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Quantum Dots Applied to Methodology on Detection of Pesticide and Veterinary Drug Residues

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ABSTRACT: The pesticide and veterinary drug residues brought by large-scale agricultural production have become one of the issues in the fields of food safety and environmental ecological security. It is necessary to develop the rapid, sensitive, qualitative and quantitative methodology for the detection of pesticide and veterinary drug residues. As one of the achievements of nanoscience, quantum dots (QDs) have been widely used in the detection of pesticide and veterinary drug residues. In these methodology studies, the used QD-signal styles include fluorescence, chemiluminescence, electrochemical luminescence, photoelectrochemistry, etc. QDs can also be assembled into sensors with different materials, such as QD-enzyme, QD-antibody, QD-aptamer, and QD-molecularly imprinted polymer sensors, etc. Plenty of study achievements in the field of detection of pesticide and veterinary drug residues have been obtained from the different combinations among these signals and sensors. They are summarized in this paper to provide a reference for the QD application in the detection of pesticide and veterinary drug residues.

KEYWORDS: *quantum dot, pesticide and veterinary drug residues, detection, biosensor*

INTRODUCTION

The use of pesticides and veterinary drugs is necessary in the modern agriculture to prevent the devastating loss from large-scale pests and diseases, which brings about the problem of pesticide and veterinary drug residues in the environment and food. These residues can bring about the risks of human health, such as cancer, birth defects, interruptions of hormone functions,[1] drug resistance,[2] etc. With the increasing concern of environmental protection and food safety, many countries in the world have enacted a variety of laws and regulations to strictly restrict pesticide and veterinary drug residues in environment, especially food. Therefore, the requirement for the limits of detection (LODs) of the corresponding methods is more and more strict. Fluorescence detection has always been known for its high sensitivity, which makes the fluorescence-related detection technology show a wide prospect in the field of pesticide and veterinary drug residue detection.

With the rapid development of nanoscience, as a type of new fluorescent probes different from the conventional fluorescence dyes, the QDs with the unique spectral characteristics and excellent photochemical stability have been used in the field of food and agriculture such as the monitoring of food pathogens, the tracking of proteins.[3] Meanwhile they have widely been used in the field of environmental and food safety detection through combining with biological, electrochemical, immunology, and other technologies.[4,5]

The QDs-based methods have become a class of new detection methods of pesticide and veterinary drug residues in recent years, which show the advantages of simplicity, fastness, and high sensitivity.[5] In view of their rapid development, a comprehensive review is necessary although the several reviews partly involving the detection of pesticide residues in the applications of QDs have been published.[6−9]

QD CHARACTERISTICS

QDs are the nanocrystals composed of inorganic nuclei and organic molecules that are coated on the surface of the nucleus, with the size between 1 and 10 nm.[10] When QD size is smaller than a certain critical value, its quantum properties will be shown.[11] The QDs include the fluorescent semiconductor nanocrystals composed of II−VI and III−V group elements,[12] the nanocrystals composed of IV−VI and V−VI elements, gold clusters, silver clusters, silicon dots, carbon dots, and complex fluorescent nanoparticles.[13−16]

Compared with the conventional organic fluorophore, QDs have the following unique optical properties.

(1) The fluorescence emission wavelength of QDs can be adjusted by controlling their chemical composition and particle size.[17] At present, the wavelength range of QDs covers from 300 nm to 2 μm.[18]

(2) QDs have broad absorption spectra and symmetrical fluorescence emission spectra, with only 25−40 nm of half width, and can emit multicolor fluorescence when excited at same wavelength. Therefore, QDs can be used in multichannel analysis, greatly increasing analytical information and detection sensitivity.[19]

(3) QDs are composed of inert inorganic materials, usually have a shell, and thus have good photochemical stability. The study results show that the ability of CdSe/ZnS QDs against photobleaching is 10−100 times higher than that of conventional fluorophore. Therefore, QDs can be used for dynamic tracer analysis for a long time.[20,21]

(4) QDs have a large absorption cross section, of which molar absorptivity can be as high as 10^6 L/(mol cm), and high

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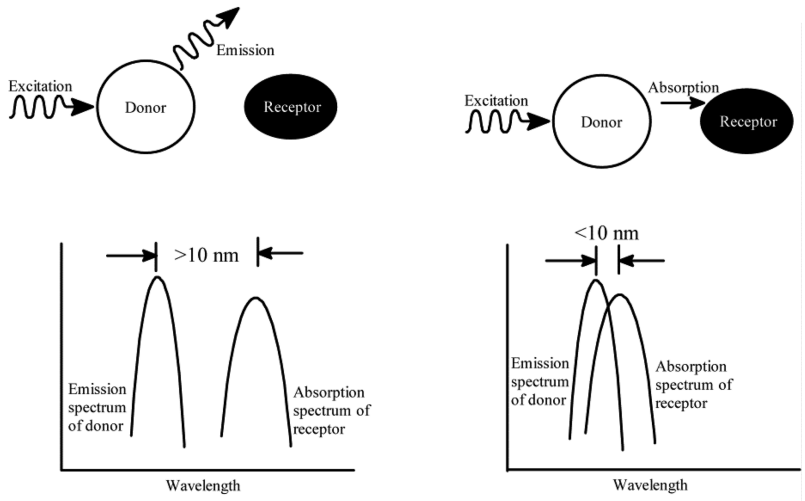

Figure 1. Principle of FRET.

fluorescence quantum yield (40−90%), which can emit intensive fluorescence. These can greatly improve the detection sensitivity and make QDs be used for single particle optical tracer imaging.[22]

(5) QDs have longer fluorescence lifetime, up to 20−50 ns, and high time resolution threshold, which can be used for time-resolved optical imaging.[23]

These excellent optical properties make QDs an ideal fluorescent probe, and they have widely been used in detection, fluorescence imaging, and other fields.

QD APPLICATION IN DETECTION OF PESTICIDE AND VETERINARY DRUG RESIDUES

In the detection of pesticide and veterinary drug residues, QDs are usually used as light signal source and chemiluminescent enhancer. They can directly be used or conjugated to other materials into complex probe when used as a signal source. The signal types of QDs include direct fluorescence, indirect fluorescence, fluorescence quenching, resonance Rayleigh scattering (RRS), and fluorescence resonance energy transfer (FRET) when QDs are directly used. The materials conjugated to QDs include antibodies, enzymes, aptamers (APTs) and molecularly imprinted polymers (MIPs) when QDs are used as a complex probe. In fact, it is from the different combinations between the signal types and probe types that the plenty of study achievements on the QDs are obtained in the field of pesticide and veterinary drug residue detection. They are reviewed as follows.

Methodologies on Direct Use of QD Themselves. This is a class of detection methods in which QDs themselves are directly used. When QDs interact directly with the analyte, their fluorescence will be dynamically quenched. The quenching degree can be used to detect pesticide and veterinary drug residues.[24,25] It was this principle that was successfully used to determine doxycycline residues in honey.[26] When thioglycolic acid-modified CdTe QDs interacts with docetaxel, electrons can be transferred from the QDs to the doxycycline molecules, resulting in fluorescence of the QDs is dynamically quenched. Doxycycline can be detected based on the change of fluorescence intensity. The principle of fluorescence quenching was also used by Durán to detect paraquat herbicide.[27] The mercaptopropionic acid-modified CdSe/ZnS QDs can interact with paraquat rather than diquat, mepiquat chloride, chlormequat chloride, malathion, fenitrothion, terbutryn, triasulfuron, ether tribenuron methyl, metsulfuron methyl, or tribenuron methyl, resulting in the fluorescence quenching. The LOD was 3.0 ng/L, and the linear range (LR) was $10-5 \times 10^3$ ng/L for paraquat. The method was directly applied to the determination of paraquat in tap water, mineral water, waste water, and groundwater.

The sensitivity of RRS method is higher than that of fluorescence quenching method. Aminoglycoside antibiotics can induce the aggregation of CdTe or CdS QDs modified with thioglycolic acid so that the RRS signal is enhanced. The signal intensity of RRS is proportional to the concentration of aminoglycoside antibiotics in a certain range. This principle was used by Liu to detect aminoglycoside antibiotics.[28,29]

QDs can promote the luminescence of some chemiluminescence systems, thus broadening the range of use of QDs. Imani-Nabiyyi et al. established a chemiluminescence system for the measurement of tetracycline and oxytetracycline.[30] L-Cysteine-modified CdTe QDs can catalyze the reaction of two tetracyclines with sodium periodate to generate reactive oxygen species in alkaline conditions, while the active oxygen species excite the chemiluminescence of luminal. This system was successfully used for the determination of water and honey samples. Tetracycline could not be degraded at the pH value of this chemiluminescence system, which was helpful to improve the accuracy of results. In the flow injection chemiluminescence system proposed by Khataee et al., CdS QDs showed another mechanism of action.[31] $KMnO_4$ can oxidize carminic acid in acidic medium to form an oxidized carminic acid, with the maximum absorption wavelength of 498 nm. Meanwhile, $KMnO_4$ can also react with CdS QDs with a particle size of 5.32 nm in acidic medium and make them emit chemiluminescence at 520 nm. The light energy at this wavelength can be absorbed by the oxidized caramelic acid to emit chemiluminescence with the range of 550−630 nm and the maximum wavelength of 580 nm. This is a chemiluminescence resonance energy transfer (CRET) system in which CdS QDs is the energy donor, and the oxidized carminic acid is the acceptor. When there is chlorzacillin sodium that consumes $KMnO_4$ in the CRET system, the system will be inhibited and the luminous intensity is decreased. Chlorzacillin sodium was detected based on the principle.

