were investigated. The aptamer is relatively stable in neutral partial alkaline environment, the pH values of 6.0, 6.5, 7.0, 7.5,



Scheme 1. Schematic diagram of the biosensor for selective detection of BPA.

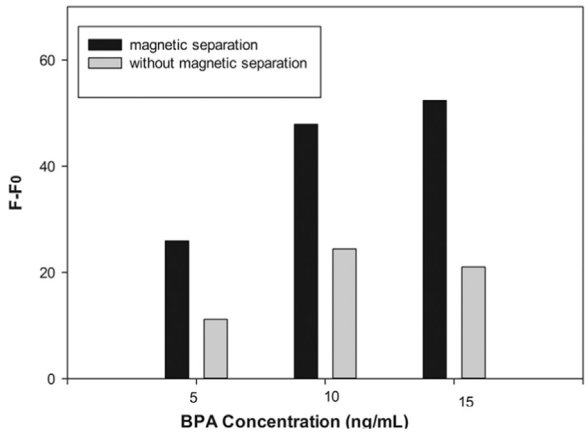


Fig. 2. Effect of the second magnetic separation.

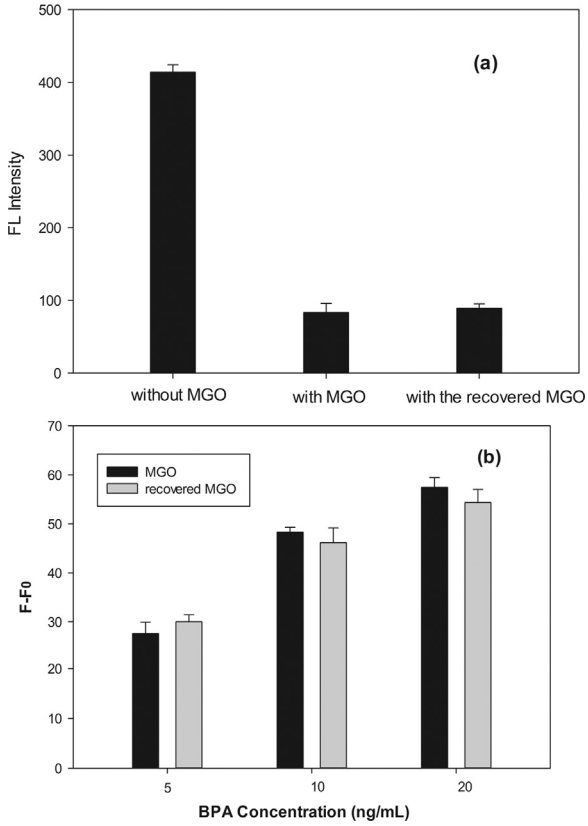


Fig. 3. (a) Comparison of fluorescence quenching of MGO and recovered MGO; (b) Effect of MGO and recovered MGO on the sensing system.

8.0, 8.5, 9.0, 9.5 and 10.0 were selected for the optimization of experimental conditions. 18 of centrifuge tubes were divided into group A (experimental group) and group B (blank group), which were respectively labeled as A1, A2, A3, A4, A5, A6, A7, A8, A9 and B1, B2, B3, B4, B5, B6, B7, B8, B9. As described above, in the experimental group, each of the tube was added of 750 μL of different pH buffer solution. 220 μL of MGO (in different pH buffer solution) was added into the tube and mixed well. Then, 20 μL of BPA aptamer was added into the mixture. And, the solution was fully mixed and incubated for a while and then magnetic separation by magnet. After that, 10 μL of BPA solution was added and incubated at room temperature. Next, the mixed solution was placed on a magnet to separate the MGO from the mixture and the final separating solution was transferred into a micro quartz cuvette for detection of fluorescence intensity. In the blank group, the experimental processes were the same as the experimental

