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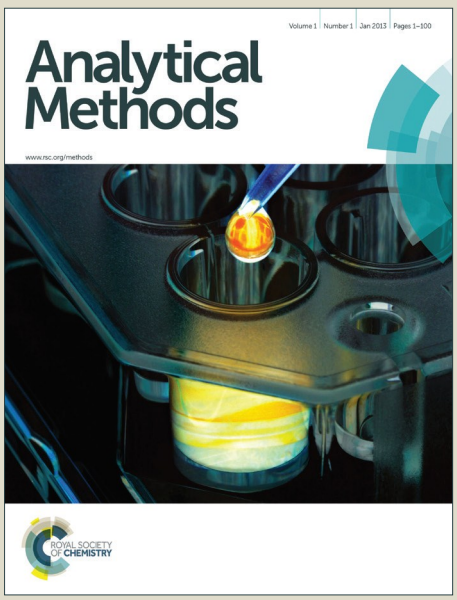

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ARTICLE TYPE

Heparin sodium-selective 'on−off' and lysine-selective 'off−on' fluorescence switching of cadmium telluride quantum dots and their analytical applications

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Sensing biomolecules such as heparin sodium and lysine is of great significance. In this work, a "turn-off-on" fluorescence switching of cadmium telluride quantum dots (CdTe QDs) was designed for both heparin sodium and lysine. Even though both heparin sodium and thioglycolic acid (TGA)-capped CdTe QDs are negatively charged, they are capable of forming self-assembly and even aggregates through hydrogen bonding, depending on the concentration of heparin sodium, which leads to the sensitive fluorescence quenching of CdTe QDs. Thus, a fluorescence 'turn-on' analytical method for heparin sodium sensing could be established with the detection range of 0.200 μg/mL-5.000 μg/mL and the detection limit was 0.033 μg/mL, which is applicable to determining heparin sodium in injection. What's more, a sensitive and selective "turn-off-on" nanosensor was developed for lysine analysis with the detection range of 2 μmol/L-200 μmol/L and the detection limit as low as 0.146 μmol/L. This approach offers a new, simple, fast and selective method for determining heparin sodium and lysine.

1. Introduction

Quantum dots (QDs), a kind of semiconductor nanocrystal, have attracted great attention in chemical and biological fields owing to the unique optical properties, such as high quantum yield, low photobleaching, long fluorescence lifetime, broad absorption and tunable emission,[1-4] depending on their size.[5, 6] Traditionally, thioglycolic acid (TGA) is functioned as a ligand to form a capping shell on the surface of CdTe core,[7] which provides sufficient repulsive force between CdTe QDs.[8, 9] It is also reported that TGA is possible to enhance the specificity to the target.

Heparin sodium is a highly negatively charged linear sulfated glycosaminoglycan (GAG).[10] Structurally, GAG is sulfated disaccharide repeating units, which consists of predominantly iduronic acid, minor glucoronic acid and glucosamine, so that heparin sodium is rich in sulfonic acid groups and secondary amine groups, as well as hydroxyl groups.[11] Heparin sodium, which is extracted from porcine or bovine intestinal mucosa, is one of the most effective and widest clinical anticoagulant drugs with its extensive medical applications, such as anti-thrombotic infarct and suppresses tumor growth.[12] The therapeutic dosing concentration range of heparin is 2-8 U/mL (10.8-43.2 μg/mL) during cardiovascular surgery and 0.2-1.2 U/mL (1.08-6.48 μg/mL) in postoperative and long-term therapy. Therefore, controlling the amount of heparin sodium during the surgery especially for postoperative and long-term care patients in anticoagulant therapy is crucially significant.[13] Recently, a variety of methods have been developed for heparin sodium sensing, such as colorimetric assays[13] spectrophotometry,[14] phosphorescence,[15] fluorescence[16] methods. and light scattering technique.[17] By now, gold nanoparticles and cationic polythiophene have been employed to determine heparin sodium by absorption or colorimetric assays. Other materials, such as rhodamine B-modified polyethyleneimine/graphene oxide[18] or gold nanoclusters/protamine,[19] have been applied to sensitive and selective detection of heparin sodium by fluorescence or phosphorescence. However, more simple, accurate and rapid assays for heparin sodium sensing with high sensitivity and selectivity is still highly desirable.

Structurally, it is possible to form hydrogen bonds between heparin sodium and TGA-CdTe QDs with =N-H—O-C- or –O-H—O-C-.[20-22] In the first part of this work, it was found that CdTe QDs were easy to aggregate in the presence of heparin sodium *via* hydrogen bonding, resulting in the fluorescence quenching of CdTe QDs. Thus, it was propitious to avoiding other negative charge disruptor. Based on this mechanism, a simple, rapid, sensitive and selective method for heparin sodium detection was established.