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Table 1. Detection Methods Using QDs Directly

QD	analyte(s)	signal type	LOD	LR	sample type	ref
CdTe	Doxycycline	fluorescence	52.90 μg/L	913.7−29330 μg/L	honey, human serum	26
CdSe/ZnS	Paraquat	fluorescence	0.003 μg/L	10^{-3}−5 μg/L	water	27
CdTe	Etimicin	RRS	5.1 μg/L	17−6000 μg/L	serum and urine	28
	isepamicin		2.0 μg/L	6.7−1200 μg/L		
	amikacin		25 μg/L	85−7200 μg/L		
CdS	Neomycin	RRS	1.7 μg/L	5.7−640 μg/L	serum and urine	29
	streptomycin		4.4 μg/L	14.7−5200 μg/L		
CdTe	Tetracycline	chemiluminescence	9.78 μg/L	22.22−2666 μg/L	water, honey, drug	30
	oxytetracycline		13.81 μg/L	23.02−3683 μg/L		
CdS	Cloxacillin	chemiluminescence	5.8 μg/L	8−22000 μg/L	water	31
CdTe	Chlorpyrifos	fluorescence	0.035 μg/L	0.035−3506 μg/L	apple	33
CdTe	Thiamethoxam	fluorescence	50 ng/g	500−30000 μg/L	vegetables	34
	acetamiprid		10 ng/g	100−30000 μg/L		
	imidacloprid		9 ng/g	100−30000 μg/L		
CdTe	Azoxystrobin	fluorescence	2 ng/g	5−2500 ng/g	fruits, vegetables	35
	kresoxim-methyl		1 ng/g			
	pyraclostrobin		2 ng/g			
CdTe	Loxacin	fluorescence	4 ng/g	10−10000 ng/g	milk	36
	enrofloxacin		7 ng/g			
	ciprofloxacin		8 ng/g			
	lomefloxacin		7 ng/g			
	norfloxacin		5 ng/g			
CdTe	Rifampicin	fluorescence	1500 μg/L	5000−80000 μg/L	human urine, drug	37
	rifaximin		1000 μg/L	3000−40000 μg/L		
CdTe	Glyphosate	fluorescence	0.01 ng/g	0.02−2.0 ng/g	apple	38
CdTe/CdS	Polymyxin b	RRS	6.36 μg/L	20−6000 μg/L	drug	39
CdTe-AuNP	Acetamiprid	fluorescence	16.8 μg/L	25−5000 μg/L	water, soil, rice	40
CdS	Dicofol	fluorescence	55 μg/L	1230−23157 μg/L		41
CdS	Pentachlorophenol	ECL	0.003 μg/L	0.01−500 μg/L	tap water	42
CdTe-AuNP	Parathion-methyl	fluorescence	0.018 μg/L	0.04−400 μg/L	tap water, milk, rice	43
ZnSe	2-chlorophenol	ECL	1.03 μg/L	2.57−1286 μg/L		
	2,4-dichlorophenol		0.33 μg/L	0.98−1467 μg/L	waste water	44
	pentachlorophenol		2.66 μg/L	15.98−2131 μg/L		
CdTe	Chlortoluron	fluorescence	0.017 μg/L	0.05−18.08 μg/L	irrigation water	45

It has been reported that the FRET system with QDs was used to detect pesticide and veterinary drug residues. When the difference between the emission wavelength of the energy donor and the absorption wavelength of the receptor is less than 10 nm, the electron excited from donor can be transferred to the receptor through nonradiative energy transfer process.[32] This is so-called FRET, as shown in Figure 1. In this process, the effectiveness of FRET can be impacted by the positions of donor and receptor, the degree of overlap between the emission spectrum of donor and the absorption spectrum of receptor, and the distance between the donor and receptor. The size dependence of emission wavelength of QDs makes them the best donor. By adjusting their particle size during synthesis, the emission wavelength of QDs can be maximally overlapped with the absorption wavelength of the receptor to improve the sensitivity of the detection system. Zhang et al. developed a rapid method for the detection of organic phosphorothioate pesticides.[33] The CdTe QDs that emitted green fluorescence at 520 nm were conjugated by dithizone of which the maximum absorption wavelength was at 510 nm in alkaline medium. This is a FRET system. The fluorescence of CdTe QDs can be immediately quenched by dithizone due to the effect of FRET. When the organic phosphorothioate pesticide is added into the system, its hydrolysis product can substitute dithizone conjugated on the surface of CdTe QDs, so that the fluorescence of CdTe QDs are restored. The highly sensitive fluorescence "on−off" system can selectively detect phosphorothioate pesticides without the need for expensive antibodies or enzyme. The LOD of chlorpyrifos was 0.1 nM, and the LOD for chlorpyrifos in apple was 5.5 ppb.

In the indirect fluorescence methods developed by Chen et al., CdTe QDs were added to the background electrolyte solution of capillary electrophoresis as a fluorescent background material, and pesticide and veterinary drug residues could be detected by the use of inverted peak height of analytes. Three kinds of nicotine insecticides,[34] three kinds of strobilurin fungicides[35] in fruits and vegetables, and five kinds of quinolones antibiotics in milk and honey[36] have been successfully detected by this kind of method. It is specially pointed out that these are all multiresidue detection methods. The detection methods in which QDs are directly used are listed in Table 1.

QD Fluorescence Immunoassay (QD-FLISA). This is a class of methods using the complex probe conjugating QDs with antibodies or antigens. FLISA is one of the earlier methods in immunoassay. In FLISA, the fluorescent substance is combined with an antibody or antigen molecule, and the analyte is determined by measuring the change of fluorescence intensity caused by the specific reaction between antigen and antibody.[2] The fluorescent dyes used to label antibodies or

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antigens must be easily combined with antibodies or antigens. They are also demanded to be stable, not to affect antibody activity, to be easily dissolved, and for the labeling method to be simple. Some components in the biological sample may emit fluorescence. The labeled fluorescent dye has both high fluorescence quantum yield and a narrow fluorescence emission spectrum in order to avoid the fluorescence interference of these components. It can be said that QDs meet all the requirements of the labeled antibody or antigen due to their excellent optical properties beyond the conventional fluorescent dyes. QD-FLISA using QDs as a fluorescent probe has become one of the important tools for the detection of pesticide and veterinary drug residues due to the advantages such as simplification, rapidness, accuracy, specification, sensitiveness, simple pretreatment, and no need for special testing equipment.[46−48]

Chen et al. first reported an indirectly competitive QD-FLISA for the determination of enrofloxacin residues in chickens.[48] The enrofloxacin-ovalbumin as coated antigen was coated on a 96-well microplate, and then sample and the monoclonal antibody of the antigen were added. The QDs conjugated to goat antimouse IgG secondary antibody were added after the micoplate was incubated and washed. The fluorescence intensity of the microplate was measured by a fluorescent microplate reader after incubating and washing. The higher the concentration of enrofloxacin in the chicken was, the lower the fluorescence intensity of the microplates was. The LR was 1−100 μg/L, and the LOD was 2.5 μg/L.

The QDs with different sizes can simultaneously be excited at same wavelength to produce multicolor fluorescence due to their broad and continuous absorption spectrum. This characteristic enables QD-FLISA to detect a variety of veterinary drug residues simultaneously.[4,49,50]

The indirect competition QD-FLISA developed by Song et al. is a very representative method.[49] Three kinds of complex fluorescent probes were prepared through conjugating three kinds of QDs with emission wavelengths of 520, 560, and 610 nm to the antibodies of streptomycin, tetracycline, and penicillin, respectively. Then, the 96-well microplates were evenly divided into three regions, and the streptomycin, tetracycline and penicillin conjugated to bovine serum albumin (BSA) as the coated antigens were immobilized in one of the regions, respectively. The free antigen standard series and the corresponding complex fluorescent probes were added into three regions, respectively. After incubating and washing, they were excited at 370 nm under the inverted fluorescence microscope, and their images were recorded with a camera to produce a color card. The same procedures were used to measure the sample, and the qualitative and quantitative analysis of the three veterinary drug residues were carried out by comparison with the color card. The LRs of streptomycin, tetracycline, and penicillin were 0.01−25 μg/L, 0.01−25 μg/L, and 0.01−10 μg/L, and their LODs were all 5 ng/L lower than 1 μg/L of enzyme-linked immunosorbent assay (ELISA).[46] Compared with the commercial ELISA kit, this method could simultaneously analyze multiple target antibiotics in multiple samples, improve the accuracy and sensitivity, and were successfully applied to the detection of three kinds of antibiotics in milk. A similar indirect competition QD-FLISA was used to determine the animal growth promoters carbadox and olaquindox in pork and liver.[4] The difference was that a fluorescent microplate reader was used for quantitative analysis, and the excitation wavelength of QDs was 335 nm and emission wavelengths were 520 and 635 nm, respectively. The LODs of carbadox and olaquindox were 0.05 and 0.07 μg/L, respectively, and the recoveries were 81.5−98.2% and 84.2−95.7%, respectively. Taranova et al. also developed the method used to detect three kinds of antibiotics in milk.[50] An immunochromatographic strip called "traffic lights" was prepared based on the principle of indirectly competitive QD-FLISA. The conjugations of ofloxacin-, chloramphenicol-, and streptomycin-protein were immobilized on the nitrocellulose membrane to form three test lines. The three kinds of complex probes were prepared through conjugating the three color QDs of red, yellow, and green with emission wavelength of 625, 585, and 525 nm to the monoclonal antibodies of ofloxacin, chloramphenicol, and streptomycin by use of activated ester method, and the mixture of these complex probes was applied onto glass fiber membrane. These two films were assembled with sample membrane and adsorption membrane into the test strip. When the end of the test strip is immersed in the sample solution without these three antibiotics, the solution is moved toward the test lines, and the three complex probes on the membrane are also moved together due to the capillary infiltration action. When moving to their respective test lines, they react with the antibiotic-protein conjugates immobilized onto lines and form lines of each color. When the sample contains one of these three antibiotics, the antibiotic competes with the antibiotic-protein conjugate on the line for binding to the complex probe, resulting in a decrease of the complex probe that is bound to the test line of this antibiotic and a lighter color. When the concentrations of ofloxacin, chloramphenicol, and streptomycin in the samples are 200, 10, and 500 μg/L, respectively, the colors of their test lines disappear. Therefore, the qualitative analysis of these antibiotics can be carried out by observing the color of the test line. If the test line of the sample containing antibiotic is excited by ultraviolet light, the weaken fluorescence can be detected with a CCD camera. The quantitative analysis of these antibiotics can be performed by measuring the fluorescence intensity of the test lines. The LODs of ofloxacin, chloramphenicol, and streptomycin were 80−200 times lower than those of ELISA, and they were 0.3, 0.12, and 0.2 μg/L, respectively. The method did not require to prepare sample, the antibiotics in milk were detected within 10 min, and the spiked recoveries were 92−101%.

QD-FLISA has also been used widely in pesticide residue detection. Vinayaka et al. established a method for the detection of herbicide 2,4-D by direct competition QD-FLISA.[51] The thioglycolic acid-modified CdTe QD was bound to alkaline phosphatase (ALP) and the QD-ALP was bound to 2,4-D to form QD-labeled antigen. The IgG antibody of 2,4-D was immobilized on CL-4B agarose particles. The immunoreactor column was fabricated by packing these particles into a glass capillary. The sample was passed through the column at a flow rate of 50 μL/L, and then 10 μL of the 2,4-D-ALP-CdTe complex with the optimum concentration was passed through the column. The residual 2,4-D-ALP-CdTe complex was collected, and detected on fluorescence spectrophotometer. The higher the concentration of 2,4-D in the sample was, the lower the measured fluorescence intensity was. The LOD of 2,4-D was down to 250 ng/L.

