

REVIEW

Electrochemiluminescent functional nucleic acids-based sensors for food analysis

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Funding information

National Sciences Foundation of China, Grant/Award Numbers: 81773894, 21775026, 212157502 and 521575027; Natural Sciences Foundation of Fujian Province, Grant/Award Numbers: 2014J05013 and 2016J01396; Program for Changjiang Scholars and Innovative Research Team in University, Grant/Award Number: No. IRT15R11; University of Fujian Province, Grant/Award Number: 2018Y4007

Abstract

Foodborne contaminants widely exist in foods, which can lead to various foodborne diseases and food safety issues. The development of quick, sensitive and universal analytical approaches for foodborne contaminants is imperative. Electrochemiluminescent functional nucleic acids (ECL FNAs)-based sensors are a series of sensing devices using FNAs as the recognition elements and ECL as the transducer. Contributing to the specific recognition ability of FNA and the high sensitivity of ECL, ECL FNA-based sensors are considered to be of great application potential for foodborne contaminants monitoring. This review mainly presents the applications of ECL FNA-based sensors for foodborne contaminants (including microorganisms, mycotoxins, allergens, antibiotics, heavy metal ions, pesticides and some illegal additives). In general, the application of ECL FNA-based sensors in the field of food analysis is just in its infancy. Although there are several limitations and challenges, it is envisaged that ECL FNA-based sensors will have broad prospects for food analysis in the future.

KEYWORDS

electrochemiluminescent (ECL), functional nucleic acids (FNAs), sensor, foodborne contaminants

1 | INTRODUCTION

At present, foodborne diseases have commanded increasing worldwide attention because they can lead to a series of food safety problems, and an increase the social and economic burden. Foodborne diseases are mainly originated from different contaminants, including heavy metal ions, biotoxins, organic dyes, food allergens, illegal additives, pathogenic microorganisms, and antibiotics. To ensure food safety and control the appearance of foodborne diseases, the monitoring of these possible contaminants in foods is very significant. Undeniably, traditional analytical techniques for these contaminants^[1,2] need

time-consuming detection processes, expensive equipment, and well-trained testing staff. In addition, antibody-based enzyme linked immunosorbent assay (ELISA)^[3] is also widely utilized to monitor various contaminants. However, the acquisition of antibodies is faced with many issues, such as ethical problems, instability of monoclonal, and the time-consuming and costly production process.

Single-stranded nucleic acids can hybridize with complementary sequences through Watson-Crick base pairing. In recent decades, some single-stranded nucleic acids have evolved through a systemic evolution of ligands by an exponential enrichment (SELEX) technique. Some of them can recognize various targets of non-DNA or RNA by

folding three-dimensional structures, called as aptamers.^[4] Others can bind with the co-factor (metal ions or hemin) exhibiting catalytic activity, called as nucleic acid enzymes (NAEs).^[5,6] Aptamers and NAEs are named as functional nucleic acids (FNAs), which exhibit high affinity to recognize various analytes. Meanwhile, FNAs exhibit several advantages that include low-cost and ease of synthesis, storage and modification, which is superior to antibodies to some extent. Due to these advantages, FNAs as promising recognition elements have been widely applied in drug screening, disease diagnosis, environmental monitoring, and national defense security.

Electrochemiluminescent (ECL) is chemiluminescence from the electrochemical reaction of ECL-active species. As a powerful analytical tool, ECL has received considerable attention owing to high sensitivity, simplicity of operation, and controllable light emission. Common ECL-active species contain transition metal complexes (i.e. ruthenium, iridium, and platinum) and polyaromatic hydrocarbons (luminol and acridinium esters).^[7,8] Nanomaterials (e.g. semiconductors,^[9–14] noble metal nanoclusters,^[15–18] and carbon materials^[19–22]) also exhibit remarkable ECL behavior. Generally, these ECL-active species can generate obvious ECL response with the help of co-reactants, such as $\text{S}_2\text{O}_8^{2-}$,^[23] tri-*n*-propylamine,^[24] dibutylaminoethanol (DBAE),^[25] H_2O_2 ,^[26–28] and $\text{C}_2\text{O}_4^{2-}$.^[29,30] The overall number of publications involving ECL has increased year-by-year.^[31,32] A great deal of ECL luminophores and the detailed ECL mechanisms have been extensively studied by many researchers,^[11,15,21,33–38] and well summarized in several reviews.^[7,31,32,39–42] Therefore, in this review, ECL substrates and their related luminescent mechanisms are not presented in detailed.