Following, a turn-on fluorescence sensor was developed for lysine sensing. As one of essential amino acids, lysine is a significant component of animals or human.[23, 24] Lysine plays important roles in synthesis of protein and polyamine,[25] as well as adjusting the somatotropic hormone in human body.[26] If lysine is not able to normally metabolize, it would trigger a lot of clinical symptoms, such as saccharopinuria and glutaric aciduria.[27] Therefore, it is vital to detect the concentration of lysine accurately. Usually, it is detected by liquid chromatography[28, 29] and colorimetric assay,[25, 30] as well as fluorescence analysis.[31] Compared with the above methods, the fluorescence 'turn-off-on'

aasay is simple, selective and sensitive with the low background for lysine analysis. As far as we are concerned, lysine possesses two NH_3^+ groups to compete heparin sodium from CdTe QDs/heparin sodium complex *via* the electrostatic interaction. In the latter part of this work, it was found that fluorescence recovered after the introdution of lysine into CdTe QDs/heparin sodium mixture. Therefore, a simple, low-cost, sensitive, and selective assay for lysine sensing has been developed with CdTe QDs/heparin sodium complex as optical probes.

2. Experimental section

2.1 Materials

Heparin sodium salt (185 IU/mg), D/L-lysine, cadmium, tellurium, thioglycolic acid were purchased from Aladdin Reagent Co., Ltd. (Shanghai, China). The molecular weight of heparin sodium was determined by disaccharide (644.2 g/mol). All other chemicals not mentioned here were of analytical grade purchased from Chengdu Kelong Chemical Reagents Factory (Sichuan, China), and were used as received without further purification. All aqueous solutions were prepared with ultrapure water (18.2 MΩ/cm).

2.2 Apparatus

Fluorescence spectra were scanned with an F-2500 fluorescence spectrophotometer (Hitachi, Tokyo, Japan), and UV-Vis absorption spectra were performed with a UV-3600 spectrophotometer (Hitachi, Tokyo, Japan). A high-resolution transmission electron microscope (TEM) (FEI Company, USA) and Zata nanosizer (ZEN3600, Malvern) were used to characterize CdTe QDs. Functional group analyses were carried out with a Fourier transform infrared spectrometer (FTIR-8400S, Toyota, Japan).

2.3 Synthesis of TGA-capped CdTe QDs

Water-soluble TGA-capped CdTe QDs were synthesized as described in previous report with slight modifications.[32] Briefly, 1 mmol $CdCl_2{\cdot}H_2O$ was dissolved into 100 mL deionized water in a three-necked flask. Then, 166 uL TGA was dispersed in 20 mL water, which was dripped slowly into the flask. Next, cadmium precursor was prepared by purging nitrogen for 30 min after pH was adjusted to 9.0 with 1 mol/L NaOH. Followingly, 0.5 mmol tellurium and 1.68 mmol $NaBH_4$ were quickly poured into a single neck flask that contained 3 mL ethanol and 1 mL water. Tellurium precursor was obtained by nitrogen purging for 30 min after incubation at 50 ^oC for 1 h, and then were quickly injected into cadmium precursor under vigorous shaking and refluxed at 100 ^oC under open-air conditions. TGA-capped CdTe QDs could be obtained with desirable emission properties *via* controlling the reaction time.

2.4 Optimizing conditions for heparin sodium detection

To optimize concentrations of TGA-capped CdTe QDs, 100μL of heparin sodium (20 μg/mL) and different concentrations of CdTe QDs were diluted with ultrapure water till the final volume to 1 mL and standing for 3 min. Besides, to optimize reaction time, the fluorescence intensity was recorded after mixing CdTe QDs (1 μg/mL) with heparin sodium (2 μg/mL) for different time.

The resulting solutions were investigated by fluorescence spectra at room temperature with excitation wavelength at 300 nm, and both the excitation and emission slit widths were set at 5 nm.

2.5 The general procedure of detecting heparin sodium

CdTe QDs (100 μL, 10 μg/mL) and different amounts of heparin sodium were added in a microtube (1.5 mL) successively, then diluted with ultrapure water to 1 mL and vortexed thoroughly. After standing for 3 min, the fluorescence spectra of resulting solutions were scanned at room temperature with excitation wavelength at 300 nm, and both the excitation and emission slit widths were set at 5 nm.

2.6 The detection of heparin sodium injection samples

The heparin sodium injection samples (Tianjin Biochem Pharmaceutical Co., Ltd.) were diluted 20,000 times with ultrapure water before detection. 100 μL injection sample and 100 μL CdTe QDs (10 μg/mL) were diluted with H_2O to 1 mL. The fluorescence intensity was recorded and the concentration of heparin sodium in the heparin sodium injection could be calculated according to the standard curve method.

2.7 Optimizing conditions for lysine detection

In order to obtain a sensitive response for the detection of lysine, the optimal concentration of heparin sodium was considered. 100 μL CdTe QDs (10 μg/mL), 100 μL of lysine (1×10^{-4} mol/L) and different concentrations of heparin sodium were diluted with ultrapure water till the final volume to 1 mL. After standing for 3 min, the fluorescence spectra of resulting solutions were recorded at room temperature with excitation wavelength at 300 nm, and both the excitation and emission slit widths were 5 nm.