Chen et al. reported two indirectly competitive QD-FLISA methods in the same year for the detection of chlorpyrifos residue in drinking water.[52,53] The principle of the first method[52] is similar to that of detection method of

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Table 2. QD-FLISA Analysis of Pesticide and Veterinary Drug Residues

QD	analyte(s)	LOD	LR	Sample type	ref.
CdTe/ZnS	Tetracyclines	1 μg/L	0.56−1.25 μg/L	bovine meat	46
QD655	Melamine	3.88 μg/L		milk	47
CdTe	Enrofloxacin	2.5 μg/L	1−100 μg/L	chicken muscle	48
CdTe	Streptomycin	0.005 μg/L	0.01−25 μg/L	milk	49
	tetracycline		0.01−25 μg/L		
	penicillin		0.01−10 μg/L		
QD520	Carbadox	0.05 μg/L		swine tissue	4
QD635	Olaquindox	0.07 μg/L	1.5−200 μg/L		
Qdot625 ITK	Ofloxacin	0.3 μg/L	0.14−10 μg/L	milk	50
Qdot585 ITK	Chloramphenicol	0.12 μg/L	0.3−500 μg/L		51
Qdot525 ITK	Streptomycin	0.2 μg/L	0.25−1 μg/L	drinking water	52
CdTe	2,4-D	0.25 μg/L		drinking water	53
QD530	Chlorpyrifos	8.4 μg/L	10.5−180.4 μg/L	river water, vegetables	54
CdTe	Chlorpyrifos	3.8 μg/L	60−3.83 × 10^6 μg/L	milk	55
CdTe	Fenvalerate	25 μg/L	10−590 ng/g	pork	56
CdTe	Gentamicin	5 ng/g	0.33−10 ng/g		
CdTe	Dexamethasone	0.13 ng/g	0.28−10 ng/g		
	gentamicin	0.16 ng/g	0.16−25 ng/g		
	clonazepam	0.07 ng/g	0.17−10 ng/g		
	medroxyprogesterone	0.06 ng/g	0.32−25 ng/g		
	ceftiofur	0.14 ng/g			
QD655	Tylosin	0.02 ng/g		chicken, pork, fish	57
	tilmicosin	0.04 ng/g			
Qdot605	Melamine	0.27 μg/L		milk, milk powder	58
Qdot705 ITK	Sulfonamides	0.13 μg/L		milk	59
	quinolones	0.062 μg/L			

enrofloxacin,[48] except that the coated antigen is replaced by BSA-chlorpyrifos, and the excitation/emission wavelength of QDs is 300/530 nm. The LOD for chlorpyrifos was as low as 8.4 μg/L. In the second method, QDs were bound to streptavidin (SA) to form QD-SA complex probes, and monoclonal antibodies against chlorpyrifos were conjugated with biotin to form biotinylated antibodies.[53] The sample and biotinylated antibodies were added into 96 well microtiter plates coated by BSA-chlorpyrifos antigens. After incubating and washing, QD-SA probes were added and the QDs were immobilized on the microtiter plate by use of the super affinity between biotin and SA. After washing the excess QD-SA probes, the fluorescence intensity was measured on a fluorescent microplate reader with an excitation/emission wavelength of 300/600 nm. The LOD of this method was 3.8 μg/L, the sensitivity was 5.5 times higher than that of the conventional ELISA, and the detection time was reduced by 1 h.

In the QD-FLISA established for the detection of fenvalerate by Liu et al., the glutathione-modified CdTe QDs were conjugated to the antifenvalerate antibodies to form a complex fluorescent probes by the activated ester method.[54] The sample and complex probes were added into a 96-well microtiter plate coated by antigen, and the fluorescence intensity was measured on a fluorescence spectrophotometer after incubating and washing. The excitation/emission wavelength was 400/564 nm. The LOD of fenvalerate was 25 μg/L, and the LR was 60 μg/L to ∼3.83 mg/L. The method was applied to the detection of river water, cabbage, and rape samples. The applications of QD-FLISA are summarized in Table 2.

QD Biosensor. The so-called biological sensor refers to the transducer of which the surface is immobilized by enzymes, antibodies, APTs, biological tissue, or other bioactive substances. The sensor can convert the signal (such as electricity, light, heat, mass, etc.) produced by a specific reaction between an analyte and an active substance into an identifiable signal for the determination of analyte content or concentration. QDs can be applied in biosensors including the complex probes and the sensor fabricated with the electrodes used in electrochemistry. The biosensor based on a specific reaction can greatly simplify the analysis of pesticide and veterinary drug residues and enhance the detection flux, with the advantages of high specificity of biological active substances and high sensitivity. In addition, the sensor is small size and easy to carry and is favorable for on-site real-time detection. These characteristics make QD biosensors become an important research field of the detection of pesticide and veterinary drug residues in the environment and food in recent years and have a very broad application prospect.

QD-Enzyme Biosensor. QD-enzyme biosensors are usually divided into two types, complex probes and electrochemical electrode-based sensors. There are all enzymes in either the probes or the sensors. Because enzymes can specifically catalyze the reaction of substrate, these biosensors have good selectivity to the special pesticides. However, the storage condition of enzymes is usually harsh.

The complex probe is a kind of mixture solution composed of QDs, enzyme, and its substrate. The detection method using the complex probe has been widely applied in the detection of pesticides, especially organophosphorus pesticides. The most commonly used enzyme is acetylcholinesterase (AChE) that exists in the nervous system. In the detection method of methyl parathion (MP) established by Tran et al., the complex probe was prepared by mixing and incubating CdTe QDs, AChE, and acetylchiocholine (ATCh), in which ATCh was reversibly hydrolyzed by AChE to produce thiocholine (TCh) and acetic

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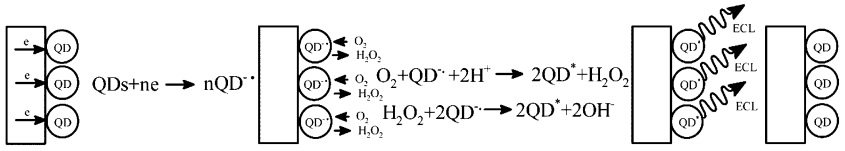

Figure 2. Principle of ECL.

acid changing the pH value around QDs.[5] The fluorescence intensity of QDs is a function of pH value. Because the concentration of ATCh and AChE in the probe is constant, the pH value of the probe solution is constant, and thus the fluorescence intensity is constant. When MP is mixed into probe solution, AChE activity is inhibited. The hydrolyzed TCh and acetic acid in probe solution are recovered into ATCh, and the pH value around QDs is changed. The higher the concentration of MP is, the more significant the fluorescence intensity of CdTe QDs is changed. There is linear relationship between fluorescence intensity and MP concentration in a certain range. The LOD of this method was as low as 0.05 ppm.

In the method established by Gao et al., the change of fluorescence intensity of QDs with the concentration of organophosphorus pesticide was based on another principle.[60] The complex probe is composed of AChE, acetylcholine (ACh), choline oxidase (ChOx), and Mn-doped ZnSe QDs solution, which is an organophosphorus biosensor in the double enzyme system. The AChE in the probe hydrolyzes ACh to choline (Ch), ChOx successively oxidize Ch to produce H_2O_2, and H_2O_2 can quench the fluorescence of QDs. When organophosphorus pesticide paraoxon is mixed into the probe solution, AChE activity is inhibited, the amount of Ch is reduced, the subsequent H_2O_2 also decreases, and the fluorescence of QDs is recovered. The LOD was 1.31×10^{-11} M. The sensor was used for the rapid determination of paraoxon in tap water and milk samples with satisfactory reproducibility and accuracy, and the spiked recoveries were 95−103%.

When QDs are synthesized in aqueous phase, their surfaces are often modified by some ligands such as thioglycolic acid. These ligands can effectively reduce the defects on the surfaces of QDs and increase their luminescent stability. When QDs and some metal ions coexist, their competition to ligands will significantly affect the luminescence of QDs.[61] By use of this feature, it is possible to fabricate a specific complex probe by appropriately selecting various ligands on QD surface. Yan et al. developed a new method for the detection of MP based on this idea.[62] They prepared a kind of sensitive new complex probe through mixing $CuInS_2$ QDs which were modified by mercaptopropionic acid (MPA) and emitted near-infrared light, Pb^{2+}, and organophosphatase (OPH) solutions. In the probe solution, the competition of Pb^{2+} and Cu^{2+} to MPA destroys the integrity of the QD surface, resulting in fluorescence quenching. When MP is mixed into the probe solution, it is hydrolyzed into *p*-nitrophenol and dimethyl phosphorothioate (DMPA) by OPH. DMPA is an excellent ligand of metal ions, and can capture the Pb^{2+} bound to MPA. The perfection of QD surface can be restored by DMPA, and then fluorescence can be recovered. The higher the concentration of MP is, the higher the fluorescence intensity is. The LR was 0.10−38.00 μM, and the LOD was 0.06 μM. The method was successfully applied to the detection of MP in rice and bananas with satisfactory result and recoveries of 90−105%.

The electrochemical electrode-based sensors are usually fabricated through depositing a coupler on the electrode, preparing the conjugation of QD and enzyme by activated ester method, and immobilizing the QD-enzyme on the electrode by the coupler. The electrochemical signal produced from the sensor is used for detection. A biosensor utilizing electrochemiluminescence (ECL) signal was used to detect MP by Liang et al.[63] They dropped grapheen oxide (GO) onto the surface of cleaned glass carbon electrode (GCE), and the GCE was immersed into phosphate solution after dried. The grapheen nanosheets (GNs) were prepared on the surface of GCE through scanning the GCE between 0 and −1.5 V for 10 cycles. The GNs were used to anchor CdTe QDs and significantly amplified the ECL signal of QDs. CdTe QDs were dropped on GNs and were conjugated with AChE by use of glutaraldehyde (GLD) after dried. The fabricated AChE-CdTe QDs-GNs/GCE sensor was used to ECL detection. The principle of ECL is shown in Figure 2. When the composite electrode is applied with a potential, the QDs is reduced. The dissolved oxygen in the solution reacts with them and makes the QDs excite and produce an ECL signal. When acetylcholineschine chloride (ATCl) is present in the solution, AChE will catalyze it to hydrolyze. This reaction consumes dissolved oxygen and cause the ECL signal to drop. When MP is added, the activity of AChE is inhibited and the hydrolysis of ATCl and the consumption of dissolved oxygen is decreased resulting in the restoration of ECL signal. It was found that there were two LRs with the change of MP concentration, 0.2−10 μg/L and 20−150 μg/L, the LOD was 0.06 μg/L, and the spiked recovery of vegetable samples was 94.5−102.6%.

A method with more excellent selectivity was used to detect MP by Du et al., in which a new amperometric biosensor was used.[64] They bound cysteine-modified CdTe QDs to methyl parathionase (MPDE), and then the composite was immobilized to GCE modified by multiwalled carbon nanotubes (MWCNTs)-gold nanoparticles (AuNPs) complex. In this composite electrode, MWCNTs can increase the electronic conduction channel, AuNPs can promote the conduction of electron and increase the surface area of the electrode to make more MPDE-CdTe QDs are connected to the electrode, and CdTe QDs is the connector between MPDE and electrode. When the electrode is immersed in the sample solution, MP is hydrolyzed by MPDE on the electrode and an electron can be released under alkaline conditions. The current passes through the electrode. The higher the MP concentration is, the higher the hydrolysis current is. The electrode showed a high sensitivity in their experiment results, and the LOD of MP was 0.1 μg/L. The electrode also showed ultrastrong anti-interference ability and only catalyzed the pesticide with P−S bond. Unlike AChE-based biosensor, the electrode cannot be destroyed by organophosphorus pesticides and therefore has the potential for repeated use and is suitable for continuous monitoring.