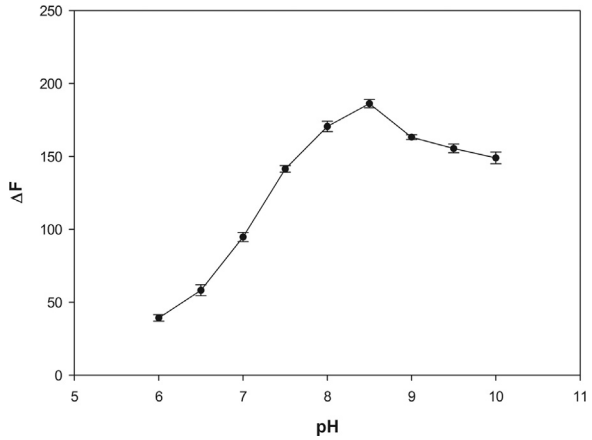


Fig. 4. Optimization of reaction pH.

group except adding 10 μL of BPA solution into each centrifuge tube replaced by adding 10 μL of water.

As shown in Fig. 4, in the presence of a certain amount of BPA, the ΔF value first increases and then decreases as the pH value increases. ΔF (ΔF=F-F_0) increased along with the increase of pH from 6.0 to 8.5. However, the value of ΔF decreased when the pH over 8.5. In order to guarantee a higher performance for the fluorescence sensing of BPA, pH 8.5 was chosen in the sensing system.

3.2.2. MGO concentration optimization

Following the above-mentioned principle, the performance of the biosensor for BPA detection was based on the competitive reaction between target BPA and MGO with the BPA aptamer. Relatively, the concentration of MGO had effect on this competitive reaction. Thus, the changes of fluorescence intensity in the reaction system with different concentration of MGO were studied. A series of concentrations of MGO (in buffer solution) were added into a centrifuge tube contained buffer solution at a fixed concentration of 20 nM anti-BPA aptamer. As shown in Fig. 5, the fluorescence quenching rate enhanced along with the increase of MGO concentration. When the concentration of MGO reached 55 mg/L, the fluorescence quenching rate was basically no longer enhanced. Indicating that the fluorescence of the solution was approximately quenched and all the anti-BPA aptamers labeled with fluorescein were adsorbed onto the surface of MGO. Therefore, 55 mg/L was selected for the optimal MGO concentration.

3.2.3. Temperature optimization

The stability of the biosensor may be affected by the temperature. And, temperature could induce the change of pH of the buffer so as to affect the activity of aptamer and the fluorescence intensity of FAM.

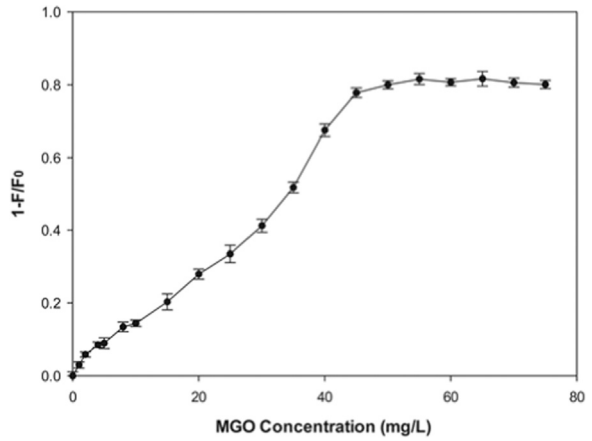


Fig. 5. Quenching efficiency with different concentration of MGO.

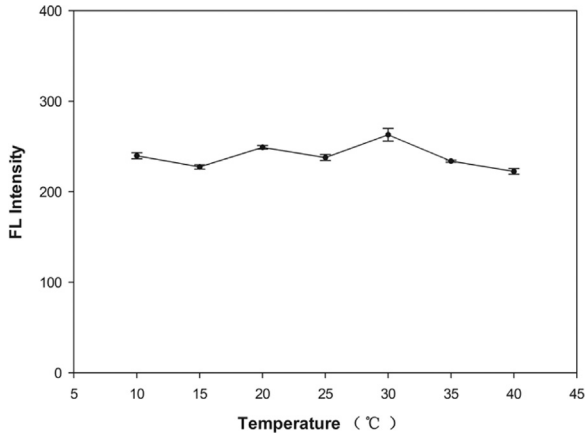


Fig. 6. Influence of temperature on the fluorescence intensity.