ECL FNA-based sensors are smart devices, where FNA and ECL are used as the recognition elements and the transducer, respectively. In addition to ECL character, ECL FNA-based sensors have good specificity owing to FNA compared with ECL chemosensors. The working principle of ECL FNA-based sensors is that target-induced FNA structure switching induces the ECL probe to move away from or get close to the electrode surface, leading to a change in the ECL intensity. According to the different signal changes, ECL FNA-based sensors mainly have two different types: signal-on and signal-off, which stand for the ECL signal enhancement and decline of ECL response with the

introduction of targets, respectively. Although these two methods have their own advantages, inevitably, these single signal changes might be affected by environmental conditions, resulting in the wrong analytical results. The development of ratiometric ECL sensors, containing two ECL probes with different excitation wavelengths or excitation potentials, can overcome this issue. The introduction of targets can give rise to signal changes of the two ECL substances. The ratio of the two ECL intensities can be used to monitor the concentration of the targets. Therefore, the ratiometric ECL FNA-based sensors are more suitable in complex samples.

In recent decades, ECL FNA-based sensors have been thriving in many fields, including food safety, drug screening, disease diagnosis, life sciences, and environmental monitoring. In this review, we focus on their application of food safety, especially for the detection of food contaminants. Thus, we list several common food contaminants, and introduce their detection methods involving ECL FNA-based sensors. Then, we present the prospect of ECL FNA sensors in the future.

2 | THE APPLICATION OF ECL FNA-BASED SENSORS IN FOOD CONTAMINANTS

2.1 | Microorganisms

Microorganisms are the most numerous organisms in the world. They are various and widely distributed in the environment. Once conditions are suitable, they can rapidly grow and breed. More importantly, microorganisms are infectious and can lead to a series of fearful food-borne diseases.^[43] *Escherichia coli* is one of the most common foodborne pathogenic bacteria. Hao et al. immobilized luminol into AgBr/3D nitrogen-doped graphene hydrogel (AgBr/3DNGH) on the electrode as a solid-state ECL platform to assay *E. coli*^[44] (Figure 1). The solid-state sensing platform had a low limit of detection (LOD, 0.17 cfu/mL), and employed to assay *E. coli* in meal samples. The development of this solid-state ECL FNA-based sensor is able to decrease the consumption of the reagent and improve the signal stability.

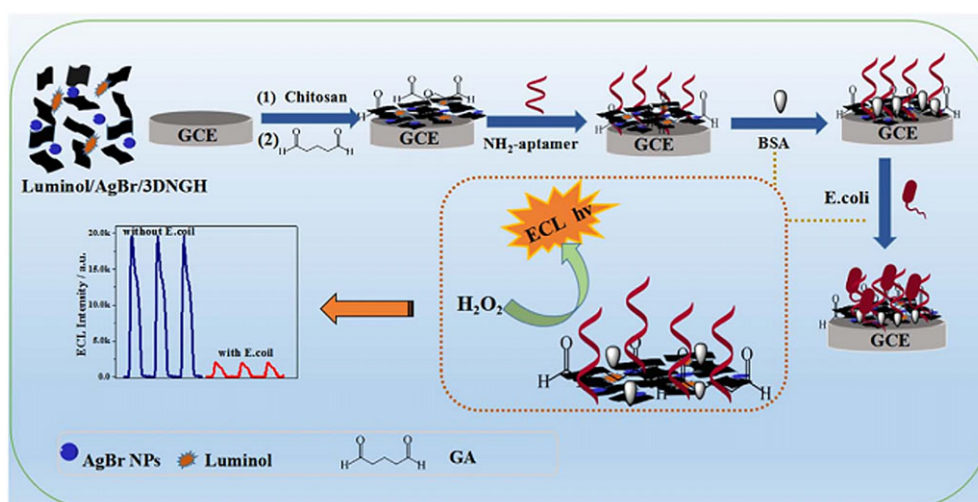
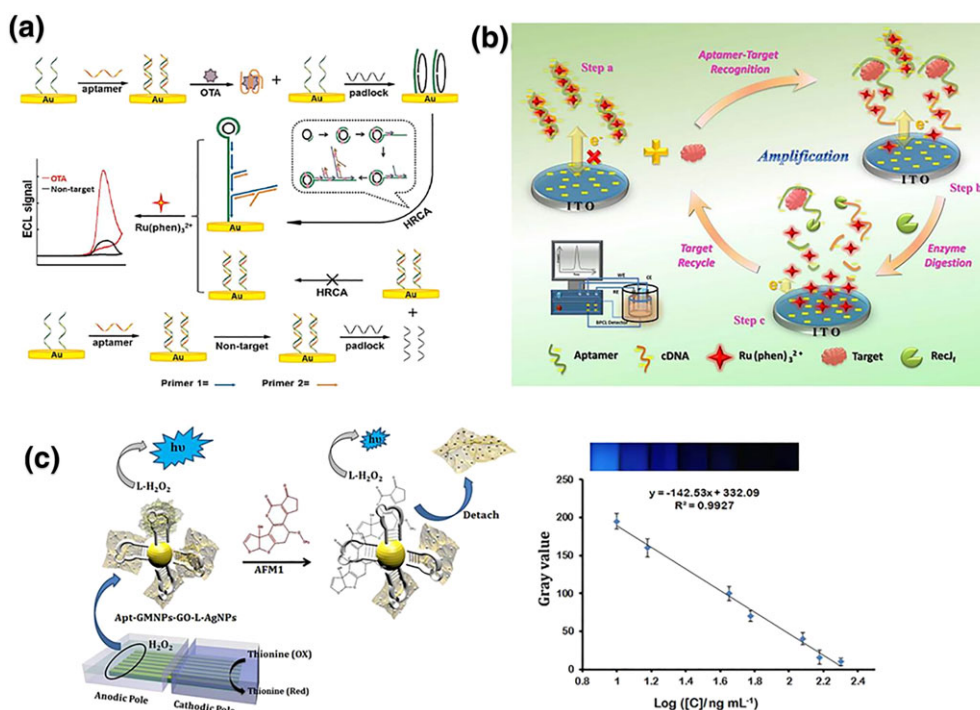


