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Molecularly imprinted polymer based on CdTe@SiO_2 quantum dots as a fluorescent sensor for the recognition of norepinephrine

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A novel molecular imprinted sensor based on CdTe@SiO_2 quantum dots (QDs) was developed for norepinephrine (NE) recognition. The molecularly imprinted polymer (MIP) on the surface of CdTe@SiO_2 QDs (CdTe@SiO_2@MIP) was characterized by Fourier transform infrared spectroscopy, transmission electron microscopy and fluorescence spectroscopy. The synthesized nanosensor had distinguished selectivity and high binding affinity to NE. Under the optimal conditions, the relative fluorescence intensity of CdTe@SiO_2@MIP decreased linearly with the increase of the concentration of NE in the range of 0.04-10 μM. The limit of detection was 8 nM (3σ/K). The proposed method was applied to the analysis of NE in rat plasma, and the results obtained by the method were in good agreement with those assayed by the fluorescence derivatization method. The method built is simple, fast, and can be applied to the determination of NE in biological samples.

1. Introduction

Quantum dots (QDs) are luminescent semiconductor nanocrystals in size range of 1-10 nm. QDs have attracted much attention in recent years due to their unique optical properties, such as high quantum yield, narrow and symmetrical spectra, broad excitation spectra and photostability.[1] Many researchers have constructed QDs-based sensing materials for sensitive determination of analytes. Huang et al.[2] utilized mercaptosuccinic acid-capped CdSe/ZnS QDs as a fluorescent sensor for quantitative analysis of urea. Huang et al.[3] developed a simple and sensitive method for L-cysteine detection based on the increment of the fluorescence intensity of mercaptoacetic acid-capped CdSe/ZnS QDs. Jin et al.[4] reported that tert-butyl-N-(2-mercaptoethyl)-carbamate modified CdSe QDs allowed a highly sensitive determination of free cyanide. However, researchers have found that the selectivity of QDs sensors is poor, which limits their usage in detecting real samples.

In recent years, many efforts have been made to improve the selectivity of QDs sensors, e.g. QDs-based immunosensor, in which QDs were conjugated with antibody to generate specific sensor for the immuno-recognition of antigen.[5-7] However, the construction of a QDs-based immunosensor is complex, and antibodies are expensive and easily denatured. Lately, a new type of molecularly imprinted polymer (MIP)-based QDs (QDs@MIP) as a selective sensor has attracted considerable interests.[8-20] MIP is a kind of biomimetic polymer, which is usually obtained by polymerization of functional and cross-linking monomers in the presence of a template molecule capable of forming complexes with the monomer. After the

removal of the template, definite cavities that are specific to both the shape and chemical functionality of the template are left. Thus, MIP can recognize the template with a high specificity, comparable to antibodies.[21,22] The remarkable advantages of a QDs@MIP sensor compared with a QDs-based immunosensor are its chemical stability, low cost and availability to recognize small molecules. Hence, QDs@MIPs have been employed as selective sensors in the field of bioanalysis, pharmaceutical and environmental analysis.

QDs@MIPs are usually prepared by sol-gel method.[23-36] Sol-gel method is a well-established way, and the rigid, highly cross-linked structure of silica allows the creation of delicate imprint sites with the potential for a high degree of shape selectivity. The chemical/mechanical stability, nontoxicity, and biocompatibility of silica also make it an attractive substrate in many fields.[37] Generally, there are two synthetic routes to obtain QDs@MIPs by sol-gel method. One is the direct method by polymerization on the surface of QDs prepared by organometallic or aqueous method,[23-33] and the other is the surface modification method by using QDs previously coated with silica.[34-36] Studies have shown that the fluorescence intensity of the QDs@MIP prepared by the direct method was very weak, and what is more, the yield was very low. However, the surface modification method could increase the fluorescence intensity and the yield of the QDs@MIP.

To the best of our knowledge, no literature has reported the application of QDs@MIP to determine neurotransmitters in biological samples. Norepinephrine (NE) is a catecholamine with multiple roles including as a neurotransmitter and a

hormone. One of the most important functions of NE is the role as the neurotransmitter released from the sympathetic neurons to affect the heart. An increase of NE from the sympathetic nervous system increases the rate of contractions in the heart. As a stress hormone, NE affects parts of the brain, such as the amygdala, where attention and responses are controlled.[38] Thus, the determination of NE is very important for the studies of the physiological role of NE and the diagnosis of several mental diseases.[39,40] Many methods have been reported for determining NE in biological samples, such as HPLC-chemiluminescent detection,[41] HPLC-MS,[42] capillary electrophoresis-UV[43] and hydrophilic interaction chromatography-electrochemical detection,[44] etc. However, these methods need expensive instruments and man-power. It is urgent to develop a simple and rapid method to detect NE in biological samples.

In the present work, a highly selective and sensitive CdTe@SiO_2@MIP sensor for the determination of NE was prepared by the surface modification method. CdTe@SiO_2 QDs were not only utilized as fluorophores to provide fluorescence signal, but also served as a highly cross-linked rigid matrix for surface molecular imprinting. The CdTe@SiO_2@MIP was characterized by Fourier transform infrared spectroscopy (FT-IR), transmission electron microscopy (TEM) and fluorescence spectroscopy. The CdTe@SiO_2@MIP was successfully applied as a fluorescent sensor to the analysis of NE in real samples. Encouraging results were obtained.

2. Materials and methods

2.1 Reagents and chemicals

$CdAc_2$ $2.5H_2O$ (98.5%), $NaBH_4$ (96%), tellurium powder and tetraethoxysilane (TEOS) were obtained from Sinopharm Chemical Reagent Co. Ltd. (Shanghai, China). Mercaptopropanoic acid (MPA; 99%), 3-aminopropyltritehoxysilane (APTES; 98%), NE (98%), epinephrine hydrochloride (E; 98%), 5-hydroxytryptamine hydrochloride (5-HT; 98%) and isoprenaline hydrochloride (ISO; 98%) were purchased from Sigma-Aldrich Chemical Company (St. Louis, MO, USA). Doubly deionized water (DDW) was obtained from a PURELAB Classic water purification system (PALL, USA).

2.2 Apparatus

The fluorescence spectra were obtained on a Hitachi F-4600 fluorescence spectrometer (Japan). The absorption spectra were measured by a Shimadzu UV-2450 UV-Visible spectrophotometer (Japan). FT-IR spectra were recorded by using a Tensor-27 FT-IR spectrometer (Bruker, Germany) with a resolution of 2 cm^{-1} and a spectral range of 4000-400cm^{-1}. TEM were performed on a Phillips FEI Tecnai G^2 20 S-TWIN (FEI Company, USA) for the estimation of average size of the as-prepared CdTe@SiO_2 QDs and CdTe@SiO_2@MIP.