Therefore, it is necessary to evaluate the effects of temperature. Generally, the analytes were detected at room temperature, thus the reaction temperature range of 5–40 °C was selected to optimize the temperature. As shown in Fig. 6, with gradually rising of temperature, the fluorescence intensity exhibited a very small variation. These results indicated that the proposed biosensor was slightly affected by the change of temperature from 5 to 40 °C and the stability of this biosensor was excellent. Considering the simplicity of the method, subsequent experiments were performed at room temperature.

3.2.4. Optimization of the incubation time

The effects of incubation time on the fluorescence intensity were investigated from two processes. The first process was the adsorption of BPA aptamer onto the surface of MGO. The second process was the specific conjugation of BPA and BPA aptamer. In the first process, MGO can quickly absorb the fluorescein-labeled BPA aptamer and quench its fluorescence due to the strong absorption of MGO for ssDNA and FRET between fluorescein and MGO. Even if a small amount of BPA aptamers that were not adsorbed onto the surface of the MGO, they were separated by magnetic force. In addition, the BPA aptamer would not be absorbed onto MGO after the combining of BPA and aptamer. And, the BPA aptamer that had not been combined with BPA could continuously be absorbed by MGO. That is to say, there were slight effects on the results even if the BPA aptamer had not been completely absorbed onto MGO when the BPA was added. Therefore, the effect of the time of the second process on the experimental results was mainly studied. The second process of this sensing system was evaluated at different times in the presence of 55 mg/L MGO, followed by the addition of 20 nM fluorescein-labeled BPA aptamer and 15 ng/mL BPA. As depicted in Fig. 7, the fluorescence intensity increased with the increase of incubation time and approximately reached the maximum within 15 min. Hence, 15 min was selected as the optimal time.

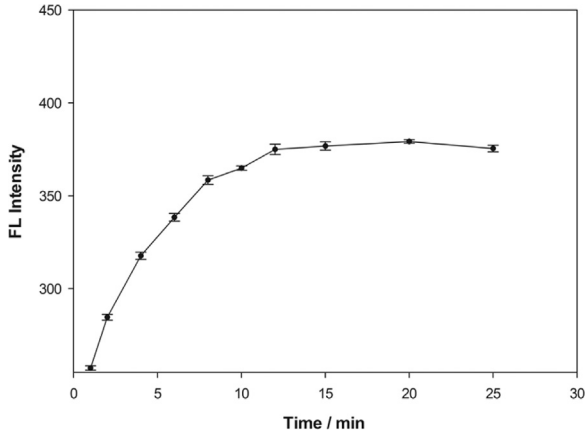


Fig. 7. Optimization of reaction time.

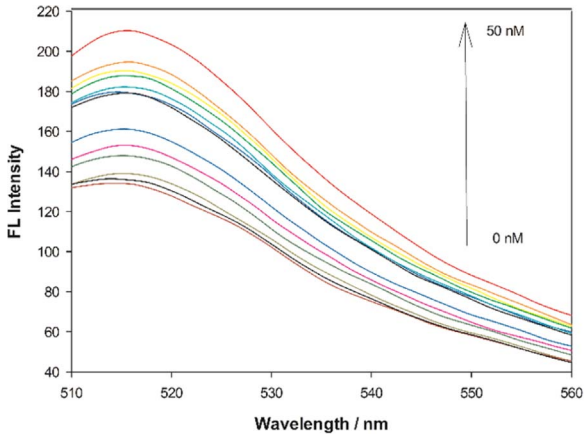


Fig. 8. Fluorescence spectrum of the sensing system with different concentrations of BPA.

