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Perspective on recent developments of nanomaterial based fluorescent sensors: Applications in safety and quality control of food and beverages

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Abstract

As the highly toxic pollutants will seriously harm human health, it is particularly important to establish the analysis and detection technology of food pollutants. Compared with the traditional detection methods, fluorescent detection techniques based on nanomaterials trigger wide interesting because of reduced detection time, simple operation, high sensitivity and selectivity, and economic. In this review, the application of fluorescent sensors in food pollutants detection is presented. Firstly, conventional fluorescent nanomaterials including metal-based quantum dots, carbon dots, graphene quantum dots and metal nanoclusters were summarized, with emphasis on the photoluminescence mechanism. Then, the fluorescence sensors based on these nanomaterials for food pollutants detection were discussed, involving in the established methods, sensor mechanisms, sensitivity, selectivity, and practicability of fluorescence sensors. The selected analytes focus on five types of higher toxic food pollutants, including mycotoxins, foodborne pathogens, pesticide residues, antibiotic residues, and heavy metal ions. Finally, outlook on the future and potential development of fluorescence detection technology in the field of food science were proposed, including green synthesis and reusability of fluorescence probes, large-scale industrialization of sensors, nondestructive testing of samples and degradation of harmful substances.

Keywords: Fluorescent nanomaterial, Food pollutant, Photoluminescence mechanism, Sensing mechanism, Toxicity

1. Introduction

F ood safety has become a major global concern because the frequent occurrence of food poisoning events that have brought great threat and harm to the public health. It is reported that there are about 1.5 billion cases of diarrhea was occurred every year on a global scale, three quarters of which are caused by ingesting contaminated foods [1]. Food pollution may occur in the whole food chain, including raw materials, processing, transportation and storage. Microorganism is one of the main reasons that affect food safety. Foodborne pathogenic bacteria, such as *salmonella*, *escherichia coli* and *staphylococcus aureus*, can easily cause vomiting, diarrhea, poisoning and intestinal infectious diseases [2–4]. Mycotoxins are the toxic metabolites of mold, which is widespread exist in cereal, corn, wheat, soybean, beer and wine, etc. Eating foods contaminated with mycotoxins may have a variety of effects on humans and animals, including hepatotoxicity, nephrotoxicity, immunotoxicity, neurotoxicity and carcinogenicity, etc. [5,6] In the

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development of agriculture and animal husbandry, a large number of pesticides or chemicals are used to control pests and diseases, resist pathogens and improve economic benefits, which is also a potential risk for food safety. The extensive use or abuse of pesticides and antibiotics will inevitably lead to the toxic residues in food and further cause adverse effects on human health [7–10]. Heavy metal ion is one of the important factors of water pollution that is closely related to the quality of food and human health [11–15]. Therefore, it is very necessary to realize the accurate, sensitive and effective determination of food pollutants.

Conventional analytical techniques for food safety include high-performance liquid chromatography (HPLC), gas chromatography, size exclusion chromatography, liquid chromatography-mass spectrometer (LC-MS), gas chromatograph-mass spectrometer (GC-MS), and enzyme-linked immunosorbent assay (ELISA), etc. Although the conventional analytical methods have been widely employed, these methods refer to complex multi-step sample pretreatment, expensive instruments, labor intensive and high requirements for testing personnel. With the rapid development of nanotechnology, many detection methods are established based on novel nanomaterials. The nanomaterial based fluorescent sensors are nonnegligible, which realized fast, convenient, accurate and reliable detection of analytes and are widely used for biosensing, bioimaging, biomedical, environmental analysis and food science [16-19].

Fluorescent nanomaterials, such as metal-based quantum dots (QDs), carbon dots (CDs), graphene QDs (GQDs), and metal nanoclusters (NCs), have been verified as excellent nanoprobes for detection of target analytes attributed to their high photoluminescence (PL) intensity, photobleaching resistance, controllable synthesis, easy surface modification and cost-effectiveness [19-21]. With the clear studies on the structures and properties of these nanomaterials, the complicated PL mechanism of nanomaterials has been gradually illustrated. The PL of nanoprobes is closely related to both its cores and surface chemistry [21-24]. Therefore, the probes prepared by different methods show different PL properties, which make them can identify different targets. And the fluorescent probes also can be modified with various signal recognition probe for the selective determination of more target analytes.

In this review, we focus on the reported fluorescent sensors based on metal-based QDs, CDs, GCDs and metal NCs for detection of food pollutants. Considering the toxicity and universality of various pollutants, mycotoxins, foodborne pathogens, pesticide residues, antibiotic residues, and heavy metal ions are chosen as target analytes. The sensing mechanism of sensing systems are emphatically discussed. And utilized nanoprobes, established methods, sensing performance (including the linear response range and the limits of detection (LOD)) and the application of the real sample are also introduced (see Table 1). Finally, the challenges and future outlooks of nanomaterial based fluorescent sensors in food safety analysis are discussed.

2. Fluorescent nanomaterials

2.1. Metal-based quantum dots (QDs)

Metal-based semiconductor QDs are generally spherical or quasi spherical with radius smaller than that of bulk exciton Bohr radius [25]. The quantum confinement of electrons and holes in three-dimensions leads to the increase of effective band gap with decrease of crystallite size. Conventional metalbased QDs are composed of the periodic groups of IV, II-VI, IV-VI or III-V, such as Si, CdS, CdSe, CdTe, ZnSe, ZnS, ZnSe and PbS, etc. [21] As a substitute of organic dyes, QDs exhibit super bright and colorful emission with high quantum yield and resistance to photobleaching. Considering the quantum confinement effect, the PL wavelength of QDs could be tuned by changing their size. The optical spectrum of QDs show broad absorbance, narrow emission and larger Stokes shift, which facilitates the analysis of multiple targeted molecules [26,27]. Core-shell type composite QDs alleviate the problems of electron-hole pair recombination and leaching, which improved the stability and quantum yield [21]. For example, coating QDs with higher band-gap inorganic materials passivates surface nonradiative recombination sites, resulting in improvement of the PL quantum yields [25]. Notably, the cytotoxicity of QDs induced by the metal ions that leach out has always been under debate since their discovery. It is reported that both the synthetic protocols, surface ligands, excitation light source, as well as the concentration, size, and charge of QDs have impact on the level of toxicity [28]. After decades of development, present preparation method of QDs improves the adaptability of QDs for versatile bioconjugation that further expand the application in analytical sensing [21].

2.2. Carbon-based quantum dots

2.2.1. Carbon dots (CDs)

CDs are considered to be discrete, quasi-spherical particles with sizes below 10 nm, which generally

Table 1. List of various fluorescent sensors for the detection of food contaminants.