FIGURE 1 The principle of electrochemiluminescent (ECL) aptasensor for *Escherichia coli*.^[44] Copyright 2017, Elsevier

TABLE 1 Electrochemiluminescent (ECL) aptasensors for the toxins in food

Analytes	ECL probe	Limit of detection (LOD)	Real samples	Reference
OTA	Dissolved O ₂	75 fg/mL	Red wine	46
OTA	Ru(phen) ₃ ²⁺	2.0 pg/mL	Corn	47
OTA	Nitrogen-doped graphene Quantum dots	0.5 pg/mL	Peanut	48
OTA	Ru(bpy) ₃ ²⁺	3.0 fg/mL	Corn	49
OTA	N-(Aminobutyl)-N-ethylisoluminol	0.06 ng/mL	Wheat	50
OTA	Ru(phen) ₃ ²⁺	0.02 pg/mL	Corn	51
OTA	CdTe quantum dot	0.64 pg/mL	Red wine	52
OTA	Ru(phen) ₃ ²⁺	10 fM	Red wine	53
AFM 1	Luminol	0.05 ng/mL	Milk	54

**FIGURE 2** Several electrochemiluminescent functional nucleic acid (ECL FNA)-based sensors for biotoxins. (a) The ECL aptasensor based on hyperbranched rolling circle amplification (HRCA) for ochratoxin A (OTA).^[51] Copyright 2015, Elsevier. (b) The immobilization-free and label-free ECL aptasensor for OTA.^[47] Copyright 2018, Elsevier. (c) The visual ECL array for aflatoxin M1 (AFM 1).^[54] Copyright 2018, Elsevier

2.2 | Mycotoxins

Mycotoxins are toxic secondary metabolites of filamentous fungi, which have severe toxicity, and may give rise to teratogenic effects on people and animals. They are usually found in moldy foodstuffs, containing crops and animal feed, even beverages and dried fruits.^[45] In more than 300 found toxins, zearalenone, deoxynivalenol, aflatoxins, ochratoxins, and fumonisins have more fatal toxicity. Table 1 lists the application of ECL aptasensor for common toxins in food. Ochratoxin A (OTA), one kind of ochratoxins, has been extensively studied because it is a potential carcinogen.^[46–53,55] Using *N*-(4-aminobutyl)-*N*-ethyl-isoluminol (ABEI) as the ECL probe, Wang et al. reported a simple ECL aptasensor for OTA with a LOD of 0.007 ng/mL.^[50] For the sake of improving the sensitivity, various amplification strategies were introduced. Our group fabricated a signal-on ECL aptasensor for OTA^[51] (Figure 2a). With the assistance of DNA polymerase,