A sensitive photoelectrochemical (PEC) biosensor was fabricated by Li et al.[65] to detect paraoxon and dichlorvos as

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organophosphorus pesticides. The surface of glass electrode coated by indium-doped tin oxide (ITO) was functionalized with (3-aminopropyl) trimethoxysilane, and then grapheen, poly(ethylenimine) (PEI), CdSe@ZnS QDs, and PEI were successively deposited on the surface. AChE and PEI were alternately prepared on the film composed of (grapheen/PEI/QDs/PEI)$_4$ for four layers. The principle of PEC is shown in Figure 3. When the QDs on the PEC biosensor are excited, the

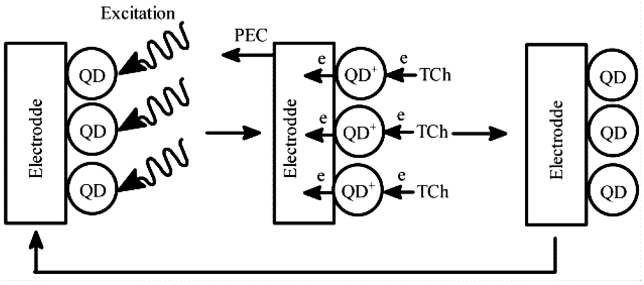

Figure 3. Principle of PEC.

electrons on the valence band of QDs will jump to the conduction band, and the photoexcited holes in the valence band will be released. The recombination of electron and hole can effectively be blocked by graphene due to its ability to separate the carriers. If the solution in which the electrode is immersed contains ATCh, AChE catalyzes it to hydrolyze into acetic acid and TCh which provides an electron as donor into the hole in the valence band of QDs. Thus, a stable photocurrent is produced on the electrode under the excitation of the light source. When the sample was added into the ATCh solution, the organophosphorus pesticides inhibit the activity of AChE, which the amount of TCh produced from ATCh is reduced and the photocurrent is decreased. It was observed that the logarithm of the concentration of paraoxon and dichlorvos was proportional to the photocurrent in the range of 10^{-12} to $\sim 10^{-6}$ M, and the LODs were 10^{-14} M and 10^{-12} M, respectively. The method was successfully applied to the detection of organophosphorus pesticides in apple samples.

The pesticides that inhibit the activity of AChE, such as organophosphorus or carbamate pesticides, can be all identified by the QD-enzyme biosensors using AChE. However, the types of these pesticides cannot be distinguished by these sensors. The applications of QD-enzyme sensors are listed in Table 3.

QD-Antibody Biosensors. The difference of QD-antibody biosensor and QD-FLISA is that the former mainly utilizes electrochemical signals when used to detect pesticide and veterinary drug residues, with the advantages of relatively simple operation and sample pretreatment. The sensitivity is greatly increased. The disadvantages of this kind of sensor are that the preparation procedure of antibodies is usually complicated, and its storage condition is harsh. The QD-antibody biosensors are composed of electrochemical electrode and the conjugations of QDs and antibodies immobilized on the surface of the electrode. QDs and antibodies are conjugated by activated ester or adsorption method.

Table 3. Detection Methods Based on QD-Enzyme Sensors

QD	enzyme	analyte(s)	signal type	LOD	LR	sample type	ref
CdTe/CdS	AChE	MP	fluorescence	50 μg/L	50−100 μg/L		5
Mn:ZnSe	AChE, ChOx	Paraoxon	fluorescence	0.004 μg/L	0.01−1332 μg/L	tap water, milk	60
$CuInS_2$	OPH	MP	fluorescence	6 μg/L	10.02−3806 μg/L	banana, rice	62
CdTe	AChE	MP	ECL	0.06 μg/L		vegetable	63
CdTe	MPDE	MP	current	1.0 μg/L	5.0−200 μg/L	garlic	64
CdSe/ZnS	AChE	Paraoxon,	photocurrent	1.7×10^{-5} μg/L	2.8×10^{-4}−275.2 μg/L	apple	65
		dichlorvos		5.5×10^{-4} μg/L	2.2×10^{-4}−221 μg/L		
CdTe	AChE	Carbaryl	current	0.6 μg/L	1−50, 50−500 μg/L	garlic	66
CdTe	AChE	Methamidophos	fluorescence	2 ng/g	60−780 ng/g	Chinese cabbage	67
CdTe	AChE	Parathion	fluorescence	10 μg/L	5−100 μg/L	fruits, water	68
		paraoxon					
CdSe/ZnSe/ZnS	AChE	Trichlorfon	fluorescence		100−5000 μg/L		69
CdTe	AChE	Paraoxon	fluorescence	0.003 μg/L		apple, bean, tap water	70
		parathion		0.001 μg/L			
CdTe, CdSe/ZnS14[a]ML	AChE	MP	fluorescence		0.05−8 μg/L		71
CdSe/ZnSe2ML/ZnS8ML		acetamiprid			2.5−10 μg/L		
CdTe	AChE, ChOx	Paraoxon	fluorescence	8×10^{-4} μg/L	2.8×10^{-4}−275.2 μg/L	apple	72
		dichlorvos		0.005 μg/L	2.2×10^{-4}−221.0 μg/L		
		parathion		0.001 μg/L	2.9×10^{-4}−291.3 μg/L		
CdS	AChE	Paraoxon	fluorescence	0.022 μg/L	0.017−31.65 μg/L		73
CdTe	AChE, ChOx	Paraoxon	fluorescence	0.001 μg/L	0.003−275.2 μg/L	apple	74
		parathion		7×10^{-4} μg/L	0.003−291.3 μg/L		
CdTe	AChE, ChOx	Dichlorvos	fluorescence	0.992 μg/L	0.992−198, 10139−30688 μg/L	apple	75
	AChE	Paraoxon	phosphorescence	2.9×10^{-4} μg/L		lake water, apple juice	76
		parathion		5.9×10^{-4} μg/L			
		omethoate		6.7×10^{-4} μg/L			
		DDVP[b]		4.4×10^{-4} μg/L			
Mn:ZnS	AChE, ChOx	Paraoxon	phosphorescence	2.8×10^{-5} μg/L	2.8×10^{-4}−275.2 μg/L	vegetable	77

[a]ML, monolayer. [b]DDVP, dimethyl dichlorovinyl phosphate.

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Zhang et al. established an ECL immunoassay by use of this sensor for rapid and sensitive detection of salbutamol (SAL).[78] First, cysteamine was bound to the surface of cleaned gold electrode by use of the strong interaction between its −SH and gold through immersing the electrode into 4 °C cysteamine solution for 16 h, and then GLD was combined with the surface of the gold electrode by use of the reaction of cysteamine and GLD. The SAL-ovalbumin as coating antigen was dropped to the electrode and coated onto the gold electrode by its reaction with GLD. Second, the SAL polyclonal antibody was bound to the surface of CdTe QDs modified by thiolacetic acid through the activated ester method. After the prepared electrode was incubated in the SAL antibody-QD solution and washed, it was electrochemically scanned in the phosphate buffer and made the QDs on it produce ECL signal. When the prepared electrode was immersed in a mixed solution of sample and SAL antibody-QDs, the SAL in the sample would compete with the SAL immobilized on the electrode for SAL antibody, resulting in the decrease of QDs bound to the electrode. Finally, the ECL signal would be weakened. The decrease of ECL intensity was proportional to the logarithm of SAL concentration in the range of 0.05−100 μg/L, and the LOD of SAL was as low as 5.6 ng/L. This method is high sensitivity and easy to use and has been used for the detection of pork and liver samples. The similar method was also reported by Cai et al.[79]

Zhang et al. fabricated a kind of electrochemical immunosensor using QDs-antibodies for the detection of trace clenbuterol (CH) by use of electrochemical impedance spectroscopy (EIS).[80] They synthesized the polyaniline (PANI)-modified ZnS QDs (ZnS QD@PANI) nanocomposite utilizing a wet chemical method, and then ZnS@PANI was dropped on the surface of the cleaned gold electrode. After drying, the electrode was immersed into the CH antibody solution for 2 h, and the final electrode was used for measurement. There are many NH_2 in the PANI on the electrode, which can improve the adsorption capacity of CH antibody and increase the selectivity and sensitivity of the electrode. Compared with the bare gold electrode, the impedance of the electrode is successively increased after ZnS@PANI, CH antibody is modified and CH is combined. The difference of impedance of the electrode with and without CH was proportional to the logarithm of CH concentration in the range of 0.01−10 μg/L, and the LOD was as low as 5.5 ng/L.

QD-APT Biosensor. APTs are oligonucleotide sequences with lengths less than 100 nt, which have high specificity and affinity to specific target materials. When the target material is present, APT can form specific target binding sites through conformational adaptation and three-dimensional folding. Compared with antibodies, APTs show the many similar even better properties. For example, APTs can be artificially synthesized without the dependence on animals and cells, are easy to preserve, and their target molecules can be small molecules without immunogenicity. APTs are more specific, stable, and easier to be modified and marked.[81,82] APTs are usually obtained from random oligonucleotide library through many screening cycles. In recent years, there have been the new methods in which highly sensitive QDs were combined with high specific APTs for the detection of pesticide and veterinary drug residues. Similar as QD-enzyme biosensors, QD-APT sensors are also divided into two types: the mixture solution composed of QDs, quenchers, and APTs; electrochemical electrode-based sensors, QDs, and APTs are immobilized on the surface of the electrode. APTs are conjugated to QDs (or AuNPs) by use of activated ester, adsorption, or hybridization method in the QD-APT sensors. The signal types of QD-APT sensors used to the detection of pesticide and veterinary drug residues are mainly FRET,[83−85] fluorescence quenching,[86] ECL,[87] PEC,[88] etc.

Alibolandi et al. prepared the APT-QDs of chloramphenicol by binding the thioglycolic acid-modified CdTe QDs to the amino terminus of chloramphenicol APT with the activated ester method.[84] Then, GO was added to the APT-QD solution, and the APT-QD was bound to the GO through the $\pi-\pi$ stacking interaction between the base of APT and sp^2 hybrid orbital of GO. When the QDs in GO/APT-QD solution are excited, the excitation energy can be absorbed by the GO in the FRET system composed of QD and GO, and the fluorescence of QDs at 630 nm will be quenched. When the sample is added to this solution, chloramphenicol will be bound by APT, and the chloramphenicol-bound APT will fall off from GO, and the fluorescence of QDs will be restored due to the disintegration of FRET system. It was observed that the fluorescence intensity was proportional to chloramphenicol concentration in the range of 0.1−10 nM, and the LOD was 98 pM. The method was applied in the detection of milk samples. The same principle was also applied by Lin et al. to the detection of acetamiprid.[85] In the sensors fabricated by them, the QDs were changed from CdTe to ZnS:Mn and GO was changed to MWCNTs. The LOD of acetamiprid was 0.7 nM. The method is simple and rapid and has the potential for in-site vision detection.