2.8 The general procedure of lysine analysis

100 μL CdTe QDs (10 μg/mL), 100 μL heparin sodium (50 μg/mL) and different amounts of lysine were successively added into a microtube (1.5 mL). Then the mixture was diluted with ultrapure water to 1 mL and vortexed thoroughly. After waiting for 3 min, the fluorescence spectra of the resulting solutions studied at room temperature with excitation wavelength at 300 nm, and both the excitation and emission slit widths at 5 nm.

3. Results and discussion

3.1 Characterization of CdTe QDs

The CdTe QDs were prepared by wet-chemical method with $CdCl_2{\cdot}H_2O$, tellurium and thioglycolic acid, thus the surface of the obtained CdTe QDs was covered with carboxylate groups, which were orange in visible light, and displayed a yellow emission under a UV light at 254 nm or 365 nm.

Fig. 1a illustrates the absorbance and fluorescence spectra of CdTe QDs, since absorbance and fluorescence spectra were powerful tools to confirm quantum-confined property of semiconductor QDs. The fluorescence excitation spectrum of QDs showed no any characteristic peak, which was consistent with broad wavelength absorption in the UV-Vis absorption spectrum. The maximum emission intensity at 565 nm was obtained at the excitation of 300 nm. Fig. 1b shows TEM images of CdTe QDs with the interplanar spacing of CdTe QDs was 0.36 nm and the average size about 4 nm.

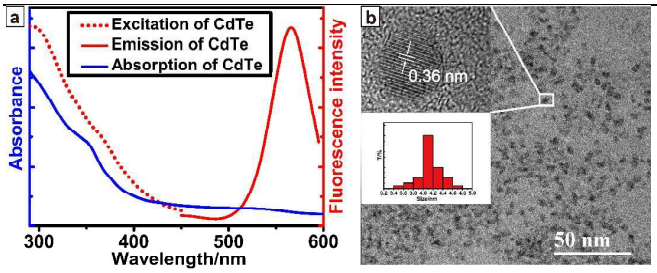
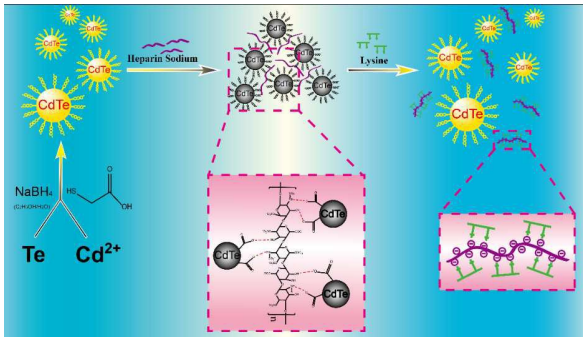


Fig. 1 Characterization of TGA-capped CdTe QDs. (a) Spectral features of CdTe QDs. (b) TEM images of CdTe QDs. The inset displays an enlarged image of region marked by a white pane and the size distribution of CdTe QDs, respectively. Scale bar: 50 nm.

3.2 Mechanism for detection of heparin sodium and lysine

The "turn off-on" fluorescence switch for heparin sodium and lysine analyses is presented in Scheme 1. The TGA-capped CdTe QDs are well dispersed and highly fluorescent. However, the introduction of heparin sodium into the TGA-capped CdTe QDs results in the aggregation and fluorescence quenching of CdTe QDs. The quenching is attributed to the aggregation of CdTe QDs by the hydrogen bonding between heparin sodium and TGA-capped CdTe QDs, since TGA-capped CdTe QDs are abundant in carboxylate groups, while heparin sodium is sulfate glycosaminoglycan segment, so it is easy to form hydrogen bonds between N-H from the sulfated glycosaminoglycan and C-O from the carboxylate groups.[20-22] The aggregated CdTe QDs become dispersive again when lysine is present in the mixture of CdTe QDs and heparin sodium because of the strong electrostatic interaction between lysine and heparin sodium, leading to the fluorescence recovery of CdTe QDs.



Scheme 1 Schematic representation of heparin sodium and lysine detection based on "turn off-on" fluorescent switch of CdTe QDs.

In order to confirm that this fluorescence quenching resulted from the hydrogen-bond interaction, the FTIR spectroscopy was employed to investigate the functional groups. Fig. 3a shows the FTIR spectra of CdTe QDs, heparin sodium and heparin sodium–CdTe QD. The bands assigned to the vibration of O−H and N−H for heparin are at 3452.72 $cm^{-1}$and 1037.70 cm^{-1}, respectively, which shift to 3441.01 cm^{-1} and 1029.99 cm^{-1} when the CdTe/heparin complex is formed. The peaks at 3448.72 cm^{-1} and 1631.78 cm^{-1} are attributed to O-H and C=O vibrations of the carboxylic groups on the surface of CdTe QDs, which shift to lower wavenumbers. Thus, this can be explicated by the strong hydrogen bonding interactions between the heparin and CdTe QDs.[20, 33, 34] As mentioned in Fig. 1a, it presented a downward curve without characteristic peak for CdTe QDs. For heparin sodium, it showed no absorption from 250 nm to 600 nm. However, the mixing of CdTe QDs and heparin sodium led to a reduction in the UV-Vis absorption spectrum of CdTe QDs, which is possible to result from the aggregation of CdTe QDs (Fig. 2b).

