



Aptamer-Based Detection Methodology Studies in Food Safety

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Abstract

Oligonucleotide aptamers as a new type of molecular recognition element, compared with conventional antibodies, have not only high affinity and specificity to target molecules but also many advantages such as a wide range of target molecule recognition, synthesis *in vitro*, and chemical stability. With deep concerns of human beings about food safety issues, various aptamer-based methods for detecting harmful substances in foods have been extensively studied in recent years, including fluorescent, colorimetric, electrochemical, photoelectrochemical, electrochemiluminescent methods, etc. They have the methodology characteristics such as on-site detection, rapidness and high sensitivity. The hazardous substances that were detected mainly involved pesticide and veterinary drug residues, pathogenic organisms, biotoxins, allergens and organic pollutants. The methodology studies on the applications of aptamers in the detection of harmful substances in foods are comprehensively reviewed.

Keywords Aptamer · Detection · Food safety · Aptasensor

Introduction

In the whole industry chain of food, the hazardous factors for human health can be introduced from various ways including production, processing, storage, and circulation of agricultural and animal husbandry raw materials. These hazardous factors include all kinds of chemical and microbial sources, such as pesticide and veterinary drug residues, pathogenic organisms, biotoxins, and organic pollutants. Some of the hazardous factors are produced from food itself, such as allergens, which is harmful to their sensitive populations. With more attention to food safety, many countries around the world have enacted more and more rigorous regulations for the control of hazardous substances in foods. Therefore, it is urgent to develop highly sensitive detection methods for the hazards in food.

The analytical instrument-based detection methods and the antibody-based enzyme-linked immunosorbent assays (ELISA) have widely been applied to detect pesticide and veterinary drug residues, biotoxins, organic pollutants, and allergens. The detection methods of pathogens are mainly culture methods and polymerase chain reaction (PCR)-based methods. However, most detection methods are time-consuming and offsite, and require professional operations,

which is a great challenge for the real-time and onsite testing of samples. PCR-based methods have high sensitivity and can detect multiple samples at a time. However, these methods often produce a high percentage of false positives. The conventional ELISA has the advantage of simplicity, speed, and high reproducibility, but it is limited by the stability and production efficiency of antibodies. Furthermore, not all antigens are immunogenic.

With the successful screening of aptamers, their high affinity, high specificity, and wide applicability to target materials hint at their great application potential in the field of food safety detection. It has been proven that the various aptamer-based determination methods could be used to detect all factors hazardous to human health such as pesticide residues (Bala et al. 2017), veterinary drug residues (Yang et al. 2017), pathogenic organisms (Kim et al. 2017), biotoxins (Wang et al. 2018), allergens (Mishra et al. 2017), and organic pollutants (Cheng et al. 2018). The applicable scope of these methods to targets is much more than that of conventional detection methods. Many researchers have developed various biosensors by fixing the aptamer to a carrier such as quantum dots (QDs) (Tang et al. 2016), gold nanoparticles (AuNPs) (Yan et al. 2017), electrochemical electrode (Wang et al. 2017b), optical fiber (Gao et al. 2017), etc., which make these methods show extremely flexible and distinctive features. The signal types used in these methods can include fluorescence (Sadeghi et al. 2018), absorption (Wang et al. 2017a), electrochemiluminescence (Jiang et al. 2017a), surface-enhanced Raman spectra (SERS) (Duan et al. 2017b),

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photoelectrochemistry (Li et al. 2016a), electrochemistry (Wang et al. 2016b), etc. Some topic reviews on the applications of aptamers in food safety detection have been published (Xu et al. 2011; Wu et al. 2014; Liu and Zhang 2015; Tombelli et al. 2005; Sharma et al. 2015; Yüce et al. 2015; Dong et al. 2014). However, many new study achievements have been published again since 2015. A new topic review for the achievements mainly from 2015 is very necessary. They are summarized in this review, expecting to provide reference for their further research.

Aptamers

An aptamer is a type of single-stranded DNA (ssDNA) or RNA screened from a large random oligonucleotide pool synthesized artificially. There are approximately 10^{15} sequences with a length of 20–220 nt in the random library. The complementary base pairing makes these sequences folded into complex and stable three-dimensional structures which can bind to the specific targets and identify the difference of the only one hydroxyl or methyl group on the targets (Jenison et al. 1994). The excellent power for aptamers to distinguish the difference of chemical structure of targets makes them recognize one of chiral enantiomers (Michaud et al. 2003; Geiger et al. 1996). As the recognition result of aptamers to targets, they can be bound into a supramolecular complex through the non-covalent interactions such as hydrogen bonding, van der Waals forces, hydrophobic effects, and electrostatic interactions. The interaction can encapsulate the small-molecule targets, such as aminoglycoside antibiotic tobramycin, into the aptamer, and it can insert aptamers into the cavities of the structure of large-molecule targets, such as protein (Hermann and Patel 2000). The high specificity and affinity of aptamers to targets make them similar to antibodies. However, compared with antibodies, the several notable advantages of aptamers are mainly reflected in the following features: (1) aptamers have high chemical stability, are insensitive to changes in pH value, and can stand long-term storage at ambient temperature; (2) the denaturation of aptamers is highly reversible, that is to say, they can be denatured at high temperature and renatured at low temperature; (3) aptamers are easy to be obtained because they can be non-biologically screened *in vitro* and high purely synthesized when the sequence is determined; (4) aptamers can recognize a wide range of targets including proteins, nucleic acids, cells, and various micromolecular compounds; (5) aptamers are highly affinitive to targets with the dissociation constants (K_d) in the range of 10^{-6} – 10^{-12} mol/L; and (6) aptamers are easily modified and are suitable for combination with nanomaterials. Given this, aptamers can be widely applied in biomedicine, analysis and other research fields (Hamula et al. 2011;

Tombelli et al. 2007; Groff et al. 2015; Hamula et al. 2006; Dunn et al. 2017).

Applications of Aptamers in Food Safety Inspection

In the published studies, aptamers are usually conjugated to carriers, fabricating various biosensors. The developed aptamer biosensors generally include the composite probes and the electrochemical sensors. The former is prepared with aptamers and microcarriers such as QDs and AuNPs. They are easily prepared, and the limits of detection (LODs) of methods can be at the level of nanomoles per liter. The latter is fabricated with aptamers and electrochemical electrodes. Their preparation is usually time-consuming, but the LODs of the methods can be down to the level of picomoles per liter and even femtomoles per liter. The methods of conjugating the aptamer with other materials include directly adsorbing the sulfhydryl aptamer through the Au-S interaction, conjugating the aptamer with a carboxylation carrier by use of the activated ester method, and the hybridization between aptamers and their complementary sequences. The aptamer biosensors can be combined with various technologies (Dunn et al. 2017), mainly including electrochemistry (Vasilescu and Marty 2016; Liu et al. 2014b; Radi 2011) and optical methods (Feng et al. 2014; Lan et al. 2017) such as fluorescence, colorimetry, and so on, producing the various signals that can be utilized.

Pesticide and Veterinary Drug Residues

Detection of Pesticide Residues

The applications of aptamers in the detection of pesticide residues mainly include the spectral or electrochemical detection of the pesticide residues through fabricating composite probes or electrochemical sensors.

In the detection method of four kinds of organophosphorus pesticide residues including phorate, profenofos, isocarbophos, and omethoates, the aptamer that is highly affinitive to all four organophosphorus pesticides was selected. A molecular beacon with low background fluorescence intensity was designed, in which there was a nucleotide sequence to be partially complementary to the aptamer. The molecular beacon was conjugated with the fluorescein (FAM)-labeled aptamer by hybridization to fabricate a kind of detection reagent used for the four organophosphorus pesticides. The resulting reagent could emit intensive fluorescence (Zhang et al. 2014). When a certain amount of the reagent is mixed with the sample containing one of the four organophosphorus pesticides, the aptamer is melted from the molecular beacon because of its affinity to the target. As a result, the fluorescence intensity is decreased,

and the decrease degree is linear with the increase of organophosphorus pesticide concentration. The four organophosphorus pesticide residues can be quantitatively analyzed. The limits of quantification (LOQs) for phorate, profenofos, isocarbophos, and omethoate are 19.2, 13.4, 17.2, and 23.4 nmol/L, respectively. The method has been applied to the detection of Chinese cabbage samples. It is clear that the method cannot be used for accurately qualitative analysis of one of these four organophosphorus pesticides. This suggests the importance of aptamers that can selectively recognize a single target. The selectivity of an aptamer can also be combined with the fluorescence features of QDs for the detection of these four organophosphorus pesticides. The carboxylation QDs were first conjugated with the amino-modified oligonucleotides (AMOs) which were partial complementary to the aptamer of these four organophosphorus pesticides by amidation reaction. The resulting QD-AMO complexes were conjugated with the aptamers to be the QD-AMO-aptamer duplexes by hybridization (Tang et al. 2016). When the target pesticides are added, the binding of the aptamers to the pesticides makes the QD-AMO-aptamer duplexes melted into QD-AMOs and aptamer-target complexes. The ratio of the fluorescent intensity of QD-AMOs and QD-AMO-aptamer duplexes is determined by a laser-induced fluorescence detector after their CE separation. The higher the ratio is, the higher the pesticide concentration in the sample is. The LODs of isocarbophos, omethoate, phorate, and profenofos are 0.17, 0.23, 0.20, and 0.10 $\mu\text{mol/L}$, respectively. This method had been successfully used for the detection of the four organophosphorus pesticide residues in apple peels. The same thiol aptamers were also conjugated with silver dendrites via Ag-S bonds for the detection of these four organophosphorus pesticide residues by SERS (Pang et al. 2014). When they are incubated with target pesticide and then determined under a Raman microscope, the Raman fingerprint spectrum of the pesticide can be enhanced by silver dendrites. The LODs of isocarbophos, omethoate, phorate, and profenofos are 3.4, 24, 0.4, and 14 $\mu\text{mol/L}$, respectively. This method has also been applied in the detection of apple juice. The combination of aptamer and SERS suggests the method that can accurately recognize one of these four organophosphorus pesticides.