The absorption of absorber (quencher) in the detection system to the excitation light and/or the emission light of fluorophore is called internal filter effect (IFE). The IFE will occur when the absorption band of the absorber in the system can be well overlapped with the excitation and/or emission band of the fluorophore. It is unnecessary to modify QDs and AuNPs when they are used to construct an IFE system, which will favor the design of IFE system. However, the modification is necessary in FRET system to obtain specific distances or geometries between them for the interaction.[89] Guo et al. reported a method by combining the IFE of the AuNPs on the CdTe QDs with the APT specificity for the detection of acetamiprid.[86] When CdTe QDs are mixed with AuNPs, their fluorescence is significantly quenched due to IFE. When salt is present in the solution, the aggregation of AuNPs can be induced and the fluorescence of QDs is restored due to the disappearance of IEF. When the APT of acetamiprid (ABA) is adsorbed to the surface of negatively charged AuNPs, it can prevent AuNPs from salt-induced aggregation and the fluorescence of CdTe QDs will be quenched by AuNPs. However, ABA will be released from the surface of AuNPs when specifically bound to acetamiprid. The AuNPs are aggregated again by salt, and the fluorescence of CdTe QDs will be restored. On the basis of this principle, a method for the detection of acetamiprid was established, LR was 0.05−1.0 M and LOD was 7.29 nM. The method was successfully used to detect acetamiprid in six vegetables.

In addition to fluorescence signals, ECL[87] and PEC[88] signals were also used to detection. Feng et al. designed a screen-printed carbon electrode (SPCE) array consisting of an Ag/AgCl reference electrode, a carbon counter electrode, and two space-resolved carbon working electrodes (WE1, WE2).[87] In the system, WE1 were modified by luminol-AuNPs as working signal tags, the DNA complementary (DNA1) of chloramphe-

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nicol APT and chloramphenicol APT (DNA2) tagged with chlorogenic acid as quenchers of luminol-AuNPs, on which DNA1 and DNA2 were combined by hybridization. WE2 was modified by CdS QDs as internal reference to provide a correction for avoiding the environmental effects. When the system is run, the QDs on WE2 can emit fluorescence normally, the ECL of luminol-AuNPs on WE1 can be quenched by chlorogenic acid and the ratio of light intensities of WE1 and WE2 is small. When WE1 is immersed into sample, the high affinity of chloramphenicol toward DNA2 makes DNA1 and DAN2 be partially unbound. Meanwhile, the ECL of luminol-AuNPs on WE1 is partially restored due to releasing chlorogenic acid, and the ratio of light intensities of WE1 and WE2 is increased. This ratio of ECL signals can be used to detect chloramphenicol. The design that these two ECL signal labels are immobilized on two separated working electrodes can be avoid potential crosstalk as much as possible. The LOD of chloramphenicol was 0.5953 nM.

Li et al. constructed a sensitive aptasensor for the detection of oxytetracycline (OTC) by use of PEC signal.[88] First, a TiO_2 film was uniformly prepared on the ITO conducting glass with TiO_2 nanorods by the sol method, and AuNPs were electrodeposited on the surface of TiO_2 film. Then the conjugates of hairpin DNA and CdTe QD were immobilized on the electrode by Au−S bonds. Because CdTe QDs at 3′ end of hairpin DNAs are close to the electrode surface, the stronger photocurrent can be produced from the effective electron transfer under visible light irradiation. When the electrode is immersed in OTC APT solution, the hairpin DNAs on the electrode can be specifically bound to OTC APTs. The binding makes CdTe QDs far away from the electrode surface, and the photocurrent is significantly decreased. When the electrode bound with APTs is immersed in the target OTC solution, the photocurrent signal can be restored because the APTs are combined with OTC molecules and unlinked from hairpin DNAs. The photocurrent value increased with the increase of OTC concentration. The LOD of OTC was 0.19 nM and the LR was 2−300 nM.

QD-MIP Sensor. Molecular imprinting is derived from immunology, which refers to the process of synthesizing polymers that have specific selectivity to a kind of particular target molecule (detection substance). In the process, the cross-linked polymer is assembled around the template molecule by intermolecular forces. After the template molecule is removed, the specific recognition site that is complementary to the template molecule remains in the polymer and can specifically recognize the template molecule.[90] In general, the synthesis of MIP includes the following three steps: the template molecule and the functional monomer are preassembled; the cross-linker is used to carry out the polymerization reaction; and the template molecules are eluted from the MIP. The synthesized MIP can maintain stable performance for a long time in a harsh physical environment without changing its specific adsorption to template molecules.[91]

In recent years, the special optical properties of QDs have been combined with the high selectivity of MIP by synthesizing MIP on the surface of QDs. This is so-called QD-MIP sensor. In the sensors, the QDs are usually modified with silylating reagent or mercaptan carboxylic acid and surfactant to form the surface on which MIP can easily be synthesized. The QD-MIP sensors have been used to the selective identification and detection of pesticide and veterinary drug residues.

Wang and Ren, respectively, synthesized MIPs on the surface of Mn-doped ZnS QDs for selective detection of pentachlorophenol and nicosulfuron.[92,93] The 3-mercaptopropyltriethoxysilane-modified Mn:ZnS QDs were first synthesized by Wang et al, and then the MIP film was subsequently synthesized on the surface of the QDs, in which pentachlorophenol was the template molecule, 3-aminopropyltriethoxysilane was the functional monomer, and tetraethoxysilane was the cross-linker.[92] The MIP-coated QDs were obtained after removal of template molecules, which recognized pentachlorophenol. When the MIP-coated QDs are added to the sample, pentachlorophenol enters into the MIP film and was bound to the blotting site and the phosphorescence of QDs is quenched. The linear relationship was presented between quenching degree and pentachlorophenol concentration in a certain range, and the LOD was 86 nM. The method was applied to the analysis of river water samples, and the spiked recoveries were 93−106%. Ren et al. also prepared MIP film on the surface of cysteine-modified Mn:ZnS QDs by use of the same method as Wang except that the template molecule was changed to nicosulfuron.[93] The principle of detection is also the charge transfer quenching. The LOD of the method was as low as 1.1 nM, and the LR was 12−6000 nM. The method was applied to the analysis of river water samples, and the spiked recoveries were 89.6−96.5% with the relative standard deviations of 2.5−5.7%. Compared with the chromatography, the method has the advantages of simplicity, low energy consumption, and fastness.

A kind of CdTe@SiO_2@MIP composite nanoparticles were prepared by Wei et al.[94] The MIPs of cyhalothrin as template were synthesized on the surface of CdTe QDs modified by mercapto succinic acid (MSA) with reverse phase microemulsion method. The CdTe@SiO_2@MIP composite nanoparticles were successfully used to the detection of cyhalothrin in water based on the same fluorescence quenching principle. The LR was 5.0−60 μM, and the recoveries were 93.7−108.3%. Afterward, the MIPs of the same template were also synthesized on the surface of CdTe QDs by them.[95] In the synthesizing process, the aqueous CdTe QDs were transferred into the organic phase through using octadecyl-4-vinylphenyldimethylammonium chloride as surfactant. There was linear relationship in the range of 0.1−16 μM, and the recoveries were 97.25−105.5%.

Wang et al. designed a novel paper-based molecular imprinted-PEC (MI-PEC) sensor for the detection of S-fenvalerate.[96] The detection device was composed of a square auxiliary table and a square sample table fabricated with wax-printed paper. A circular SPCE as WE was prepared in the hydrophobic barrier on the sample table, and an arch carbon counter electrode and an arch Ag/AgCl reference electrode were prepared on the auxiliary table. First, they synthesized the mercaptoacetic acid-modified CdTe QDs. The MIP film was successively synthesized on the surface of QDs constructing CdTe QDs@MIP, in which S-fenvalerate was used as template, acrylamide as functional monomer, and ethylene glycol dimethacrylate as cross-linker. Then, the AuNPs film was prepared on WE with $HAuCl_4$, and the prepared CdTe QDs@MIP was dropped to the Au film reacting for 1 h. The CdTe QDs@MIP was bound to WE through covalent bond between the amino group on the surface of MIP and Au. After the sample was dropped on the WE and incubated, the sample table and the auxiliary table were closely contacted with each other face to face, and the photocurrent was measured under

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Table 4. Detection Methods Based on QD-MIP Sensors

QD	analyte(s)	signal type	LOD	LR	sample type	ref
Mn:ZnS	Pentachlorophenol	phosphorescence	22.91 μg/L	53.3−1039 μg/L	river water	92
Mn:ZnS	Nicosulfuron	fluorescence	0.451 μg/L	4.9−2463 μg/L	river water	93
CdTe	λ-cyhalothrin	fluorescence		2249−26991 μg/L	river water	94
CdTe	λ-cyhalothrin	fluorescence	13.50 μg/L	45−7198 μg/L	river water	95
CdTe	S-fenvalerate	photocurrent	1.343 μg/L	4.2−419.9 μg/L	fruit, vegetable	96
CdTe/ZnS	Ractopamine	fluorescence	0.044 μg/L	0.15−105.5 μg/L	feeding stuffs, pork	97
CdSe	Ractopamine	fluorescence	0.228 μg/L	0.365−913.2 μg/L	pork	98
Mn:ZnS	Diazinon	fluorescence	50 μg/L	50−600 μg/L	tap water	99
Mn:ZnS	Cyphenothrin	fluorescence	3.379 μg/L	37.55−30037 μg/L	river water	100
Mn:ZnS	Chlorpyrifos	fluorescence	5.96 μg/L	105.2−21035 μg/L	river water	101
CdTe	Parathion	fluorescence	63.50 μg/L	14.56−291260 μg/L	river water, tap water	102
QD605	Cypermethrin	fluorescence	1.2 ng/g	50−60000 ng/g	fish	103
CdTe	Deltmethrin	fluorescence	160 μg/L	500−35000 μg/L	fruit, vegetable	104

the irradiation of excitation light at 365 nm after dropping ascorbic acid. When the sample is not added to the device, the QDs are excited and the electrons can transit from the valence band to the conduction band, leaving holes at the valence band. The electrons supplied by strong reducing ascorbic acid can enter these holes, which allow the electrons continuous transiting from valence band of QDs to the conduction band. The AuNPs can quickly transfer these electrons, forming stable photocurrent. When the sample is added, S-fenvalerate will enter the MIP, where the excited electrons of QDs can be absorbed by S-fenvalerate and the photocurrent will decrease. It was observed that the photocurrent decreased linearly with the increase of S-fenvalerate concentration in the range of 10^{-8} to 10^{-6} M, and the LOD was as low as 3.2×10^{-9} M. The method was applied to the detection of S-fenvalerate in fruit and vegetable samples.

Liu et al. prepared the MIP film of ractopamine on CdTe/ZnS QDs and CdSe QDs, respectively, by the sol−gel and reverse microemulsion method.[97,98] The constructed CdTe/ZnS QDs@MIP and CdSe QDs@MIP were used for the detection of ractopamine in feeding stuffs and pork samples. The principle of detection is also that the fluorescence of QDs is quenched by the analytes bound into MIP. The LODs of the two methods were 1.47×10^{-10} and 7.57×10^{-10} M, respectively. The applications of QD-MIP sensors are listed in Table 4.

The fluorescence properties of QDs in QDs@MIP are often lost in the polymerization process. It is difficult to stabilize the water-soluble QDs in the MIP matrix through a relatively easy way. The preparation of bright and stable QDs and the functionalization of their surface are still the direction of research in future.