2.3 Preparation of CdTe@SiO_2 QDs

The water-soluble CdTe@SiO_2 QDs were synthesized by using a one-pot method[45] with some modification. Freshly prepared oxygen-free NaHTe solution was added to N_2-saturated Cd^{2+} aqueous solution at pH 9~10 in the presence of MPA at 90 ℃. The mixture was refluxed for 10 min. Then, TEOS was dropped into the solution by a syringe and the mixture was refluxed at 90 ℃ for 5 h. The as-prepared CdTe@SiO_2

solution was dried out by rotary evaporation and washed with ethanol three times. The concentration of Cd^{2+} was set as 2 mM and the molar ratio of Cd:Te:MPA:TEOS was 1:0.5:2.4:50 in the present experiment.

2.4 Preparation of CdTe@SiO_2@MIP

The CdTe@SiO_2 QDs obtained above were dispersed in 25 mL of mixture of ethanol and DDW (2:1, v:v) by ultrasonic vibration. After the mixture was degassed with N_2 for 20 min, 250 mg of NE (1.48 mmol), 1.4 mL of APTES (5.98 mmol) and 2 mL of TEOS (8.97 mmol) were sequentially added and stirred under N_2 for 20 h. Finally, CdTe@SiO_2@MIP was isolated by centrifugation at 10,000 rpm for 10 min.

To remove NE, the product was washed with DDW until no template was detected by UV-vis spectrophotometry. The polymer was then stored at -18 ℃ prior to use. As a reference, non-imprinted polymer on the surface of CdTe@SiO_2 (CdTe@SiO_2@NIP) was prepared with the same procedure except for the addition of the template molecule.

2.5 FT-IR measurements

For FT-IR measurements, the samples were prepared by using KBr pellet technique. CdTe@SiO_2, CdTe@SiO_2@MIP and CdTe@SiO_2@NIP were dried in vacuum drying oven at 50 C for 6 h before use.

2.6 Fluorescence measurements

In the experiments, all the fluorescence detections were performed under the same conditions: the slit widths of the excitation and emission were both 5.0 nm and the excitation wavelength was set at 370 nm with a recording emission range of 450-700

nm. The photomultiplier tube voltage was set at 700 V.

The as-prepared CdTe@SiO_2@MIP or CdTe@SiO_2@NIP was dispersed in an appropriate quantity of DDW by ultrasonic vibration. Then, 1 mL of the suspension was added to 1 mL of the given concentration of analyte standard solution. The mixture was mixed thoroughly for 15 min by ultrasonic vibration and scanned with a fluorescence spectrometer after being cooled to room temperature.

2.7 Sample preparation and analysis

2 mL of rat plasma was added to a 10 mL centrifuge tube. 6 mL of acetonitrile was added, and the mixture was vortexed for 3 min. After centrifugation at 13000 rpm for 5 min, the supernatant was collected and dried by using nitrogen blowing. The dried extract was dissolved with 1 mL of DDW for the analysis of NE by using the method described in section 2.6.

3. Results and discussion

3.1 Preparation of CdTe@SiO_2@MIP

In sol-gel method, QDs@MIPs are usually prepared by two different routes, i.e. direct way[23-33] and surface modification way.[34-36] In the direct method, QDs was first prepared by organometallic or aqueous method, and then either the raw solution of QDs[23-30] or the purified QDs[31-33] was utilized in the polymerization reaction. However, when the raw solution of QDs was employed, the remaining materials, such as the stabilizer and sodium hydroxide, would adversely affect the polymerization. On the other hand, since the purification procedure usually led to a significant decrease of the photoluminescent quantum yield (PLQY) of QDs which

decided the optical quality of QDs@MIP, the fluorescence intensity of the QDs@MIP prepared by the direct way was very weak. The yield was also very low due to the loss of QDs during the purification process.

As for the surface modification way using QDs previously coated with silica, the fluorescence intensity of the QDs@MIP could be greatly increased since the studies have shown that the PLQY of the silica coated QDs was much higher than that of the neat QDs.[45-49] The common route for coating silica shell on QDs needs multistep complicated manipulations in which the QDs have to be presynthesized and separated before the SiO_2-coating reaction.[34,35,46-49] In our experiment, CdTe@SiO_2 QDs was prepared using a one-pot method[36, 45] by adding TEOS directly into the mixture of NaHTe, Cd^{2+}, MPA and NaOH at 90 ℃. The coating approach is simple and low-cost.

The yields (*Y*) and fluorescence intensities of CdTe@SiO_2@MIPs prepared by the direct and surface modification methods under the same amount of the starting materials are compared in Table 1. *Y* was defined as the following equation:

$$Y = \frac{m_{\text{QDs@MIP}} - m_{\text{QDs}}}{m_{\text{QDs}}} \times 100$$

Where $m_{\text{QDs@MIP}}$ and m_{QDs} represented the mass of the QDs@MIP produced and QDs added, respectively.

Table 1 Comparison of the yields and fluorescence intensities of CdTe@SiO_2@MIPs between the direct and surface modification way.

	Y (%)	fluorescence intensity (a.u.)
direct way	43	3070
surface modification way	68	9850

Table 1 showed that both *Y* and the fluorescence intensity of the QDs@MIP prepared by the surface modification way were much higher than those of the QDs@MIP prepared by the direct way.

CdTe@SiO_2@MIP was prepared via a surface molecular imprinting process. APTES was used as the functional monomer and TEOS as the cross-linker. The mixture of ethanol and DDW (2:1, v:v) was chosen as the porogen through experiments. Because acid could destroy the surface environment of QDs and alkali could accelerate the oxidation of NE, acid or alkali as a catalyst was not used in the molecular imprinting procedure and the reaction time was prolonged to 20 h to ensure the yield of the products. The template NE was self-assembled and immobilized on