3.3. Sensitivity of detection method

In order to investigate the sensitivity of this developed method, a series of different concentrations of BPA were added into the sensing system to measure the change of fluorescence intensity and their fluorescence spectra were recorded. As shown in Fig. 8, we found that fluorescence intensity was changed following addition of BPA. From the results showed in Fig. 9, the fluorescence intensity increased with the increase of the BPA concentration, and the fluorescence intensity

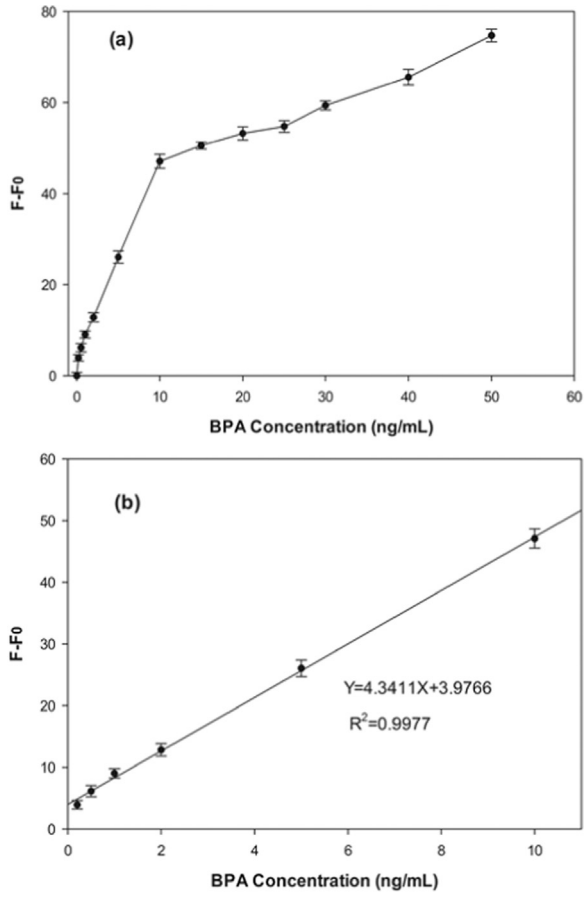


Fig. 9. (a) Plot of fluorescence intensity as a function of BPA concentrations; (b) Linear relationship between fluorescence intensity and BPA concentration.

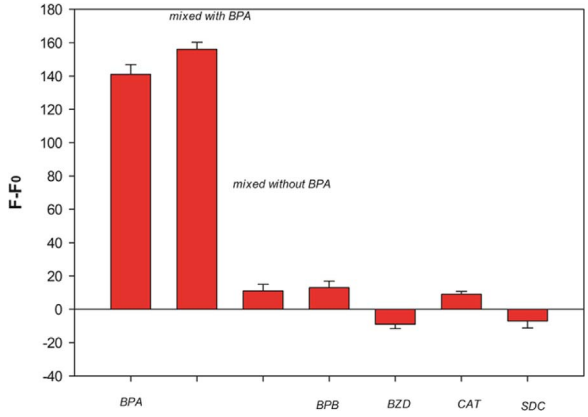


Fig. 10. Selectivity of proposed method. The concentration of BPA was 5 ng/mL, the concentration of interfering substances was 50 ng/mL.

Table 1
Detecting the actual water samples by the proposed method and HPLC.

Samples	BPA Added (ng/mL)	Propose method mean ± SD (ng/mL)	HPLC mean ± SD (ng/mL)
Tap water	0.00	0.050 ± 0.040[a]	0.110 ± 0.090
	0.25	0.357 ± 0.009	0.371 ± 0.107
	0.50	0.597 ± 0.013	0.607 ± 0.076
	1.00	1.143 ± 0.047	1.09 ± 0.214
Pure water	0.00	0.000	0.000
	1.00	1.015 ± 0.021	0.974 ± 0.093
	2.00	1.969 ± 0.046	2.036 ± 0.186
	4.00	4.126 ± 0.152	4.089 ± 0.062
River water	0.00	0.160 ± 0.110[a]	0.190 ± 0.120
	1.00	1.207 ± 0.054	1.163 ± 0.227
	2.00	2.181 ± 0.140	2.252 ± 0.0146
	4.00	4.163 ± 0.315	4.235 ± 0.094

mean: The mean of three experiments. SD=standard deviation.
[a] Not within the linear range, the value obtained by extrapolating the linear equation.