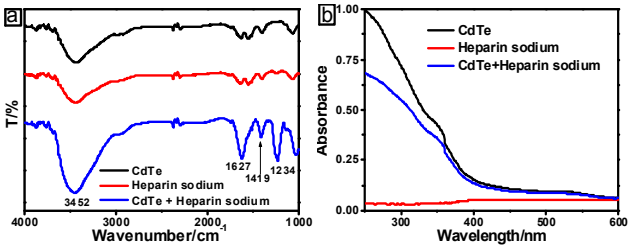


Fig. 2 (a) FTIR spectra. (b) UV-Vis absorption spectra. Concentrations: CdTe QDs, 1 μg/mL; heparin sodium, 2 μg/mL.

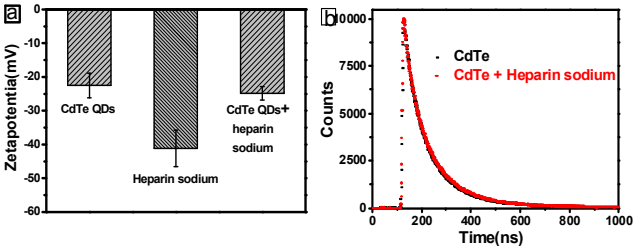


Fig. 3 (a) Zeta-potential before and after added heparin sodium into CdTe QDs. (b) Lifetimes of steady-state fluorescence of CdTe QDs. Concentrations: CdTe QDs, 1 μg/mL; heparin sodium, 2 μg/mL.

Furthermore, the changes of Zeta-potential and steady-state fluorescence lifetime were performed to discuss the mechanism. As shown in Fig. 3a, the negative potential of the TGA-capped CdTe QDs and heparin sodium were -22.5 mV and -41.2 mV, respectively. When mixed, the Zeta potential of mixture was -24.8 mV, indicating that the binding between CdTe QDs and heparin sodium is not caused by electrostatic interaction. On the other hand, there was not obvious change in the fluorescence lifetime of CdTe QDs, which just increased from 45.9 ns to 50.9 ns (Fig. 3b). Therefore, it was extremely likely to be static quenching by aggregation. These results demonstrated that the CdTe QDs were induced to assembly or aggregate *via* hydrogen-bonding between heparin sodium, and thus the fluorescence of CdTe QDs was quenched.

3.3 Sensitive and selective detection of heparin sodium

In order to gain a sensitive response for detecting heparin sodium, the optimizations of TGA-capped CdTe QDs concentrations and reaction time were carried out, respectively. The fluorescence quenching capability of heparin sodium to various concentrations of CdTe QDs was considered (Fig. S1, ESI†). With increasing the concentration of TGA-capped CdTe QDs, the fluorescence intensity was enhanced gradually, while quenching effect was weakened gradually. 1 μg/mL CdTe QDs were employed for the following work to obtain a relatively high quenching effect. Then, the fluorescence intensity of CdTe QDs/heparin sodium mixture was recorded for 10 min, which was decreased gradually. In the other words, the quenching effect was enhanced with extending the reaction time, and it reached the maximum within 3 min, which is applicable for the rapid sensing of heparin sodium (Fig. S2, ESI†).

Fig. 4 depicts the fluorescence intensity of CdTe QDs mixed with different concentrations of heparin sodium, which was quenched gradually owing to the aggregation of CdTe QDs. The inset of Fig. 4 shows the linear plot of fluorescence quenching effect versus heparin sodium concentrations, which could be expressed as $(I_0-I)/I_0=0.0076+0.1789c$ ($R^2=0.9926$), wherein I_0 is

the fluorescence intensity of CdTe QDs, and I is the fluorescence intensity of CdTe QDs /heparin sodium mixture, and c is the concentration of heparin sodium. The linear response toward concentration of heparin sodium ranges from 0.2 to 5.0 μg/mL with the limit of detection as low as 33 ng/mL ($3\sigma/k$). In comparison with other assays for heparin sodium (Table S1), this proposed method presents high sensitivity.