SITUATION AND PROSPECT

As a class of new luminescent materials, QDs have been more and more widely used in the detection of pesticide and veterinary drug residues, and the relative research is still deepening and expanding. The goal pursued in detection method of the pesticide and veterinary drug residues is sensitive, rapid, qualitative, quantitative, and multiresidue detection. Among the published research results, the goal of fast and sensitive detection could be realized by use of the signal of QDs. However, the selectivity of qualitative analysis methods in which the optical signal of QDs themselves was directly used was inadequate. The excellent selectivity was usually obtained when QDs were conjugated to the material for analyte to be selective to construct complex probes or sensors, such as QD-enzymes, QD-antibodies, QD-APTs, or QD-MIPs. However, it is still necessary to continuously increase the selectivity of QD-enzyme sensors. Searching for the enzymes of which the activities are selectively inhibited by special pesticide or veterinary drug is the future development direction of this kind of sensors. Without doubt, the most methods of using QDs signal were the monoresidue detection, multiresidue detection still needed to be combined with the separation method. The detection methods without the dependence of separation will be a development direction in the future. In this respect, the combination of QDs with highly selective APTs or MIPs will show a broad application prospect.

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Notes

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ABBREVIATIONS USED

QD, quantum dot; LOD, limit of detection; RRS, resonance Rayleigh scattering; FRET, fluorescence resonance energy transfer; APT, aptamer; MIP, molecularly imprinted polymers; LR, linear range; CRET, chemiluminescence resonance energy transfer; FLISA, fluorescence immunoassay; BSA, bovine serum albumin; ELISA, enzyme-linked immunosorbent assay; ALP, alkaline phosphatase; SA, streptavidin; AChE, acetylcholinesterase; MP, methyl parathion; ATCh, acetylchiocholine; TCh, thiocholine; Ach, acetylcholine; ChOx, choline oxidase; Ch, choline; MPA, mercaptopropionic acid; OPH, organophosphatase; DMPA, dimethyl phosphorothioate; ECL, electrochemiluminescence; GO, grapheen oxide; GCE, glass carbon electrode; GN, grapheen nanosheet; GLD, glutaraldehyde; ATCl, acetylcholineschine chloride; MPDE, methyl parathionase; MWCNT, multiwalled carbon nanotubes; AuNP, gold nanoparticle; PEC, photoelectrochemical; ITO, indium-

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doped tin oxide; PEI, poly(ethylenimine); SAL, salbutamol; CH, clenbuterol; EIS, electrochemical impedance spectroscopy; PANI, polyaniline; IFE, internal filter effect; ABA, APT of acetamiprid; SPCE, screen-printed carbon electrode; MSA, mercapto succinic acid; DDVP, dimethyl dichlorovinyl phosphate; MI-PEC, molecular imprinted-PEC

REFERENCES

(1) Fang, R.; Chen, G. H.; Yi, L. X.; Shao, Y. X.; Zhang, L.; Cai, Q. H.; Xiao, J. Determination of eight triazine herbicide residues in cereal and vegetable by micellar electrokinetic capillary chromatography with on-line sweeping. *Food Chem.* **2014**, *145*, 41−48.

(2) Tian, Y. F.; Chen, G. H.; Guo, L. H.; Guo, X.; Mei, X. Y. Methodology studies on detection of aminoglycoside residues. *Food Anal. Method* **2015**, *8*, 1842−1857.

(3) Bonilla, J. C.; Bozkurt, F.; Ansari, S.; Sozer, N.; Kokini, J. L. Applications of quantum dots in food science and biology. *Trends Food Sci. Technol.* **2016**, *53*, 75−89.

(4) Le, T.; Zhu, L. Q.; Yu, H. Dual-label quantum dot-based immunoassay for simultaneous determination of Carbadox and Olaquindox metabolites in animal tissues. *Food Chem.* **2016**, *199*, 70−74.

(5) Tran, T. K. C.; Vu, D. C.; Ung, T. D. T.; Nguyen, H. Y.; Nguyen, N. H.; Dao, T. C.; Pham, T. N.; Nguyen, Q. L. Fabrication of fluorescence-based biosensors from functionalized CdSe and CdTe quantum dots for pesticide detection. *Adv. Nat. Sci.: Nanosci. Nanotechnol.* **2012**, *3*, 035008.

(6) Nsibande, S. A.; Forbes, P. B. Fluorescence detection of pesticides using quantum dot materials - A review. *Anal. Chim. Acta* **2016**, *945*, 9−22.

(7) Stanisavljevic, M.; Krizkova, S.; Vaculovicova, M.; Kizek, R.; Adam, V. Quantum dots-fluorescence resonance energy transfer-based nanosensors and their application. *Biosens. Bioelectron.* **2015**, *74*, 562−574.

(8) Frigerio, C.; Ribeiro, D. S. M.; Rodrigues, S. S. M.; Abreu, V. L.; Barbosa, J. A.; Prior, J. A.; Marques, K. L.; Santos, J. L. Application of quantum dots as analytical tools in automated chemical analysis: A review. *Anal. Chim. Acta* **2012**, *735*, 9−22.

(9) Kuang, H.; Zhao, Y.; Ma, W.; Xu, L. G.; Wang, L. B.; Xu, C. L. Recent developments in analytical applications of quantum dots. *TrAC, Trends Anal. Chem.* **2011**, *30*, 1620−1636.

(10) Lesnyak, V.; Gaponik, N.; Eychmueller, A. Colloidal semiconductor nanocrystals: the aqueous approach. *Chem. Soc. Rev.* **2013**, *42*, 2905−2929.

(11) Alivisatos, A. P. Semiconductor clusters, nanocrystals, and quantum dots. *Science* **1996**, *271*, 933−937.

(12) Chestnoy, N.; Harris, T. D.; Hull, R.; Brus, L. E. Luminescence and photophysics of cadmium sulfide semiconductor clusters: the nature of the emitting electronic state. *J. Phys. Chem.* **1986**, *90*, 3393−3399.

(13) Lee, D. C.; Pietryga, J. M.; Robel, I.; Werder, D. J.; Schaller, R. D.; Klimov, V. I. Colloidal synthesis of infrared-emitting germanium nanocrystals. *J. Am. Chem. Soc.* **2009**, *131*, 3436−3437.

(14) Li, L.; Coates, N.; Moses, D. Solution-processed inorganic solar cell based on in situ synthesis and film deposition of $CuInS_2$ nanocrystals. *J. Am. Chem. Soc.* **2010**, *132*, 22−23.

(15) Shiohara, A.; Hanada, S.; Prabakar, S.; Fujioka, K.; Lim, T. H.; Yamamoto, K.; Northcote, P. T.; Tilley, R. D. Chemical reactions on surface molecules attached to silicon quantum dots. *J. Am. Chem. Soc.* **2010**, *132*, 248−253.

(16) Guo, Q. J.; Hillhouse, H. W.; Agrawal, R. Synthesis of Cu_2ZnSnS_4 nanocrystal ink and its use for solar cells. *J. Am. Chem. Soc.* **2009**, *131*, 11672−11673.

(17) Rossetti, R.; Brus, L. Electron-hole recombination emission as a probe of surface chemistry in aqueous cadmium sulfide colloids. *J. Phys. Chem.* **1982**, *86*, 4470−4472.

(18) Bruchez, M., Jr.; Moronne, M.; Gin, P.; Weiss, S.; Alivisatos, A. P. Semiconductor nanocrystals as fluorescent biological labels. *Science* **1998**, *281*, 2013−2016.

(19) Alivisatos, A. P.; Gu, W. W.; Larabell, C. Quantum dots as cellular probes. *Annu. Rev. Biomed. Eng.* **2005**, *7*, 55−76.

(20) Sun, J. J.; Goldys, E. M. Linear absorption and molar extinction coefficients in direct semiconductor quantum dots. *J. Phys. Chem. C* **2008**, *112*, 9261−9266.

(21) Yu, W. W.; Qu, L. H.; Guo, W. Z.; Peng, X. G. Experimental determination of the extinction coefficient of CdTe, CdSe, and CdS nanocrystals. *Chem. Mater.* **2003**, *15*, 2854−2860.

(22) Zrazhevskiy, P.; Sena, M.; Gao, X. H. Designing multifunctional quantum dots for bioimaging, detection, and drug delivery. *Chem. Soc. Rev.* **2010**, *39*, 4326−4354.

(23) Walling, M.; Novak, J.; Shepard, J. R. E. Quantum Dots for Live Cell and In Vivo Imaging. *Int. J. Mol. Sci.* **2009**, *10*, 441−491.

(24) Zhao, S. M.; Han, S. Q. Thioglycolic Acid Capped CdS Quantum Dots as Fluorescence Probe for Ultrasensitive Determination of Tetracycline and Oxytetracycline. *J. Chin. Chem. Soc.* **2010**, *57*, 1353−1360.

(25) Qu, F. G.; Zhou, X. F.; Xu, J.; Li, H. B.; Xie, G. Y. Luminescence switching of CdTe quantum dots in presence of p-sulfonatocalix[4]-arene to detect pesticides in aqueous solution. *Talanta* **2009**, *78*, 1359−1363.

(26) Tashkhourian, J.; Absalan, G.; Jafari, M.; Zare, S. A rapid and sensitive assay for determination of doxycycline using thioglycolic acid-capped cadmium telluride quantum dots. *Spectrochim. Acta, Part A* **2016**, *152*, 119−125.

(27) Durán, G. M.; Contento, A. M.; Ríos, Á. Use of Cdse/ZnS quantum dots for sensitive detection and quantification of paraquat in water samples. *Anal. Chim. Acta* **2013**, *801*, 84−90.

(28) Wang, L.; Peng, J. J.; Liu, Z. W.; He, Y. Q. Resonance Rayleigh-scattering spectral method for the determination of some amino-glycoside antibiotics using CdTe quantum dots as a probe. *Luminescence* **2010**, *25*, 424−430.

(29) Liu, Z. W.; Liu, S. P.; Wang, L.; Peng, J. J.; He, Y. Q. Resonance Rayleigh scattering and resonance non-linear scattering method for the determination of aminoglycoside antibiotics with water solubility CdS quantum dots as probe. *Spectrochim. Acta, Part A* **2009**, *74*, 36−41.

(30) Imani-Nabiyyi, A.; Sorouraddin, M. H.; Amjadi, M.; Naseri, A. Luminol/CdTe quantum dots/sodium periodate system in conjunction with response-surface methodology for chemiluminometric determination of some tetracyclines. *J. Lumin.* **2014**, *151*, 57−65.

(31) Khataee, A.; Hasanzadeh, A.; Lotfi, R.; Joo, S. W. Enhanced chemiluminescence of carminic acid-permanganate by CdS quantum dots and its application for sensitive quenchometric flow injection assays of cloxacillin. *Talanta* **2016**, *152*, 171−178.

(32) Förster, T. Zwischenmolekulare energiewanderung und fluoreszenz. *Ann. Phys.* **1948**, *437*, 55−75.

(33) Zhang, K.; Mei, Q. S.; Guan, G. J.; Liu, B. H.; Wang, S. H.; Zhang, Z. P Ligand replacement-induced fluorescence switch of quantum dots for ultrasensitive detection of organophosphorothioate pesticides. *Anal. Chem.* **2010**, *82*, 9579−9586.