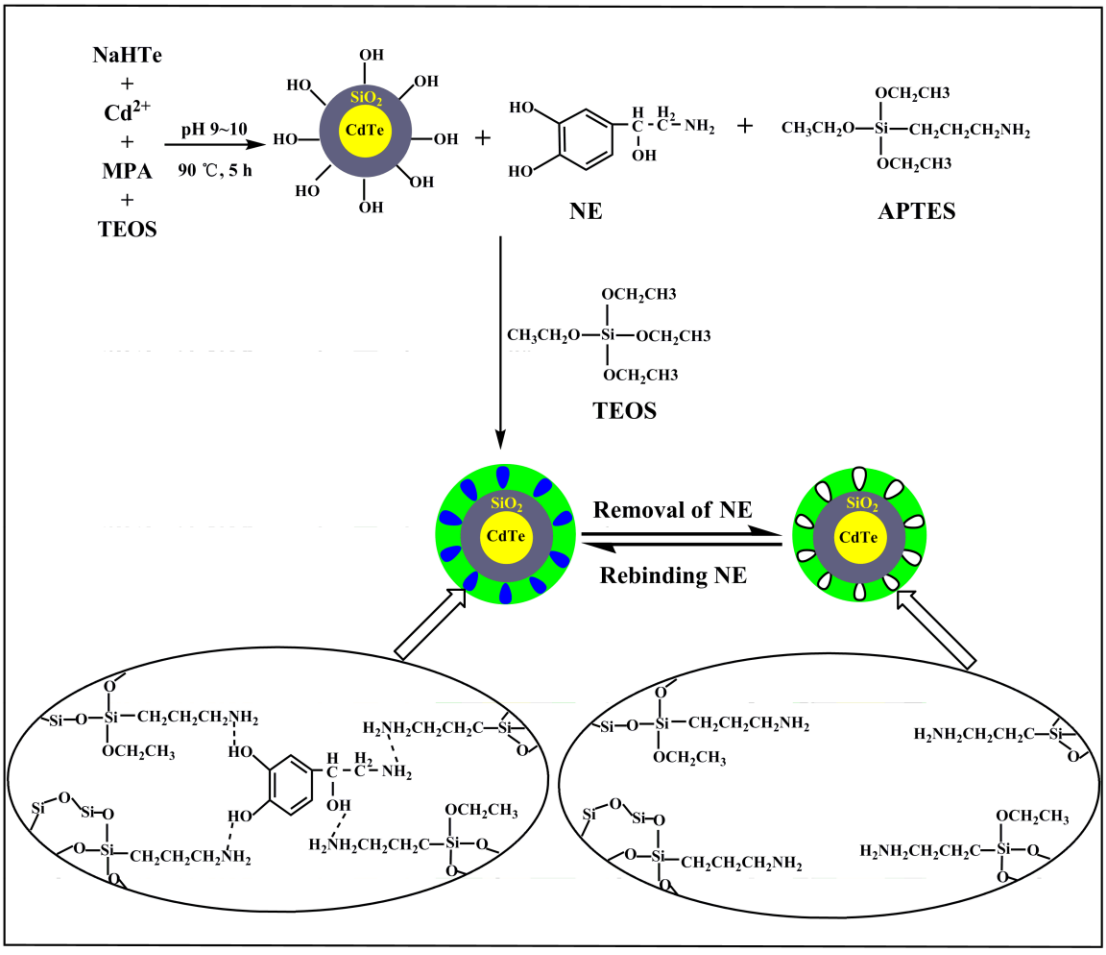

Fig. 1 Schematic illustration of fabricating CdTe@SiO_2@MIP.

the surface of CdTe@SiO_2 QDs through the hydrolysis and condensation reaction of APTES and TEOS,[31] and thus CdTe@SiO_2@MIP with specific NE recognition sites was obtained after the residues of the template and reactants were removed by DDW elution (Fig. 1).

CdTe@SiO_2@MIP stored in a freezer at -18 ℃ would remain stable for at least 30 days. When dispersed in DDW, the fluorescence intensity of the CdTe@SiO_2@MIP remained almost unchanged for 24 h under dark and 6 h under continuous UV irradiation (365 nm), respectively. So, the as-prepared CdTe@SiO_2@MIP fluorescent sensor showed good photochemical stability.

3.2 Characterization of FT-IR

To ascertain the successful synthesis of MIP on the surface of CdTe@SiO_2 QDs, FT-IR spectra of CdTe@SiO_2 QDs, CdTe@SiO_2@MIP and CdTe@SiO_2@NIP are compared in Fig. 2. Since SiO_2 existed in the above three substances, the peaks of the Si-O stretching vibration (1105 cm^{-1}) and Si-O bending vibration (802 cm^{-1}) could be seen in all the spectra. MPA was used as a stabilizer in the preparation of CdTe@SiO_2 QDs, and it existed in the form of carboxylate anion in the synthesis condition (pH 9~10). According to the reference,[50] the peaks of the symmetric and asymmetric stretching vibration of carboxylate anion were around 1409 and 1558 cm^{-1} in the spectrum of CdTe@SiO_2 QDs (Fig. 2A), respectively. However, these two peaks disappeared in Fig. 2B and 2C since CdTe@SiO_2 QDs were tightly wrapped by the MIP and NIP layer in CdTe@SiO_2@MIP and CdTe@SiO_2@NIP. This indicated that MIP and NIP layers generated from the sol-gel condensation of APTES and TEOS

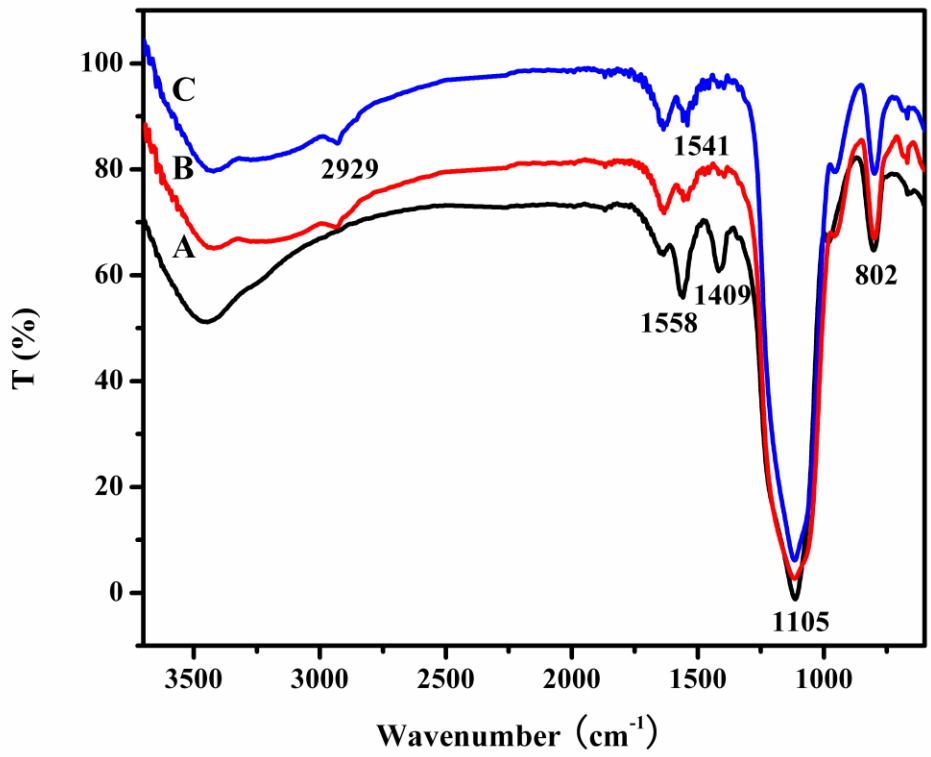

Fig. 2 FT-IR spectra of CdTe@SiO_2 QDs (A), CdTe@SiO_2@MIP (B) and CdTe@SiO_2@NIP (C).