CdTe QDs and AuNPs can constitute a fluorescence inner filter effect system. The fluorescence emitted by QDs can be absorbed by AuNPs, making the fluorescence of QDs disappear. This property was used to detect acetamiprid residues in vegetables (Guo et al. 2016). When there is salt in the mixture solution of CdTe QDs and AuNPs, the salt can induce the aggregation of AuNPs, resulting in the disassembly of the fluorescence inner filter effect system. As a result, the fluorescence of the QDs is restored. If the AuNPs are modified by acetamiprid aptamers with a K_d of 4.98 μM through coordination, their salt concentration effect disappears (He et al. 2011). The fluorescence of QDs is still quenched by AuNPs

in the mixture solution of QDs and aptamer-AuNPs. When target pesticide is added, the aptamers are specifically bound to the targets, making them dissociated from the surface of the AuNPs. As a result, the salt concentration effect reoccurs, and the fluorescence of QDs is recovered. The linear range of this method is 0.05–1.0 $\mu\text{mol/L}$ with a LOD of 7.29 nmol/L. The system with a similar principle also included the fluorescence resonance energy transfer (FRET) system (Lin et al. 2016a). ZnS QDs are conjugated with the aptamers of acetamiprid. A multi-walled carbon nanotubes (MWCNTs)/aptamer-QDs FRET system was fabricated by use of the π - π stacking interaction between aptamer bases and MWCNTs. When QDs are excited, their excitation energy can be absorbed by MWCNTs, and the fluorescence of the QDs is quenched. When targets are added, the aptamers are specially bound to the targets, resulting in the dissociation of aptamers from the MWCNTs. The disassembly of the FRET system makes the fluorescence of the QDs recover. The LOD of acetamiprid is 0.7 nmol/L.

The method of combining an aptamer with electrochemistry was also applied for the detection of acetamiprid residues. The AuNPs were electrodeposited on the surface of a gold electrode as a coupling agent. The thiol aptamer of acetamiprid was modified on the gold electrode by a Au-S bond to fabricate an aptamer/AuNPs/gold electrode with high selectivity for acetamiprid (Fan et al. 2013). When the resulting electrode contacts with a sample containing acetamiprid, acetamiprid can be recognized by the aptamer, forming target-aptamer complexes on the surface of the electrode. As a result, the resistance of electron transfer (RET) of the electrode increases with the increase of acetamiprid concentration. The linear range of this method is 5–600 nmol/L, and the LOD is 1 nmol/L. The method has been used for the detection of wastewater and tomato samples.

The applications of aptamers in the detection of pesticide residues are shown in Table 1.

Detection of Veterinary Drug Residues

Veterinary drug residues refer to the prototype drugs or their metabolites that are accumulated or remained in the animal body or products such as eggs, milk, and meat after medication. The application types of aptamers in the detection of veterinary drug residues mainly includes fabricating composite fluorescence probes or electrochemical sensors through conjugating aptamers with fluorophore or electrode, and AuNPs colorimetry.

A method to detect ampicillin in milk was developed by Song et al., in which the ampicillin aptamer with a K_d of 13.4 nmol/L was used. The 5'-FAM-modified aptamers were conjugated with AuNPs by coordination to prepare AuNPs-aptamer-FAM in which AuNPs were used as fluorescence quenchers by interacting with fluorophore (Song et al. 2012a). When a sample containing ampicillin is added, the

Table 1 Applications of aptamers in the detection of pesticide residues

Analyte	Detection system	Aptamer sequence (5' to 3')	K_d	Linear range	LOD	Sample type	Ref
Acetamiprid	Fluorescence	CTGACACCATATTATGAAGA	–	0.05–1.0 $\mu\text{mol/L}$ 0–150 nmol/L	7.29 nmol/L 0.7 nmol/L	Chinese cabbage River water, cabbage leaves	Guo et al. (2016) Lin et al. (2016a)
	EIS			100–1200 nmol/L 5–600 nmol/L	9.12 nmol/L 1 nmol/L	Chinese cabbage Wastewater, tomatoes	Liu et al. (2016) Fan et al. (2013)
	CL			0.8–630 nmol/L	62 pmol/L	Cucumber	Qi et al. (2016)
	Colorimetry	GCAGCGTTTCTTGA TCGCTGACACCATATTA TGAAGA or GATCGCTGA CACCATATTATGAAGA	–	–	0.4 $\mu\text{mol/L}$	–	Tian et al. (2016)
	RLS	TGTAATTGTCGTC	4.98 $\mu\text{mol/L}$	0–100 nmol/L	1.2 nmol/L	Lake water	Wang et al. (2016a)
Atrazine	EIS	AGCGTTCTTGATCGCTG ACACCATATTATGAAGA		5×10^{-8} –10 $\mu\text{mol/L}$ 0.25–2.0 $\mu\text{mol/L}$ 0.5–800 nmol/L	17 fmol/L 0.09 $\mu\text{mol/L}$ 0.18 nmol/L	Water Juice Cucumber	Fei et al. (2015) Rapini et al. (2016) Li et al. (2016a)
	PEC			–	40 pmol/L	–	Madianos et al. (2018a)
	EIS	TACTGTTTGCACTG GCGGATTAGCCAGT CAGTG	0.62 ± 0.21 nmol/L	0.1–1000 $\mu\text{mol/L}$	10 pmol/L	Tap water, bottled mineral water	Madianos et al. (2018b)
	Colorimetry	ATCCGTCACACCTGCTCTTA TACACAATTGTTTCTCT TAACCTTCTGACTGCTGG TGTGGCTCCCGTAT	–	0.01–0.75 nmol/L 0.5–1000 pmol/L 0.5–6 $\mu\text{g/L}$	1.94 pmol/L 0.06 pmol/L 0.13 $\mu\text{g/L}$	Lake water, bottled mineral water, apple Lake water, apple Surface water, rice	Bala et al. (2017) Bala et al. (2016a) Arvand and Mirroshandel (2017)
	Fluorescence	CGTACGGAATTCGC TAGCTAAGGGATTCCTGT AGAAGGAGCAGTCTG GATCC	–	–	–	–	–
Iprobenfos, edifenphos	Colorimetry	CGTACGGAATTCGC TAGCTAAGGGATTCCTGT AGAAGGAGCAGT CTGGATCCGAGCTCC ACGTG	1.67 $\mu\text{mol/L}$, 38 nmol/L	10–100 nmol/L, 5–25 nmol/L	10 nmol/L, 5 nmol/L	Rice	Kwon et al. (2015)
	Colorimetry	AAGCTTGCTTTATAGCCTGC AGCGATTCTTGATCGGAA AAGGCTGAGAGCTACGC	0.8–25 $\mu\text{mol/L}$	0.01–1300 nmol/L	0.01 nmol/L	Apple juice River water	Bala et al. (2016b) Bai et al. (2015)
Phorate Isocarbophos, phosalone, methamidophos, acephate, trichlorfon, dursban Isocarbophos, profenofos, phorate, omethoate	Fluorescence	AGCTTGCTGCAGCGATTCTTGATCGCCACAGAGCT	–	–	0.035 $\mu\text{mol/L}$, 0.134 $\mu\text{mol/L}$	Dried tangerine peel	Dou et al. (2015)

Table 1 (continued)

Analyte	Detection system	Aptamer sequence (5' to 3')	K_d	Linear range	LOD	Sample type	Ref
SERS				0.01–10.0 mg/kg	0.384 $\mu\text{mol/L}$, 2.35 $\mu\text{mol/L}$	Chinese cabbage	Zhang et al. (2014)
					17.2 nmol/L		
					13.4 nmol/L		
					19.2 nmol/L		
				0.50–10.0 $\mu\text{mol/L}$ 0.30–10.0 $\mu\text{mol/L}$ 0.60–10.0 $\mu\text{mol/L}$ 0.70–10.0 $\mu\text{mol/L}$	23.4 nmol/L	Apple peels	Tang et al. (2016)
					0.17 $\mu\text{mol/L}$		
					0.10 $\mu\text{mol/L}$		
					0.20 $\mu\text{mol/L}$		
				–	0.23 $\mu\text{mol/L}$	Apple juice	Pang et al. (2014)
					3.4 $\mu\text{mol/L}$		

EIS electrochemical impedance spectroscopy, *CL* chemiluminescence, *RLS* resonance light scattering, *DPV* differential pulse voltammetry, *PEC* photoelectrochemistry

aptamers are changed in configuration due to their binding to ampicillin, and dissociated from AuNPs. As a result, the FAM fluorescence is restored. Ampicillin can be quantified by detecting the change of fluorescence intensity. The LOD of ampicillin in milk is 2 ng/mL. A similar principle was also used to detect chloramphenicol (CAP) residues in milk samples (Alibolandi et al. 2015). The CdTe QDs modified with thioglycolic acid were first conjugated to the amino-terminus of the CAP aptamer with activated ester method. Then, a FRET system was fabricated by conjugating the QD–aptamer complex with graphene oxide (GO) through π – π stacking interaction. The detection principle of the system is the same as that reported by Lin et al. (Lin et al. 2016a). The linear range is 0.1–10 nmol/L, and the LOD is 98 pmol/L.

The AuNP colorimetry was also used for the detection of veterinary drug residues. The solution of AuNPs appears red when being in the dispersed state. If salt is added into the solution, it will appear purple due to the aggregation of AuNPs. When the aptamers are modified to the surface of AuNPs, they can prevent the AuNPs from aggregating in saline solution. However, when the sample containing targets is added, the aptamers will specially bind to the targets, resulting in the dissociation of aptamers from the surfaces of AuNPs. As a result, the AuNPs are reaggregated, and the absorbance of the solution is changed. The ratio of the absorbance before and after the sample is added can reflect the concentration of the targets in the sample. This method and the methods with a similar principle have been used to detect ampicillin in milk with the LOD of 10 ng/mL (Song et al. 2012a), sulfadimethoxine in milk with the LOD of 100 ng/mL (Yan et al. 2017), kanamycin with the LOD of 25 nmol/L (Song et al. 2011), and 17 β -estradiol (E2) with the LOD of 0.10 ng/mL (Liu et al. 2014a).

