Academic Journal of Science and Technology
ISSN: 2771-3032 | Vol. 11, No. 2, 2024

Research Progress on Electrochemical Sensors based on Metal-Organic Framework Materials for the Detection of Mycotoxins in Food

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Abstract: Mycotoxins, with their teratogenic, carcinogenic, and mutagenic effects, pose a significant threat to food safety, socio-economic development, and human health. They are commonly found in cereal crops at concentrations that are difficult to detect, necessitating rapid, sensitive, and accurate detection methods. Metal-Organic Framework (MOF) boasts advantages such as a high specific surface area, high porosity, tunable structures, good conductivity, and stability, making them widely used as excellent metallic materials. Recently, many have made progress in constructing electrochemical sensors based on MOF in combination with metal nanoparticles, porphyrins, polycyclic aromatic hydrocarbons, graphene, etc., for the detection of mycotoxins in food, achieving promising results. In this review, we discuss the harmful effects of mycotoxins, list the regulatory standards for mycotoxins in food set by different organizations and countries, and highlight the methods for detecting common mycotoxins in food using MOF-based electrochemical sensors, providing a reference for subsequent detection of mycotoxins in food.

Keywords: Metal-Organic Framework; Electrochemical Sensor; Mycotoxins; Aflatoxins; Ochratoxin A; Zearalenone; Deoxynivalenol.

1. Introduction

Food constitutes the material foundation for the development of human society. In recent years, with the outbreak of foodborne pathogen incidents, such as the detection of dioxins in eggs and Salmonella in fast food, food safety has become a global concern, affecting people's physical and mental health and life safety [1]. However, improper operations by producers during the processes of food raw material cultivation, food processing, packaging, transportation, and storage can often lead to the introduction of harmful substances.

Mycotoxins are one of the common harmful substances found in food [2]. Produced by fungi, which are eukaryotic organisms lacking chloroplasts and plastids and are typical heterotrophic organisms that reproduce in the form of spores with a rapid reproduction rate, mycotoxins are secondary metabolites produced by fungi in food or feed under mild environmental conditions. They are a class of harmful substances with very strong toxicity, mainly contaminating agricultural products, and are thus commonly found in grains such as soybeans, wheat, oats, peanuts, corn, and feed [3]. Mycotoxins vary in type, including Aflatoxin (AF), Ochratoxin A (OTA), Zearalenone (ZEN), Citrinin (CIT), Patulin (PAT), Mucoryne, Ergot alkaloids (EAs), Citrinin (CIT), Fumonisins (FUM), Deoxynivalenol (DON), among others. Among them, Aflatoxin B1 (AFB1) is the most toxic type of mycotoxin, and the most commonly observed mixture of mycotoxins in grains and products includes Deoxynivalenol, Zearalenone, Fumonisins, and the combination of Fumonisins and Aflatoxins [4]. Mycotoxins can easily enter the food chain, not only destroying the nutrients in food and causing the loss of nutritional components but also leading to corresponding economic losses for contaminated agricultural products or feed and posing severe health risks to humans. More than 30 types of mycotoxins are known to pose potential hazards to humans. Intake of more than 1mg can potentially lead to food poisoning, weight loss, decreased immunity, and an increased risk of cancer, while an intake exceeding 20mg could be fatal [5]. Zhu and others have observed various toxic effects of mycotoxins in animals and humans, such as immunosuppression, carcinogenicity, genotoxicity, teratogenicity, and mutagenicity [6]. In 2002, the World Health Organization pinpointed contamination of agricultural products with mycotoxins as a principal factor behind foodborne illnesses [7]. Therefore, the development of methods for detecting mycotoxins is of great significance in ensuring human health, highlighting the concentration and residue of contaminants like mycotoxins as important indicators of food safety and health.

To limit the presence of mycotoxins in food and ensure food safety, countries and organizations such as China, the United States, Japan, the European Union Committee (EU), and the Codex Alimentarius Commission (CAC) have established regulatory standards based on the dietary structures of their populations and food safety monitoring data. A comparative study on the regulatory standards for different mycotoxins established by various organizations and countries shows discrepancies that stem from distinct climatic conditions, geographical settings, and the types of crops that are characteristic to each area. The regulatory standards for AFB1, FB, and DON are relatively similar between China and the United States, while France and Chile have similar regulatory standards for ZEN. China and the EU have similar standards for OTA, as shown in Table 1.