was linear with the concentration of BPA in the range of 0.2–10 ng/mL. The linear equation was fitted as $Y=4.3411X+3.9766$ with a linearity correlation coefficient of R^2 =0.9977 ($Y=F-F_O$, F was the fluorescence intensity, F_O was the fluorescence intensity of the blank, and X was the concentration of BPA). Moreover, the limit of detection (LOD) of 0.071 ng/mL was obtained. This LOD is lower than some other detected methods for BPA [42–44]. From these comparisons, the LOD of the method developed here was acceptable and the proposed sensor was sensitive.

3.4. Specificity and selectively of this developed sensor

To investigate the specificity and selectivity of this biosensor, two aspects of the experiment were carried out. On the one hand, four kinds of interferents (SDC, CAT, BZD and BPB) were added to the sensing system as four independent samples to observe whether the interferents can lead to fluorescence intensity changes. On the other hand, the anti-interference capability was studied; the interferents were mixed with BPA and then added to the sensing system. As shown in Fig. 10, only the samples containing BPA caused a significant enhancement of fluorescence intensity, the interferents did not cause significant changes in fluorescence. The anti-interference test also showed that the mixed solution of interferents containing BPA had no obvious change compared with the sample only containing BPA. These results might be attributed to the high affinity and strong specificity of aptamer, when the target is present, the conformation of the aptamer changes and is folded into a specific three-dimensional structure such as stem, inner ring, convex ring, hairpin, quadrangular ring, fake body, triple body and G-quadruplex structure. Through the shape matching, the pairing of complementary bases in the chain, the accumulation between the aromatic compounds, the accumulation of the base of the ligand, the van der Waals force, the electrostatic interaction or the hydrogen bonding, the aptamer is complementary to the target molecule and form a stable three-dimensional space structure to achieve specific binding to the target [45–47]. And, these results clearly demonstrated that the biosensor was of high specificity and selectivity for BPA detection and had a strong capability to resist interference.

3.5. Application in actual water samples

In order to investigate the practical application of the method in the actual water samples, the experiments were performed to compare the proposed detection method by high performance liquid chromatography (HPLC). Different standard concentrations of BPA were added into the real water samples (river water, tap water and pure water) and measured using the proposed detection method and HPLC. As shown in Table 1, the value of BPA in these samples measured by the proposed method was close to the value of BPA measured by HPLC. These results indicated that the agreement of the proposed method with HPLC for BPA detection. And, the detection results of the proposed method are acceptable and very slight affected by the components of the actual environmental samples. In other words, this proposed method is an alternative and practical approach for the analysis of BPA in actual water samples.

4. Conclusion

In this study, a simple, sensitive and selective detection method was proposed to detect BPA in environmental water based on MGO and the specific binding of aptamer to PBA. The MGO synthesized in this paper retains the characteristics of both graphene oxide and magnetic material, and exhibits excellent properties as fluorescence quencher and ssDNA adsorbent, and also plays a good role as separation medium. In addition, the proposed method has high selectivity and anti-interference capability, the recovery experiments shown that this method could be applied to the detection of real environmental samples.

Acknowledgement

This work was financially supported by the National Natural Science Foundation of China (21507034, 51541801, 51521006), the Natural Science Foundation of Guangdong Province, China (2016A030310022), and the Pearl River S&T Nova Program of Guangzhou (201710010134).