Probe	Target analyte	Linear range	LOD	Sensing time	Real sample	Ref.
CdSe/ZnS QDs	aflatoxin B1	0.005–0.15 ng/mL	0.003 ng/mL	15 min	dark soy sauce	[<mark>61</mark>]
CdSe/ZnS QDs	aflatoxin B1	0.001-10 ng/mL	0.005 ng/mL	10 min	rice, peanut	[60]
CdSe QDs	zearalenone	0.78–25 ng/mL	0.58 ng/mL	8 min	corn	[65]
CdTe QDs	zearalenone	0.0024-1.25 ng/mL	0.0041 ng/mL	15 min	corn	[<mark>66</mark>]
GQDs	ochratoxin A	0–1 ng/mL	0.013 ng/mL	120 min	red wine	[69]
CdTe QDs	ochratoxin A	1.0–1000 ng/mL	1.0 ng/mL	40 min	red wine	[70]
Ag NCs	ochratoxin A	0.01-0.3 ng/mL	0.002 ng/mL	15 min	wheat	[71]
CdSe/ZnS QDs	S. typhi	$1.88 imes 10^4 {-} 1.88 imes 10^7$	3.75×10^3	35 min	tap water, milk,	[72]
		CFU/mL	CFU/mL		fetal bovine serum,	
					whole blood	
CdSe/ZnS QDs	S. typhi	$6.6 \times 10^2 - 6.6 \times 10^4$ CFU/mL	3.3×10^2 CFU/mL	_	_	[75]
Ag NCs	E. coli	$1 \times 10^2 - 1 \times 10^7$	60 CFU/mL	60 min	tap water, milk	[76]
CD-	E1:	CFU/mL	FF2 CELU	70		[77]
CDs	E. COII	7.63 × 10 –3.90 × 10 CFU/mL	552 CFU/mL	70 min	orange juice	[//]
Au NCs	S. aureus	$32 - 10^8$ CFU/mL	16 CFU/mL	210 min	milk, human serum	[80]
Au NCs	S. aureus	$20-10^{8}$ CFU/mL	10 CFU/mL	30 min	milk, orange juice	[81]
CDs	S. aureus	1–200 CFU/mL	1 CFU/mL	60 min	milk	[82]
Si QDs	carbaryl	0.00749–749 ng/mL	0.00725 ng/mL	25min	apple, tomato, cucumber	[90]
	diazinon	0.0749–749 ng/mL	0.0325 ng/mL			
	parathion	0.0749–749 ng/mL	0.0676 ng/mL			
	phorate	0.749–749 ng/mL	0.19 ng/mL			
CDs	dichlorvos	10–2000 ng/mL	3.2 ng/mL	56 min	tap water, lettuce,	[91]
	methyl-parathion	20–20000 ng/mL	13 ng/mL		cabbage, pear, rice	
CDs	chlorpyrifos	10–1000 ng/mL	3 ng/mL	30 min	cabbage	[92]
Au NCs	parathion-methyl	0.33–6.67 ng/mL	0.14 ng/mL	35 min	lake water, apple, and cucumber	[93]
Cu NCs	paraoxon	0.1–1000 ng/mL	0.0333 ng/mL	_	tap water	[94]
CdTe QDs	parathion-methyl	0.04–400 ng/mL	0.018 ng/mL	94 min	tap water, milk, rice	[95]
CDs	tetracycline	0–7875 nM	11.7 nM	_	tap water, lake water	[98]
Au NCs	tetracycline	$10-6 \times 10^4 \text{ nM}$	4 nM	10 min	human serum, lake water	[104]
GQDs	tetracycline	22.5–225 nM	21 nM	40 min	fish, chicken muscle,	[105]
A11 NCs	tetracycline	$1125-1125 \times 10^5 \text{ nM}$	11 9 nM	_	pure water tap water	[106]
Cu NCs	tetracycline	$3.6 \times 10^3 - 1.0 \times 10^6 \text{ nM}$	920 nM	10 min	milk	[107]
Cu NCs	tetracycline	$0.1-1.1 \times 10^5 \text{ nM}$	47 nM	1 min	lake water	[107]
CdS Sea ODs	chloramphenicol	97–1547 4 nM	28 nM	2 min	milk	[111]
CdTe ODs	chloramphenicol	1238 - 15474 nM	15.5 nM	15 min	human and boyine	[110]
cure QD0	emorumphemeor	120.0 1017.1 1101	10.0 1101	10 1111	serum, milk	[110]
CDs	penicillin	1–32 nM	0.34 nM	5 min	milk	[112]
CDs	D-penicillamine	250–1500 nM	85 nM	15 min	tap water	[113]
Au NCs	D-penicillamine	$1\times10^31.05\times10^4~nM$	80 nM	_	lake water	[114]
CDs	norfloxacin	$50-5 imes10^4~nM$	17 nM	_	tablet, milk	[115]
	ciprofloxacin	$200{-}2.5\times10^4~nM$	35 nM			
	ofloxacin	$4001.0 \times 10^4 \text{ nM}$	67 nM			
	nalidixic acid	20-100 nM	2 nM	15 min	tablet, human urine	
Ag NCs	cinoxacin	5–120 nM	1.2 nM			[116]
-	ciprofloxacin	5–100 nM	1 nM			
	moxifloxacin	1-60 nM	0.096 nM			
CDs	Hg ²⁺	$0-8 \times 10^4 \text{ nM}$	201 nM	_	lake water, urine of cattle	[139]
CDs	Hg^{2+}	$04\times10^4~nM$	9 nM	30 min	human serum, river water	[140]
A11 NCs	$H\sigma^{2+}$	1–20 nM	0.5 nM	_		[141]
Ag NCs	$H_{\sigma^{2+}}$	0.1 - 10 nM	0.024 nM	50 min	tan water sea water	[147]
CdS/ZnS ODs	$H_{\sigma^{2+}}$	0-1/1-10 nM	0.18 nM	51 min	tan water, lake water	[143]
CDs	Ph^{2+}	$16.7-1 \times 10^3 \text{ nM}$	4.6 nM	10 min	water, urine	[145]
CDs	Pb ²⁺	$1 \times 10^2 - 6 \times 10^3 \text{ nM}$	15 nM	_	ultrapure water	[146]
GQDs	Pb^{2+}	0.01–1 nM	0.009 nM	_	rat brain microdialysate	[147]

(continued on next page)

	,							
Probe	Target analyte	Linear range	LOD	Sensing time	Real sample	Ref.		
GQDs	Pb^{2+}	9.9–435 nM	0.6 nM	3 min	_	[148]		
Ag NCs	Pb^{2+}	5–50 nM	3 nM	_	tap water, lake water	[144]		
CDs	Cr ⁶⁺	$10{-}5 imes10^4~nM$	_	1 min	_	[149]		
CDs	Cr^{6+}	$1 imes 10^3 extsf{-}4 imes 10^5 \ extsf{n}M$	240 nM	2 min	tap water, river water	[150]		
CDs	Cr ⁶⁺	$2 \times 10^3 1 \times 10^5 \text{ nM}$	210 nM	3 min	tap water, river water	[151]		

Table 1. (continued)

has a sp^2 conjugated core and contain suitable oxygen content in the forms of various oxygen-containing species represented by hydroxyl, aldehyde, and carboxyl groups [22]. The CDs are prepared from carbon precursors through chemical ablation, hydrothermal treatment, electrochemical carbonization, laser ablation, and microwave irradiation [29]. Both the carbon materials, biomass and molecules, such as chicken egg, coffee, orange juice, Chinese ink, carbohydrate and citric acid, can be used as carbon source of CDs. Compared with classical metal-based QDs, CDs exhibit unique advantages of colorful emitting, excellent biocompatibility, convenient synthesis and low cost. Until now, CDs have been widely employed for bioimaging, sensing, optoelectronics, catalysis, nanomedicine and energy conversion. Therefore, PL is the most fascinating features of CDs in application-oriented perspectives.

The PL mechanisms and properties of CDs synthesized by different methods are varied in the reported literature. The emissive wavelength of CDs is related to the size, microstructure of the sp^2 carbon core and surface state. Normally, the emissions of CDs prepared from graphitized materials attributed to the quantum-sized graphite structure, which is red-shifted with the increase of size [30]. Contrast with CDs with graphitized core, the emission of CDs with an amorphous core is red-shifted with the decrease of size [31]. For smaller CDs with abundant bared oxygen-related surface states, the red-shifted of emission attributed to variation in surface states emerged as the sizes decreased [32]. It is know that one distinctive PL feature of the CDs was the emission wavelength and intensity dependence on excitation wavelength [33]. The green emitting CDs prepared through oxidation of graphite oxide with nitric acid showed an excitation wavelength independent emission profile. After reduction by NaBH₄, the blue emissive CDs with higher quantum yield were produced. The emission spectra of reduced CDs was remained by excitation from 260 to 360 nm, while the maximum emission wavelength of CDs was shifted to lower energies at longer excitation wavelength. It is suggested that the intrinsic emission from graphitic core networks may responsible for the emission be at short wavelengths, but other deactivation pathwavs dependent on the synthetic methods and the posttreatment of CDs dominate the PL at longer wavelengths [34]. The PL properties of CDs prepared by thermal condensation using molecules as carbon source is dependent on the formation of carbonaceous cores and the organic fluorophores. Pyrolysis of precursors at low temperature generated molecular fluorophore with excellently high quantum yield, which exhibited single, excitation-independent emitting. At higher temperature, spherical particles with lower quantum yield were observed. And the emission position was red-shifted by excitation with longer wavelengths (above 400 nm), a generic feature of CDs [35]. As a result, wide variations exist in the PL mechanisms of CDs produced from different synthetic methods.

2.2.2. Graphene quantum dots (GQDs)

GQDs are defined as single-, double- and few-(<10) layers of graphene sheets with lateral dimensions less than 100 nm [36]. Unlike the CDs, which are crystalline or amorphous, GQDs clearly possess graphene lattices in the dots. The GQDs can be synthesized through top-down and bottom-up routes. For top-down approach, GQDs are synthesized by cutting of graphene sheets, which include chemical ablation, electrochemical oxidation, oxygen plasma treatment and microwave-assisted hydrothermal synthesis. Bottom-up approach refer to synthesis of graphene moieties contained precise number of conjugated carbon atoms, which involving the solution chemistry, carbonizing some special organic precursor, cyclodehydrogenation of polyphenylene precursors, and the fragmentation of suitable precursors [37,38]. Owing to the excellent quantum confinement and edge effects, GQDs possess numerous attractive physical and chemical properties. The chemical inertia, excellent solubility, stable PL, better surface grafting, and low cytotoxicity of GQDs enable them employing for bioimaging, sensors, and optoelectronic devices, etc. [23].