(34) Chen, G. H.; Sun, J.; Dai, Y. J.; Dong, M. Determination of nicotinyl pesticide residues in vegetables by micellar electrokinetic capillary chromatography with quantum dot indirect laser-induced fluorescence. *Electrophoresis* **2012**, *33*, 2192−2196.

(35) Guo, X.; Wang, K.; Chen, G. H.; Shi, J.; Wu, X.; Di, L. L.; Wang, Y. Determination of strobilurin fungicide residues in fruits and vegetables by nonaqueous micellar electrokinetic capillary chromatography with indirect laser-induced fluorescence. *Electrophoresis* **2017**, *38*, 2004−2010.

(36) Meng, H. L.; Chen, G. H.; Guo, X.; Chen, P.; Cai, Q. H.; Tian, Y. F. Determination of five quinolone antibiotic residues in foods by micellar electrokinetic capillary chromatography with quantum dot indirect laser-induced fluorescence. *Anal. Bioanal. Chem.* **2014**, *406*, 3201−3208.

(37) Jimenez-López, J.; Molina-García, L.; Rodrigues, S. S. M.; Santos, J. L. M.; Ortega-Barrales, P.; Ruiz-Medina, A. Automated

DOI: 10.1021/acs.jafc.7b05119
J. Agric. Food Chem. 2018, 66, 1307−1319

determination of rifamycins making use of MPA−CdTe quantum dots. *J. Lumin.* **2016**, *175*, 158−164.
(38) Guo, J. J.; Zhang, Y.; Luo, Y. L.; Shen, F.; Sun, C. Efficient fluorescence resonance energy transfer between oppositely charged CdTe quantum dots and gold nanoparticles for turn-on fluorescence detection of glyphosate. *Talanta* **2014**, *125*, 385−392.
(39) Shen, Y. Z.; Liu, S. P.; Kong, L.; Li, D.; He, Y. Q. Sensitive detection of polymyxin B sulfate at the nanogram level using enhanced resonance scattering signals and decreased fluorescence signals with thioglycolic acid capped CdTe/CdS quantum dots as probe. *Sens. Actuators, B* **2013**, *188*, 555−563.
(40) Yan, X.; Li, H. X.; Li, Y.; Su, X. G. Visual and fluorescent detection of acetamiprid based on the inner filter effect of gold nanoparticles on ratiometric fluorescence quantum dots. *Anal. Chim. Acta* **2014**, *852*, 189−195.
(41) Walia, S.; Acharya, A. Fluorescent cadmium sulfide nanoparticles for selective and sensitive detection of toxic pesticides in aqueous medium. *J. Nanopart. Res.* **2014**, *16*, 1−10.
(42) Liu, Q.; Wang, K.; Huan, J.; Zhu, G. B.; Qian, J.; Mao, H. P.; Cai, J. R. Graphene quantum dots enhanced electrochemiluminescence of cadmium sulfide nanocrystals for ultrasensitive determination of pentachlorophenol. *Analyst* **2014**, *139*, 2912−2918.
(43) Yan, X.; Li, H. X.; Han, X. S.; Su, X. G. A ratiometric fluorescent quantum dots based biosensor for organophosphorus pesticides detection by inner-filter effect. *Biosens. Bioelectron.* **2015**, *74*, 277−283.
(44) Li, J. J.; Li, X.; Yang, R.; Qu, L. B.; Harrington, P. D. A sensitive electrochemical chlorophenols sensor based on nanocomposite of ZnSe quantum dots and cetyltrimethylammonium bromide. *Anal. Chim. Acta* **2013**, *804*, 76−83.
(45) Tao, H. L.; Liao, X. F.; Sun, C.; Xie, X. L.; Zhong, F. X.; Yi, Z. S.; Huang, Y. P. A carbon dots-CdTe quantum dots fluorescence resonance energy transfer system for the analysis of ultra-trace chlortoluron in water. *Spectrochim. Acta, Part A* **2015**, *136*, 1328−1334.
(46) García-Fernández, J.; Trapiella-Alfonso, L.; Costa-Fernández, J. M.; Pereiro, R.; Sanz-Medel, A. A quantum dot-based immunoassay for screening of tetracyclines in bovine muscle. *J. Agric. Food Chem.* **2014**, *62*, 1733−1740.
(47) Wu, J.; Xu, F.; Zhu, K.; Wang, Z. H.; Wang, Y. H.; Zhao, K. X.; Li, X. W.; Jiang, H. Y.; Ding, S. Y. Rapid and sensitive fluoroimmunoassay based on quantum dots for detection of melamine in milk. *Anal. Lett.* **2013**, *46*, 275−285.
(48) Chen, J. X.; Xu, F.; Jiang, H. Y.; Hou, Y. L.; Rao, Q. X.; Guo, P. J.; Ding, S. Y. A novel quantum dot-based fluoroimmunoassay method for detection of enrofloxacin residue in chicken muscle tissue. *Food Chem.* **2009**, *113*, 1197−1201.
(49) Song, E. Q.; Yu, M. Q.; Wang, Y. Y.; Hu, W. H.; Cheng, D.; Swihart, M. T.; Song, Y. Multi-color quantum dot-based fluorescence immunoassay array for simultaneous visual detection of multiple antibiotic residues in milk. *Biosens. Bioelectron.* **2015**, *72*, 320−325.
(50) Taranova, N. A.; Berlina, A. N.; Zherdev, A. V.; Dzantiev, B. B. 'Traffic light' immunochromatographic test based on multicolor quantum dots for the simultaneous detection of several antibiotics in milk. *Biosens. Bioelectron.* **2015**, *63*, 255−261.
(51) Vinayaka, A. C.; Basheer, S.; Thakur, M. S. Bioconjugation of CdTe quantum dot for the detection of 2, 4-dichlorophenoxyacetic acid by competitive fluoroimmunoassay based biosensor. *Biosens. Bioelectron.* **2009**, *24*, 1615−1620.
(52) Chen, Y. P.; Ning, B. A.; Liu, N.; Feng, Y.; Liu, Z.; Liu, X. Y.; Gao, Z. X. A rapid and sensitive fluoroimmunoassay based on quantum dot for the detection of chlorpyrifos residue in drinking water. *J. Environ. Sci. Health, Part B* **2010**, *45*, 508−515.
(53) Chen, Y. P.; Ren, H. L.; Liu, N.; Sai, N.; Liu, X. Y.; Liu, Z.; Gao, Z. X.; Ning, B. A. A fluoroimmunoassay based on quantum dot-streptavidin conjugate for the detection of chlorpyrifos. *J. Agric. Food Chem.* **2010**, *58*, 8895−8903.
(54) Liu, J. K.; Zhang, Q.; Zhang, W.; Ding, X. X.; Hu, X. F.; Zhao, F. F.; Li, P. W. Development of a fluorescence-linked immunoassay based on quantum dots for fenvalerate. *Food Agric. Immunol.* **2014**, *25*, 82−93.
(55) Beloglazova, N. V.; Shmelin, P. S.; Eremin, S. A. Sensitive immunochemical approaches for quantitative (FPIA) and qualitative (lateral flow tests) determination of gentamicin in milk. *Talanta* **2016**, *149*, 217−224.
(56) Peng, C. F.; Li, Z. K.; Zhu, Y. Y.; Chen, W.; Yuan, Y.; Liu, L. Q.; Li, Q. S.; Xu, D. H.; Qiao, R. R.; Wang, L. B.; Zhu, S. F.; Jin, Z. Y.; Xu, C. L. Simultaneous and sensitive determination of multiplex chemical residues based on multicolor quantum dot probes. *Biosens. Bioelectron.* **2009**, *24*, 3657−3662.
(57) Le, T.; Zhu, L. Q.; Yang, X. A quantum dot-based immunoassay for screening of tylosin and tilmicosin in edible animal tissues. *Food Addit. Contam. Part A Che. Anal. Control Expo. Risk Assess.* **2015**, *32*, 719−724.
(58) Luan, C. L. A fluoroimmunoassay method using quantum dot labels for detection of melamine. *Adv. Mater. Res.* **2014**, *955−959*, 1484−1490.
(59) Jiang, W. X.; Beloglazova, N. V.; Wang, Z. H.; Jiang, H. Y.; Wen, K.; de Saeger, S.; Luo, P. J.; Wu, Y. N.; Shen, J. Z. Development of a multiplex flow-through immunoaffinity chromatography test for the on-site screening of 14 sulfonamide and 13 quinolone residues in milk. *Biosens. Bioelectron.* **2015**, *66*, 124−128.
(60) Gao, X.; Tang, G. C.; Su, X. G. Optical detection of organophosphorus compounds based on Mn-doped ZnSe d-dot enzymatic catalytic sensor. *Biosens. Bioelectron.* **2012**, *36*, 75−80.
(61) Fernández-Argüelles, M. T.; Jin, W. J.; Costa-Fernández, J. M.; Pereiro, R.; Sanz-Medel, A. Surface-modified CdSe quantum dots for the sensitive and selective determination of Cu(II) in aqueous solutions by luminescent measurements. *Anal. Chim. Acta* **2005**, *549*, 20−25.
(62) Yan, X.; Li, H. X.; Yan, Y.; Su, X. G. Selective detection of parathion-methyl based on near-infrared $CuInS_2$, quantum dots. *Food Chem.* **2015**, *173*, 179−184.
(63) Liang, H.; Song, D. D.; Gong, J. M. Signal-on electrochemiluminescence of biofunctional CdTe quantum dots for biosensing of organophosphate pesticides. *Biosens. Bioelectron.* **2014**, *53*, 363−369.
(64) Du, D.; Chen, W. J.; Zhang, W. Y.; Liu, D. L.; Li, H. B.; Lin, Y. H. Covalent coupling of organophosphorus hydrolase loaded quantum dots to carbon nanotube/Au nanocomposite for enhanced detection of methyl parathion. *Biosens. Bioelectron.* **2010**, *25*, 1370−1375.
(65) Li, X. Y.; Zheng, Z. Z.; Liu, X. F.; Zhao, S. L.; Liu, S. Q. Nanostructured photoelectrochemical biosensor for highly sensitive detection of organophosphorous pesticides. *Biosens. Bioelectron.* **2015**, *64*, 1−5.
(66) Du, D.; Chen, W. J.; Cai, J.; Zhang, J.; Qu, F. G.; Li, H. B. Development of acetylcholinesterase biosensor based on CdTe quantum dots modified cysteamine self-assembled monolayers. *J. Electroanal. Chem.* **2008**, *623*, 81−85.
(67) Guo, J. J.; Li, H. K.; Xue, M.; Zhang, M. W.; Cao, X. Y.; Luo, Y. L.; Shen, F.; Sun, C. Y. Highly Sensitive Detection of Organophosphorus Pesticides Represented by Methamidophos via Inner Filter Effect of Au Nanoparticles on the Fluorescence of CdTe Quantum Dots. *Food Anal. Methods* **2014**, *7* (6), 1247−1255.
(68) Luan, E. X.; Zheng, Z. Z.; Li, X. Y.; Gu, H. X.; Liu, S. Q. Inkjet-assisted layer-by-layer printing of quantum dot/enzyme microarrays for highly sensitive detection of organophosphorous pesticides. *Anal. Chim. Acta* **2016**, *916*, 77−83.
(69) Nguyen, N. H.; Duong, T. G.; Hoang, V. N.; Pham, N. T.; Dao, T. C.; Pham, T. N. Synthesis and application of quantum dots-based biosensor. *Adv. Nat. Sci.: Nanosci. Nanotechnol.* **2015**, *6*, 015015.
(70) Zheng, Z. Z.; Zhou, Y. L.; Li, X. Y.; Liu, S. Q.; Tang, Z. Y. Highly-sensitive organophosphorous pesticide biosensors based on nanostructured films of acetylcholinesterase and CdTe quantum dots. *Biosens. Bioelectron.* **2011**, *26*, 3081−3085.
(71) Hai, N. N.; Chinh, V. D.; Chi, T. K.; Ung, T. D. T.; Nghia, N. X.; Cao, D. T.; Nga, P. T. Optical detection of the pesticide by