Electrochemical sensors composed of aptamers and electrochemical electrodes have been used for the detection of various veterinary drug residues. An array of screen-printed carbon electrode (SPCE) consisting of a common Ag/AgCl reference electrode, carbon counter electrode, and two spatial-resolved carbon working electrodes (WE1 and WE2) was used for the detection of CAP residues. WE1 was modified with luminol-AuNPs, the complementary sequence of the CAP aptamer (DNA1) and the CAP aptamer (DNA2) tagged with chlorogenic acid, in which DNA1 and DNA2 could be combined by hybridization reaction. WE2 was modified with QDs which could normally emit fluorescence (Feng et al. 2016). Because the luminescence of luminol-AuNPs can be quenched by chlorogenic acid on WE1, the ratio of light intensity of WE1 to that of WE2 is small when the system is operated. When sample is added into the system, the high-affinity binding between CAP and DNA2 makes the DNA2 bound to CAP disassociate from DNA1. The ratio of the light intensity of WE1 to that of WE2 is consequently increased. The changes of the ratio signal can be used to detect CAP. The

LOD is 0.03 nmol/L. Another electrochemical sensor for the detection of CAP showed a simpler principle (Pilehvar et al. 2012). When the gold electrode modified with sulfhydryl aptamers is immersed into the sample containing CAP, the aptamers are specially bound to CAP, and changed in the configuration. As a result, the CAP gets close to the surface of the electrode, causing a significant increase in electron transfer efficiency to the electrode. The CAP concentration can be determined by measuring the current change rate. The method has been used for the determination of CAP in milk samples with a LOD of 1.6 nmol/L.

The electrochemical sensor prepared on a glassy carbon electrode (GCE) was used for the detection of tetracycline residues in milk samples. The aptamers of tetracycline were immobilized on a hydroxylated GCE with the activated ester method (Zhang et al. 2010). When the GCE is immersed into the sample, the targets in the sample are specially bound onto GCE, which makes the electric current reduce. The decrease of electric current has been used to detect tetracycline with a LOD of 1 ng/mL. The PEC method was also used to detect the residues of tetracyclines, in which QDs were conjugated to conductive glass electrodes. Firstly, AuNPs were electrodeposited on the electrode. The hairpin DNAs complementary to the aptamer were conjugated to CdTe QDs. The resulting conjugation was thus immobilized to the AuNPs on the electrode. Then, the aptamers were immobilized on the electrode by hybridization with the complementary DNAs (Li et al. 2017c). When the electrode is immersed into the sample, the aptamers bound to the targets are isolated with the complementary DNAs, restoring the DNAs to the hairpin shape. The QDs located at the 3' end of the DNAs are closer to the electrode than that before isolating, resulting in a larger photocurrent. This method has been used to detect oxytetracycline residues with a linear range of 2–300 nmol/L and a LOD of 0.19 nmol/L.

The aptamers were combined with surface plasma resonance (SPR) technology to detect neomycin B residues (Delos-Santos-Álvarez et al. 2009). Neomycin B can be immobilized on the gold-coated glass sensor by acylation reaction. When its RNA aptamers are added, they are bound to the targets immobilized on the SPR sensor, changing the SPR angular displacement signal. When the SPR sensor is exposed to a sample solution in which the fixed concentration of the RNA aptamers is added, the neomycin B in the sample will compete with the neomycin B immobilized on the sensor for the binding to the RNA aptamers. The higher the concentration of neomycin B in the sample is, the less the aptamers bound to the sensor are, and the smaller the net change of the SPR angular displacement signal is. The lower LOQ for neomycin B was measured to be 10 nmol/L.

A cantilever array sensor based on an aptamer was developed for the label-free detection of kanamycin. The cantilever array sensor consisted of sensing cantilevers and reference

cantilevers (Bai et al. 2014). The deflection of a single cantilever can be directly determined in this configuration, and the relative deflection between the sensing and reference cantilever pairs can subsequently be determined. The thiol-modified kanamycin aptamers are immobilized on the silicon cantilever. The aptamers can be changed from an unstructured single strand to a hairpin structure when combined with the targets. This change can cause the repulsion between adjacent molecules, and a compressive surface stress can be produced by the downwardly curved surface, which results in a difference in deflection between the sensing cantilever and the reference cantilever. Kanamycin can thus be detected. The change of surface stress is linearly related to kanamycin concentration in the range of 100 $\mu\text{mol/L}$ –10 mmol/L with a correlation coefficient of 0.995 and the LOD of 50 $\mu\text{mol/L}$. The sensor showed good selectivity for kanamycin.

E2 is used as an animal growth promoter in the aquaculture industry. Long-term low-dose exposure can cause drastic health problems. An aptamer-based PEC sensing platform was developed combining optics with electrochemistry for the detection of E2. Firstly, the vertically aligned TiO_2 nanotube arrays were orderly prepared on Ti foil by in situ anodization. Then, the narrow-bandgap semiconductor CdSe nanoparticles were electrodeposited on the TiO_2 nanotubes. Finally, the aptamers were immobilized on CdSe– TiO_2 nanotubes with glutaric dialdehyde as the coupling agent to prepare aptamer-based PEC sensors (Fan et al. 2014). The sensor is immersed in a phosphate buffer containing ascorbic acid when determining. The CdSe on the sensor can absorb the photon of 430 nm when being excited, and their valence band electrons can transit to the conduction band, leaving a hole in the valence band. When the hole is transferred to the CdSe surface, it is trapped by electron donor ascorbic acid in the solution, providing an electron into the hole. At the same time, the electrons that entered the conduction band are transferred to TiO_2 nanotubes and converted into external currents through the Ti foil. As a result, the photocurrent can continuously be generated under excitation light irradiation. When there is E2 in the sample solution, it can be bound with the aptamer, which limits the diffusion of the electron donor to the sensor surface, resulting in a decrease in photocurrent. Therefore, E2 can be detected by measuring the change of the photocurrent. The method has been used to detect E2 in medical wastewater, tap water, and lake water with the linear range of 0.05–15 pmol/L, the LOD of 33 fmol/L, and the spiked recoveries of 90.0–102.8%.

Dopamine is also used as a kind of animal growth promoter, and eating animal foods containing its residuals may cause Parkinson's disease, hypertension, gastrointestinal disorders, and so on. A system based on FRET was developed for the detection of dopamine, in which rhodamine B was the donor and AuNP was the acceptor. The sample was incubated with dopamine aptamers, and AuNPs were successively added into

the mixture. The free aptamers that were not bound to dopamine were bound to the surface of AuNPs. Then, NaCl was added into the solution, and the AuNPs that have not been bound by the aptamers were induced to aggregate. The rhodamine B was finally added. Those AuNPs bound to the surface by the aptamer and a portion of the rhodamine B can form a FRET system, making the fluorescence of this portion of the rhodamine B quench. The higher the concentration of dopamine in the sample is, the higher the concentration of AuNPs that can be aggregated is, and thus the higher the fluorescence intensity of rhodamine B is. This method has been successfully applied to the determination of dopamine in swine feeds and chicken liver with the linear range of $26\text{--}2.90 \times 10^3$ nmol/L, the LOD of 2 nmol/L, and the spiked recoveries of 91.4–103.5% (Xu et al. 2015a).

The applications of aptamers in the detection of veterinary drug residues are shown in Table 2.

Pathogens

Foodborne pathogens refer to the pathogenic organisms that can cause food poisoning or are mediated by food, including pathogenic bacteria, viruses, and parasites. They can directly or indirectly contaminate food and the water source, causing infectious diseases of the intestine and food poisoning. Foodborne pathogens are one of the important sources of food safety problems. The conventional detection method of foodborne pathogens is mainly the observation of samples cultured with special biochemical media. However, it takes 4–5 days to finish the detection, which means it takes a long time to complete the detection after the outbreak of the disease. Therefore, it is important to fast detect pathogenic organisms. The introduction of aptamers has made the detection of foodborne pathogens a revolutionary change.

AuNP colorimetry was used by Kim et al. for the detection of *Cronobacter sakazakii* (Kim et al. 2017). The longer aptamers cannot be bound to AuNPs efficiently due to steric hindrance. In order to solve this problem, the CS4 which had random regions with high adenine- and cytosine-to-thymine ratios is chosen as an actual aptamer, and CS4A is made up by appending an adenine base at each terminal of CS4 because adenine and cytosine had higher affinity to AuNPs than thymine. The two-phase method different from the normal AuNP colorimetry was used in the test by them. In the first phase, the sample and the aptamer were incubated in a binding buffer, and further centrifuged to obtain the supernatant containing excess aptamers that failed to bind to the target. In the second phase, the resulting supernatant was mixed with the citrate-coated AuNP solution (red), and the aptamers were bound to a portion of the AuNPs. NaCl 2 mol/L was slowly added to the solution, and the part of AuNPs that were not bound by the aptamers were aggregated; this part of the AuNPs turned purple. The concentration of the target bacteria in the sample was

determined by visually observing or measuring the absorbance ratio A₆₃₀/A₅₂₀ at 630 and 520 nm. The change in the color/absorbance indirectly depends on the concentration of target bacteria in the sample. The two-phase method can avoid the serious interference from coexisting components due to the direct contact of the sample with the aptamer–AuNP complexes. The assay can be completed within 30 min with a linear range of 7.1×10^3 to 10^7 CFU/mL under optimal conditions. The same principle was used for the rapid on-site detection of *Campylobacter jejuni* and *Campylobacter coli* in chicken carcass samples (Kim et al. 2018). The method is with the linear range of 10^5 to 10^8 CFU/mL and the LOD of 7.2×10^5 CFU/mL for *Campylobacter jejuni* and 5.6×10^5 CFU/mL for *Campylobacter coli*. A similar colorimetry was also used for the detection of *Campylobacter jejuni* in a milk sample with the linear range of $10\text{--}10^6$ cells/mL and the LOD of 10 cells/mL, in which the AuNPs were replaced by the Au@Pd nanoparticles that had peroxidase-like activity and could catalyze tetramethylbenzidine to be oxidized as blue product (Dehghani et al. 2018).

For the detection of *Campylobacter jejuni* in poultry samples, the strategy adopted by Suh et al. was quantitative PCR for the DNAs extracted from the *Campylobacter jejuni* that were captured by aptamers immobilized on magnetic beads, with the LOD of 42 cells/mL (Suh et al. 2014). A similar PCR method was also used for the detection of human noroviruses in human stool and lettuce samples, in which the PCR templates were RNAs extracted from the noroviruses rather than their DNAs (Escudero-Abarca et al. 2014). The fabrication of aptamer-based composite probes or electrochemical sensors can be avoided in this kind of PCR method, but the steps of extracting DNAs or RNAs from the targets are needed.