PL of GQDs is due to combination or competition effect of intrinsic state emission and defect state emission. Therefore, the distinct PL properties of GQDs, such as the dependence on size, excitation wavelength, and pH, etc, are varied with synthetic method [23]. Similar to CDs, GQDs show sizedependent PL due to quantum confinement effect. As the graphene fragments increased, the band gap of π - π * transition is decreased resulting in the redshifted of PL emissions [39,40]. The excitation dependence of the emission intensity and wavelength is also discovered in fluorescent GODs, resulting from selection of different sized and emissive sites of GQDs [41]. Inversely, GQDs with uniform size and emissive sites exhibited excitationindependent behavior [42]. The edge types (armchair and zigzag edges) of GCDs also play an significant role in optical properties. The carbynelike armchair edges are commonly shown a singlet ground state, while carbene-like zigzag edges are commonly shown a triplet ground state [43]. And the graphene nanoribbons with higher proportion of zigzag edges possess a smaller energy gap than predominantly armchair-edge ribbons with similar width [23]. The oxygen-containing functional groups have various energy levels between π - π * states of C=C, which may lead to a series of surface state emissive traps. The higher the surface oxidation degree, the more surface defects, which results in the red-shifted of emission [44]. The pH has effects in the PL intensities of GQDs rather than the PL wavelength. GQDs with emissive zigzag sites exhibited strong PL upon alkaline condition, whereas the PL was nearly completely quenched upon acidic conditions. The formation of reversible complex between H⁺ and zigzag sites induces the damage and inactivation of emissive triple carbene state [45], For GQDs without zigzag edges, the pHdependent PL behaviors of GQDs are related to the surface emissive traps of GQDs, which could transform by surface passivated [46]. Similarly, the solvent-dependent PL peak shifted of GQDs contained oxygen-containing functional groups might also be attributed to defect states, whereas m-GQDs and r-GQDs show negligible solvent-dependent behaviors [23,41].

2.3. Metal nanoclusters (NCs)

Metal NCs, also known as ultra-small metal nanoparticles (NPs), occupy the gap between discrete atoms and plasmonic nanomaterials [20]. The plasmonic metal NPs with size larger than 2 nm show semi-continuous electronic structures, while the metal NCs with size smaller than 2 nm exhibit discrete electronic states attributed to the strong quantum confinement effects. Therefore, the metal NCs possess unique physical-chemical properties and some molecular-like properties, such as PL, catalysis, HOMO-LUMO transition, redox behavior, chirality, electrochemistry, and magnetism [24,47,48]. The metal NCs are usually prepared by chemical reduction of metal ions precursors in the presence of ligand molecules. The reductive metal cores of NCs are protected and stabilized by surface ligands of biological templates such as proteins, polypeptide, and DNA or molecular ligands such as alkyl mercaptan and aromatic mercaptan. The atomically precise nature and recent progress in their structural determination enables elucidation of the correlation between the structure and the properties. PL is one of the most attractive properties of metal NCs, which enables it used as promising probe for sensing applications.

The PL of dendrimer and protein protected metal NCs is attributed to the metal core and shows size-dependent PL property. Jellium energy scaling law ($\lambda = E_{\text{Fermi}}/N^{1/3}$, E_{Fermi} is the Fermi energy of bulk metal and N is the number of metal atoms) can accurately illustrate the size dependence of the emission wavelength of metal NCs, which due to the electronic structure of NCs with few metal atoms is closely defined by the cluster size and number of free electrons [24,49–51]. However, the above mechanism is not appropriate for all metal NCs. For metal NCs protected with thiolate ligands, the metal core is not only factor responsible for PL properties of NCs. The PL of thiolated metal NCs exhibited large Stokes shift, emission red-shift under low temperature, and long lifetime, which is attributed to metal-centered ligand-to-metal charge transfer or ligand-to-metal-metal charge transfer process. Therefore, except the metal core, valence state of the metal atoms, metal-ligand shell, and the nature of thiolate ligands also affect the PL properties of metal NCs [20,52]. It is reported that the PL of thiolated metal NCs can be enhanced by many approaches, such as increased electro-positivity of metal core, doped other atoms in metal core, ensured the percentage of metal monovalent oxidation state, used ligands with long ligand chain and electron-rich atoms or functional groups, and ensured the ligand density [53-56]. In addition, the aggregation of metal NCs can effectively enhanced its PL intensity. The compact structure of aggregated NCs induces stronger coprophilic interaction of intra- and inter-NCs and inhibits intramolecular rotation and vibration of capping ligands, resulting in higher emitting and quantum yield [24,57] (see Fig. 1).

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3. Fluorescent sensors

The fluorescent nanomaterials are used as signal probes for fluorescent sensors. Some target analytes, such as metal ions and biothiols, can combine with the core or surface ligand of nanoprobe by bonding or other molecular interactions and further induced the change of fluorescent signal. So, the nanoprobes can directly utilize for capturing and detecting of analytes. For other analytes, the identified units were introduced into the sensing system to capture and recognize the target molecules. The conventional recognition units included antibody, DNA aptamer, molecularly imprinted polymer, enzyme and molecules with specific functional groups, which was the connector between the signal probe and the analyte.

In the presence of analytes, the PL intensity of fluorescent probe increased or decreased that denoted as "turn-on" or "turn-off" sensor, respectively. Another conventional sensing type is"on-offon" sensor. By mixing the nanoprobe and fluorescent quencher (such as Au NPs, graphene oxide and MoS₂ nanosheets), the PL of nanoprobe was quenched and then recovered in the presence of analytes. A very important question is how the analyte affects the fluorescence of the probe. It is found that the sensing mechanism mainly include: fluorescence resonance energy transfer, electronic energy transfer, photo induced electron transfer, intramolecular charge transfer, twisted intramolecular charge transfer, metal-ligand charge transfer [58]. Moreover, the detected types of fluorescence technique can be divided into single wavelength detection and dual wavelength detection. Dual wavelength detection, known as ratiointegrates metric fluorescence method, the reference and response signals, which can eliminate the false signals generated from matrix effects and further improve the sensitivity and accuracy of sensor (see Fig. 2).



Fig. 1. (A) Photograph of CdTe QDs with different size under UV light (350 nm) and the corresponding PL spectra [21]. Copyright 2017 Elsevier. (B) Absorbance and PL spectra with increasingly longer excitation wavelengths (in 20 nm increments starting from 400 nm) of CDs [33]. Copyright 2006 American Chemical Society. (C) Schematic illustration of the PL mechanism of Class I and Class II CDs [31]. Copyright 2013 The Royal Society of Chemistry. (D) Schematic diagram of the top-down and bottom-up methods for synthesizing GQDs [37]. Copyright 2013 The Royal Society of Chemistry. (E) Energy gap of π - π * transitions calculated based on DFT as a function of the graphene molecules (top). Models of the GQDs in acidic and alkali media, the pairing of σ (\bullet) and π (\bigcirc) localized electrons at carbene-like zigzag sites and the presence of triple bonds at the carbyne-like armchair sites are represented (middle). Typical electronic transitions of triple carbenes at zigzag sites of GQDs (bottom) [40]. Copyright 2010 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim. (F) Schematic illustrations of the strategies for controlling the PL properties of nanoclusters, including: (a) engineering the peripheral ligand, (b) controlling the metallic kernel, (c) AIE, and (d) self-assembly of nanocluster building blocks into cluster-based networks [20]. Copyright 2019 The Royal Society of Chemistry.



Fig. 2. Schematic illustration of established fluorescent sensor based on nanomaterials.

4. Fluorescent sensors for detection of food contaminants

4.1. Mycotoxin detection

Mycotoxins are the toxic metabolites of mold, which is widespread occurrence in cereals, wheat, barley, oat, corn, soybeans, coffee beans, beer and grape juice, etc. It is evident that the products contaminated with mycotoxins might have various toxic effects on humans, such as carcinogenicity, hepatotoxicity, nephrotoxicity, immunotoxicity, neurotoxicity, teratogenesis, and abortion. Therefore, methods for sensitive and rapid detection of mycotoxins are very important particularly in the aspect of food safety. Based on the signalization of



Fig. 3. (A) Schematic illustration of the MFBs formation and the principle of the MFB-based ICA. Reprinted with permission from Ref. [61]. Copyright 2019 American Chemical Society. (B) Schematic of catalase-mediated fluorescent ELISA for sensitive detection of ZEN. Reprinted with permission from Refs. [66]. Copyright 2016 Elsevier. (C) Schematic illustration on the fluorescent signal-on sensing platform for OTA detection based on GQDs. Reprinted with permission from Refs. [69]. Copyright 2016 American Chemical Society.

fluorescent nanomaterials and recognition effect of antibody and DNA aptamer, fluorescent sensors for selective, sensitive and rapid detection of mycotoxins has been established.