DOI: 10.1021/acs.jafc.7b05119
J. Agric. Food Chem. 2018, 66, 1307−1319

functionalized quantum dots as fluorescence-based biosensor. *Key Eng. Mater.* **2011**, *495*, 314−318.
(72) Zheng, Z. Z.; Li, X. Y.; Dai, Z. F.; Liu, S. Q.; Tang, Z. Y. Detection of mixed organophosphorus pesticides in real samples using quantum dots/bi-enzyme assembly multilayers. *J. Mater. Chem.* **2011**, *21*, 16955−16962.
(73) Garai-Ibabe, G.; Saa, L.; Pavlov, V. Thiocholine mediated stabilization of in situ produced CdS quantum dots: application for the detection of acetylcholinesterase activity and inhibitors. *Analyst* **2014**, *139*, 280−284.
(74) Gao, X.; Zhao, Y.; Zhang, B.; Tang, Y. W.; Liu, X. Y.; Li, J. R. Highly-sensitive organophosphorus pesticide biosensors based on CdTe quantum dots and bi-enzyme immobilized eggshell membranes. *Analyst* **2016**, *141*, 1105−1111.
(75) Meng, X. W.; Wei, J. F.; Ren, X. L.; Ren, J.; Tang, F. Q. A simple and sensitive fluorescence biosensor for detection of organophosphorus pesticides using H_2O_2-sensitive quantum dots/bi-enzyme. *Biosens. Bioelectron.* **2013**, *47*, 402−407.
(76) Zhang, R.; Li, N.; Sun, J. Y.; Gao, F. Colorimetric and phosphorimetric dual-signaling strategy mediated by inner filter effect for highly sensitive assay of organophosphorus pesticides. *J. Agric. Food Chem.* **2015**, *63*, 8947−8954.
(77) Ban, R.; Zhu, J. J.; Zhang, J. R. Manganese-doped ZnS quantum dots as a phosphorescent probe for use in the bi-enzymatic determination of organophosphorus pesticides. *Microchim. Acta* **2014**, *181*, 1591−1599.
(78) Zhang, J.; Cai, F. D.; Deng, A. P.; Li, J. G. CdSe quantum dots based electrochemiluminescence immunosensor with simple structure for ultrasensitive detection of salbutamol. *Electroanalysis* **2014**, *26*, 873−881.
(79) Cai, F. D.; Wang, N.; Dong, T. T.; Deng, A. P.; Li, J. G. Dual-signal amplified electrochemiluminescent immunoassay for salbutamol based on quantum dots and gold nanoparticles-labeled horseradish peroxidase. *Analyst* **2015**, *140*, 5885−5890.
(80) Zhang, Z. H.; Duan, F. H.; He, L. H.; Peng, D. L.; Yan, F. F.; Wang, M. H.; Zong, W.; Jia, C. X. Electrochemical clenbuterol immunosensor based on a gold electrode modified with zinc sulfide quantum dots and polyaniline. *Microchim. Acta* **2016**, *183*, 1089−1097.
(81) Tombelli, S.; Minunni, M.; Mascini, A. Analytical applications of aptamers. *Biosens. Bioelectron.* **2005**, *20*, 2424−2434.
(82) Cho, E. J.; Lee, J. W.; Ellington, A. D. Applications of aptamers as sensors. *Annu. Rev. Anal. Chem.* **2009**, *2*, 241−264.
(83) Miao, Y. B.; Ren, H. X.; Gan, N.; Zhou, Y.; Cao, Y. T.; Li, T. H.; Chen, Y. J. A homogeneous and "off-on" fluorescence aptamer-based assay for chloramphenicol using vesicle quantum dot-gold colloid composite probes. *Anal. Chim. Acta* **2016**, *929*, 49−55.
(84) Alibolandi, M.; Hadizadeh, F.; Vajhedin, F.; Abnous, K.; Ramezani, M. Design and fabrication of an aptasensor for chloramphenicol based on energy transfer of CdTe quantum dots to graphene oxide sheet. *Mater. Sci. Eng., C* **2015**, *48*, 611−619.
(85) Lin, B. X.; Yu, Y.; Li, R. Y.; Cao, Y. J.; Guo, M. L. Turn-on sensor for quantification and imaging of acetamiprid residues based on quantum dots functionalized with aptamer. *Sens. Actuators, B* **2016**, *229*, 100−109.
(86) Guo, J. J.; Li, Y.; Wang, L. K.; Xu, J. Y.; Huang, Y. J.; Luo, Y. L.; Shen, F.; Sun, C. Y.; Meng, R. Z. Aptamer-based fluorescent screening assay for acetamiprid via inner filter effect of gold nanoparticles on the fluorescence of CdTe quantum dots. *Anal. Bioanal. Chem.* **2016**, *408*, 557−566.
(87) Feng, X. B.; Gan, N.; Lin, S. C.; Li, T. H.; Cao, Y. T.; Hu, F. T.; Jiang, Q. L.; Chen, Y. J. Ratiometric electrochemiluminescent aptasensor array for antibiotic based on internal standard method and spatial-resolved technique. *Sens. Actuators, B* **2016**, *226*, 305−311.
(88) Li, Y.; Tian, J. Y.; Yuan, T.; Wang, P.; Lu, J. S. A sensitive photoelectrochemical aptasensor for oxytetracycline based on a signal "switch off-on" strategy. *Sens. Actuators, B* **2017**, *240*, 785−792.
(89) Tang, B.; Cao, L. H.; Xu, K. H.; Zhuo, L. H.; Ge, J. H.; Li, Q. F.; Yu, L. J. A new nanobiosensor for glucose with high sensitivity and selectivity in serum based on fluorescence resonance Energy transfer (FRET) between CdTe quantum dots and Au nanoparticles. *Chem. - Eur. J.* **2008**, *14*, 3637−3644.
(90) Monier, M.; Abdel-Latif, D. A. Synthesis and characterization of ion-imprinted chelating fibers based on PET for selective removal of Hg^{2+}. *Chem. Eng. J.* **2013**, *221*, 452−460.
(91) Ciardelli, G.; Borrelli, C.; Silvestri, D.; Cristallini, C.; Barbani, N.; Giusti, P. Supported imprinted nanospheres for the selective recognition of cholesterol. *Biosens. Bioelectron.* **2006**, *21*, 2329−2338.
(92) Wang, H. F.; He, Y.; Ji, T. R.; Yan, X. P. Surface molecular imprinting on Mn-doped ZnS quantum dots for room-temperature phosphorescence optosensing of pentachlorophenol in water. *Anal. Chem.* **2009**, *81*, 1615−1621.
(93) Ren, X. H.; Chen, L. G. Preparation of molecularly imprinted polymer coated quantum dots to detect nicosulfuron in water samples. *Anal. Bioanal. Chem.* **2015**, *407*, 8087−8095.
(94) Wei, X.; Meng, M. J.; Song, Z. L.; Gao, L.; Li, H. J.; Dai, J. D.; Zhou, Z. P.; Li, C. X.; Pan, J. M.; Yu, P.; Yan, Y. S. Synthesis of molecularly imprinted silica nanospheres embedded mercaptosuccinic acid-coated CdTe quantum dots for selective recognition of λ-cyhalothrin. *J. Lumin.* **2014**, *153*, 326−332.
(95) Wei, X.; Hao, T. F.; Xu, Y. Q.; Lu, K.; Li, H. J.; Yan, Y. S.; Zhou, Z. P. Facile polymerizable surfactant inspired synthesis of fluorescent molecularly imprinted composite sensor via aqueous CdTe quantum dots for highly selective detection of λ-cyhalothrin. *Sens. Actuators, B* **2016**, *224*, 315−324.
(96) Wang, Y. H.; Zang, D. J.; Ge, S. G.; Ge, L.; Yu, J. H.; Yan, M. A novel microfluidic origami photoelectrochemical sensor based on CdTe quantum dots modified molecularly imprinted polymer and its highly selective detection of S-fenvalerate. *Electrochim. Acta* **2013**, *107*, 147−154.
(97) Liu, H. L.; Liu, D. R.; Fang, G. Z.; Liu, F. F.; Liu, C. C.; Yang, Y. K.; Wang, S. A novel dual-function molecularly imprinted polymer on CdTe/ZnS quantum dots for highly selective and sensitive determination of ractopamine. *Anal. Chim. Acta* **2013**, *762*, 76−82.
(98) Liu, H. L.; Fang, G. Z.; Wang, S. Molecularly imprinted optosensing material based on hydrophobic CdSe quantum dots via a reverse microemulsion for specific recognition of ractopamine. *Biosens. Bioelectron.* **2014**, *55*, 127−132.
(99) Zhao, Y. Y.; Ma, Y. X.; Li, H.; Wang, L. Y. Composite QDs@MIP nanospheres for specific recognition and direct fluorescent quantification of pesticides in aqueous media. *Anal. Chem.* **2012**, *84*, 386−395.
(100) Ren, X. H.; Chen, L. G. Quantum dots coated with molecularly imprinted polymer as fluorescence probe for detection of cyphenothrin. *Biosens. Bioelectron.* **2015**, *64*, 182−188.
(101) Ren, X. H.; Liu, H. C.; Chen, L. G. Fluorescent detection of chlorpyrifos using Mn(II)-doped ZnS quantum dots coated with a molecularly imprinted polymer. *Microchim. Acta* **2015**, *182*, 193−200.
(102) Tang, J. S.; Xiang, L. Development of a probe based on quantum dots embedded with molecularly imprinted polymers to detect parathion. *Pol. J. Environ. Stud.* **2016**, *25*, 787−793.
(103) Xiao, T. T.; Shi, X. Z.; Jiao, H. F.; Sun, A. L.; Ding, H.; Zhang, R. R.; Pan, D. D.; Li, D. X.; Chen, J. Selective and sensitive determination of cypermethrin in fish via enzyme-linked immunosorbent assay-like method based on molecularly imprinted artificial antibody-quantum dot optosensing materials. *Biosens. Bioelectron.* **2016**, *75*, 34−40.
(104) Ge, S.; Lu, J. J.; Ge, L.; Yan, M.; Yu, J. H. Development of a novel deltamethrin sensor based on molecularly imprinted silica nanospheres embedded CdTe quantum dots. *Spectrochim. Acta, Part A* **2011**, *79*, 1704−1709.

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