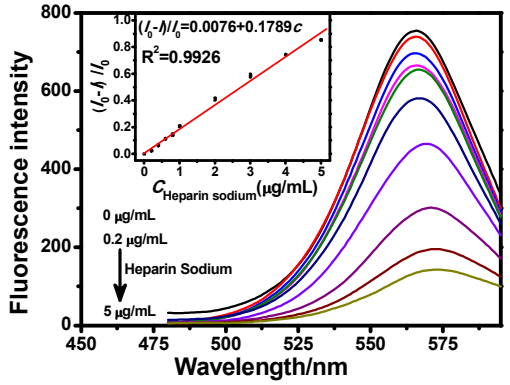


Fig. 4 The fluorescence quenching of TGA-capped CdTe QDs with different concentrations of heparin sodium. The inset displays the linear plot of fluorescence intensity quenching versus heparin sodium concentrations. Conditions: CdTe QDs, 1 μg/mL; λ_{em}, 565 nm; λ_{ex}, 300 nm; t, 3min.

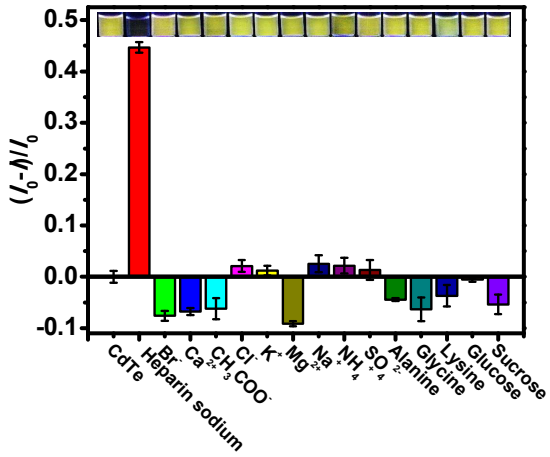


Fig. 5 Selectivity of heparin sodium over other substances. Conditions: CdTe QDs, 1 μg/mL; heparin sodium, 2 μg/mL; Mg^{2+} and Ca^{2+}, 0.2 mmol/L; other substances, 2 mmol/L; λ_{em}, 565 nm; λ_{ex}, 300 nm; t, 3min. The inset images were TGA-capped CdTe QDs with the corresponding substances under a 365 nm UV light source.

This fluorescence assay presented high selectivity for heparin sodium detection, even if they were kept at a concentration more than 100 times higher than heparin sodium.[18] The selectivity was analyzed by monitoring the fluorescence quenching responses of CdTe QDs upon addition of heparin sodium or other coexisting substances, including Br^-, Ca^{2+}, CH_3COO^-, Cl^-, K^+, Mg^{2+}, Na^+, NH_4^+, SO_4^{2-}, alanine, glycine, lysine, glucose, sucrose. As shown in Fig. 5, other ions and amino acids presented minor or negligible restoration effects on the fluorescence intensity of CdTe QDs, which confirmed that the high selectivity of CdTe QDs probes towards heparin sodium was owing to the specific hydrogen bonding.

In order to demonstrate the practical application of the fluorescence assay, heparin sodium in injection samples was detected with our proposed method. The heparin sodium injection it was diluted 20,000 times with ultrapure water for final detection, which obtained similar results to the labelled concentration (Table 1). The results obtained by standard addition method showed that recovery reached to 100±5% (not shown here), suggesting that the proposed assay for heparin sodium analysis was feasible.

Table 1 Results of heparin sodium determination by this method in real samples

No.	Heparin sodium found (IU/2 mL)	Mean (IU/2 mL)	RSD(%) (n=5)	Labelled (IU/2mL)
1	13126, 13030, 12999, 12185, 11730	12614	4.9	12500
2	13141, 13009, 12529, 12408, 11831	12584	4.1	12500

The injection samples were diluted 20000 times before determination (185 IU=1 mg). Conditions: CdTe QDs; 1 μg/mL. λ_{em}=565 nm; λ_{ex}=300 nm; t, 3min.

3.4 Sensitive and selective detection of lysine

It was found that lysine could not induce the quenching of CdTe QDs fluorescence; however, it could the recover CdTe QDs fluorescence that quenched by heparin sodium, which probable to develop for lysine sensing. It is noticeable that the off-on fluorescence process induced by lysine was conducted after the fluorescence quenching by heparin sodium, thus, the concentration of heparin sodium was an important parameter for the sensitive detection of lysine, which was essential to optimize (Fig. S3, ESI†). It showed that fluorescence intensity at 565 nm gradually decreased with increasing the concentrations of heparin sodium when in the absence of lysine. Nevertheless, when lysine was present, the fluorescence of CdTe QDs recovered and it reached maximum when heparin sodium was 5 μg/mL. Hence, 1 μg/mL CdTe QDs and 5 μg/mL heparin sodium were optimal for lysine analysis.

Fig. 6 depicts the fluorescence of CdTe QDs in the presence of heparin sodium and lysine, which presents a gradual enhancement with increasing the concentration of lysine. The inset of Fig. 6 shows the linear plot of fluorescence recovery versus lysine concentrations, which could be expressed as $(I'-I_0')/I_0'=19.683+1.571(\ln c')$ (R^2=0.9967), wherein I_0' is the fluorescence intensity of CdTe QDs in the presence of 5 μg/mL heparin sodium, I' is the fluorescence intensity of CdTe QDs/heparin sodium in the presence of lysine and c' is the concentrations of lysine. The linear response toward lysine concentrations ranges from 2 μmol/L to 200 μmol/L with a detection limit of 0.146 μmol/L. In comparison with other assays for lysine (Table S2), our proposed method presents satisfied sensitivity.