4.1.1. Aflatoxins (AFs)

AFs are secondary metabolites of Aspergillus flavus and Aspergillus parasiticus [59]. Among the identified AFs, aflatoxin B1 (AFB1) is the highest toxic and has been classified as Group I carcinogen by the International Agency for Research on Cancer (IARC). The allowable concentration of Food and Drug Administration (FDA) and European Commission (EC) are 20 mg/kg and 2.0 mg/ kg, respectively [60]. Based on the signalization of QDs and recognition effect of anti-AFB1 monoclonal antibodies (mAbs), Guo et al. established immunochromatographic assay (ICA) for sensing of AFB1 (Fig. 3A). Firstly, the core-shell bifunctional magnetic fluorescent beads (MFBs) were synthesized by encapsulating oleic acid-coated iron oxide nanoparticles and octadecylaminemodified CdSe/ZnS QDs into polymer nanobeads through ultrasonic emulsification method. Then anti-AFB1 mAbs combined with carboxyl group functionalized MFBs via the EDC conjugation method. As a result, the MFBs successfully recognized and enriched the AFB1 of dark soy sauce and also used as a fluorescent indicator of ICA for monitoring of AFB1. Upon the optimal test conditions, the MFBs-based ICA shown a linear response to AFB1 of sauce extract in the range from 0.005 to 0.15 pg/mL with the LOD of 3 pg/mL. The selective and accurate performances of the reported ICA strategy were investigated in AFB1 spiked dark soy sauce samples and confirmed by HPLC with fluorescence detection [61]. Similarly, Li et al. also fabricated lateral flow immunoassay strips for determination of AFB1. The CdSe/ZnS ODs were functionalized by amphiphilic N-alkylated branched polv(ethyleneimine) to obtain amino-modified QDs, which attached to anti-AFB1 antibodies through thiol-maleimide conjugation. The strip displayed a linear response to AFB1 in range from 0.001 to 10 ng/mL with a LOD of 5 pg/mL. The quantitative results of test strip were verified by recovery and reproducibility assay, which could be employed for rapidly detecting AFB1 of cereal samples [60].

4.1.2. Zearalenone (ZEN)

ZEN, a nonsteroidal estrogenic mycotoxin, is biosynthesized via a polyketide pathway by several *Fusarium fungi*, which has been classified as group III carcinogen by IARC [62-64]. Using CdSe ODs and anti-ZEN mAbs as sensing and identification probes, Chen et al. developed a fluorescent lateral flow assay for determination of ZEN. The gold nanoflowers combined with anti-ZEN mAbs (mAbs-Au NFs) were used as PL quencher of QDs and loaded on conjugation pad. The BSA-QDs and ZEN-BSA-QDs were coated on nitrocellulose membrane to form C-line and T-line, respectively. When low concentration ZEN samples are applied, the mAbs-Au NFs could combine with the ZEN-BSA-QDs leading to PL quenching of T-line. While high concentration ZEN samples are applied, ZEN competitively bound with mAbs-Au NFs resulting in PL recovery of T-line. The fluorescent lateral flow assay for ZEN shown a linear sensing range from 0.78 to 25 ng/mL with a LOD of 0.58 ng/mL, which is utilized to detect the ZEN in corn samples [65]. It is found that the PL of mercaptopropionic acid capped CdTe QDs was sensitive to H₂O₂. On the basis of catalysis of catalase, Zhan and coworkers designed a competitive fluorescent ELISA for ZEN detection (Fig. 3B). When ZEN was absent, the ZEN labeled catalase (ZEN-CAT) was captured by the anti-ZEN mAbs on the microplates. The PL of QDs was remained because of the H₂O₂ was expended by CAT. Inversely, ZEN could competitively bind with anti-ZEN mAbs and the mount of ZEN-CAT immobilized on the microplate was decreased, resulting the PL quenching of QDs by excessive H₂O₂. Under optimal test conditions, the fluorescent ELISA displayed a dynamic linear response to ZEN in the range of 2.4 pg/mL - 1.25 ng/mL and a LOD of 4.1 pg/mL. Moreover, the developed method accurately detected of ZEN in real corn samples, and closely agreement with LC-MS [66].

4.1.3. Ochratoxins

Ochratoxins is a typical mycotoxin produced by Aspergillus ochraceus, Aspergillus carbonarius and Penicillium viridicatum [67,68]. Among the identified species, ochratoxin A (OTA) is the highest toxic and widely spread pollution in agricultural products. The toxicities of OTA on human beings include nephrotoxicity, hepatotoxicity, teratogenicity, carcinogenesis, mutagenicity and immunosuppression effect. Similar to antibody, the DNA aptamer is also excellent recognition probe for analytes. As shown on Fig. 3C, Wang et al. designed a "turn-on" fluorescent sensor employed for OTA sensing based on GQDs and OTA aptamer. The amino-modified aptamer and cDNA (complementary with partial OTA aptamer) were combined with carboxyl groups of GQDs to form GQDs-aptamer and GQDs-cDNA conjugates, respectively. Mixing the two types

GODs-DNA complex, the hybridization between aptamer and cDNA induced aggregation of GQD, accompany with the PL quenching of GQD via exciton energy transfer. In the presence of OTA, the duplex structure of aptamer-cDNA switched to aptamer-OTA complex, leading to disaggregation of GODs accompanied PL recovery. This fluorescent detection platform for OTA shown a linear range from 0 to 1 ng/mL and the LOD of 13 pg/mL, which also successfully detected OTA of red wine sample [69]. Considering the conformational change of OTA aptamer, Lu et al. also proposed a fluorescence analyzing strategy for OTA. The aptamer modified CdTe QDs was initially assembled on the MoS₂ nanosheets, which caused the PL quenching of QDs via fluorescence resonance energy transfer. After addition of OTA, the structure of aptamer varied from linear to folded conformation that has low affinity effect to MoS₂ nanosheets, resulting in release of QDs from MoS₂ nanosheets and restoration of PL intensity. The designed platform shown a dynamic range over 1.0–1000 ng/mL and a LOD of 1.0 ng/mL in laboratory buffers. And the feasibility of platform in real sample analysis was verified in spiked red wine sample [70]. As mentioned before, DNA could be utilized as template for synthesis of fluorescent metal NCs. Based on the PL of DNA-templated Ag NCs, Chen et al. designed a more sensitive "turnon" fluorescent sensor for OTA monitoring. Firstly, the biotin group functionalized OTA aptamer was bind with streptavidin modified magnetic beads (MBs). Then a cytosine rich cDNA (complementary with partial OTA aptamer) was attached to MBs through hybridization with OTA aptamer forming a duplex conformation. Upon addition of OTA, aptamer recognized and captured OTA forming Gquadruplex structure while released the single strand cDNA. After magnetic separation, the liberated cDNA was left and used as template to synthesize Ag NCs in the presence of Ag^+ and $NaBH_4$. Therefore, PL intensity of Ag NCs was enhanced as the OTA concentration increased, which exhibited a linear dynamic range from 0.01 to 0.3 ng/mL with a LOD of 2 pg/mL. The practicability of designed fluorescent biosensor was demonstrated by detect-

4.2. Foodborne pathogenic bacteria detection

ing OTA of wheat sample [71].

Infectious diseases induced by foodborne pathogenic bacteria continue to pose a significant threat to public health [72]. The foodborne bacteria mainly include salmonella, escherichia coli (Escherichia coli), staphylococcus aureus (Staphylococcus aureus), vibrio cholerae, etc. [73] Pathogenic bacteria can contaminate food directly or indirectly, and then cause intestinal infectious diseases, food poisoning through oral infection [74]. Thus, it is of significant importance to quickly and sensitively detect pathogenic bacteria.

4.2.1. Salmonella typhimurium (S. typhi)

S.almonellatyphi, a group of non-adaptive or pantropic Salmonella, has a wide range of hosts. It can cause various infectious diseases of poultry and mammals, and also human infection, which has important significance for public health. Based on antibody labeled colorimetric-fluorescent-magnetic nanospheres (CFMNs), Hu et al. reported a multisignal readout sensor for determination of S. typhi (Fig. 4A). The CFMNs were prepared by coating Fe₃O₄ and CdSe/ZnS QDs on polymer nanospheres through layer-by-layer assembly method and then carboxylation by succinic anhydride, which was further used for coupling with antibody. Therefore, as-prepared CFMNs possessed multifunction of target recognized and enrichment, multi-signal readout, and double quantitated formats. The S. tuphi were firstly separated and enriched by CFMNs from matrix, and then the suspension contained S. *typhi* was added into the sample pad of test strip for detection. For fluorescence signal reader, the assay shown a quantitation range from 1.88×10^4 to 1.88×10^7 CFU/mL and the LOD of 3.75 \times 10^3 CFU/ mL. The naked eye detection assay for S. typhi was as low as of 1.88×10^4 CFU/mL. Moreover, the practical application of sensing platform was indicated by successfully detecting S. typhi in real samples including milk, tap water, whole blood and fetal bovine serum [72]. Employing fluorescent amino groups-modified CdSe/ZnS@SiO2 nanoparticles as probe, Wang et al. directly detected the bacteria. The CdSe/ZnS QDs were embedded into SiO₂ nanospheres through self-modified reversemicroemulsion method. And then amino groups were introduced on CdSe/ZnS@SiO₂ nanoparticles for covalently combining with the bacteria. Take S. typhi as representative sample, the PL intensity of probe shown a good linear response to S. typhi concentration in the range from 6.6×10^2 to 6.6×10^4 CFU/mL with a LOD of 3.3×10^2 CFU/mL [75].