were successfully grafted on the surface of CdTe@SiO_2 QDs. The N-H band around 1541 cm^{-1} in Fig. 2B and 2C, resulting from APTES, also proved the presence of MIP and NIP on the surface of CdTe@SiO_2 QDs. Another characteristic feature of CdTe@SiO_2@MIP and CdTe@SiO_2@NIP compared with CdTe@SiO_2 was the aliphatic C-H stretching band around 2929 cm^{-1}. Theoretically, there exist C-H bonds in the three materials, and the C-H stretching band should appear in all the spectra. However, the C-H stretching band did not appear in the spectrum of CdTe@SiO_2 (Fig. 2A) and appeared as a very weak peak in the spectra of CdTe@SiO_2@MIP and CdTe@SiO_2@NIP (Fig. 2B and 2C). This might be due to the low sensitivity of IR spectrophotometry and relatively less number of C-H bonds in the CdTe@SiO_2 QDs.

The major bands of FT-IR spectra of CdTe@SiO_2@MIP and CdTe@SiO_2@NIP were in similar locations due to their similar compositions.

3.3 Characterization of TEM

TEM images were taken for CdTe@SiO_2 QDs and CdTe@SiO_2@MIP. As shown in Fig. 3, CdTe@SiO_2 QDs were highly spherical and monodispersed with the average size of about 10 nm, while the obtained CdTe@SiO_2@MIP was relatively mono-dispersive and about 20 nm in size. Thus, the thickness of NE-imprinted layer was estimated to be about 5 nm.

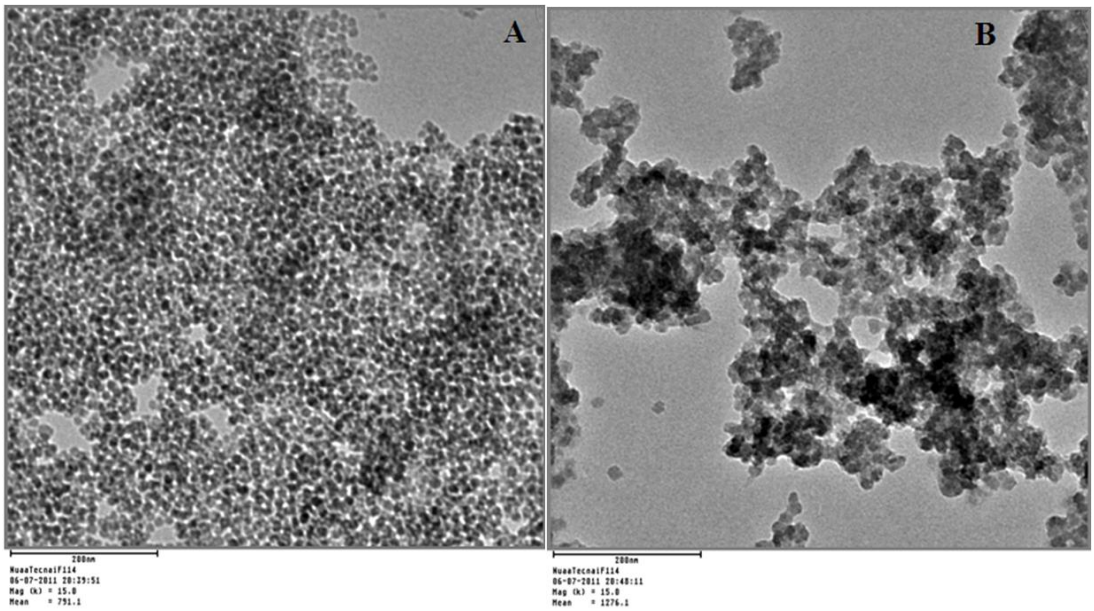

Fig. 3 TEM images of CdTe@SiO_2 QDs (A) and CdTe@SiO_2@MIP (B).

3.4 Optimization of recognition conditions

There are many factors influencing the recognition performance of CdTe@SiO_2@MIP. Solvent, pH value and reaction time were investigated to acquire optimized recognition conditions. The photoluminescence quench was measured in several solvents such as methanol, ethanol, chloroform and DDW as well. The largest response was obtained when DDW was used as the solvent. This was ideal for the

detection of NE in biological samples. In addition, the maximum fluorescence quenching was obtained when the mixture of CdTe@SiO_2@MIP and NE was ultrasoniced for 15 min in DDW without buffer solution. CdTe@SiO_2@MIP was prepared via a surface molecular imprinting process in the experiment, and the binding sites of the CdTe@SiO_2@MIP were at the surface or in the proximity of the surface. So it was an easy diffusion for template to access the recognition sites and fast recognition could be acquired. The above results showed that the CdTe@SiO_2@MIP could be used as a fluorescent sensor to develop a simple, rapid and green method to detect NE in biological samples.

3.5 Selectivity of the CdTe@SiO_2@MIP as a fluorescent sensor for NE

The selectivity of the CdTe@SiO_2@MIP was investigated by using E, 5-HT and ISO as the structural analogues of the NE template. As reported in the previous literatures,[18-20, 26-35] the fluorescence quenching in this system followed the Stern-Volmer equation:

$$F_0/F = 1 + K_{sv}[Q]$$

where F and F_0 are the fluorescence intensities of the probe in the presence and absence of the quencher, respectively. [Q] is the quencher concentration and K_{sv} is the Stern-Volmer constant. Usually, K_{sv} is used to estimate the extent of quenching and sensitivity, and the ratio of $K_{sv,MIP}$ to $K_{sv,NIP}$, known as imprinting factor (IF), is employed to evaluate the selectivity of the sensor.

It is well known that a molecule with the optimal size and shape complementarity has more chance to enter the imprinted cavity and bind with the functional group on

the binding site in the cavity. [51] Compared with its analogs, NE as the template has the superiority to enter the NE-made recognition cavities, and forms the hydrogen bonding with the functional group on the specific binding site in CdTe@SiO_2@MIP. So, the $K_{sv,MIP}$ for NE was much higher than those of its structural analogs and the IF for NE was the highest, just as shown in Fig. 4. It is worth mentioning that although the structure of E differs from that of NE by only a methyl group, the $K_{sv,MIP}$ for E was much lower than that for NE. This might be due to the fact that the steric hindrance caused by the methyl group of E not only reduced the chance of E to enter the recognition cavities, but also affected the formation of the hydrogen bonding between E and the functional group on the binding site.