OTA-induced the hyperbranched rolling circle amplification (HRCA) generated a great deal of double-stranded DNAs (dsDNAs).^[56] Thus, dichlorotris(1,10-phenanthroline)ruthenium(II) hydrate (Ru(phen)₃²⁺), as an ECL indicator, can intercalate into the grooves of dsDNAs on the electrode. As a result, this aptasensor exhibited high sensitivity (LOD of 0.02 pg/mL) and selectivity, and was used to assay OTA in corn samples. In this work, the application of the intercalated ECL probe not only enhances the ECL signal, but also avoids the complex functionalization of the probe. In consideration of the complexity and reproducibility of the immobilization of DNA,^[57,58] taking advantage of this intercalated ECL probe, we also designed a label-free ECL aptasensor via different electrostatic interactions and exonuclease-catalyzed amplification^[47] (Figure 2b). Recently, the nano-scale DNA structures have attracted more interest due to their predictable geometric structures, which can be obtained by self-assembly of DNA without enzyme.^[59] The DNA nanostructures also

have been employed to develop aptasensors. Chen et al. demonstrated an ECL aptasensor based on the target-initiated hybridization chain reaction (HCR).^[46] It had a low LOD of 75 fg/mL for OTA, and was employed in the real sample (red wine). Similarly, they also reported another ECL aptasensor for OTA based on loop-mediated isothermal amplification.^[53] Semiconductor quantum dots (QDs, also named as semiconductor nanocrystals) are very important luminescent nanomaterials, whose ECL behaviors can be tunable by changing elemental composition and preparation technology. Using CdTe QDs as the ECL nanomaterials, Yang et al. introduced an ECL aptasensor for OTA.^[52] With the help of exonuclease-catalyzed target recycling amplification, this highly sensitive ECL aptasensor showed a LOD of 0.64 pg/mL, and is able to detect OTA in red wine. In the earlier mentioned ECL strategies, ECL signals were usually monitored by a photomultiplier tube. Interestingly, a smartphone with ImageJ software used to recognize the images was also applied to monitor ECL intensity. Khoshfetrat et al. chose aflatoxin M1 (AFM 1, the highest toxic aflatoxin) as the target to present a visual ECL aptamer bipolar electrode (BPE) array^[54] (Figure 2c). The ECL response was visualized by transferring ECL intensity to ECL image gray value through ImageJ software. As a result, this visual ECL array showed a wide linear range (10–200 ng/mL) and low LOD.

2.3 | Allergens

Food allergens are ingredients in food that can cause an abnormal immune response.^[60] They influence about more than 2% of adults and 8% of children because they can trigger different levels of allergic reactions.^[61] The range of allergic reactions can range from mild local reactions to severe life-threatening allergies. At present, it is difficult to understand the pathogenesis of food allergies and cure allergic constitution. However, it is still possible to monitor allergens to avoid the exposure of allergens to susceptible populations. Lysozyme, as one of the major food allergens, has been studied in the past decade. Wang and coworkers used 2-(dimethylamino)ethanethiol (DMAET) as an

efficient co-reactant to fabricate an ECL aptasensor for lysozyme. The addition of lysozyme could displace DMAET-capped lysozyme to achieve the detection of lysozyme.^[62] They also demonstrated another similar displacement ECL aptasensor for lysozyme with a LOD of 1.0×10^{-13} mol/L.^[63] Beside these displacement assays, Zhu and coworkers reported a QD-based ECL aptasensor based on lysozyme-induced structure switching.^[64] In these ECL aptasensors, ECL probes-labeled DNAs or targets are obtained by complex cross-linkers and purification processes, which were time-consuming and of low yield. The development of label-free ECL aptasensors could overcome these drawbacks.^[47–49] Wang et al. used $\text{Ru}(\text{phen})_3^{2+}$ as the probe to develop an aptasensor for adenosine and lysozyme,^[65] with the linear ranges of 0.5×10^{-9} to 7×10^{-9} mol/L and 0.5 to 9 ng/mL, respectively. As indicated in Figure 3, Liu et al. prepared the ordered mesoporous silica films (MSFs) by *in situ* growth on an ITO electrode.^[66] Aptamer, as the gate, adsorbed on to the MSFs to seal ECL reagents ($\text{Ru}(\text{bipy})_3^{2+}$) in the pores of the MSFs. The introduction of target lysozyme opened the gate (aptamer), and released ECL reagents, reducing ECL intensity. This sensor had a LOD of 9.43×10^{-9} mol/L for lysozyme.