4.2.2. E. coli

E. coli, as the representative of *Escherichia*, is a resident bacterium in human and animal intestines and generally not pathogenic. However, it can cause extraintestinal infection in some case, and some serotypes have high pathogenicity. By detecting the lysate of *E. coli*, Zheng and coworkers reported a



Fig. 4. (A) Schematic diagram for multi-signal readout detection of S. typhi by CFMNs-based lateral flow immunoassay. Reprinted with permission from Ref. [72]. Copyright 2018 American Chemical Society. (B) Schematic representation of DNA-templated fluorescent Ag NCs based sensing system for pathogenic bacterial detection integrated with MNP-DNAzyme-AChE complex. Reprinted with permission from Ref. [76]. Copyright 2018 Elsevier. (C) Schematic illustrations of preparation of AuNCs@Van and determination of S. aureus in mixtures using the Apt-MB and AuNCs@Van dual recognition strategy. Reprinted with permission from Ref. [80]. Copyright 2015 American Chemical Society. (D) Illustration of the detection of pathogen bacteria with the proposed method and conventional method. Reprinted with permission from Ref. [82]. Copyright 2018 American Chemical Society.

fluorescent sensing platform for E. coli (Fig. 4B). The magnetic nanoparticles-DNAzyme-AChE (MNP-DNAzyme-AChE) complex and DNA-templated Ag NCs were prepared firstly. Upon addition of E. coli lysate, the target molecules lysed by bacteria were MNP-DNAzyme-AChE attached to complex through reaction with DNAzyme. And then the DNAzyme substrate was cleaved into two sections, releasing AChE from MNP-DNAzyme-AChE complex. After the magnetic separation, the liberated AChE was moved into the Ag NCs contained solution and catalyzed the hydrolyzation of acetylthiocholine thiocholine, to generate which significantly enhanced the PL of Ag NCs. The sensing platform shown a linear response to logarithm of E. coli concentrations in range of $1 \times 10^2 - 1 \times 10^7$ CFU/mL with a LOD of 60 CFU/mL. In addition, the platform could be applied to detect other target bacteria by simply changing the corresponding DNAzyme as recognition unit [76]. On the basis of the antibacterial activity of antibiotics, Chandra et al. synthesized amikacin modified CDs

as fluorescent probe for *E. coli* detection. The probe captured *E. coli* through the interaction between amikacin and *E. coli*. The CDs-based fluorescent sensor is utilized to detect *E. coli*, which exhibited a linear response range from 7.625×10^2 to 3.904×10^5 CFU/mL with a LOD of 552 CFU/mL. Then the sensor was also successfully employed for sensing of *E. coli* in different fruit juice samples like orange, pineapple, and apple [77].

4.2.3. S. aureus

S. aureus is the most common pathogen of human suppurative infection, which can induce local suppurative infection, pericarditis, pseudomembranous enteritis, pneumonia, and even septicemia or other systemic infections [78,79]. The vancomycin could adhere to the surface of *S. aureus* by binding with N-acetylglucosamine peptide subunits and terminal residues D-alanyl-D-alanine of N-acetylmuramic acid on the cell wall of the gram-positive bacteria. Song and coworkers prepared vancomycin-stabilized fluorescent Au NCs through a one-step

approach and utilized it for S. aureus detection (Fig. 4C). Combined the aptamer-modified magnetic beads, the fluorescent sensor with double recognition units could selectively and sensitively detect S. *aureus* with a linear range of $32-10^8$ CFU/mL and the LOD of 16 CFU/mL [80]. Replaced aptamer-coated magnetic beads with aptamer-coated Au NPs, a sensing platform for S. aureus built on fluorescence resonance energy transfer was established. The vancomycin-functionalized Au NCs and aptamerlabeled Au NCs were employed for energy donor and acceptor. The sensing platform shown a linear response to S. aureus concentration in range of 20-10⁸ CFU/mL and a LOD of 10 CFU/mL [81]. In order to improve the detection sensitivity for S. aureus, Yang et al. utilized CDs-encapsulated breakable organosilica nanocapsules (CDs@BONs) as fluorescent probe (Fig. 4D). The hundreds of CDs could be successfully encapsulated into one nanocapsule, which was realized through cohydrolyzation of tetraethyl orthosilicate and bis[3-(triethoxysilyl) propyl] disulfide. Immunofluorescent nanocapsules were prepared by binding the anti-S. aureus antibody with CDs@BONs and applied to recognize and capture S. aureus. Before fluorescent monitor assay, CDs were released from CDs@BONs on the basis of NaBH₄ reduction. Compared with conventional fluorescent immunoassay based on CDs, the fluorescent signal of CDs@BONs were amplified about 2 orders magnitude. And the CDs@BONs shown a linear response to S. aureus concentration in range of 1-200 CFU/mL and a LOD of 1 CFU/mL [82].

4.3. Pesticides residues detection

Pesticides, as commercial farming chemicals employed for pest control, have been widely used to prevent crop loss in the past few decades. However, the excessive use of pesticides induces the pesticides residues in foods and the environment, which leads to severe public health concerns attributed to their high toxicity for humans [83–87]. The OPs pesticide is the most widely used pesticides in modern agriculture, more studies focus on the detection of OPs in food samples have been reported by researchers [88,89].

The toxicity of OPs pesticide to human body is mainly due to the inhibition of OPs on the catalytic activities of some enzyme. For example, some fluorescent sensors established on the basis of the significant inhibition of OPs on acetylcholinesterase (AChE). Acetylcholine chloride was hydrolyzed by AChE to generate choline which was then catalytically oxidized by choline oxidase to produce H_2O_2 . Using Si QDs sensitive to H_2O_2 as fluorescent prob, Yi et al. reported a sensing method for pesticides. In the presence of pesticides, the catalytic activity of AChE was inhibited leading to decrease of produced H₂O₂, while the PL intensity Si QDs was enhanced. Eventually, four kinds of pesticides (including phorate, diazinon, parathion, and carbaryl) were detected by the proposed sensing strategy with the LOD of 1.9×10^{-7} , 6.76×10^{-8} , 3.25×10^{-8} and 7.25×10^{-9} g/L, respectively. The practicability of sensing method was verified by monitoring pesticide residues in apple, cucumber, and tomato samples, which was consisted with the detection results of HPLC [90]. The o-phenylenediamine generate fluorophore 2,3-diaminophenazine (DAP) in the presence of H₂O₂ and horseradish peroxidase. Huang and coworkers found that DAP effectively quenched the PL of nitrogen-doped CDs via inner filter effect. As shown on Fig. 5A, a ratiometric fluorescent sensor was fabricated for determination of OPs based on fluorescent CDs and DAP. The OPs inhibited AChE activity and eventually resulting in reduction of DAP, which induced the PL enhanced of CDs at 450 nm and the PL decreased of DAP at 574 nm. Under optimal conditions, the ratiometric fluorescent probe exhibited a LOD of 3.2 pg/mL for dichlorvos, and 13 pg/mL for methyl-parathion, respectively. Moreover, the sensing platform was employed for detection OPs of tap water, cabbage, pear, and rice samples and obtained detection results are well agree with those by GC-MS [91]. In addition, Fe^{3+} was generated through redox reaction between Fe^{2+} and H_2O_2 . The CDs sensitive to Fe^{3+} were synthesized by Lin et al. using waste paper ash as precursor and utilized it as sensing probe for OPs. The OPs could impede the production of H₂O₂ via effectively inhibiting catalytic activity of AChE, inducing the decrease of Fe^{3+} . Aa a result, the PL intensity of CDs was enhanced with the increased of OPs concentration. Take chlorpyrifos for example, the sensing system shown a linear response range from 0.01 to 1.0 μ g/mL with the LOD of 3 ng/mL [92]. Acetylthiocholine iodide was catalyzed hydrolysis by AChE to produce thiocholine. Then thiocholine could attach to BSA protected Au NCs via Au-S bonds, which leading to the PL weaken of Au NCs. Inversely, OPs could prevent the generation of thiocholine through inhibiting the AChE activity, and then the PL of Au NCs was recovered. Upon optimized test conditions, parathion-methyl was detected with a linear response range from 0.33 ng/mL to 6.67 ng/mL and a LOD of 0.14 ng/mL. Moreover, practical applications of were demonstrated by quantitatively detecting OPs of lake water, apple, and cucumber samples [93].