The selectivity for lysine analysis was achieved by monitoring the fluorescence recovery responses of the heparin/CdTe QDs complex upon introduction of lysine or other amino acids. As shown in Fig. 7, other amino acids (except arginine) exerted minor or negligible restoration effects on the fluorescence intensity of the heparin/CdTe QDs complex, even if they were kept at a concentration 20 times higher than lysine, which confirmed the high selectivity of the heparin sodium/CdTe QDs probes towards lysine.[25, 30] It was found that only arginine, another positively charged amino acid, could slightly recover the fluorescence of CdTe QDs. However, heparin/CdTe QDs complex can distinguish lysine and argentine, since lysine and argentine follow different rules. For lysine, the regression equation for lysine concentrations has been presented as above, but the regression equation for argentine was much different from lysine (Fig. S4, ESI†). Furthermore, lysine and argentine were mixed at different ratios to check the fluorescence, which could be expressed in respective regression equations depending on the

ratios, further confirming that lysine and argentine were different form each other (Fig. S5, ESI†).

TEM and fluorescence lifetime were employed to prove the completion between lysine and CdTe QDs to bind heparin sodium, leading to the release of CdTe QDs and recovery their fluorescence. As shown in Fig. 8, CdTe QDs presented the dispersive state (Fig. 8a). However, the addition of heparin sodium induced the aggregation (Fig. 8b) and fluorescence quenching of CdTe QDs (Fig. 4). Following, CdTe QDs got dispersed again (Fig. 8c) and their fluorescence recovered (Fig. 4). It presumed that force of electrostatic interaction between heparin sodium and lysine was greater than that of the hydrogen bonding between heparin sodium and TGA-capped CdTe QDs.

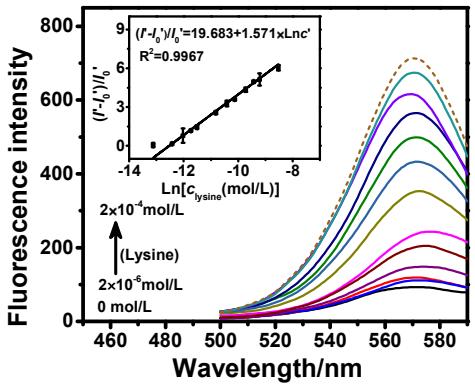


Fig. 6 The fluorescence recovery of TGA-capped CdTe QDs in the presence of heparin sodium with the addition of different concentrations of lysine. The inset displays the linear plot of fluorescence intensity recovery versus lysine concentration. Conditions: CdTe QDs: 1 μg/mL; heparin sodium, 5 μg/mL. λ_{em}, 565 nm; λ_{ex}, 300 nm; *t*, 3min.

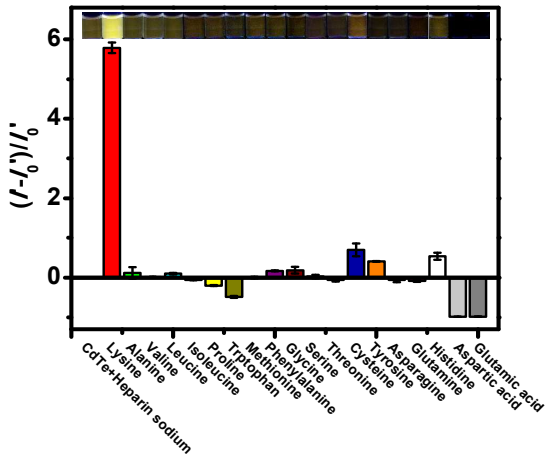


Fig. 7 Selectivity of lysine over other amino acids. Conditions: CdTe QDs, 1 μg/mL; heparin sodium, 2 μg/mL; lysine, 100 μmol/L; other amino acids, 2 mmol/L; λ_{em}, 565 nm; λ_{ex}, 300 nm; *t*, 3min. The inset: images of TGA-capped CdTe QDs in the presence of heparin sodium with the addition of amino acids under a 365 nm UV light source.

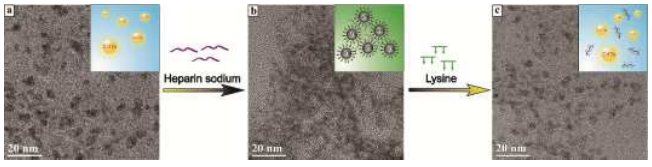


Fig. 8 TEM images of the CdTe QDs. (a), CdTe QDs; (b), CdTe QDs+heparin sodium; (c), CdTe QDs+heparin sodium+lysine. The inset shows the schematic diagrams.