2.4 | Antibiotics

Antibiotics have been widely used in the aquaculture industry and animal husbandry to reduce animal diseases or promote animal growth. However, there are a large amount of antibiotics stored in animals due to their misuse. Thus, accumulation of antibiotics in the human body after uptaking these contaminated food will result in fearful antimicrobial resistance and various side effects. For example, the abuse of kanamycin, an aminoglycoside antibiotic, may lead to severe ototoxicity, nephrotoxicity and antibiotic resistance. Yuan and coworkers reported a label-free ECL sensing platform on tri-layer composite films on a glassy carbon electrode.^[67] This ECL sensor was employed to assay kanamycin in the milk with good selectivity. Recently, it has been noticed that gold nanoparticles

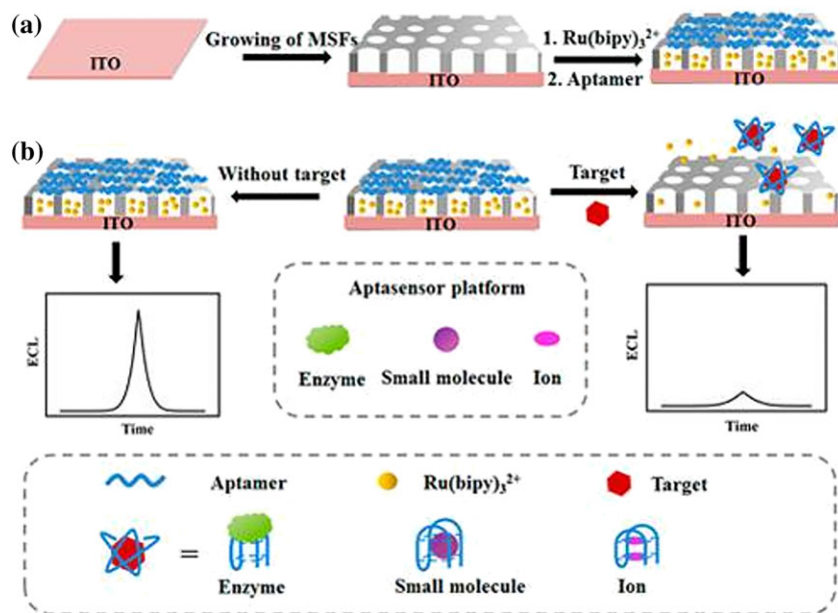


FIGURE 3 Electrochemiluminescent (ECL) aptasensor for ochratoxin A (OTA) based on aptamer-Ru@MSFs/ITO.^[66] Copyright 2016, ACS publications

(AuNPs) can effectively enhance ECL intensity from QDs when their distance was more than 10 nm, resulting from the energy transfer between surface plasmon resonance (SPR) from AuNPs and the QDs.^[38] Based on this interesting phenomenon, Miao et al. demonstrated a multi-amplification SPR ECL aptasensor for chloramphenicol (CAP), an antibiotic.^[68] This sensor was applied to assay CAP in fish samples with good accuracy. Li et al. proposed a dual recognition sensor comprising molecularly imprinted polymers (MIPs, artificially synthesized molecular recognition elements) and aptamer.^[69] This sensing platform can achieve a reversible ECL resonance energy transfer (ECRET) process by removal and re-adsorption of target lincomycin (an antibiotic against bacteria), which was used to assay lincomycin in meat samples, including chicken, duck, pork and beef. In above ECL aptasensors, the ECL response comes from the single ECL probe. This single signal output might be influenced by the external environment, resulting in the wrong analytical results. To overcome this issue, ratiometric ECL sensors were developed, where two ECL probes with different excitation wavelengths or excitation potentials were applied. Feng et al. designed a ratiometric ECL array using luminol and CdS QDs as the ECL probes, which generated an anode ECL signal and a cathode ECL signal, respectively.^[70] This ratiometric ECL array had the capacity to monitor CAP in fish samples.