Also for the detection of noroviruses, a FRET system similar to that reported by Lin et al. (2016a) was constructed by Weng and Neethirajan, in which the FAM-labeled aptamers and MWCNTs or GO were used (Weng and Neethirajan 2017). The linear range of the method is from 13 µg/L to 13 mg/L, and the LOD is 4.4 µg/L when using MWCNT and 3.3 µg/L when using GO.

Bagheryan et al. developed a label-free impedimetric aptamer-based biosensor for the fast detection of *Salmonella typhimurium* in food. A diazonium-supporting layer was electrochemically or chemically grafted onto SPCE. The aminated aptamers of *S. typhimurium* were successively conjugated to the carboxylated diazonium-supporting layer with the activated ester method. The fabricated biosensor was immersed into the sample solution and incubated with *S. typhimurium* in the sample. The SPCE after washing was immersed in phosphate buffer containing $\text{K}_3\text{Fe}(\text{CN})_6/\text{K}_4\text{Fe}(\text{CN})_6$ where EIS was recorded (Bagheryan et al. 2016). The EIS can reflect the decrease of the electron transfer rate on the interface of the $\text{Fe}(\text{CN})_6^{4-/3-}$ redox couple due to the presence of the negatively charged aptamers or target-bound aptamers on SPCE

Table 2 Applications of aptamers in the detection of veterinary drug residues

Analyte	Detection system	Aptamer sequence (5' to 3')	K_d	Linear range	LOD	Sample type	Ref
Ampicillin	DPV	GCGGGCGGTTGTATAGCGG	13.4 nmol/L	0.02–40 nmol/L	4 pmol/L	Milk	Wang et al. (2016b)
	EIS			0.10–1000 nmol/L	10 pmol/L	Milk	Dapra et al. (2013)
	SWV			0.10–1000 nmol/L	10 pmol/L	Lake water	Yang et al. (2017)
Kanamycin	Colorimetry			0.5–500 ng/mL	10 ng/mL	Milk	Song et al. (2012a)
	Fluorescence			0.5–50 ng/mL	2 ng/mL	Lake water	
	Colorimetry	TGGGGGTTGAGGCTAAGCCGA	78.8 nmol/L	–	10 nmol/L	–	Song et al. (2011)
	Deflection			0.05–0.6 μ g/mL	2.6 ng/mL	Milk	Xu et al. (2015b)
	Fluorescence			1–500 nmol/L	1 nmol/L	Milk	Zhou et al. (2014b)
				0.1–10 nmol/L	50 μ mol/L	–	Bai et al. (2014)
Kanamycin A				1–50 ng/mL	0.92 ng/mL	Pork, milk, honey	Liu et al. (2015a)
		AGATGGGGTTGAGGCTAAGCCGA	–	–	321 pmol/L	Milk	Ramezani et al. (2016)
	EIS	TGGGGGTTGAGGCTAAGCCGAC	–	0.05–9.0 μ mol/L	9.4 $\pm$ 0.4 nmol/L	–	Zhu et al. (2012)
		TGGGGGTTGAGGCTAAGCCGA	78.8 nmol/L	1.2–75 ng/mL	0.11 ng/mL	Milk	Sharma et al. (2017)
	Fluorescence		78.8 nmol/L	0.80–350 nmol/L	0.30 nmol/L	Milk	Chen et al. (2015a)
	EIS	TGGGGGTTGAGGCTAAGCCGA	–	0.01–1000 μ mol/L	–	Milk	Dapra et al. (2013)
CAP		TGGGGGTTGAGGCTAAGCCGAG	–	1–10,000 nmol/L	–	Lake water	Liu et al. (2015b)
		TCACCTAT					
	ECL ⁵⁵	ACTTCAGTGAGTTGTCCACGGT	0.766 μ mol/L	0.1–120 nmol/L	0.03 nmol/L	Fish	Feng et al. (2016)
	Fluorescence	CGGCGAGTCGGTGGTAG		0.005–100 ng/mL	3 pg/mL	–	Wang et al. (2017c)
				0.001–10 ng/mL	0.0002 ng/mL	Fish	Miao et al. (2016)
				0.008–1 ng/mL	0.003 ng/mL	Fish, milk	Zhou et al. (2017)
Streptomycin		AGCAGCACAGAGGTCAGATGCACT	–	–	98 pmol/L	Milk	Alibolandi et al. (2015)
	SWV	CGGACCCCATCTCCTTCCATCCC		1.6–420 nmol/L	1.6 nmol/L	Milk	Pilehvar et al. (2012)
		TCATCCGTCCACCCATATGCGTGCT					
		ACCGTGAA					
	Colorimetry	GCGGCCCTAGGTACGATCGCGC	132.3 nmol/L	180–1000 nmol/L	47.20 nmol/L	Milk	Soheli et al. (2016)
		GCGGCTCTGGTGTCTGCTTT	199.1 nmol/L	0.2–1.2 μ mol/L	–	Honey	Zhou et al. (2013)
		GTTCTG					
		TCGGGTCGT					
		TAGGGAATTCGTGACGGATCCGGG	–	–	73.1 nmol/L	Milk	Emrani et al. (2016)
	Fluorescence	GTCTGGTGTCTGCTTTGT		–	54.50 nmol/L	Milk	Taghdisi et al. (2016)
		TCTGTCCGGTCTGCTGCA		–	47.6 nmol/L	Milk	Emrani et al. (2016)
Neomycin B		GGTCGACGCATGCGCCG		30–1500 nmol/L	14.10 nmol/L	Milk	Danesh et al. (2016)
	DPV		–	0.01–100 μ mol/L	10 nmol/L	–	De-los-Santos-Álvarez et al. (2009)
	SPR	GGCCUGGGCGAGAAGUUAGGCC	–				

Table 2 (continued)

Analyte	Detection system	Aptamer sequence (5' to 3')	K_d	Linear range	LOD	Sample type	Ref
Tetracycline	RLS	CGTACGGAAATTCGCTAGCCCCCGG	63.6 nmol/L	–	11.60 nmol/L	Milk	Luo et al. (2014)
	DPV	CAGGCCACGGCTTGGTTGGTC CCACTGCGCGTGGATCCGAGCTC CACGTG	–	10^{-11} –1 mmol/L or 10^{-6} –1 μ mol/L	3.8 fmol/L or 0.31 pmol/L	Milk, honey	Jahanbani and Bervidi (2016)
	PEC	–	–	0.3–1600 nmol/L	0.1 nmol/L	Liquid milk	Li et al. (2017a)
	Colorimetry	–	–	0.20–2.0 μ g/mL	0.039 μ g/mL	Raw milk	Luo et al. (2015)
	SPR	–	–	10–200 fmol/L	–	River water	Kim and Lee (2017)
Oxytetracycline	SWV	TTTTTCGTACGGAATTCGCTAGCC CCCCGGCAGGCCACGGCTTGGGT TGGTCCCACTGCGCGTGGATCC GAGCTCCACGTG	–	0.01–10 μ mol/L	10 nmol/L	–	Kim et al. (2010)
	CV	–	–	0.1–100 ng/mL	1 ng/mL	Milk	Zhang et al. (2010)
	DPV	CGACGCACAGTCGCTGGTGCCTA CCTGGTTGCCGTTGTGT	–	0.5–2000 μ g/mL	0.498 μ g/mL	Honey	Liu et al. (2017a)
	Fluorescence	GGAATTCGTAGCAGCTTGACGCT GGTGCCGGTTGTGTGCGAGTG TTGTGTGGATCCGAGTCCACGTG	9.61 nmol/L	1–50 ng/mL	0.85 ng/mL	Pork, milk, honey	Liu et al. (2015a)
	ELISA	–	–	0.50–100 ng/mL	0.88 ng/mL	Chicken, milk, honey	Lu et al. (2015)
Penicillin G	PEC	–	–	2–300 nmol/L	0.19 nmol/L	Chicken, raw milk, tap water, lake water	Li et al. (2017c)
	EIS	GGGAGGACGAAGCGGAACGAGAT GTAGATGAGGCTCGATCCGAATG CGTGACGTCTATCGGAATACTCG TTTTACGCCCTCAGAAACACAG CCCGACA	–	0.4–1000 ng/mL	0.17 ng/mL	Milk	Paniel et al. (2017)
	CL	CCCATCAGGGGGCTAGGCTAACAC GGTTCGGCTCTCTGAGCCCGG TTATTTACAGGGGA	–	–	0.04 ng/mL	Fish	Liu et al. (2017b)
	DPV	TCTAACGTGAATGATAGACCTGGCT TGGGTGGTGGCGACTGACTGGC GGTGCACCGTTAACTTAITCGA CCATA	–	100–1300 pmol/L	33 pmol/L	Pharmaceutical preparations	Azadbakht and Derikvandi (2018)
	Fluorescence	GGTCCATTCAAGTCGTAGGTTTGCC TTCAGCTCAACGCTTAC	52.78 nmol/L	5–1200 nmol/L	5.75 nmol/L	Milk	Sadeghi et al. (2018)
Sulfadimethoxine	SWV	GAGGGCAACGAGTGTTTATAGA	84 nmol/L	10^{-6} –1 mmol/L	1 nmol/L	Lake water	Yang et al. (2017)
	Fluorescence	–	–	–	10 ng/mL	Milk	Song et al. (2012b)
	Colorimetry	–	–	1–500 ng/mL	0.7 ng/mL	Lake water	Wang et al. (2017a)
		–	–	50–1000 ng/mL	50 ng/mL	–	Chen et al. (2013)
		–	–	0.01–1000 μ g/mL	10 ng/mL	Milk	Yan et al. (2017)

Table 2 (continued)