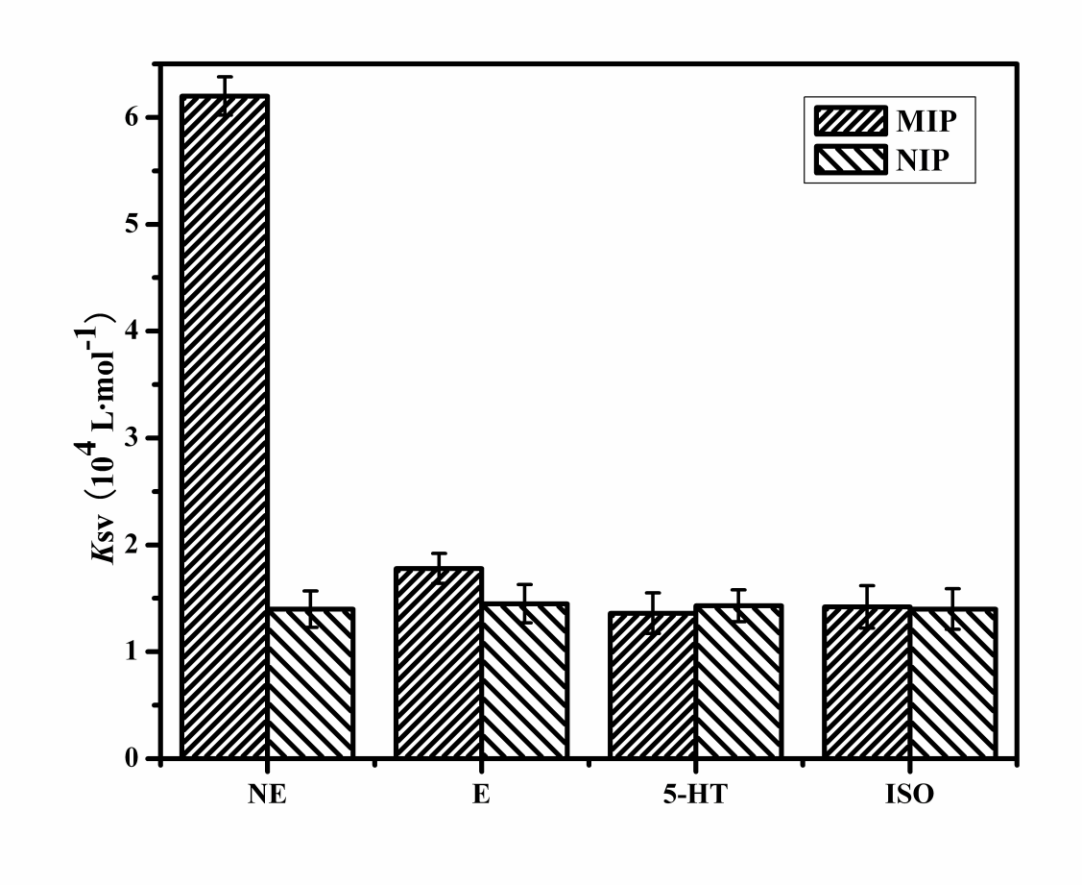

Fig. 4 Selectivity of the CdTe@SiO_2@MIP.

As for CdTe@SiO_2@NIP, since there was no tailor-made recognition cavity formed but -NH_2 groups existed on the surface of CdTe@SiO_2@NIP, NE and its structural analogs were physically adsorbed on the surface of CdTe@SiO_2@NIP by hydrogen bonding (Fig. 5). So, CdTe@SiO_2@NIP adsorbed the template molecules much less than CdTe@SiO_2@MIP, and the binding capacities of CdTe@SiO_2@NIP for NE and its structural analogues were almost the same, just as shown in Fig.4.

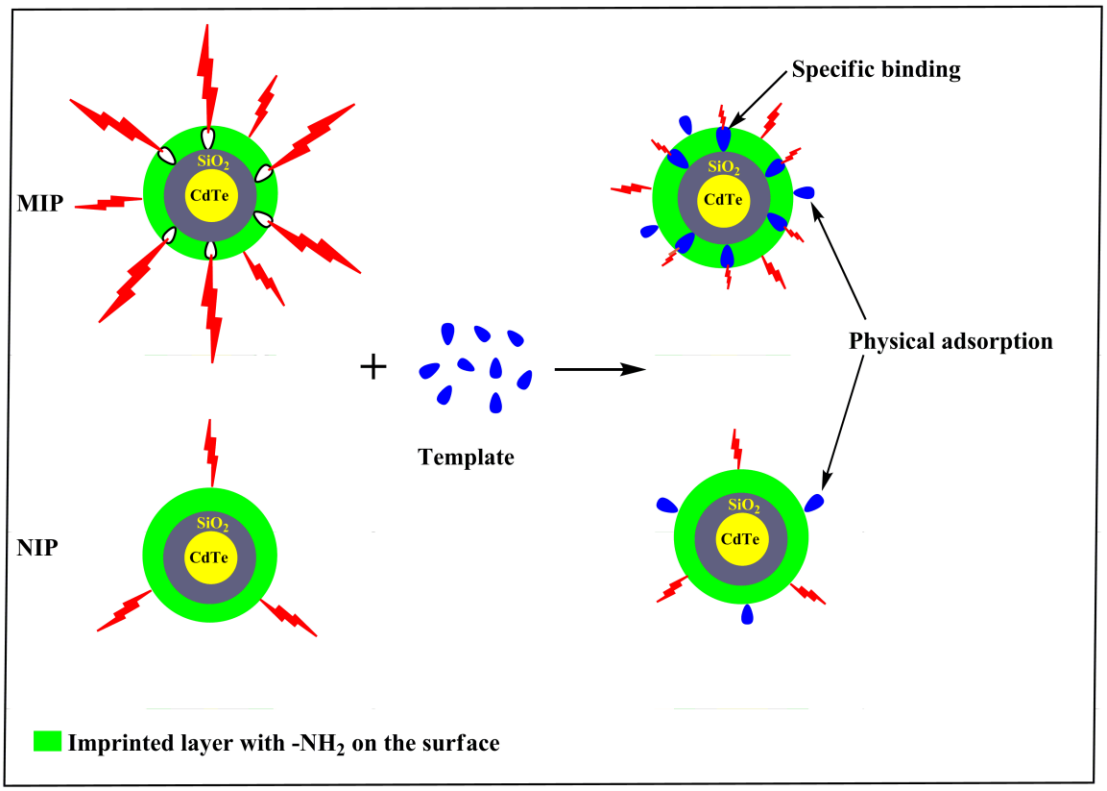

Fig.5 Schematic illustration of the mechanism of interaction between MIP and NIP.