Common methods for the detection of mycotoxins include bioassay, chromatographic analysis (high-performance liquid chromatography, gas chromatography, thin-layer chromatography), immunological methods (enzyme-linked immunosorbent assay, colloidal gold immunochromatography, thin-layer chromatography), and

mass spectrometry analysis (inductively coupled plasma mass spectrometry) [8]. The bioassay is straightforward and yields direct results but lacks selectivity and sensitivity [9]. Chromatographic analysis has a high separation efficiency and fast analysis speed but is relatively poor in qualitative capability. Among these, thin-layer chromatography is cost-effective and simple in equipment but involves complex sample preparation, low sensitivity, and lacks quantitative analysis capabilities; high-performance liquid chromatography boasts high sensitivity, efficiency, and a broad application range but comes with high equipment costs. Table 2 encapsulates the core principles, benefits, and drawbacks of these techniques. It highlights that both thin-layer chromatography and enzyme-linked immunosorbent assay are challenged by their limited sensitivity. Moreover, the transformation of mycotoxins' original molecules into diverse structures can render traditional detection techniques ineffective in identifying the various forms of mycotoxins [4]. As a result, there is a need for detection techniques that are efficient, sensitive, and precise, while also being accessible to users. Lately, there's been a shift towards adopting innovative sensor-based strategies for detecting mycotoxins in food. This trend is due to their cost-effectiveness, exceptional stability, dependable consistency, and high sensitivity.

Recent sensor-based innovations utilize diverse sensors for the rapid detection of contaminants, converting biological responses into signals that are easy to interpret. These techniques vary based on the principle of signal transduction used by the sensor, encompassing methods such as electrochemical, fluorescence, colorimetric, biosensing, electrochemiluminescence, electrochemical immunosensing, and Surface Enhanced Raman Scattering (SERS), among others. Due to their ease of use, cost-effectiveness, and time-saving capabilities, these methods are widely applied in food safety testing. Specifically, electrochemical sensing techniques are notable for their affordability, user-friendliness, remarkable reproducibility, high specificity and sensitivity, excellent stability, and quick response times.

Electrochemical sensors are thus far the most commonly used type of sensors, divided into various types such as amperometric, conductometric, potentiometric, impedimetric, electrochemiluminescence, and photoelectrochemical, among others. They possess advantages such as portability, low detection limits, and miniaturization, and are widely applied in the detection of fungal toxins in food.[12] Electrochemical sensors can convert the chemical signals of fungal toxins contained in the food to be tested into electrochemical signals. They are sensors that obtain analytical information from the electrical signals produced by the interaction of fungal toxins in food with the recognition layer. Depending on the nature of the fungal toxins, the characteristics of the food matrix, and the requirements for sensitivity or selectivity, various electrochemical devices can be used for environmental monitoring.[13] Electrochemical sensors consist of conductive materials (electrodes) and non-conductive components (electrolytes or the reactor cells, electrodes, and piping systems required for gas circulation).[14] Over the years, a series of electrode materials (such as carbon fiber, gold, platinum, glassy carbon, etc.) have been mixed with various nanomaterials to enhance the analytical performance of electrochemical sensors. By improving the surface area and conductivity of 2D/3D multidimensional materials, as well as introducing new means of interaction with the target analytes (such as π-π interactions), 2D/3D materials have been proven to improve the analytical performance of electrochemical sensors. Nanomaterials with different properties, such as nanocarbon materials, semiconductor materials, metals and metal oxides, quantum dots, and polymers, have been widely applied in electrochemical sensors. Therefore, electrode materials are a crucial part of electrochemical sensors, and enhancing the conductivity of electrode materials can improve the efficiency of detecting fungal toxins.[12]