Analyte	Detection system	Aptamer sequence (5' to 3')	K_d	Linear range	LOD	Sample type	Ref
Dopamine	SWV Colorimetry Fluorescence	GTCTCTGTGTGCGCCAGAGACACT GGGCGAGATATGGCCAGCACA GAATGAGGCCC	0.4 $\mu\text{mol/L}$	100–1000 $\mu\text{mol/L}$ 0.54–5.4 $\mu\text{mol/L}$ 26–2900 nmol/L	100 $\mu\text{mol/L}$ 0.36 $\mu\text{mol/L}$ 2 nmol/L	– – Swine feeds, chicken, livers	Walsh et al. (2015) Zheng et al. (2011) Xu et al. (2015a)
Lincomycin	ECL	CGCGTGATGTGTGTCGATGCGATACG GTGAGTCGCGCCACGGCTACACA CGTCTCAGCGA	–	5×10^{-3} –1 nmol/L	0.16 pmol/L	Chicken, beef, mutton, duck, crucian, pork, crab	Li et al. (2017b)
Diethylstilbestrol	ECL	GGCGATGGGTAGGGGGTGTGGAG GGGCCGACGGAGGGG	–	0.3 – 10^5 pg/mL	0.1 pg/mL	Fish	Jiang et al. (2017a)
E2	Colorimetry PEC	GCTTCCAGCTTATTGAATTACACGC AGAGGTAGCGGCTCTGCGCATT CAATTGCTGCGCGCTGAAGCGCG GAAGC	0.13 $\mu\text{mol/L}$	0.1 – 10^5 ng/mL 0.05 – 15 pmol/L	0.1 ng/mL 33 fmol/L	– Lake water, tap water, medical wastewater	Liu et al. (2014a) Fan et al. (2014)
Clenbuterol	Fluorescence	AGCAGCACAGAGGTCAGATGTCAT CTGAAAGTGAATGAAGGTAAACA TTATTTCAATTAACACCTATGCGTG CTACCGTGAA	76.61 ± 12.70 nmol/L	0.1–50 ng/mL	0.07 ng/mL	Pork	Duan et al. (2017a)
Malachite green	Fluorescence	GGAUCCCGACUGGCGAGAGCCAGG UAACGAAUGGAUCC	46.6 nmol/L	10–100 nmol/L	5 nmol/L	Salmon tissue	Stead et al. (2010)

SWV square wave voltammetry, ECL electrochemiluminescence, CV cyclic voltammetry

(Witte and Lisdat 2011). The linear response range of the target concentration logarithm of the developed aptamer-biosensor is 10 – 10^8 CFU/mL, and the LOD is 6 CFU/mL. It has been shown that the aptamer biosensor could discriminate *S. typhimurium* from six other model bacteria strains. The method has been applied to the detection of *Salmonella typhimurium* in spiked apple juice samples.

The similar principle was also used for the detection of avian influenza virus H5N1 (Fu et al. 2014). Concanavalin A (ConA)/glucose oxidase (GOx)/AuNPs were prepared through the interaction between ConA and GOx on the GOx-modified AuNPs. The biotinylated H5N1 aptamers were conjugated on the streptavidin-coated magnetic beads by use of the interaction between biotin and streptavidin. The aptamer/magnetic beads were incubated with the solution containing H5N1 viruses. The viruses-bound aptamer/magnetic beads were conjugated to ConA/GOx/AuNPs through the interaction between ConA and glycoproteins on the surface of H5N1 viruses. The final complex was dispersed in glucose solution, and the EIS was measured by SPCE. The linear range of the method is from 0.001 to 1 hemagglutinin unit (HAU) and the LOD, 8×10^{-4} HAU. It is obvious that the complicated modification for the electrode can be avoided in the method.

A microfluidic platform made with poly (dimethyl siloxane) and glass substrate was developed for the detection of *E. coli* O157:H7, in which there was a microchannel of which the inner surface was modified by the carboxylated poly (amido amine) dendrimers (Jiang et al. 2017b). The capturing aptamers capped with $-\text{NH}_2$ were thus immobilized to the dendrimers on the inner surface of the microchannel by the active ester method. Sequentially, the aptamer–primer was hybridized with the padlock probe of which the two ends were complementary to the primer part of aptamer–primer to form a circular template, as shown in Fig. 1a. The reaction called rolling circle amplification (RCA) was employed to enhance the signals in the detection of *E. coli* O157:H7, in which the complementary sequences of the circular templates produced from padlock probes were repeatedly amplified by use of RCA reagents to form the RCA products, as shown in Fig. 1b. When the sample is injected into the microchannel, the target bacteria in the sample can be captured by the aptamers immobilized on the surface of the microchannel. The aptamer–primer solution is successively introduced, and the aptamer part of the aptamer–primer can also be bound to the bacterium to form the aptamer/bacterium/aptamer–primer sandwich structure. After washing, the padlock probes and RCA reagents are introduced into the microchannel to start the RCA reaction. The RCA products will be synthesized to the aptamers bound to the bacteria. Finally, the fluorescent dye Cy3-labeled ssDNAs complementary to the RCA product are introduced into the microchannel. Because there are many sequences complementary to the ssDNA in the every RCA product, every target bacterium can be labeled by many Cy3 fluorophores, making the

detection signal largely enhanced. In the absence of target bacteria in the sample, the aptamer–primer will be washed away from the microchannel and no signals will be detected. As a result, the method offered a low LOD at 10^2 cells/mL.

A quartz crystal microbalance (QCM)-based aptasensor was developed by Wang et al. for the detection of *Salmonella typhimurium* after they obtained the aptamer of *S. typhimurium* using the QCM method (Wang et al. 2017b). The aptamers were immobilized on the surface of the gold electrode by the activated ester method, and further incubated with the sample. The targets in the sample were bound by the aptamers on the electrode, causing the change of QCM frequency. The frequency changes before and after incubation with the sample can be used for the detection of *Salmonella typhimurium*. The linear response range of the target concentration logarithm of the aptasensor is 7.9×10^2 – 7.9×10^6 CFU/mL. It takes less than 1 h to detect 10^3 CFU/mL of *Salmonella typhimurium*.

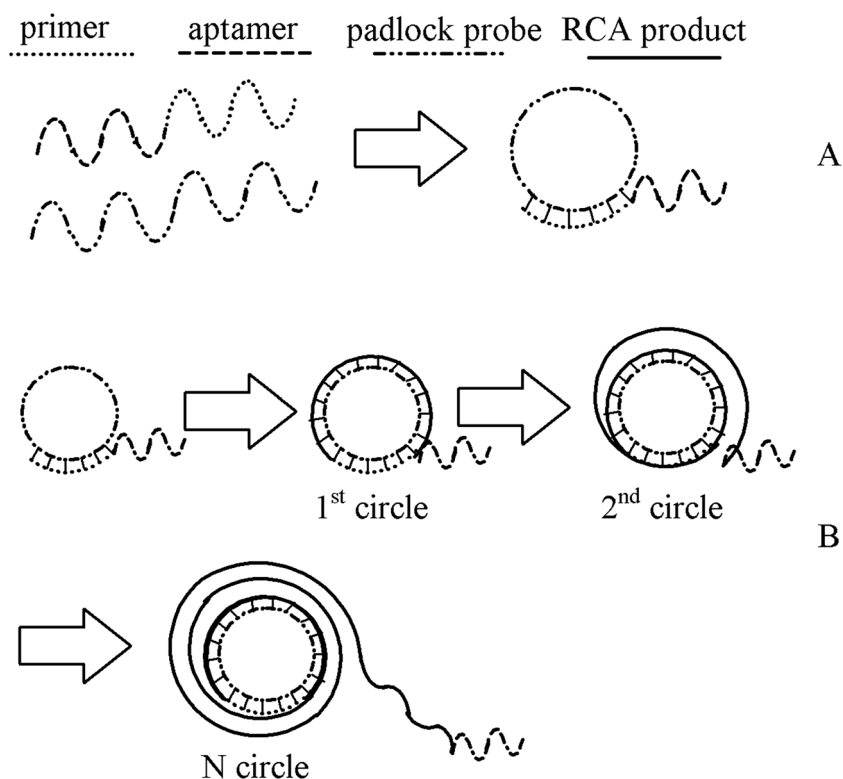
Cryptosporidium is a kind of common protozoan parasite found in the intestinal tract of humans and many animal species. Its transmission routes include water-borne way, human to human (fecal–oral), zoonoses, and foodborne way. The water-borne way is the main transmission route. An electrochemical aptasensor was developed for the detection of cryptosporidium oocysts (Iqbal et al. 2015). The thiol-modified complementary strands of aptamers were immobilized on the AuNP-modified SPCE by Au–S interaction, and were further incubated with aptamers. The conjugation of the aptamers and their complementary strands can block the external redox probe $\text{K}_4\text{Fe}(\text{CN})_6/\text{K}_3\text{Fe}(\text{CN})_6$, and thus, electrons cannot be transferred to the electrode. When the targets are bound to aptamers, the conformation of aptamers can be changed and their surface is remodeled, which allowed the outer redox probe to freely penetrate the electrode. The ability to transfer electrons back to the electrode is restored. Therefore, cryptosporidium oocysts can be detected based on the changes of current intensity, with a linear range of 150–800 oocysts and a LOD of 100 oocysts.

The applications of aptamers in the detection of pathogens are shown in Table 3.

Biotoxins

Biotoxins refer to the toxic substances produced by various organisms. If the food that contains the biotoxins is accidentally ingested by humans, the various poisoning symptoms and even death may happen. The okadaic acid aptamers were applied to fabricate a kind of electrochemical biosensor for the detection of okadaic acid (Eissa et al. 2013). The aptamers were first immobilized on the surface of a gold electrode by a self-assembly approach through Au–S interaction. The negatively charged aptamer repels the negatively charged redox probe $\text{Fe}(\text{CN})_6^{4-/3-}$, hindering the electron transfer between $\text{Fe}(\text{CN})_6^{4-/3-}$ and the electrode surface. As a result, the redox

Fig. 1 Formation of circular template (a) and RCA product (b)



peak current is decreased, and the RET is increased. When the target is bound to the aptamer, the conformation of the aptamer is changed, thereby facilitating $\text{Fe}(\text{CN})_6^{4-/3-}$ redox pair entry into the sensor surface. As a result, the redox peak current is increased, and the RET monitored by EIS is decreased significantly. The linear detection range of the aptasensor was finally determined to be 0.1–60 ng/mL and the LOD was 70 pg/mL.