References

[1] S.F. Li, Y.B. Jin, J. Wang, Z. Tang, S.Q. Xu, T.J. Wang, Z.W. Cai, Urinary profiling of cis-diol-containing metabolites in rats with bisphenol A exposure by liquid chromatography-mass spectrometry and isotope labeling, Analyst 141 (2016) 1144–1153.
[2] Z.X. Zheng, Y.L. Du, Z.H. Wang, Q.L. Feng, C.M. Wang, Pt/graphene–CNTs nanocomposite based electrochemical sensors for the determination of endocrine disruptor bisphenol A in thermal printing papers, Analyst 138 (2013) 693–701.
[3] M. Muz, M.S. Sönmez, O.T. Komesli, S. Bakırderecd, C.F. Gökçaya, Determination of selected natural hormones and endocrine disrupting compounds in domestic wastewater treatment plants by liquid chromatography electrospray ionization tandem mass spectrometry after solid phase extraction, Analyst 137 (2012) 884–889.
[4] J.A. Rather, S. Pilehvara, K.D. Wael, A biosensor fabricated by incorporation of a redox mediator into a carbon nanotube/nafion composite for tyrosinase immobilization: detection of matairesinol, an endocrine disruptor, Analyst 138 (2013) 204–210.
[5] S. Manzetti, E.R. Spoel, D. Spoel, Chemical properties, environmental fate, and degradation of seven classes of pollutants, Chem. Res. Toxicol. 27 (2014) 713–737.
[6] E. Simon, M.H. Lamoree, T. Hamers, J.M. Weiss, J. Balaam, J. Boer, P.E.G. Leonards, Testing endocrine disruption in biota samples: a method to