3.6 Detection range and limit

To further evaluate the analytical performance of the CdTe@SiO_2@MIP, the linear rang and detection limit were investigated. Under the optimum conditions, the CdTe@SiO_2@MIP exhibited a distinctly linear decrease in fluorescence upon NE binding over 0.04-10 μM concentration range. The regression equation was F_0/F=0.0593[Q]+1.0317 with a correlation coefficient of 0.9950. As shown in the

regression equation, the intercept was very close to the theoretical value. The systematic error with 3.2% was in the allowed range of fluorimetry (Fig. 6). The limit of detection, which was calculated as the concentration of NE that quenched three times the standard deviation of the blank signal divided by the slope of the standard curve (3σ/K), was 8 nM.

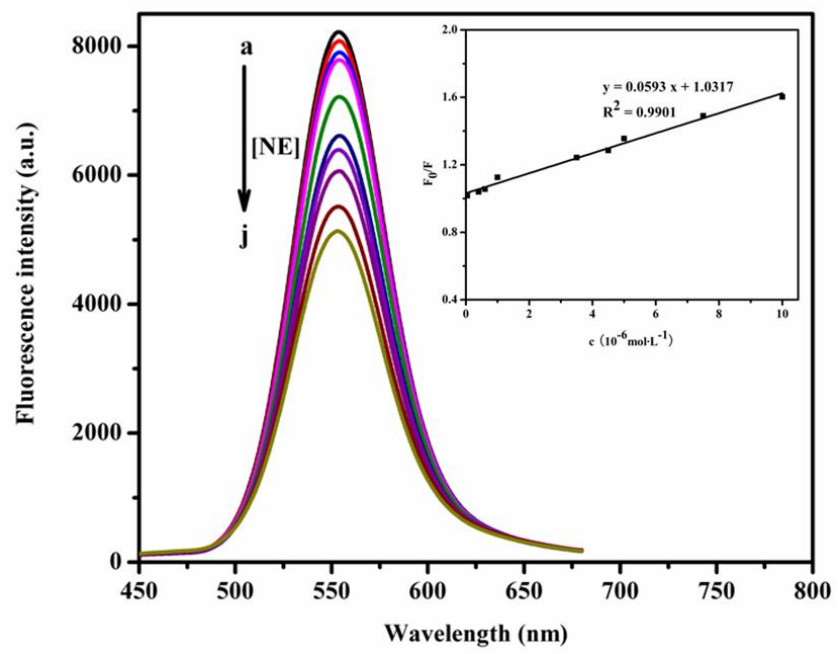

Fig. 6 Fluorescence spectra of CdTe@SiO_2@MIP at different concentrations of NE and the corresponding Stern-Volmer curve (inset).

3.7 Application

The practical feasibility of the CdTe@SiO_2@MIP sensor was tested with rat plasma sample. As shown in Table 2, trace amount of NE in rat plasma was detected. The recoveries of the spiked NE standard solutions in rat plasma sample at three different concentration levels were in the range of 98.20-106.1 % with the relative standard deviations less than 10%. It indicated that the detection results were reliable.

To further verify the accuracy of the proposed method, the level of NE in rat

plasma were also determined by the fluorescence derivatization method reported in the literature[52]. Table 2 displayed that the concentration of NE in the sample obtained by the proposed method was in good agreement with that determined by the reference method. The relative deviation of 3.35% is allowed for analysis of biological samples.

In the fluorescence derivatization method used above, NE was first oxidized by oxidizer under acidic condition, and then fuorescent substance 3-hydroxyindole was generated by alkali treatment. This method was multistep and time-consuming. But in our developed method, the assay time was greatly reduced to less than 1 h if CdTe@SiO_2@MIP was pre-prepared. And the other reported methods as mentioned in the introduction[41-44] need expensive instruments and man-power. Therefore, the proposed method is expected to be a powerful tool for simple, fast and cheap determination of NE in biological samples.

Table 2 Determination of NE in rat plasma sample (n=3).

Proposed method (μM)	Reported method (μM)	Added (μM)	Found (μM)	Recovery (%)	RSD (%)
0.185±0.017	0.179±0.015	0.148	0.157	106.1	9.8
		0.185	0.190	102.7	5.4
		0.222	0.218	98.20	6.9

3.8 Mechanism of the recognition

Fig. 7 revealed the changes in the fluorescence spectra of the original CdTe@SiO_2 QDs, CdTe@SiO_2@MIP before and after the removal of NE, CdTe@SiO_2@MIP and CdTe@SiO_2 QDs with addition of NE. As shown in Fig. 7a, the fluorescence intensity

of the original CdTe@SiO_2 QDs was very strong. After the polymerization process, the fluorescence of the raw material of CdTe@SiO_2@MIP was almost quenched (Fig. 7b). Although, after the removal of the template, the fluorescence intensity of CdTe@SiO_2@MIP did not recover to the previous level of the CdTe@SiO_2 QDs, the CdTe@SiO_2@MIP showed very bright fluorescence (Fig. 7c). The fluorescence intensity of CdTe@SiO_2@MIP was quenched again with the addition of NE (Fig. 7d). On the other hand, the fluorescence intensity of CdTe@SiO_2 remained almost unchanged when the same concentration of NE was added (Fig. 7e). Therefore, it could be concluded that the fluorescence quenching of CdTe@SiO_2@MIP resulted from the interaction between NE molecules and the specific sites of CdTe@SiO_2@MIP. When NE molecules interacted with the functional groups in the imprinting cavities by hydrogen bonding, electron transfer would occur, and thus led to the fluorescence quenching of CdTe@SiO_2@MIP. Meanwhile, the fluorescence of CdTe@SiO_2@MIP would be blocked by NE, just like shading plates.

Fig. 7 also showed that the fluorescence peak of CdTe@SiO_2@MIP shifted from 534 to 552 nm in comparison with that of CdTe@SiO_2 QDs. Since a single charge (Si-O- groups, hydroxylions or ammonium) close to the QDs surface could generate a sufficiently large electric field to cause significant quenching and a red-shift of the QDs emission,[31] the red-shift of CdTe@SiO_2@MIP might be due to the attachment of fully hydrolyzed and subsequently condensed APTES and TEOS to the CdTe@SiO_2 QDs. On the other hand, the imprinting process could increase the size of QDs, thereby reducing the quantum size effect and causing red-shift of the fluorescence

peak of CdTe@SiO_2@MIP.