Fig. 5. (A) Schematic illustration of OPs determinations using CDs-based ratiometric fluorescent probes. Reprinted with permission from Ref. [91]. Copyright 2019 American Chemical Society. (B) Illustration of the fluorescent detection of OPs through the inner-filter effect of Au NPs on RF-QDs. Reprinted with permission from Ref. [95]. Copyright 2015 Elsevier. (C) Schematic illustrating the principle of "On-off-on" mode for nano-ZnTPyP combined with double QDs and OPs and the principle of visual paper chip combined with chemometrics for OPs assay. Reprinted with permission from Ref. [96]. Copyright 2019 Elsevier. (D) Simple schematic illustration of the wearable target OPs monitoring device (a); the swiping pictures for the wearable glove sensor on different samples (b); fluorescence emission spectra of the sensing glove on different samples contaminated target OPs (c), EtOH (d) and diisopropyl methylphosphonate (e), $\lambda_{ex} = 365$ nm. Reprinted with permission from Ref. [97]. Copyright 2018 The Royal Society of Chemistry.

Except for AChE, OPs also could inhibit the activity of other enzymes. Chen et al. used polythymine DNA templated Cu NCs as probe for detection of OPs. Initially, the bright emitting of Cu NCs was remarkably quenched by tyrosinase. After addition of OPs, catalytic activity of tyrosinase was restrained and then the PL of Cu NCs was recovered. Owing to the good performance of fluorescent probe, functionalized hydrogel built on Cu NCs was prepared for visible determination of OPs. The reported sensing approach had been employed for rapid detection of paraoxon and exhibited a linear response range of 1.0×10^{-4} -1.0 ng/µL with LOD of 3.33×10^{-5} ng/µL [94] Moreover, based on the inhibition of OPs on trypsin, Yan and coworkers developed a ratiometric fluorescent sensor for OPs sensing (Fig. 5B). The dual-emission QDs were prepared by hybridizing two kinds of CdTe QDs with different color emitting. The green emitting (540 nm) QDs were coated on the surface of silica sphere and acted as the response signal, while the red emitting (657 nm) QDs were embedded into silica sphere and used as reference signal. Initially, the PL of green emissive QDs was quenched by Au

NPs via the inner-filter effect. After addition of protamine, protamine combined with AuNPs through electrostatic attraction while released the QDs from AuNPs, leading to turn on the PL of QDs. When the protamine was hydrolyzed by trypsin, the recovered PL was quenched again. Finally, due to the restriction of OPs on catalytic activity of trypsin, the PL was recovered by adding parathion-methyl. In brief, the PL intensity of blue emissive QDs was enhanced with the increase of parathion-methyl concentration. Upon the optimized conditions, ratiometric fluorescent sensor showed a linear response range from 0.04 ng/mL to 400 ng/mL with the LOD of 0.018 ng/mL. The applicability of reported sensor was demonstrated in real samples including tap water, milk and rice [95].

Additionally, some rapid detection devices for OPs detection had also been reported. As shown on Fig. 5C, Wang et al. developed a paper-based fluorescence visualization sensor and applied to detect of three OPs including dimethoate, dichlorvos, and demeton. The sensing mechanism of paper-based sensor was an "on-off-on" detection mode. The PL emissions of CdTe ODs and ZnCdSe ODs were quenched by Zn-nano porphyrin (nano-ZnTPyP) attributed to fluorescence resonance energy transfer. However, the PL could be recovered by adding OPs due to conjugation between OPs and nano-ZnTPyP. Mixing the blue emissive ZnCdSe QDs and red emissive CdTe QDs, the sensing-paper displayed various color responses to three kinds of OPs under 365 nm UV lamp. The RGB information of sensing-paper was collected by smartphone and software, and then identified and analyzed through chemometric analysis models. Notably, this mothed was established on the basis of Partial least squares discriminant analysis for fingerprint spectrum analysis of three kinds of OPs in cabbage and apple. As a result, simultaneous detection for various concentration of OPs was achieved and shown 100% accuracy in both prediction and training test [96]. Xv et al. developed a wearable glove-based fluorescent sensor for non-invasive detection of OPs (Fig. 5D). The "lab-on-a-glove" device was consisted of two fluorophores (blue emissive CDs and red emissive Eu MOFs) and the flexible host material (carboxymethyl cellulose aerogel) and. The designed sensor was based on the ratiometric fluorescent monitor mode, in which Eu MOFs were used as the working fluorophore and CDs were acted as the reference fluorophore. With the increased of OPs concentration, the sensor displayed the red to blue emitting transition that was easily distinguished by naked eye. Owing to the porous structures of carboxymethyl cellulose aerogel and Eu MOFs, the

response time of sensor was decreased to 30 s. Employing ratiometric fluorescence probe based wearable device, the qualitative and quantitative detections of OPs were successfully carried out on the surfaces of fruits and vegetable samples using swipe collection [97].

4.4. Antibiotic residues detection

Antibiotics play a significant role in the treatment and prevention of diseases due to the inhibiting effect on growth of bacteria [98]. Antibiotics are widely used in animal husbandry production for promoting the development of breeding industry and improving the economic benefits. However, the large-scale use and even abuse of antibiotics results in antibiotic residues in environment and animal food, which has serious threat to humans [99,100]. According to chemical structures, antibiotics in animal-derived food can be divided into: tetracyclines antibiotics, β-lactams antibiotics, aminoglycoside antibiotics, macrolide antibiotics, aniline antibiotics quinolones antibiotics and sulfonamides antibiotics. Here, we summarize the detection of some versatile broad-spectrum antibiotics in foods.

4.4.1. Tetracycline (TC)

TC has been extensive utilized in medicine and animal feed additives on account of excellent effectiveness and low cost. Repeatedly intake TC causes some side effects including colony disorders, bacterial resistance, and affecting teeth health, etc. [101–103] Due to the ring-like structure of TC, the TC easily to combine with metal ions. When TC combined with Eu³⁺, TC would transfer the absorbed energy to Eu³⁺ through energy transfer, resulting in the PL enhancement of Eu³⁺. Based on this, Shen et al. designed a ratiometric fluorescent sensor for TC (Fig. 6A). The bright blue-emitting CDs were synthesized using citric acid and cyclen contained azamacrocyclic ring as precursors by the microwave method. The ring-like structure was still remained on the surface of CDs, which combined with Eu^{3+} to form CD-Eu³⁺ ratiometric probe. Then TC was captured by CD-Eu³⁺ and further formed CDs-Eu³⁺-TC ternary complex, which induced a red emitting at 616 nm of Eu^{3+} . And the blue emitting at 442 nm of CDs was remained, realizing accurate detection of TC by recording the ratio of PL intensity at 442 and 616 nm. The value of F₆₁₆/F₄₄₂ was increased as the concentration of TC increased with a linear range of $0-3.5 \ \mu g/mL$ and a LOD of 5.2 ng/mL. Besides, the color of sensing system was varied from blue to red with

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Fig. 6. (A) Schematic illustration of the ratiometric sensing mechanism for TC and schematic drawing for the detection of TC using a smartphone. Reprinted with permission from Refs. [98]. Copyright 2018 The Royal Society of Chemistry. (B) Schematic illustration of the preparation of $CdS_{x}Se_{1-x}$ QDs by Phomopsis sp. XP-8 and the sensing mechanism of CAP. Reprinted with permission from Refs. [111]. Copyright 2020 American Chemical Society. (C) Schematic illustration of the fabrication process B/Y CDs@MIPs ratiometric sensor and the sensing mechanism of penicillin. Reprinted with permission from Ref. [112]. Copyright 2020 Elsevier. (D) Schematic illustrating the sensing mechanism of CDs to FQs. Reprinted with permission from Ref. [115]. Copyright 2018 American Chemical Society.

concentration increased of TC. Smartphone-based detection approach for TC was carried out by analyzing the corresponding RGB value [98]. Replacing the fluorescent probe with L-histidine capped Au NCs, Li and coworkers designed a ratiometric fluorescent platform for TC sensing. The Au NCs-Eu³⁺ system exhibited dual-wavelength emission at 475 and 620 nm attributed to Au NCs and Eu³⁺, respectively. After addition of TC, the PL of Au NCs was quenched while the Eu³⁺ emission greatly enhanced. So, a ratiometric signal of F620/F475 could be utilized to detect of TC by simply mixing Eu³⁺ and Au NCs. Upon the optimized test conditions, the ratiometric sensor shown a linear response range from 10 nM to 60 µM and the LOD of 4 nM for TC [104]. Utilizing aptamer as recognition unit, Zhang et al. reported a fluorescent "on-off-on" sensor based on aptamer modified nitrogen-doped GQDs and quencher of cobalt oxyhydroxide (CoOOH) nanoflakes. The PL of GQDs was remarkably quenched by CoOOH nanoflakes through fluorescence resonance energy transfer. Upon addition of TC, the aptamer captured the TC

and the linear conformation of aptamer changed to hairpin structure, releasing the GQDs from CoOOH nanoflakes leaded to PL recovery. This method exhibited better behavior for TC determination: a linear response range of 1-100 ng/mL and a LOD of 0.95 ng/mL. Furthermore, practical applicability of proposed method demonstrated in five food samples including fish, chicken muscle, eggs, honey, and milk [105]. Liu et al. found that the TC could attach to GSH protected Au NCs via electrostatic interaction and then quenched the PL of Au NCs through the electron transfer. The PL quenching ratio of Au NCs shown a linear response to TC in range of 50 µg/L-50 mg/L with a LOD of 5.31 μ g/L. The test papers prepared with Au NCs could monitor the TC as low as 1 mg/L by naked eyes [106]. Similarly, TC could interact with the surface groups of dopamine protected Cu NCs and histidine stabilized Cu NCs, which facilitating energy trapping of Cu NCs by forming new bonds and inducing the PL quenching of Cu NCs [107,108].