remove interfering lipids and natural hormones, Environ. Sci. Technol. 44 (2010) 8322–8329.
[7] M.G. Diana, G.J.L. Bernardes, O.V. Jesus, Urban endocrine disruptors targeting breast cancer proteins, Chem. Res. Toxicol. 29 (2016) 150–161.
[8] C.A. Harris, P. Henttu, M.G. Parker, J.P. Sumpter, The estrogenic activity of phthalate esters in vitro, Environ. Health Perspect. 105 (1997) 802–811.
[9] H.W. Xu, M.M. Masila, O.A. Sadik, Chemical and Biological Sensors for Environmental Monitoring, (ACS Symposium Series), American Chemical Society, Washington DC, 2000.
[10] Z. Mei, H. Chu, W. Chen, F. Xue, J. Liu, H. Xu, R. Zhang, L. Zheng, Ultrasensitive one-step rapid visual detection of bisphenol A in water samples by label-free aptasensor, Biosens. Bioelectron. 39 (2013) 26–30.
[11] H. Kuang, H. Yin, L. Liu, L. Xu, W. Ma, C. Xu, Asymmetric plasmonic aptasensor for sensitive detection of bisphenol A, ACS Appl. Mater. Interfaces 6 (2014) 364–369.
[12] A. Schecter, N. Malik, D. Haffner, S. Smith, T.R. Harris, O. Paepke, L. Birnbaum, Bisphenol A (BPA) in U.S. food, Environ. Sci. Technol. 44 (2010) 9425–9430.
[13] L.N. Vandenberg, Human exposure to bisphenol A (BPA), Reprod. Toxicol. 24 (2007) 139–177.
[14] C.Y. Liao, K. Kannan, Widespread occurrence of bisphenol A in paper and paper products: implications for human exposure, Environ. Sci. Technol. 45 (2011) 9372–9379.
[15] L. Zhao, Y.F. Ji, D.Y. Kong, J.H. Lu, Q.S. Zhou, X.M. Yin, Simultaneous removal of bisphenol A and phosphate in zero-valent iron activated persulfate oxidation process, Chem. Eng. J. 303 (2016) 458–466.
[16] D. Li, Z. Zhou, D. Qing, Y. He, T. Wu, M. Miao, J. Wang, X. Weng, J.R. Ferber, L.J. Herrinton, Q. Zhu, E. Gao, H. Checkoway, W. Yuan, Occupational exposure to bisphenol-A(BPA) and the risk of self-reported male sexual dysfunction, Hum. Reprod. 25 (2010) 519–527.
[17] D. Melzer, N.E. Rice, C. Lewis, W.E. Henley, T.S. Galloway, Association of urinary bisphenol A concentration with heart disease: evidence from NHANES 2003/06, PLoS One 5 (2010) e8673.
[18] M.D. Shelby, NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Bisphenol A, National Institute of Health, Research Triangle Park, 2008.
[19] F. Pan, L. Liu, S. Dong, C. Lu, A new approach for bisphenol A detection employing fluorosurfactant-capped gold nanoparticle-amplified chemilumine scence from cobalt (II) and peroxymonocarbonate, Spectrochim. Acta 128 (2014) 393–397.
[20] K.L. Van Landuyt, T. Nawrot, B. Geebelen, J. De Munck, J. Snauwaert, K. Yoshihara, How much do resin-baseddental materials release* A meta-analytical approach, Dent. Mater. 27 (2011) 723–747.
[21] V. Becerra, J. Odermatt, Detection and quantification of traces of bisphenol A and bisphenol S in paper samples using analytical pyrolysis-GC/MS, Analyst 137 (2012) 2250–2259.
[22] C.Y. Liao, F. Liu, H.B. Moon, N. Yamashita, S. Yun, K. Kannan, Bisphenol analogues in sediments from industrialized areas in the United States, Japan, and Korea: spatial and temporal distributions, Environ. Sci. Technol. 46 (2012) 11558–11565.
[23] E.H. Hernandez, R.C. Martinez, E.R. Gonzalo, Use of a bisphenol-A imprinted polymer as a selective sorbent for the determination of phenols and phenoxyacids in honey by liquid chromatography with diode array and tandem mass spectrometric detection, Anal. Chim. Acta 650 (2009) 195–201.
[24] M.A. Rahman, M.J.A. Shiddiky, J.S. Park, Y.B. Shim, An impedimetric immunosensor for the label-free detection of bisphenol A, Biosens. Bioelectron. 22 (2007) 2464–2470.
[25] G.R. Marchesini, E. Meulenberg, W. Haasnoot, H. Irth, Biosensor immunoassays for the detection of bisphenol A, Anal. Chim. Acta 528 (2005) 37–45.
[26] W.V. Welshons, S.C. Nagel, F.S. vom Saal, Large effects from small exposures. III. endocrine mechanisms mediating effects of bisphenol A at levels of human exposure, Endocrinology 147 (2006) S56–S69.