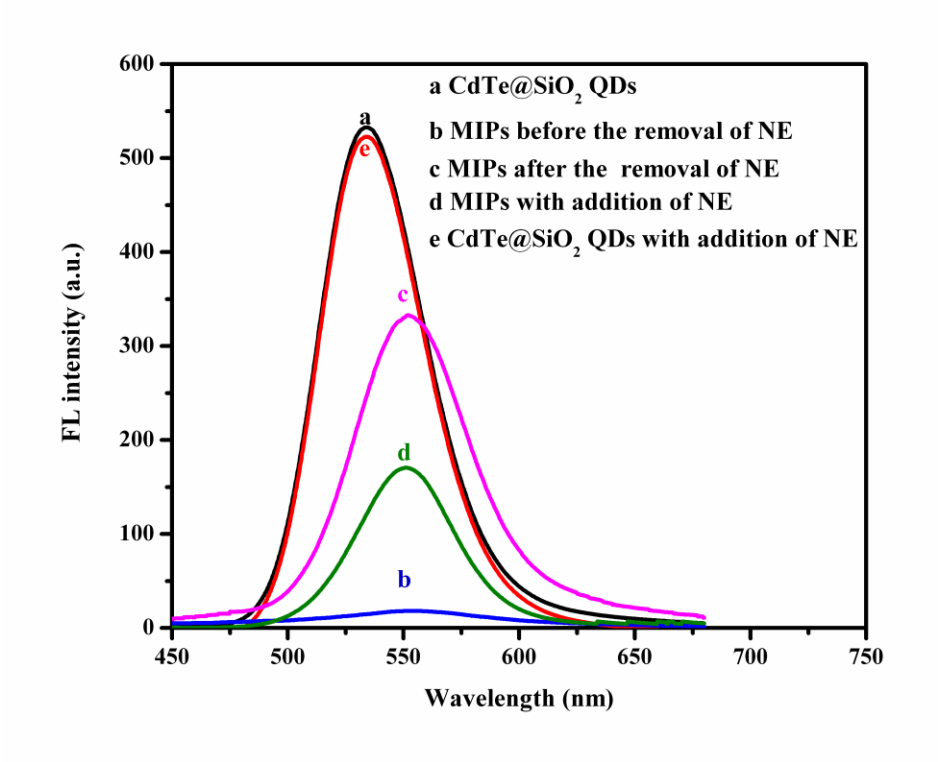

Fig. 7 Fluorescence spectra of CdTe@SiO_2 QDs, CdTe@SiO_2 QDs with addition of NE, CdTe@SiO_2@MIP before and after the removal of NE and CdTe@SiO_2@MIP with addition of NE.

4. Conclusions

A simple, rapid and high-yield method was developed to synthesize molecular imprinted sensor on the surface of CdTe@SiO_2 QDs. The sensor had attractive characteristics, such as uniform morphology, good dispersibility, high binding capacity and selectivity for NE. The analytical method based on CdTe@SiO_2@MIP as the sensing material was successfully applied to the determination of NE in rat plasma samples and the results agreed with those obtained by the method in reference. Compared with the methods previously mentioned in the introduction for determining NE in biological samples, our approach is simpler, faster and cheaper. This work

provides a method for imprinting various neurotransmitter molecules, and forms the basis for selective recognition and rapid detection of neurotransmitters in complicated matrices.

Acknowledgement

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References

1 Q. Sun, Y. A. Wang, L. S. Li, D. Y. Wang, T. Zhu, J. Xu, C. H. Yang and Y. F. Li, *Nat. Photonics*, 2007, 1, 717-722.

2 C. P. Huang, Y. K. Li and T. M. Chen, *Biosens. Bioelectron*., 2007, 22, 1835-1838.

3 S. Huang, Q. Xiao, R. Li, H. L. Guan, J. Liu, X. R. Liu, Z. K. He and Y. Liu, *Anal. Chim. Acta*, 2009, **645**, 73-78.

4 W. J. Jin, J. M. Costa-Fernández, R. Pereiro and A. Sanz-Medel, *Anal. Chim. Acta*, 2004, **522**, 1-8.

5 G. P. Anderson, R. H. Glaven, W. R. Algar, K. Susumu, M. H. Stewart, I. L. Medintz and E. R. Goldman, *Anal. Chim. Acta*, 2013, **786**, 132-138.

6 A. Chopra, S. Tuteja, N. Sachdeva, K. K. Bhasin, V. Bhalla and C. Raman Suri, *Biosens. Bioelectron*., 2013, **44**, 132-135.

7 T. Jamieson, R. Bakhshi, D. Petrova, R. Pocock, M. Imani and A. M. Seifalian, *Biomaterials*, 2007, **28**, 4717-4732.

8 N. Tomczak, D. Janczewski, M. Y. Han and G. J. Vancso, *Prog. Polym. Sci*., 2009, **34**, 393-430.

9 K. Flavin and M. Resmini, *Anal. Bioanal. Chem*., 2009, **393**, 437-444.

10 H. Y. Lin, M. S. Ho and M. H. Lee, *Biosens. Bioelectron*., 2009, **25**, 579-586.

11 M. H. Lee, Y. C. Chen, M. H. Ho and H. Y. Lin, *Anal. Bioanal. Chem*., 2010, **397**, 1457-1466.

12 J. Inoue, T. Ooya and T. Takeuchi, *Soft Matter*., 2011, **7**, 9681-9684.

13 Y. X. Li, Y. J. Li, L. H. Huang, Q. Bin, Z. Y. Lin, H. H. Yang, Z. W. Cai and G. N. Chen, *J. Mater. Chem. B*, 2013, **1**, 1256-1262.

14 C. I. Lin, A. K. Joseph, C. K. Chang and Y. D. Lee, *Biosens. Bioelectron*., 2004, **20**, 127-131.

15 C. I. Lin, A. K. Joseph, C. K. Chang and Y. D. Lee, *J. Chromatogr. A*, 2004, **1027**, 259-262.

16 S. E. Diltemiz, R. Say, S. Büyüktiryaki, D. Hür, A. Denizli and A. Ersöz, *Talanta*, 2008, **75**, 890-896.

17 S. G. Ge, C. C. Zhang, F. Yu, M. Yan and J. H. Yu, *Sensors Actuators B*, 2011, **156**, 222-227.

18 H. L. Liu, G. Z. Fang, C. M. Li, M. F. Pan, C. C. Liu, C. Fan and S. Wang, *J. Mater. Chem*., 2012, **22**, 19882-19887.

19 H. L. Liu, G. Z. Fang, H. D. Zhu, C. M. Li, C. C. Liu and S. Wang, *Biosens. Bioelectron*., 2013, **47**, 127-132.

20 G. Z. Fang, C. Fan, H. L. Liu, M. F. Pan, H. D. Zhu and S. Wang, *RSC Adv*., 2014, **4**, 2764-2771.

21 R. Zhu, W. H. Zhao, M. J. Zhai, F. D. Wei, Z. Cai, N. Sheng, Q. Hu, *Anal. Chim*.

Acta, 2010, **658**, 209-216.

22 J. Matsui, S. Goji, T. Murashima, D. Miyoshi, S. Komai, A. Shigeyasu, T. Kushida, T. Miyazawa, T. Yamada, K. Tamaki and N. Sugimoto, *Anal. Chem*., 2007, **79**, 1749-1757.