4.4.2. Chloramphenicol (CAP)

CAP is a class of aniline antibiotics and has effect on inhibiting bacterial protein synthesis. CAP can effectively treated of some infectious diseases, but it also has adverse negative effects on humans such as anaemia, bone marrow suppression, and aplastic [109,110]. CdS_xSe_{1-x} QDs with CdS_{0.75}Se_{0.25}@oligopeptide transporter structure were synthesized by a biological method using Phomopsis sp. XP-8, which could be extracted and directly used as a probe for detection of CAP (Fig. 6B). The PL of QDs was quenched by CAP through static fluorescence quenching approach, which displayed a linear range of 3.13–500 µg/L and a LOD of 0.89 µg/L. And the probe was successfully employed for detection of CAP in milk samples [111]. Employed CdTe QDs and molecularly imprinted polymer for sensing and recognition unit, Amjadi and coworker designed a fluorescent probe for CAP sensing. The probe was prepared by embedding the CdTe QDs into molecularly imprinted silica nanospheres, which could recognize and capture of CAP. In the presence of CAP, the PL of QDs was remarkably quenched attributed to electron transfer mechanism. Upon the optimal test conditions, PL intensity of as-prepared probe sensitive to the concentration of CAP with a linear range from 40 μ g/L to 500 μ g/L and LOD of 5.0 µg/L. And the reported probe had a well selectivity and was employed for detection of CAP in spiked milk samples with satisfactory results [110].

4.4.3. Penicillin and penicillamine

Penicillin, a class of β -lactams antibiotics, is a broad-spectrum antibiotic with high efficiency, low toxicity and widely used in clinical medicine. Using blue emitting and yellow emitting CDs as probes and mesoporous structured molecularly imprinted polymer as receptor of penicillin, Jalili and coworker established a ratiometric fluorescent sensor for penicillin sensing (Fig. 6C). In the presence of penicillin, PL of yellow emissive CDs was quenched by analyte blockage, while PL intensity of the blue emissive CDs was remained. The PL intensity ratio of two kind CDs was sensitive to the concentration of penicillin with a linear response range from 1 nM to 32 nM and a LOD of 0.34 nM [112]. Penicillamine is the hydrolytic metabolite of penicillin and belongs to the group of aminothiols, which includes L- and D-enantiomeric forms. D-penicillamine is a zwitterionic compound and its form in solution depend on the pH ranges. On the basis of this, Ge et al. proposed a "on-off-on" fluorescent sensing strategy for D-penicillamine detection. Initially, PL of CDs was quenched by Au NPs due to fluorescence resonance energy transfer. When pH value was

closed to the its isoelectrical point, the D-penicillamine induced Au NPs aggregated by electrostatic interactions and hydrogen bonding, resulting in the dissociation of CDs from Au NPs. Therefore, PL of CDs was enhanced as the concentration of D-penicillamine increased, which shown a linear range of 0.25-1.5 µM with a LOD of 0.085 µM [113]. Based on the strong affinities between Cu²⁺ and D-penicillamine, Yu et al. also designed a "on-off-on" fluorescent sensor. The Au NCs were prepared using 11mercaptoundecanoic acid as both the protecting and reducing agent. Firstly, PL of Au NCs was dynamic quenched by Cu²⁺ via electron transfer. After addition of D-penicillamine, the Cu²⁺ was captured by D-penicillamine and then the PL Au NCs was recovered. The PL intensity of Au NCs shown a linear response to D-penicillamine in the range of 1.0–10.5 μ M with a LOD of 0.08 μ M. Furthermore, this fluorescent sensing strategy for D-penicillamine assay was utilized to monitor of D-penicillamine in real water samples [114].

4.4.4. Quinolones antibiotics

Ouinolones antibiotics are used to treat human and animal infectious diseases, which cannot be completely metabolized by organisms. It is widely found in wastewater of pharmaceutical industry, medical, animal husbandry and aquaculture and even surface water. So, the development of appropriate methods to remove quinolones from the water environment and the detection of trace quinolones in water are important. Lu and coworkers developed CDs based sensor for detection of fluoroquinolones (FQs) (Fig. 6D). The yellow emitting CDs were synthesized using 4-aminobutyric acid and o-phenylenediamine as precursors by one-step hydrothermal method. The carboxyl group of 4-aminobutyric acid precursor was remained on the surface of produced CDs, which enabled the CDs specifically interact with FQs. When the FQs combined with CDs, the surface states CDs were disrupted leading to PL quenching. And the PL of CDs could be effectively recovered in the presence of histidine. The sensing platform displayed high sensitivity to three kinds of FQs (from 0.05 to 50 μ M for norfloxacin with the LOD of 17 nM, from 0.2 to 25 μM for ciprofloxacin hydrochloride with the LOD of 35 nM and from 0.4 to 10 μ M for ofloxacin with the LOD of 67 nM, respectively). And the CDs was employed for accurate determination of FQs in milk products [115]. Due to the strong affinity between quinolones and Cu²⁺, Wang and coworker reported a "on-off-on" sensor for quinolones sensing. The PL of DNAtemplated Ag NCs was firstly quenched by Cu^{2+} ,



Fig. 7. (A) Schematic illustration for the preparation of CDs-based nanohybrid sensor for the detection of Hg^{2+} . Reprinted with permission from Refs. [140]. Copyright 2017 American Chemical Society. (B) Schematic illustration of Hg^{2+} fluorescent sensing strategy based on label-free hairpin DNAscaffolded Ag NCs. Reprinted with permission from Ref. [142]. Copyright 2015 Elsevier. (C) Schematic representation of fluorescence detection of Pb²⁺ based on the GQD-DMA-tryptophan compound system. Reprinted with permission from Refs. [147]. Copyright 2013 The Royal Society of Chemistry. (D) Schematic illustration of the sensing method for the detection of Pb²⁺ by using ssDNA-scaffolded Ag NCs combined with aptamer. Reprinted with permission from Ref. [144]. Copyright 2018 Elsevier. (E) Schematic illustration of fluorescence assays for Cr⁶⁺ based on the inner filter effect of CDs. Reprinted with permission from Refs. [149]. Copyright 2013 American Chemical Society.

and then recovered after addition of quinolones. This assaying platform exhibited good sensitivities to four kinds of quinolones. Such as, a linear ranges of 20–100 nM for nalidixic acid with a LOD of 2.0 nM, 5–120 nM for cinoxacin with a LOD of 1.2 nM, 5–100 nM for ciprofloxacin with a LOD of 1.0 nM, and 1–60 nM for moxifloxacin with a LOD of 96 pM, respectively [116].

4.5. Heavy metal ions sensors

Heavy metals contaminated foods have serious health threats to human being. After a long time of intake and accumulation, heavy metals caused chronic damage to the liver, kidney, cardiovascular system, and nerves system of human body. There are many kinds of toxic metals, like Hg [117–120], Pb [121,122], Cd [123], Cr [124–126], Fe [127–131], Cu [132–134], Zn [135,136] and Ag [137], etc. Herein, we take three the most common and highly toxic heavy metal (Hg, Pb and Cr) as an example.