In order to prove the point, the DLS measurement was performed for demonstration of the dispersive or aggregation state. The hydrodynamic size of CdTe QDs was about 8 nm in the scattering intensity distribution. After the introduction of heparin sodium, it increased to about 530 nm. Then, it decreased to about 11 nm when lysine was present (Fig. S6, ESI†), further confirming the aggregation induced by heparin sodium and the dispersion caused by lysine. What's more, the Zeta potential of QDs/herparin sodium complex was increased from -24.8 mV to -22.6 mV when lysine was present (Fig. S7, ESI†), suggesting the electrostatic binding between QDs/herparin sodium complex and lysine since the isoelectric point of lysine is 9.74, which could be positively charged under the working conditions. Thus, lysine could bind heparin sodium to release CdTe QDs, resulting in the fluorescence recovery, which is applicable to lysine analysis. Furthermore, the fluorescence lifetime did not change greatly (Fig. S8, ESI†), suggesting that the fluorescent probe CdTe QDs was released from the aggregation owing to the electrostatic binding between herparin sodium and lysine.

4. Conclusion

TGA-capped CdTe QDs with strong fluorescence were successfully prepared, which possessed a large number of carboxylate groups to form CdTe QDs/heparin sodium complex *via* hydrogen bonding, leading to the selective fluorescence quenching of CdTe QDs. Thus, a new 'turn-off' fluorescence assay was developed for heparin sodium. Here, TGA acted as both the capping reagent to keep CdTe QDs dispersive and the linking reagent to form hydrogen bonding with heparin sodium. Moreover, the fluorescence of CdTe QDs/heparin sodium complex was effectively recovered by lysine due to the stronger electrostatic interaction between the negatively charged heparin sodium and positively charged lysine. Thus, lysine could be sensitively detected by a 'turn-off-on' fluorescence switching with a low fluorescence background. The novel fluorescent probe showed a number of attractive analytical features in the following terms, including high sensitivity, excellent selectivity, low-cost and great accuracy. It is expect that this strategy can offer a new approach to developing low-cost sensors for other drugs or small biological molecules in the pharmaceutical analysis.

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Notes and references

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1 W. W. Yu, L. Qu, W. Guo and X. Peng, *Chem. Mater.*, 2003, **15**, 2854-2860.

2 V. K. Komarala, Y. P. Rakovich, A. L. Bradley, S. J. Byrne, S. A. Corr and Y. K. Gun'ko, *Nanotechnology*, 2006, **17**, 4117-4122.

3 M. X. Gao, J. L. Xu, Y. F. Li and C. Z. Huang, *Anal. Methods*, 2013, **5**, 673-677.

4 S. J. Zhen, H. L. Zhuang, J. Wang and C. Z. Huang, *Anal. Methods*, 2013, **5**, 6904-6907.

5 A. Mandal, J. Nakayama, N. Tamai, V. Biju and M. Isikawa, *J. Phys. Chem. B*, 2007, **111**, 12765-12771.

6 S. M. Farkhani and A. Valizadeh, *IET Nanobiotechnol*, 2014, **8**, 59-76.

7 H. Jiang and H. X. Ju, *Anal. Chem.*, 2007, **79**, 6690-6696.

8 I. G. Dance, M. L. Scudder and R. Secomb, *Inorg. Chem.*, 1983, **22**, 1794-1797.

9 K. Zhao, J. Li, H. Z. Wang, J. Q. Zhuang and W. S. Yang, *J. Phys. Chem. C*, 2007, **111**, 5618-5621.

10 M. Kalita, S. Balivada, V. P. Swarup, C. Mencio, K. Raman, U. R. Desai, D. Troyer and B. Kuberan, *J. Am. Chem. Soc.*, 2014, **136**, 554-557.