23 H. F. Wang, Y. He, T. R. Ji and X. P. Yan, *Anal. Chem*., 2009, **81**, 1615-1621.

24 L. Dan and H. F. Wang, *Anal. Chem*., 2013, **85**, 4844-4848

25 W. Zhang, X. W. He, Y. Chen, W. Y. Li and Y. K. Zhang, *Biosens. Bioelectron*., 2011, **26**, 2553-2558.

26 Y. P. Chen, D. N. Wang, Y. M. Yin, L. Y. Wang, X. F. Wang and M. X. Xie, *J. Agric. Food Chem*., 2012, **60**, 10472-10479.

27 S. G. Ge, J. J. Lu, L. Ge, M. Yan and J. H. Yu, *Spectrochimica Acta Part A*, 2011, **79**, 1704-1709.

28 Y. Kim, J. B. Jeon and J. Y. Chang, *J. Mater. Chem*., 2012, **22**, 24075-24080.

29 W. Zhang, X. W. He, Y. Chen, W. Y. Li and Y. K. Zhang, *Biosens. Bioelectron*., 2012, **31**, 84-89.

30 S. F. Xu, H. Z. Lu, J. H. Li, X. L. Song, A. X. Wang, L. X. Chen and S. B. Han, *ACS Appl. Mater. Inter*., 2013, **5**, 8146-8154.

31 H. B. Li, Y. L. Li and J. Cheng, *Chem. Mater*., 2010, **22**, 2451-2457.

32 M. Yang, A. J. Han, J. L. Duan, Z. P. Li, Y. C. Lai and J. H. Zhan, *J. Hazard. Mater*., 2012, **237-238**, 63-70.

33 H. L. Liu, D. R. Liu, G. Z. Fang, F. F. Liu, C. C. Liu, Y. K. Yang and S. Wang, *Anal. Chim. Acta*, 2013, **762**, 76-82.

34 W. Zhang, X. W. He, W. Y. Li and Y. K. Zhang, *Chem. Commun.*, 2012, **48**, 1757-1759.

35 D. Y. Li, X. W. He, Y. Chen, W. Y. Li and Y. K. Zhang, *ACS Appl. Mater. Inter.*, 2013, **5**, 12609-12616.

36 T. Ye, S. Y. Lu, Q. Q. Hu, X. Jiang, G. F. Wei, J. J. Wang and J. Q. Lu, *Chinese Chem. Lett.*, 2011, **22**, 1253-1256.

37 J. E. Lofgreen and G. A. Ozin, Chem. *Soc. Rev.*, 2014, **43**, 911-933.

38 B. Kagedal, D. S. Goldstein, *J. Chromatogr.*, 1988, **429**, 177-233.

39 F. C. Cheng and J. S. Kuo, *J. Chromatogr. B*, 1995, **665**, 1-13.

40 W. Zhang, X. N. Cao, F. L. Wan, S. Zhang and L. T. Jin, *Anal. Chim. Acta*, 2002, **472**, 27-35.

41 N. Li, J. Z. Guo, B. Liu, Y. Q. Yu, H. Cui, L. Q. Mao and Y. Q. Lin, *Anal. Chim. Acta*, 2009, **645**, 48-55.

42 V. Carrera, E. Sabater, E. Vilanova and M. A. Sogorb, *J. Chromatogr. B*, 2007, **847**, 88-94.

43 B. Claude, R. Nehmé and P. Morin, *Anal. Chim. Acta*, 2011, **699**, 242-248.

44 A. Kumar, J. P. Hart and D. V. Mccalley, *J. Chromatogr. A*, 2011, **1218**, 3854-3861.

45 L. Zhou, C. Gao, X. Z. Hu and W. J. Xu, *Acs Appl. Mater. Inter.*, 2010, **4**, 1211-1219.

46 L. Jin, D. D. Yu, Y. Liu, X. L. Zhao and J. G. Zhou, *Talanta*, 2008, **76**, 1053-1057.

47 P. Yang and N. Murase, *Adv. Funct. Mater.*, 2010, **20**, 1258-1265.

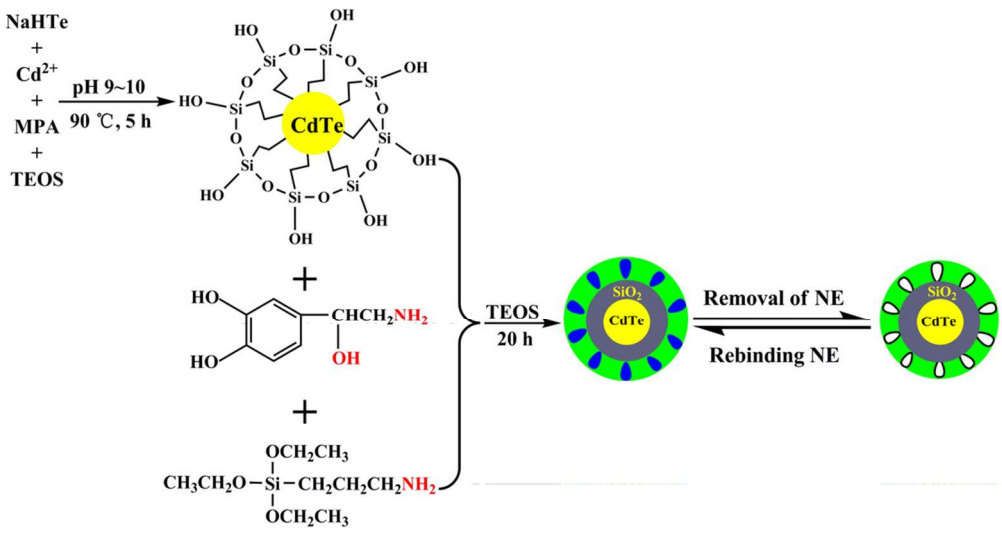
48 N. Murase and P. Yang, *Small*, 2009, **5**, 800-803.

49 K. Han, Z. Xiang, Z. H. Zhao, C. L. Wang, M. J. Li, H. Zhang, X. Yan, J. H. Zhang and B. Yang, *Colloid. Surface. A*, 2006, **280**, 169-176.

50 R. M. Silverstein, F. X. Webster and D. J. Kiemle, *Spectrometric identification of organic compounds*, 7nd ed; John Wiley & Sons, Inc.: Hoboken, 2005, pp. 95-96.

51 B. R. Hart, D. J. Rush and K. J. Shea. *J. Am. Chem. Soc.*, 2000, **122**, 460-465.

52 A. S. Welch and B. L. Welch, *Anal. Biochem.*, 1969, **30**, 161-169.



100x53mm (300 x 300 DPI)

A fluorescent sensor with recognition ability for norepinephrine was simply prepared and actually used to determine norepinephrine in rat plasma.