The strategy that makes up the system of fluorescence quenching was applied in the detection of aflatoxin M1 (AFM1) in milk. The AFM1 aptamer was labeled with FAM to be F-aptamer, and the complementary sequence of the aptamer was labeled with quencher TAMRA to be Q-aptamer. F-aptamer and Q-aptamer were hybridized to be a duplex complex in which the fluorescence of FAM could be quenched by TAMRA (Sharma et al. 2016). When the complex is added into the sample, the AFM1 in the sample can be bound to the F-aptamer, and makes the conformation of aptamer–AFM1 complexes change to antiparallel G-quadruplex, and the F-aptamer and the Q-aptamer are unbound from each other. As a result, the FAM is away from the quencher TAMRA, and its fluorescence intensity is recovered. The LOD of AFM1 was determined to be 5.0 ng/kg, and the recoveries of spiked milk were 94.40–95.28% ($n=3$).

The novel sandwich composites that combine capture probes with separation probes were developed for the colorimetric detection of patulin (PAT) (Wu et al. 2016b). Firstly, the

capture probe was fabricated by binding PAT aptamer to the glucose oxidase immobilized on AuNPs. The separation probe was fabricated by immobilizing the complementary strand of aptamer (cDNA) on the surface of magnetic nanoparticles. The capture probe was combined with the separation probe to be the sandwich composite by hybridization reaction. When the sample containing PAT is added to the composite solution, the PAT-bound capture probes are unbound from the separation probes. These separation probes and the sandwich composites that are not bound to PAT can be separated from the solution by applying a magnetic field. Glucose is added into the supernatant, and the glucose oxidase on the capture probe in the solution can catalyze the glucose to gluconic acid and H_2O_2 . The iron(II) is successively added, and oxidized by H_2O_2 to iron(III). Squaric acid is subsequently added, and the iron squarate complex is rapidly generated. As a result, the solution color is changed from colorless to brownish red accompanying the increasing absorbance, and the absorbance value could be measured at 469 nm. The higher the concentration of PAT in the sample is, the larger the absorbance value at that wavelength is. The linear range of the method was determined to be 50–2500 pg/mL, and the LOD was 48 pg/mL. The recoveries of spiked apple juice sample were from 93.0 to 108.88%.

A new strategy for sensitive fluorescence polarization analysis was proposed by Samokhvalov et al. to detect ochratoxin A (OTA) (Samokhvalov et al. 2017). The detection system is

Table 3 Applications of aptamers in the detection of pathogens

Analyte	Detection system	Aptamer sequence (5' to 3')	K_d	Linear range (CFU/mL)	LOD (CFU/mL)	Sample type	Ref
<i>Cronobacter sakazakii</i>	Colorimetry	GGTATTAGGGTCGCATCGTGGTCGG GGTGGTGGGTGGAGGGCGACTTC ATCTGCGCGATGGCTCTAACTCTC CTCT	–	7.1×10^3 – 7.1×10^7	7.1×10^3	Powdered infant formula	Kim et al. (2017)
<i>Staphylococcus aureus</i>	DPV	TCCCTACGGCGCTAACCTCCCAACCG CTCCACCCCTGCCCTCCGCTCGCCA CCGTGCTACAAC	–	10 – 10^6	1.0	Tap water, river water	Abbaspour et al. (2015)
	Colorimetry	GCAATGGTACGGTACTTCTCTCGGCAC GTTCACAGTACGGCTCGCTGGTCA TCCCACAGCTACGTCAAAAAGTGCA CGTACTTTTGCTAA	–	10 – 10^6	9	Milk	Yuan et al. (2014)
	SPQC		–	41 – 4.1×10^5	41	Milk	Lian et al. (2015)
	SERS		–	10^2 – 10^7	35	Pork	Zhang et al. (2015)
	Fluorescence	GCAATGGTACGGTACTTCTCTCCACG ATCTCATTAAGTCTGTGGATAAGCG TGGGACGTCTATGACAAAAGTGCA CGTACTTTTGCTAA	–	–	–	Milk	He et al. (2014)
<i>Salmonella typhimurium</i>	QCM	CAGTCCAGGACAGATTTCGCGAGCCCA CTCCAAAACAGACCAACTCACGCT CTATCAACATCGCTATCCACGTGG ATTTCATTACGCGATT	58.5 nmol/L	7.9×10^2 – 7.9×10^6	7.9×10^3	–	Wang et al. (2017b)
	SERS	AGTAATGCCGGTAGTTATTCAAAAGA TGAGTAGGAAAAGA	6.33 ± 0.58 nmol/L	15 – 1.5×10^6	15	Milk	Duan et al. (2016)
	EIS	TTTGGTCTGTCTTAIGTCCAGAAT GCGAGGAAAGTCTATAGCAGAGGA GATGTGTGAACCGAGTAAATTTCT CTACTGGGATAGGTGGATTAT	–	10^2 – 10^8	3	Apple juice	Sheikhzadeh et al. (2016)
<i>Salmonella enteritidis</i>	Colorimetry	AAGGGCTGGCTGGATGGACCCCTCCC GAAACGAGCTGTCTTTAACGGAA GCTAATCTGCCTCACTCCACGGAC CCCACT AAGGGCTGGCTGGG ATGGATGTAAGAAGGGAGGAAAGG ACCTAAGACCTGTATATTGCGAT CACTCCACGGACCCCACT	0.971 μ mol/L 0.309 μ mol/L	–	10^3	Milk	Bagheryan et al. (2016) Bayraç et al. (2017)
<i>Salmonella</i>	EIS	TATGGCGGTCACCCGACGGGGACT TGACATTATGACAG	–	2.4 – 2.4×10^3	3	Pork	Ma et al. (2014)
<i>Escherichia coli</i> O111	DPV	ATCCGTCACACCTGCTCTACTGGCCG GCTCAGCATGACTAAGAGGAAGT TATGTGGTGTGGCTCCCGTAT	–	2×10^2 – 2×10^6	112	Milk	Luo et al. (2012)
<i>Escherichia coli</i> O157:H7	Fluorescence	ATCCGTCACACCTGCTCTATCAAAATG TGCAGATATCAAGACGATTTGTAC AAGATGGTGTGGCTCCCGTAT	–	10^2 – 10^5 cells/mL	10^2 cells/mL	–	Jiang et al. (2017b)
<i>Vibrio parahaemolyticus</i>	SERS	TCTAAAAATGGCAAAAAGAACAGTGA CTCGTTGAGATACT	16.88 ± 1.92 nmol/L	1.4×10^2 – 1.4×10^6	14	Salmon	Duan et al. (2017b)

Table 3 (continued)

Analyte	Detection system	Aptamer sequence (5' to 3')	K_d	Linear range (CFU/mL)	LOD (CFU/mL)	Sample type	Ref
<i>Shigella sonnei</i>	Fluorescence	ATACCAGCTTATTCAATTCCATGGTC CCTCGTGTATTAATATGTGTCTGA ACTGGCTGAGAITGCATTAATCT ATACCAGCTTATTCAATTCCACACAT ACCAAAAAACACAGCACACTTCATC AATTCACGAGAITGCATTAATCT ACAAGGACAGTAGACCAACACAGGAAA TCAAAAGGCCGTGGGAA	39.32 ± 5.02 nmol/L 15.89 ± 1.77 nmol/L	10^3 – 10^7 cells/mL	10^3 cells/mL	–	Song et al. (2017)
<i>Campylobacter coli</i>	Colorimetry	–	–	10^5 – 10^8	5.6×10^5 7.2×10^5	Chicken carcass	Kim et al. (2018)
<i>Campylobacter jejuni</i>	Colorimetry	–	–	10 – 10^6 cells/mL	10 cells/mL	Milk	Dehghani et al. (2018)
	Quantitative PCR	GTATACT AGTATACGTATTACCTGCAGCACAAAG GGGCTGGTTGTGTTGGGTCGGTTG TTTTGGTTGGGCTGCAGGTAATAC GTATACT AGTATACGTATTACCTGCAGCACAAAG GGACAGTAGACCAACACAGGAAATCA AAGGCGTGGGAAAGCAAGATCTCCG AGATATCG CATCTGTGTGAAGACTATATGGCGCT CACATATTTCTTTC	292.8 ± 53.1 nmol/L	–	42 cells/mL	–	Suh et al. (2014)
Norovirus	Fluorescence	AGTATACGTATTACCTGCAGCCCCATG TTTTGTAGGTGTAATAGGTCATGT TAGGGTTTCTGCGATATCTCGGAG ATCTTGC GTGTGCATGGATAGCACGTAAACGGTG TAGTAGTAACGTGCGGGTAGGAAG AAAGGGAATAGTTGTCGTGTTG	–	13 – 13×10^3 μ g/L	3.3 or 4.4 μ g/L	Lettuce, human stool Mussel	Escudero-Abarca et al. (2014) Weng and Neethirajan (2017)
Avian influenza virus H5N1	QCM EIS Impedance	–	4.65 nmol/L	–	0.0128 HAU 8×10^{-4} HAU 0.0128 HAU	–	Wang and Li (2013) Fu et al. (2014) Lum et al. (2015)
<i>Cryptosporidium parvum</i> oocysts	SWV	GTGGTCCCGCAAAATGCACGACGAGT CTTGCTTCTGATCT	–	150–800 oocysts HAU	100 oocysts	Pineapple, mango	Iqbal et al. (2015)

SPQC series electrode piezoelectric quartz crystal

composed of the fixed amount of FAM-labeled OTA and the protein-anchored OTA aptamers. When the sample is added into the system, the OTA in the sample can compete with the fluorophore-labeled OTA in the system for the binding to the OTA aptamer. The higher the OTA content in the sample is, the higher the concentration of the FAM-labeled OTA that is released from the OTA aptamers is. The FAM-labeled OTA is a small molecule that rotates fast in the liquid phase and has a low degree of fluorescence polarization. However, the FAM-labeled OTA that is bound to the protein-anchored aptamer has a high degree of fluorescence polarization due to the large molecular weight of the protein. The strategy was applied to detect OTA in white wine with the LOD of 2.8 nmol/L (1.1 mg/kg). The recoveries of spiked wine ranged from 83 to 113%.