11 Z. Zhong and E. V. Anslyn, *J. Am. Chem. Soc.*, 2002, **124**, 9014-9015.

12 A. Falanga and M. Marchetti, *Semin. Thromb. Hemost.*, 2007, **33**, 688-694.

13 R. Zhan, Z. Fang and B. Liu, *Anal. Chem.*, 2010, **82**, 1326-1333.

14 Y. Liu, Y. Yang, X. Zhao, Z. Liu and Y. Li, *Anal. Methods*, 2013, **5**, 3242-3247.

15 H. Yan and H. F. Wang, *Anal. Chem.*, 2011, **83**, 8589-8595.

16 C. D. Sommers, D. J. Mans, L. C. Mecker and D. A. Keire, *Anal. Chem.*, 2011, **83**, 3422-3430.

17 C. Z. Huang, X. B. Pang, Y. F. Li and Y. J. Long, *Talanta*, 2006, **69**, 180-186.

18 J. S. Liu, G. N. Liu, W. X. Liu and Y. R. Wang, *Biosens. Bioelectron.*, 2015, **64**, 300-305.

19 S. N. Ding, C. M. Li and N. Bao, *Biosens. Bioelectron.*, 2015, **64**, 333-337.

20 Y. Ling, Z. F. Gao, Q. Zhou, N. B. Li and H. Q. Luo, *Anal. Chem.*, 2015, **87**, 1575-1581.

21 Y. Cao, S. Shi, L. Wang, J. Yao and T. Yao, *Biosens. Bioelectron.*, 2014, **55**, 174-179.

22 Z. Houjuan, Z. Wen, Z. Kui and W. Suhua, *Nanotechnology*, 2012, **23**, 315502.

23 D. Wellner and A. Meister, *Annu. Rev. Biochem.*, 1981, **50**, 911-968.

24 V. I. Chalova, I. B. Zabala-Diaz, C. L. Woodward and S. C. Ricke, *World J. Microbiol. Biotechnol.*, 2008, **24**, 353-359.

25 Y. Zhou, J. Won, J. Y. Lee and J. Yoon, *Chem. Commun.*, 2011, **47**, 1997-1999.

26 P. Felig, *Annu. Rev. Biochem.*, 1975, **44**, 933-955.

27 G. L. Tang, D. Miron, J. X. ZhuShimoni and G. Galili, *Plant Cell*, 1997, **9**, 1305-1316.

28 R. I. Khan, R. Onodera, M. R. Amin and N. Mohammed, *Amino Acids*, 2002, **22**, 167-177.

29 J. Haneef, M. Shaharyar, A. Husain, M. Rashid, R. Mishra, S. Parveen, N. Ahmed, M. Pal and D. Kumar, *J. Pharm. Anal.*, 2013, **3**, 341-348.

30 J. Wang, P. Zhang, C. M. Li, Y. F. Li and C. Z. Huang, *Biosens. Bioelectron.*, 2012, **34**, 197-201.

31 M. Vendrell, D. Zhai, J. C. Er and Y.-T. Chang, *Chem. Rev.*, 2012, **112**, 4391-4420.

32 M. Gao, S. Kirstein, H. Möhwald, A. L. Rogach, A. Kornowski, A. Eychmüller and H. Weller, *J. Phys. Chem. B*, 1998, **102**, 8360-8363.

33 S. Kubo and J. F. Kadla, *Biomacromolecules*, 2005, **6**, 2815-2821.

34 T. Yang, H. Yang, S. J. Zhen and C. Z. Huang, *ACS Appl. Mater. Interfaces* 2015, **7**, 1586-1594.

Graphical Abstract

for

"Turn-off-on" fluorescence switching of cadmium telluride quantum dots for rapid and selective analysis of heparin sodium and lysine †

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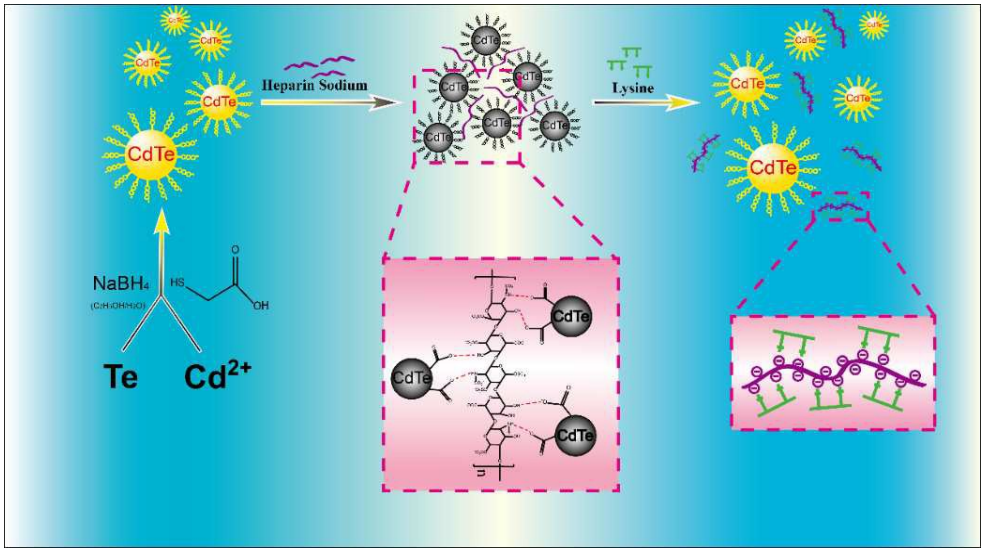

The water-soluble and highly fluorescent TGA-capped CdTe QDs are well dispersed. However, the introduction of heparin sodium results in the aggregation and fluorescence quenching of CdTe QD *via* hydrogen bonding between heparin sodium and TGA-capped CdTe QDs. The aggregated CdTe QDs become dispersive again when lysine is present in the mixture of CdTe QDs and heparin sodium because of the stronger electrostatic interaction between lysine and heparin sodium, leading to the fluorescence recovery of CdTe QDs. This approach can be developed for both heparin sodium and lysine analysis with high specificity.