2.5 | Heavy metal ions

With rapid industrialization and modern agricultural activities, vast heavy metal ions have entered into the natural environment. Once water and food is contaminated the heavy metals can enter humans by the food chain, which may give rise to adverse effects on human

health. Among these heavy metal ions, lead(II) ion (Pb^{2+}) and mercury ion (Hg^{2+}) are extensively investigated due to their toxicity. Since '8-17' DNAzyme (also named Pb^{2+} -specific DNAzyme) for Pb^{2+} was obtained,^[71] the sensors for Pb^{2+} were widely reported. Our group, for the first time, reported a highly sensitive ECL sensor for Pb^{2+} (Figure 4).^[72] DNAzyme, immobilized on the gold electrode, hybridized with Ru complex functionalized substrate strand. The introduction of Pb^{2+} catalytic hydrolyzed substrate strand into two pieces, removed away the electrode. TBR-NHS ester on the electrode decreased, causing the reduction of the ECL intensity. This ECL sensor had wide linear range ($2.5 \times 10^{-10} \sim 1.0 \times 10^{-9}$ mol/L) with a LOD of 1.1×10^{-11} mol/L. In addition, the immobilization of the ECL probe is another effective strategy for the fabrication of aptasensor. Li et al. demonstrated a solid-state ECL aptamer platform on indium tin oxide electrode consisting of CdS QDs and gold nanodendrites.^[73] Using this sensing platform, they achieved the detection of Pb^{2+} with a LOD of 9.6×10^{-13} mol/L. Apart from '8-17' DNAzyme, other oligonucleotides also can bind with Pb^{2+} . Guanine-rich (G-rich) oligonucleotides were capable of forming stacked arrays of G-quartets, also called as G-quadruplexes.^[74] Potassium ion (K^+)-stabilized G-quadruplexes show prominent peroxidase-like activity with the help of cofactor (hemin).^[75,76] It is indicated that Pb^{2+} can replace K^+ to obtain more stable G-quadruplexes with the switching of the structure,^[77] which would destroy its peroxidase-like activity.^[78] Thus, based on Pb^{2+} -stabilized G-quadruplexes, the researchers also developed an ECL platform for Pb^{2+} .^[79,80]

The mercury ion, a stable inorganic form of mercury, exhibits high cell toxicity. The lowest content of Hg^{2+} in drinking water must be less than 10×10^{-9} mol/L according to the Environment Protection Agency (EPA) guidelines. It is reported that Hg^{2+} can insert into T-T mismatch base pairs to form the complex T- Hg^{2+} -T by binding of the N3 nitrogen of the individual thymine base. Taking advantage of this complex structure, a large number of ECL sensors for Hg^{2+} have been designed. Li et al. developed an Hg^{2+} sensor using a collection process of magnetic beads.^[81] In this sensor, one DNA strand was linked with one ECL probe, $\text{Ru}(\text{bpy})_3^{2+}$, that is, the ratio of DNA to $\text{Ru}(\text{bpy})_3^{2+}$ was 1:1. In order to achieve signal amplification, ECL reagents are usually doped into silica nanoparticles (SNPs) as the novel ECL probe instead of single ECL reagent.^[82,83] Our group prepared $\text{Ru}(\text{bpy})_3^{2+}$ -doped SNPs (Ru-SNPs) with strong ECL signal.^[82,84] Using Ru-SNPs as the ECL probe, a highly sensitive ECL sensor was established for Hg^{2+} with a LOD of 2.3×10^{-9} mol/L. The low LOD was attributed to the ratio of DNA to ECL reagent of 1:n. Rolling circle amplification (RCA), an isothermal enzyme-assisted amplification technique, can yield vast long DNA stands with constant repeat units.^[85,86] Zhou et al. introduced the amplification of RCA to report a highly sensitive ECL sensor for Hg^{2+} .^[87] Besides the polymerase, Jiang et al. also used exonuclease I to develop ECL sensor for Hg^{2+} .^[88] Embedded ECL reagents owning high affinity with dsDNA, $\text{Ru}(\text{phen})_3^{2+}$ ^[89,90] and Ru-dppz ,^[91] have been also employed to develop label-free ECL sensors for Hg^{2+} . Except for Pb^{2+} and Hg^{2+} , other heavy metal ions (Cu^{2+} ^[92] and Ag^{+} ^[93]) were assayed using ECL FNA-based sensors. In addition, the researchers also developed ECL sensors for simultaneous detection of multi metal ions.^[94,95]