[27] H. Yin, Y. Zhou, S. Ai, R. Han, T. Tang, L. Zhu, Electrochemical behavior of bisphenol A at glassy carbon electrode modified with gold nanoparticles, silk fibroin, and PAMAM dendrimers, Microchim. Acta 170 (2010) 99–105.
[28] D.R. Thévenot, K. Toth, R.A. Durst, G.S. Wilson, Electrochemical biosensors: recommended definitions and classification, Biosens. Bioelectron. 16 (2001) 121–131.
[29] H. Wang, Y. Zou, C. Li, W. Wang, M. Zhang, R.A. Dahlgren, X. Wang, Fluorescence characteristics of Bisphenol A in room temperature ionic liquids, J. Fluoresc. 23 (2013) 1157–1165.
[30] A.D. Batista, F.R. Rocha, A green flow-injection procedure for fluorimetric determination of bisphenol A in tap waters based on the inclusion complex with B-cyclodextrin, Int. J. Environ. Anal. Chem. 93 (2013) 1402–1412.
[31] X.X. Lv, Z.Z. Li, C.G. Niu, M. Ruan, D.W. Huang, G.M. Zeng, Determination of ammonia-oxidizing bacteria based on time-resolved fluorescence and tandem probe, Water Sci. Technol. 6 (2012) 1361–1368.
[32] D.W. Huang, C.G. Niu, M. Ruan, X.Y. Wang, G.M. Zeng, C.H. Deng, Highly sensitive strategy for Hg^{2+} detection in environmental water samples using long lifetime fluorescence quantum dots and gold nanoparticles, Environ. Sci. Technol. 47 (2013) 4392–4398.
[33] D.W. Huang, C.G. Niu, G.M. Zeng, X.Y. Wang, X.X. Lv, A highly sensitive protocol for the determination of Hg^{2+} in environmental water using time-gated mode, Talanta 132 (2015) 606–612.
[34] S.G. Kim, J.S. Lee, J. Jun, D.H. Shin, J. Jang, Ultrasensitive bisphenol A field-effect transistor sensor using an aptamer-modified multichannel carbon nanofiber transducer, ACS Appl. Mater. Interfaces 8 (2016) 6602–6610.
[35] S.S. Oh, B.F. Lee, F.A. Leibfarth, M. Eisenstein, M.J. Robb, N.A. Lynd, C.J. Hawker, H.T. Soh, Synthetic aptamer-polymer hybrid constructs for programmed drug delivery into specific target cells, J. Am. Chem. Soc. 136 (2014) 15010–15015.
[36] O.N. Oliveira, R.M. Iost, J.R. Siqueira, F.N. Crespilho, L. Caseli, Nanomaterials for diagnosis: challenges and applications in smart devices based on molecular recognition, ACS Appl. Mater. Interfaces 6 (2014) 14745–14766.
[37] Y.H. Lao, K.K.L. Phua, K.W. Leong, Aptamer nanomedicine for cancer therapeutics: barriers and potential for translation, ACS Nano 9 (2015) 2235–2254.
[38] D.W. Huang, C.G. Niu, Z.Z. Li, M. Ruan, X.Y. Wang, G.M. Zeng, A sensitive strategy for label-free and time-resolved fluorescence assay of thrombin using Tb-complex and unmodified gold nanoparticles, Analyst 137 (2012) 5607–5613.
[39] K.L. Hong, L.J. Sooter, Single-stranded DNA aptamers against pathogens and toxins: identification and biosensing applications, Biomed. Res. Int. 2015 (2015) 31.
[40] W.S. Hummers, R.E. Offema, Preparation of graphitic oxide, J. Am. Chem. Soc. 80 (1958) 1339.
[41] J.H. Zhu, S.Y. Wei, H.B. Gu, S.B. Rapole, Q. Wang, Z.Q. Luo, N. Haldolaarachchige, D.P. Young, Z.H. Guo, One-pot synthesis of magnetic graphene nanocomposites decorated with core@double-shell nanoparticles for fast chromium removal, Environ. Sci. Technol. 46 (2012) 977–985.
[42] L.D. Wu, D.H. Deng, J. Jin, X.B. Lu, J.P. Chen, Nanographene-based tyrosinase biosensor for rapid detection of bisphenol A, Biosens. Bioelectron. 35 (2012) 193–199.
[43] L.Y. Zhang, J.C. Er, W. Xu, X. Qin, “Orange alert”: a fluorescent detector for bisphenol A in water environments, Anal. Chim. Acta 815 (2014) 51–56.
[44] L. Zhou, J.P. Wang, D.J. Li, Y.B. Li, An electrochemical aptasensor based on gold nanoparticles dotted graphene modified glassy carbon electrode for label-free detection of bisphenol A in milk samples, Food Chem. 162 (2014) 34–40.
[45] K. Padmanabhan, K.P. Padmanabhan, J.D. Ferrara, J.E. Sadler, A. Tulinsky, The structure of alpha-thrombin inhibited by a 15-mer single-stranded DNA aptamer, J. Biol. Chem. 268 (1993) 17651–17654.
[46] J. Feigon, T. Diekmann, F.W. Smith, Aptamer structures from A to zeta, Chem. Biol. 3 (1996) 611–617.
[47] D.J. Patel, Structural analysis of nucleic acid aptamer, Curr. Opin. Chem. Biol. 1 (1997) 32–46.