Gao et al. developed a kind of sensor using biolayer interferometry for the detection of palytoxin (PTX) (Gao et al. 2017). PTXs were immobilized on the biolayer of the fiber sensor surface. The PTX aptamers labeled with horseradish peroxidase (HRP) were used as biorecognition receptors. The optimum amounts of HRP-labeled aptamers are added into the sample. When the fiber sensor is immersed into the sample, the PTXs immobilized on the sensor biolayer can compete with the PTXs in the sample for the binding to the HRP-labeled aptamers, making these HRP-aptamers bind to the biolayer of the fiber sensor. Then, the fiber sensor bound by HRP-aptamers is immersed in a 3, 3'-diaminobenzidine solution. The HRP can catalyze 3, 3'-diaminobenzidine to produce the polymerization product that can precipitate on the biolayer of the fiber sensor, causing the optical thickness and mass density of the biolayer to be largely changed. When only the PTXs are immobilized on the biolayer of the fiber sensor, the reflection ray of the white light irradiated on the reference surface of the fiber and the reflection ray of the white light irradiated on the biolayer surface of the fiber can interfere with each other, which generates the interference pattern with wavelength λ . When the HRP-aptamers are bound to the biolayer of the fiber sensor, the optical thickness between the two surfaces is increased due to the formation of the polymerization product, which makes the interference pattern obviously shift $\Delta\lambda$ and generates a response profile on the biolayer-interferometric sensor. The higher the reciprocal of the PTX concentration in the sample is, the more the precipitates on the biolayer surface of fiber are, and thus the larger the $\Delta\lambda$ is. The linear range of the biosensor is 200–700 pg/mL, and the LOD is 0.04 pg/mL. The biosensor has been used for the detection of PTX in shellfish and seawater samples.

The applications of aptamers in the detection of biotoxins are shown in Table 4.

Allergens

Allergens, the substances that cause allergic reactions in the body, can be divided into many types. However, the foods that cause allergies mainly include nuts, fish, shellfish, soybeans,

and milk. What's more, most of the allergens in the foods are proteins. In recent years, researchers have developed the aptamer-based biosensors for various allergens, such as lysozyme (Ocaña et al. 2015), gluten (Amaya-González et al. 2015), the peanut allergen Ara h 1 (Peeters et al. 2014), etc.

Trashin et al. developed a label-free impedance aptasensor for the detection of the peanut allergen Ara h 1. The thiol-modified aptamers were immobilized on the gold electrode surface via Au–S bonds. The electrode was incubated with the sample containing Arah1, and EIS was recorded for the measurement (Trashin et al. 2014). The detection principle of the method is as follows: when the macromolecular proteins are captured by the aptamers immobilized on the gold electrode, the RET can be increased due to the insulation effect of these macromolecules. The Arah1 equivalent to the K_d concentration can increase the RET by more than “three times, which makes the detectable protein concentration is as low as 1/3 of K_d . Ocaña et al. reported the detection method of lysozyme by use of a novel electrochemical biosensor in which the aptamer–antibody sandwich was used (Ocaña et al. 2015). The aptamers of lysozyme were covalently bound to the surface of carbon electrode by diazo reaction. After the aptamers were incubated with lysozyme, the biotinylated antibodies were bound to lysozyme to fabricate the sandwich complex. Then the avidin-labeled alkaline phosphatases (ALPs) were bound to the sandwich electrode by use of avidin-biotin reaction. When the electrode is immersed into the sample containing ALP substrate 1-naphthyl phosphate, the lysozyme in the sample can compete with the lysozyme immobilized on the electrode to bind the aptamers, allowing the biotin-conjugated antibodies enter to the solution. The ALPs that simultaneously enter the solution can catalyze the substrate of ALP to produce 1-naphthol, and the generated electrochemical response signal can be detected by DPV. As a result, lysozyme can be detected. The sensor has a wide detection range from 5 fmol/L to 5 nmol/L, and a LOD of 4.3 fmol/L. The recoveries of lysozyme-spiked wine samples were determined to be 95.2–102.0%. The control experiments were carried out with BSA, cytochrome c, and casein. The results showed that the biosensor had a good specificity for lysozyme.

The applications of aptamers in the detection of allergens are shown in Table 5.

Organic Pollutants

Polychlorinated biphenyls (PCBs) are composed of 209 different PCB congeners and are one class of persistent organic pollutants. Meat, dairy products, and fish are the main intake routes of the general population for PCBs. A novel aptamer-functionalized stir bar sorptive extraction was developed by Lin et al. for the enrichment of the low-abundance PCBs from fish samples (Lin et al. 2016b). Firstly, a layer of organometallic framework (MOF) film was prepared by

Table 4 Applications of aptamers in biotoxin detection

Analyte	Detection system	Aptamer sequence (5' to 3')	K_d	Linear range	LOD	Sample type	Ref
Okadaic acid	CV	GGTCACCAACAAACAGGGAGC GCTACGGGAAGGTCAAT GTGACGTCATCGGATGT GTGG	77 nmol/L	0.1–60 ng/mL	70 pg/mL	Shellfish	Eissa et al. (2013)
PAT	Colorimetry	GGCCCGCAACCCGCATCAT CTACACTGATATTACCTT	21.83 ± 5.022 nmol/L	50–2500 pg/mL	48 pg/mL	Apple juice	Wu et al. (2016b)
OTA	Fluorescence	GATCGGGTGTGGTGGCGTA AAGGAGCATCGGACA	–	–	3.6 nmol/L	White wine	Samokhvalov et al. (2017)
	EIS			0.12–5.5 ng/L	0.12 ng/L	Beer	Hayat et al. (2013)
	SPR			0.094–10 ng/mL	0.005 ng/mL	Wine, peanut oil	Zhu et al. (2015)
	DPV			0.78–8.74 ng/mL	0.07 ± 0.01 ng/mL	Wheat	Bonel et al. (2011)
		GGAGGACGAAGCGAACCGG GTGTGGGTGCCTTGATCC AGGAGTCTCAGAAAGACA CGCCCGACA	–	–	0.11 ng/mL	Wine	Barthelmebs et al. (2011)
	Colorimetry	CTGGGAGGAGGGAGGGATC GGGTGTGGTGGCGTAAA GGGAGCATCGGACACCG ATCC	–	–	2.5 nmol/L	Wine	Yang et al. (2012)
	Fluorescence	GATCGGTGTGGTGGCGTA AAGGAGCATCGGACACG CCACCCACACA	–	10–5000 nmol/L	8.7 nmol/L	Flour, beer	Wang et al. (2018)
	LEWIF	AAAAAAGATCGGTGTGGGT GGCGTAAAGGAGCATCG GACA	–	6–500 nmol/L	3 nmol/L	Oat	Wang et al. (2015)
PTX	Wavelength shift	ACCGACCGTGTGGACTCAG GAGGTGTGGGACTTTG CTTGACTGGGCGCCCG TTGAAACTATGAGCGAGC CTGGCG	0.843 nmol/L	200–700 pg/mL	0.04 pg/mL	Mussels, clams, water, scallops	Gao et al. (2017)
AFB1	Fluorescence	TGGGTTTTGTGGCGGGTG GTGTACGGCGAGGG GTGGGCAGTGTGTCTCT CTGTCTCGTGCCCTTC GCTAGGCC GTGGGCAGTGTGTCTCT CTGTCTCGTGCCCTTC GCTAGGCCACA	–	0.25–32 ng/mL	0.2 ng/mL	Beer, wine	Goud et al. (2016)
			–	5–100 ng/mL	1.6 ng/mL	Infant rice cereal	Chen et al. (2017)
			–	10–400 nmol/L	3.4 nmol/L	Rice, peanuts	Sabet et al. (2017)
AFM1	Fluorescence	ACTGCTAGAGATTTCACAT	–	25–2000 ng/kg	5.0 ng/kg	Milk	Sharma et al. (2016)
	EIS		–	2–150 ng/L	1.15 ng/L	Milk	Istamboulié et al. (2016)
<i>Staphylococcus aureus</i> enterotoxins A	Fluorescence	AGCAGCACAGAGGTCAGATG TACTATGCATTTCCTCC CAGCATCTTATTGAGAG	–	0.08–10 ng/mL	0.062 ng/mL	Milk	Huang et al. (2015b)

Table 4 (continued)

Analyte	Detection system	Aptamer sequence (5' to 3')	K_d	Linear range	LOD	Sample type	Ref
<i>Staphylococcus aureus</i> enterotoxins B	Fluorescence	TGACCTATGCGTGCTAC					
		CGTGAA					
		GGTATGAGGGTCGCATCCA	–	0.10–9 ng/mL	0.069 pg/mL	Milk	
		CTGGTCGTTGTGTCTGT TGCTGTATGTTGTTTC GTGATGGCTCTAACTCTC CTCT					
<i>Staphylococcus aureus</i> enterotoxins C1	Fluorescence	AGCAGCACAGAGTCAGATG	–	0.05–5 ng/mL	0.040 ng/mL	Milk	
		TATACTCTAAAAATTGT					
		TTGTAICTACGATGTCT					
		TCGTCTATGCGTGCTAC					
Anatoxin-a	SWV	CGTGAA					
		TATACTTCTAAAAATTGTTT	65.14 ± 11.64 nmol/L	0.01–10 µg/mL	6 ng/mL	Milk	Huang et al. (2015a)
		GTATCTACGATGTCTTCGT					
		TGGCGACAAAGACGTACA	15.1 ± 3.1 nmol/L or 21.6 ± 0.89 nmol/L	1–100 nmol/L	0.5 nmol/L	Drinking water	Elshafey et al. (2015)
Cyanotoxin cylindrospermopsin	EIS	AACACGCACCGCCGA					
		GTGGAGTATCTGAGGTC					
		GG					
		GGCATCAGGCAACAACCGAT	57.41 nmol/L	0.1–80 nmol/L	100 pmol/L	–	Elshafey et al. (2014)
Fumonisin B1	EIS	GGTCCGGCCACCTAACA					
		ACCGCCACCCACCACC					
		CCGCCG					
		AGCAGCACAGAGGTCAGATG	–	10 ^{–4} –100 µmol/L	2 pmol/L	Corn	Chen et al. (2015b)
Zearalenone	Fluorescence	CGATCTGGATATTATTT					
		TGATACCCCTTTGGGGAG					
		ACATCTATGCGTGCTAC					
		CGTGAA					
Microcystin-LR	Fluorescence	AGCAGCACAGAGGTCAGATG	–	0.5–64 ng/mL	0.5 ng/mL	Beer, wine	Goud et al. (2017)
		TCATCTATCTATGGTACA					
		TTACTATCTGTAATGTA					
		TATGCCATGCGTGCTAC					
Colorimetry	Colorimetry	CGTGAA					
		GGCGCAACAGGACCACCA	50 ± 12 nmol/L	0.4–1200 nmol/L	138 pmol/L	Tap water	Taghdisi et al. (2017)
		TGACAAATACCCATACCA					
		CCTCAATTATGCCCCATCT					
CL	CL	CCGC					
		CACGCAACAACACAACATGC	61 ± 4 nmol/L	0.5–4.0 ng/mL	0.3 ng/mL	Lake water, tap water, pond water	Xiang et al. (2014)
		CCAGCGCCTGGAAACATAT					
		CCTATGAGTTAGTCCGCC					
EIS	EIS	CACA					
		TTTTTGGGTCCCGGGTAGG	–	50–10 ⁵ pmol/L	18 pmol/L	Lake water, tap water, river water	Lin et al. (2013)
		GATGGGAGGTATGGAGGG					
		GTCCCTGTTCCCTCTTG					