4.5.1. Mercury ion

 Hg^{2+} , a highly toxic heavy metal ion, is widely existed in the soil and water. And it can cause serious toxicological effects on human being

including brain damage, kidney failure, and various cognitive and motion disorders attributed to their high affinity to DNA [138]. Hg²⁺ could affect the PL of nanoprobes via covalently combining with the surface groups. Based on the interaction between Hg^{2+} and the surface groups of CDs including -COOH and -OH, He et al. utilized fluorescent CDs as probe for Hg^{2+} detection. The combination of Hg²⁺ and CDs induced the electron transferred from excited state of CDs to empty d orbit of Hg^{2+} , accompanying with the PL quenching of CDs. The probe enabled selective detection of Hg²⁺ with a linear range from 0 to 80 µM with a LOD of $0.201 \ \mu$ M. And the probe was successfully utilized to determinate of Hg^{2+} in real lake water [139]. Due to the interaction between electron-rich aromatic ring and Hg²⁺, Zhao et al. established a ratiometric fluorescent sensor for determination of Hg²⁺ (Fig. 7A). Solvothermal treatment of corn bracts, the end-product exhibited dual-emitting at 470 and 678 nm, which may respectively attribute to the intrinsic structure of CDs and chlorophyll-derived porphyrins. Therefore, the PL emitting at 678 nm was effectively quenched in the presence of Hg^{2+} , while the PL emitting at 470 nm was little changed. The PL intensity ratio at 470 and 678 nm displayed a

well linear response to Hg²⁺ concentration at 0-40 µM with a LOD of 9.0 nM [140]. Xie and coworkers employed BSA-templated Au NCs based probe for Hg²⁺ sensing. The surface of the as-prepared Au NCs is stabilized by a small amount of Au⁺, which could interact with Hg²⁺ through high affinity metallophilic Hg²⁺-Au⁺ interactions. Such specific and strong interaction between the Au NCs and Hg^{2+} , resulting the remarkably PL quenched of Au NCs [141]. On the basis of high affinity Hg^{2+} and DNA, the sensing strategies for Hg^{2+} were established. Built on hairpin DNA-scaffolded Ag NCs and exonuclease III-assisted target recycling amplification approach, Xu and coworkers proposed a fluorescent sensing protocol for Hg^{2+} (Fig. 7B). In the presence of Hg^{2+} , Hg^{2+} could specifically combined with thymine-thymine mismatched region to generate a complete hairpin DNA structure. Upon the catalysis of exonuclease III, the generated hairpin DNA was digested from restrained at 3' protruding terminus and blunt 3' termini leading to release of Hg²⁺. The free Hg²⁺ could initiate the next cycling, resulting in structure of hairpin DNA changed from stem-loop conformation to singlestranded DNA. Therefore, PL of the hairpin DNAscaffolded Ag NCs was weakened as increased of Hg^{2+} concentration. Under the optimal conditions, sensing system shown a dynamic linear response range of 0.1-10 nM and the LOD of 24 pM [142]. Based on the Hg²⁺ caused structural transformation of a thymine-rich single stranded DNA, Huang et al. also presented a "on-off-on" fluorescent sensor for Hg^{2+⁻} detection. The Mn-doped CdS/ZnS QDs modified by 33-mer thymine-rich single stranded DNA (strand A) were used as PL probe, while Au NPs labeled by 10-mer single stranded DNA (strand B) acted as PL quencher of QDs. The hybridization of strand A and strand B could induce the PL quenching of QDs through fluorescence resonance energy transfer. After addition of Hg²⁺, Hg²⁺-coordinated base pairs resulted in the structural change of linear strand A to form a hairpin conformation, while releasing Au NPs-labeled strand B from the hybrid structure. Therefore, PL of QDs was enhanced as increased of Hg²⁺ concentration. The sensor was utilized to determination of Hg²⁺ in lake water and tap water [143].

4.5.2. Lead ion

 Pb^{2+} is a highly toxic heavy metal ion that caused harmful effects to humans. Importantly, the Pb^{2+} delayed physical and mental development in infants and children [144]. Similar to Hg^{2+} , Pb^{2+} also could combine with the surface groups of fluorescent nanoprobe and further influenced the PL signal. Liu et al. prepared the bright-blue emitting CDs using polyacrylamide and sodium citrate through hydrothermal method. The Pb²⁺ chelated with organonitrogen and carboxylate groups on the surface of CDs to form CDs- Pb^{2+} complexes, which resulting in PL quenching of CDs due to inner filter effect [145]. Similarly, Jiang et al. utilized N-doped CDs as probe for Pb²⁺ sensing. The N-doped CDs were synthesized using glycerol and ethylenediamine as carbon source and nitrogen doped molecule, respectively. The PL of as-prepared CDs was sensitive to Pb²⁺ attributed to complexation interaction and the static quenching. Under the excitation, electron transferred from the excited state of CDs to d orbital of Pb²⁺ resulting in PL quenching of CDs. The CDs probe shown a linear response to Pb^{2+} in 0.1-6.0 µM with a LOD of 15.0 nM [146]. Based on 3,9-dithia-6-monoazaundecane modified GODs coupled with tryptophan, Qi and coworkers reported a sensing platform for Pb^{2+} (Fig. 7C). The Pb²⁺ can both combined with the sulfur atoms on the surface of the GQD and carboxylate groups of tryptophan, leading to the aromatic ring of the GQD coordinates with indole ring of tryptophan through π - π stacking. Therefore, the compact structure was formed between GOD and tryptophan in the presence of Pb^{2+} , which result in PL enhancement attributed to the energy transfer interactions between GQD and tryptophan [147]. Considering the comformational change DNA aptamer induced by of Pb²⁺, Qian and coworkers established a fluorescent "on-off-on" sensor. The aptamer modified GQDs and graphene oxide were used as probe and quencher, respectively. The PL of GQDs was efficiently quenched by graphene oxide through photo induced electron transfer. Upon addition of Pb^{2+} , the aptamer was captured Pb²⁺and subsequent formed G-quadraplex aptamer-Pb²⁺ complex. And then the GQDs was released from graphene oxide while the PL of GQDs was recovery. The detection sensor shown a linear response range from 9.9 to 435.0 nM and the LOD of 0.6 nM [148]. The DNA template consists of the aptamer region of Pb^{2+} in middle and the Ag NCs-nucleation region at two termini was designed by Zhang and coworkers. The combination between Pb2+ and aptamer induced the aptamer segment to form G-quadruplex and made the Ag NCs located at the two termini closer, which enhanced the PL of Ag NCs (Fig. 7D). The sensing system shown linear response to Pb²⁺ within the range of 5–50 nM with a LOD of 3.0 nM. And the reliability of the sensor was further demonstrated by detecting Pb²⁺ of real water samples [144].

4.5.3. Chromium ions

Cr⁶⁺ is also a severe pollutant in foods and environment due to its highly toxicity of carcinogenic and mutagenic. The UV-vis absorption spectra of Cr⁶⁺ shown a broad absorption band, which fully covered the excitative and emissive bands of CDs. Therefore, the Cr^{6+} could effectively quench the PL of CDs by inner filter effect. Zheng et al. used CDs as probe for detecting Cr6+ and the PL quenched Cr⁶⁺ by could recover by adding the reductant because of Cr⁶⁺ was reduced to low valent chromium species accompanied the elimination of inner filter effect (Fig. 7E) [149]. Bu and coworkers also reported a fluorescent sensing assay for Cr⁶⁺ using phosphate functionalized CDs as probes. Upon the optimized conditions, the PL intensity of CDs was linear response to Cr^{6+} in the range of 1.0–400 μM with a LOD of 0.24 μ M. And the probe was utilized for detecting Cr⁶⁺ in river water and tap water samples with satisfactory recovery. Moreover, Cr⁶⁺ test strips were fabricated for quick monitor of Cr⁶⁺ by the naked eyes [150]. In order to improve the detection sensitivity, Wang and coworkers designed a ratiometric fluorescent sensor for Cr⁶⁺ detection by encapsulating the blue emitting nitrogen and cobalt(II) co-doped CDs into europium metal-Cr⁶⁺ The organic frameworks (Eu-MOFs). quenched the PL of CDs via the inner filter effect while has no effect in the PL of the Eu-MOFs. Upon optimized conditions, the ratiometric fluorescent sensor shown high selectivity and sensitivity for Cr^{6+} with a linear response range of 2–100 μ M and a LOD of 0.21 µM [151].

5. Summary and out look

After decades of extensive research, fluorescence sensing technology has developed into one of the most valuable detection technologies. In this review, we have summarized the recent progresses of nanomaterials based fluorescent sensors for detection of food contaminants. The higher toxic food pollutants, including mycotoxins, foodborne pathogens, pesticide residues, antibiotic residues, and heavy metal ions, were successfully detected by the various fluorescent sensors. The sensing systems was easily established and shown fine linear responses to analytes with reasonable LODs met the limit standard of FDA or EC. Moreover, the practical application of sensors was also proved in real food samples. Although more kinds of analytes can be detected with the in-depth study of the preparation methods, optical properties and surface modification of fluorescent nanomaterials, there are still some challenges need to be solved.

The most basic is the synthesis of fluorescent probes. Although a large number of preparation methods have been reported, those with the advantages of eco-friendliness, large-scale production, and low cost are still needed. In addition, the rapid detection products based on fluorescent probes are mostly used in laboratory tests at present. In the future, manufacturing large-scale products that can be used for on-site inspection is the development trend.

Due to the complexity of food matrix, it is still a complex pretreatment process in the detection of real samples. It is necessary to build a detection system that integrates separation, enrichment and detection, which further shorten the testing time, simplify the testing steps, and even realize the nondestructive testing of samples. Then, on the basis of analytes monitoring, we should also pay attention to the effective degradation of pollutants. In the reported literature, the selected target analytes are mainly focus on harmful pollutants, but there is little or no analysis of nutritional components in food. With the development of economy and the improvement of our living standard, while ensuring the safety of food, food quality is also the focus of public concern.

Declaration of competing interest

None declared.

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