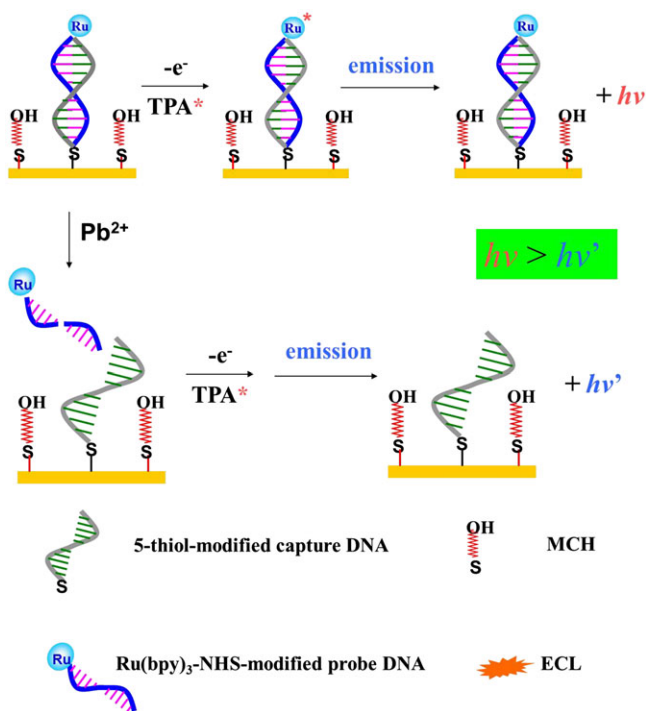


FIGURE 4 Principle of the electrochemiluminescent (ECL) DNAzyme sensor for lead(II) ion (Pb^{2+}).^[72] Copyright 2009, Royal Society of Chemistry

TABLE 2 Electrochemiluminescent (ECL) aptasensors for common illegal additives in food

Analytes	ECL probe	Limit of detection (LOD)	Real samples	Reference
MG and CAP	CdS QDs and luminol-gold nanoparticles	0.03×10^{-9} mol/L and 0.07×10^{-9} mol/L	Fishes	98
BPA	Mn ²⁺ -doped NaYF ₄ :Yb/Er upconversion nanoparticle	0.037 ng/mL	Water	99
BPA	Ru(phen) ₃ ²⁺	0.076×10^{-12} mol/L	Canned beverages	100
DES	CdS QDs	0.1 pg/mL	Fishes	101
17 β -estradiol	Ru(bpy) ₃ ²⁺	1.1×10^{-12} mol/L	Water	102

2.6 | Pesticides

Pesticides are able to destroy or control insect pests to reduce plant diseases and ensure plant growth. They have been widely used in agricultural production in many countries. Once levels of toxic pesticide residuals in the food matrices are up-taken, there is a great threat to human health.^[96] According to the chemical structure, pesticides can be classified into organochlorines, organophosphates, carbamates, and pyrethroids. Aldicarb is a carbamate insecticide, which has attracted great concern for human health due to its toxicity and widespread application. Li et al. suggested an ECL aptasensor on a self-assembled nanomaterial modified glassy carbon electrode (GCE). The complex nanomaterials were made up of AuNP, the sixth-generation poly(L-arginine) dendrimer (DPA6), Ru(bpy)₃²⁺ and multi-walled carbon nanotubes (MWCNTs).^[97] The introduction of target removed the aptamer from the electrode, reducing the ECL intensity. This ECL sensor possessed a wide linear range ($40 \times 10^{-12} \sim 4 \times 10^{-9}$ mol/L) and low LOD (9.6×10^{-12} mol/L). Aldicarb in farm products and water samples was also assayed through this method.

2.7 | Other illegal additives

Food additives, i.e. colorants, spices and antiseptic substances, are very significant compositions in the food industry because they can improve food quality and color, and are propitious to food preservation and processing. However, some illegal additives as food additives are added into foods. Various ECL FNA-based sensors have been developed to detect these illegal additives (as shown in Table 2).

Malachite green (MG), an industrial dye, is used as a fungicide and disinfectant in the fish farming industry due to its outstanding antibacterial property. However, the acute toxicity of MG threatens humans and animals. Feng et al. reported a dual-potential ECL aptamer array for the simultaneous determination of MG and CAP. Providing a LOD of 0.03×10^{-9} mol/L and 0.07×10^{-9} mol/L, respectively.^[98]