LEWIF laser evanescent wave-induced fluorescence

Table 5 Applications of aptamers in the detection of allergens

Analyte	Detection system	Aptamer sequence (5' to 3')	K_d	Linear range	LOD	Sample type	Ref
Lysozyme	FIS	CAGTGTATCTACGAATTCATCAGGGC	–	0.2–4.0 nmol/L	0.07 nmol/L	–	Peng et al. (2009)
	ECL	TAAAGAGTGCAGAGTTACTTAG ATCTACGAATTCATCAGGGC	–	–	–	–	Huang et al. (2009)
	EIS	TAAAGAGTGCAGAGTTACTTAG	–	0.01–0.5 pmol/L 0–400 µg/mL	6 fmol/L 12.09 µg/mL	Egg white	Xiao et al. (2013)
SWV	SWV	ATCAGGGCTAAAGAGTGCAG AGTTACTTAG	–	–	0.38 µg/mL	–	Rohrbach et al. (2012)
				0.1–1000 pmol/L	0.1 pmol/L	–	Erdem et al. (2014)
				1.0–50.0 pg/mL	0.3 pg/mL	Egg white	Li et al. (2010)
CV	CV	ATCAGGGCTAAAGAGTGCAG AGTTACTTAG	–	5–1000 pmol/L	0.1 pmol/L	Egg white	Xie et al. (2014)
				0.5–100 nmol/L	0.2 nmol/L	–	Chen et al. (2012)
SPR	SPR	GGGAATGGATCCACATCTACGAATTC ATCAGGGCTAAAGAG	29 ± 5 nmol/L	–	2.4 nmol/L	Red wine, white wine	Xia et al. (2013)
				–	–	–	Mihai et al. (2015)
				31 nmol/L	0.5 nmol/L	–	Subramanian et al. (2013)
DPV	DPV	GCAGCTAAGCAGCGCGCTCA CAAAACCAATTCGCAATGCGGC	2.8 ± 0.3 nmol/L	5–140 nmol/L	10 nmol/L	Wine	Mishra et al. (2017)
				5 × 10 ^{−6} –5 nmol/L	4.3 fmol/L	Wine	Ocaña et al. (2015)
Ara h 1	Fluorescence EIS	TCGCACATCCGCTTCTACC GGGGGGTCGAGCGAGTG AGCGAATCTGTGGTGGG	–	200–2000 ng/mL	56 ng/mL	Biscuit	Weng and Neethirajan (2016)
				0–10 nmol/L	1 nmol/L	–	Trashin et al. (2014)
				1–15 nmol/L	1 nmol/L	–	Peeters et al. (2014)
Gluten	Chronoamperometry	CCAGTCTCCCGTTTACCGGCCTACA CATGTCTGAATGCC or CTAGGCGA AAATAGCTACAACTGTCTGAAGG CACCCAAT	–	–	0.5 ppm or 4.9 ppm	Beer, cake, flour	Amaya-González et al. (2015)

FIS Faradic impedance spectroscopy

electrodeposition on stainless steel wire using tetrabutylammonium hexafluorophosphate, triethylamine hydrochloride, $\text{Zn}(\text{NO}_3)_2 \cdot 5\text{H}_2\text{O}$, and terephthalic as raw materials. The aptamers of 2,3',5,5'-tetrachlorobiphenyl (PCB72) and 2',3',4',5,5'-pentachlorobiphenyl (PCB106) were then bound to the stainless steel wire coated with the MOF film by self-assembly method using poly (diallyldimethylammonium chloride) as polycation to fabricate an aptamer–MOF fiber. The aptamer–MOF fiber was immersed in the sample for 1 h at room temperature during the detection. The adsorbed targets were desorbed in a pH 3.0 glycine–HCl buffer (1:10, v/v) and extracted by the methylene chloride. The sample after extraction and purification was further detected with gas chromatography–tandem mass spectrometry (GC–MS). The linear range of the method was 0.02–250 ng/mL, and the LODs were 0.003–0.004 ng/mL. The recoveries of PCB72- and PCB106-spiked fish samples ranged from 89.2 to 97.1%. The aptamer of 3,3',4,4'-tetrachlorobiphenyl (PCB77) was directly used for the detection of PCB77 by Xu et al. (Xu et al. 2012). Firstly, the complementary DNAs modified by thiol were immobilized on the surface of AuNPs through Au–S bonds. The dye-labeled aptamers were combined with the complementary DNAs by hybridization reaction. The fluorescence of dye on the aptamers was quenched by AuNPs. When this probe was mixed with the sample, the PCB 77 in the sample was bound to the aptamers, making the aptamers released from the AuNP surface, and then the fluorescence signal was restored. The linear range of the method was 0.1–100 ng/mL.

Bisphenol A (BPA) is a known endocrine disruptor and one of the most serious environmental pollutants, which can threaten human health through various water sources. A portable fiber aptasensor was developed to rapidly detect BPA on-site (Yildirim et al. 2014). The surface of the fiber sensor was first modified with 3-aminopropyl triethoxysilane and glutaraldehyde, and the aminated complementary sequences of BPA aptamers were conjugated to the surface. The BPA-containing sample was then incubated with a fixed concentration of fluorescently labeled BPA aptamers, allowing the mixture to pass through the sensor surface at a flow rate of 300 $\mu\text{L}/\text{min}$. The excess aptamers that were unbound to BPA were bound to the complementary strands on the sensor surface through a hybridization reaction. When laser is inputted into the fiber at a proper incident angle, the reflected light generated on the surface interferes with the incident light, and the interference light can pass through the surface of the fiber to form an evanescent wave used as the excitation light of the fluorescent dye bound to the surface. The higher the concentration of BPA in the sample is, the lower the fluorescent signal generated on the fiber surface is. The developed aptasensor showed a response range of 2–100 nmol/L for BPA and a LOD of 1.86 nmol/L. This method has been used for the detection of BPA in wastewater, and the recoveries were between 91 and 110%.

Table 6 Applications of aptamers in the detection of organic pollutants

Analyte	Detection system	Aptamer sequence (5' to 3')	K_d	Linear range	LOD	Sample type	Ref
BPA	Fluorescence	CCGGTGGGTGTCAGGTGGG ATAGCGTTCCGCGTATGGCCAGC GCATCACGGGTTCGCACCA	8.3 nmol/L	2–100 nmol/L	1.86 nmol/L	Wastewater	Yildirim et al. (2014)
	Colorimetry			10–80 ng/mL	1.86 ng/mL	Tap water	Li et al. (2016c)
	PEC			–	1.50 nmol/L	Tap water, river water	Zhang et al. (2016)
	SWV			1–1000 nmol/L	0.5 nmol/L	Drinking water, liquid milk	Qiao et al. (2016)
	DPV			1–100 pmol/L	0.19 pmol/L	Tap water	Yu et al. (2016)
PCB72 PCB106	GC-MS	CACTCGGACCCCAATCTCCCTCCATC CCTCATCCGTCCAC	–	0.01–10 $\mu\text{mol}/\text{L}$	5 nmol/L	Milk	Zhou et al. (2014a)
				0.02–250 ng/mL	0.003–0.004 ng/mL	Fish	Lin et al. (2016b)
PCB77	Colorimetry	GGCTACGAAGTAGTGATTTTCCGA TGGCCCGTG	–	0.5–900 nmol/L	0.05 nmol/L	Water	Cheng et al. (2018)
	Fluorescence	GGCGGGGCTACGAAGTAGTG ATTTTTCGATGGCCCGTG	4.02 $\pm$ 0.54 $\mu\text{mol}/\text{L}$	0.1–100 ng/mL	0.5 ng/mL	–	Xu et al. (2012)
	DPV			0.2–200 ng/mL	0.01 ng/mL	Tap water	Wu et al. (2016a)
	SERS			0.01–10 $\mu\text{mol}/\text{L}$	33 nmol/L	–	Sun et al. (2016)

The applications of aptamers in the detection of organic pollutants are shown in Table 6.

Development and Prospect

Aptamers are of high stability, have the wide applicability to various targets, and are easy to be high purely synthesized. These advantages that are significantly superior to antibodies make them a broad application prospect.

Aptamers considered as an ideal molecular recognition element have been fused with various detection technologies used in food safety inspection, such as fluorescence, electrochemistry, nanotechnology, SERS, SPR, colorimetry, etc. This fusion leads to the appearance of a new detection methodology with both high selectivity and high sensitivity. The aptamer-applicable analyte types are also wide. It should especially be pointed out that aptamers are used for the detection of pathogens. The aptamer-based detection methods for pathogens, compared with conventional detection methods, show greater advantages, and their improvements are revolutionary. However, compared to a great number of pesticides and veterinary drugs that have been developed, the number of aptamers that can highly specifically and selectively identify them is far from the needs of actual testing. Therefore, screening more aptamers useable for the detection of pesticides and veterinary drug residues will become a shortcut to solve this problem. Perhaps, the aptamer-based detection methods are the final resolution way of the rapid and on-site qualitative or quantitative analysis for pesticide or veterinary drug residue, especially for multi-residues of pesticide or veterinary drug with common functional groups. In addition, as far as we know, it is still very rare to apply aptamers for the detection of parasitic ovum, which suggests another potential development direction of aptamer application.

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Compliance with Ethical Standards

Conflict of Interest Guan-Hua Chen declares that he has no conflict of interest. Shang-Hong Song declares that she has no conflict of interest. Zhi-Fei Gao declares that he has no conflict of interest. Xin Guo declares that she has no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

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