Environmental hormones can influence the transport and metabolic processes of natural hormones. Bisphenol A (BPA), an endocrine disruptor, is usually used to make plastic tableware and used in the food packaging industry. Residual BPA can transfer from the package material to the food and water, and consequently pose a risk to fetuses, infants, and young children. Therefore, the determination of BPA is highly important for food safety. Our group used Ru(phen)₃²⁺ as the ECL probe to construct an ECL aptasensor for BPA.^[100] As a result, it showed a LOD of 0.076×10^{-12} mol/L for BPA. Meanwhile, using this sensor, the migration of BPA in various drinks transferred from the can was investigated. Graphite-like carbon nitride (g-C₃N₄),

a stable semiconductor, has a band gap of about 2.7 eV. It exhibits excellent ECL activity,^[103] therefore it is considered as a promising ECL probe. Chen et al. constructed an Au-g-C₃N₄ film electrode with strong ECL response. Then, polyelectrolyte and aptamers were successively assembled to form complex film onto this electrode as the ECL aptasensor for BPA.^[104] The introduction of BPA bound with aptamer, destroyed the complex films, which influenced the permeability of the film, resulting in the recovery of an ECL response. Taking advantage of this sensing platform, a LOD of 0.05 ng/mL for standard BPA was achieved. Upconversion nanoparticles (UCNPs) were also proposed as a novel ECL probe owing to their characteristic optical properties. Manganese ion (Mn²⁺)-doped NaYF₄:Yb/Er UCNP, was modified with DNA strand to fabricate ECL aptasensor for BPA with a LOD of 0.037 ng/mL.^[99] If diethylstilbestrol (DES), an additive usually added to animal feeds, is taken into the body at very low concentrations, the secretion and transport of natural hormones will be destroyed. Jiang et al. reported antibody-free ECL sensor for DES based on MMIP and CdS QDs.^[101] As a result, this sensor with a LOD of 0.1 pg/mL was applied to assay DES in fish samples.

3 | CONCLUSIONS

Food safety issues have attracted great attention with the globalization of the food market, and foodborne contaminants are the main sources of food safety issues. Therefore, it is necessary to develop simple, sensitive and universal monitoring strategies for foodborne contaminants. FNAs, consisting of aptamer and nucleic acid enzymes, could selectively bind with diverse foodborne contaminants. Furthermore, ECL exhibits lots of superiorities, including high sensitivity, good operability, and low background signal. With the combination of the merits of FNA and ECL, FNA-based ECL sensors have broad prospects in the food safety fields.

Although FNA-based ECL sensors have been employed to assay various foodborne contaminants, they are still faced with several challenges. Firstly, a single foodstuff matrix is a very complex system, which may contain numerous co-existent contaminants. However, the present FNA-based technologies always aim at a single target, which might be unadaptable for simultaneous detection of multi-analyte. For different FNAs, the affinities to their targets and the optimal operational conditions may be of great difference. This will hamper the development of high-throughput and multi-analyte FNA-based sensors. Secondly, since the selection process of aptamers is complex and time-consuming, many types of foodborne contaminants do not yet have a corresponding FNA. In this case, the monitoring of the contaminants without a corresponding FNA have to resort to

antibodies or other recognition elements. Additionally, the structural and functional characteristics of some FNAs might be vulnerable to the change in the environment, and ECL signal is also susceptible in complex solutions, which make it difficult for real sample detection.

Although the FNAs-based ECL method for foodborne contaminants is still faced with challenges, in general, it is holding promising prospects with dealing with the earlier mentioned issues. Several novel equipment and methods are used to monitor ECL intensity. It is reported that ECL intensity also can be monitored through some portable devices, such as smartphone and CCD camera, even the naked eye, which is beneficial to achieve quick and online detection of food foodborne contaminants. In the future, the development of low-cost, quick and miniaturized analytical technologies will be an important mainstream in this field. Furthermore, with the evolution of effective FNA selection techniques, like Microfluidic SELEX, Automated SELEX, more FNA involved foodborne contaminants will be obtained, which can boost the development of ECL FNA-based sensors.

ACKNOWLEDGEMENTS

This project was financially supported by National Sciences Foundation of China (81773894, 21775026, 2121575025, and 21575027), the Natural Sciences Foundation of Fujian Province (2014J05013, and 2016J01396), the Program for Changjiang Scholars and Innovative Research Team in University (No. IRT15R11), and the cooperative project of production and study in University of Fujian Province (2018Y4007). Dr. H. Xu and Dr. X. Zhu also thank the University Distinguished Young Research Talent Training Program of Fujian Province.

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How to cite this article: Xu H, Zhu X, Wang J, Lin Z, Chen G. Electrochemiluminescent functional nucleic acids-based sensors for food analysis. *Luminescence*. 2019;1-8. <https://doi.org/10.1002/bio.3596>