Metal-organic framework (MOF) is a new type of nanomaterial, consisting of crystalline porous polymers formed by the coordination of organic ligands and metal particles. The synthesis methods include solvothermal synthesis under specific conditions, microwave-assisted, mechanochemical, electrochemical, sonochemical, in-situ synthesis, and layer-by-layer growth, among others. Due to their ordered porous structure, high porosity, adjustable specific surface area, and high affinity, MOF has been proven to be promising materials for the detection of fungal toxins in food.[15] The high surface area of MOF can concentrate fungal toxins, thereby increasing the sensitivity of fungal toxin detection; specific functional sites can achieve the specific recognition of fungal toxins through host-guest interactions; high porosity is advantageous for adsorbing a large number of molecules to be tested, strong adsorptivity, improving detection efficiency.[16] Although MOF is an ideal material for modifying electrode surfaces, its poor conductivity and mechanical properties prevent them from being used directly as electrode materials. To overcome these limitations, MOF has been modified, for example, Xu et al. [17] used MOF as carriers for metal nanoparticles (MNPs), forming MNPs/MOF composite materials to enhance the conductivity of MOF.

Electrochemical sensors based on MOF utilize MOF as materials on the electrode surface, combining the advantages of MOF and electrochemical sensing technology. The porosity, morphology, pore size, high specific surface area, electro-optical characteristics, and multifunctional features of MOF are applied in electrochemical sensors. MOF possesses channels of specific dimensions, which enable selective screening of specific analytes through size exclusion, acting as molecular sieves. The extensive specific surface area and significant porosity of MOFs support the electron movement of analytes, while their proficient charge transmission greatly augments signal outputs, thereby improving the sensitivity of detection.[18] Consequently, electrochemical sensors derived from MOF are capable of conducting straightforward, swift, and highly sensitive identification of fungal toxins in foodstuffs.

This paper categorizes the types of fungal toxins in food, reviews the detection methods of foodborne fungal toxins by MOF-based electrochemical sensors, and looks forward to the application prospects of MOF-based electrochemical sensors in the detection of fungal toxins in food. This aims to provide references and lessons for establishing sensitive and accurate detection methods for fungal toxins in the food system.

Table 1. Regulatory Limits for Mycotoxins in Food by Different Countries or Institutions

Type of Mycotoxin	Country/Institution	Food Category	Limit Standard (μg/kg)
AF (using AFB1 as an example)	EU	Infant food	0.1
		Cereals and products, herbal medicines	2
		Dried figs	6
		Peanuts, hazelnuts, Brazil nuts	8
		Directly consumed almonds, pistachios	12
	China	Infant food	0.5
		Other cereals, nuts, and products	5
		Rice and products, herbal medicines	10
		Peanuts, corn and products	20
	CAC	Directly consumed hazelnuts, pistachios, etc.	10
		Peanuts, hazelnuts, pistachios requiring processing, etc.	15
	Japan	All food items	10
	United States	Herbal medicines	5
		Peanuts and products	20
OTA	China	Wine	2
		Cereals and products, legumes and products	5
	CAC	Wheat, barley, rye	5
	EU	Infant food	0.5
		Wine and fruit wine	2
		Cereals and products	3
		Unprocessed grains	5
		Herbal medicines	20
ZEN	China	Cereals and products	60
	EU	Infant food	20
		Biscuits, bread, and other baked goods	50
		Cereal products	75
		Unprocessed crops (except corn)	100
		Processed corn and products	200
		Unprocessed corn	350
	France	Vegetable oils	200
	Chile	All food items	200
DON	EU	Infant food	200
		Baked goods	500
		Unprocessed grains (except durum wheat, corn)	1250
		Unprocessed corn	1750
	CAC	Infant food	200
		Wheat, barley, corn products	1000
		Grains for further processing	200
	China	Corn, cornmeal, barley, wheat	1000
	United States	Wheat products	1000

Note: Data sourced from [19-21].

Table 2. Principles and Advantages/Disadvantages of Different Detection Methods

Method	Principle		Advantages	Disadvantages
Bioassay [22]	Direct observation of changes in cellular metabolism and poisoning symptoms in organisms after ingestion of mycotoxins to identify the presence and quantify the levels of mycotoxins.		Simple operation, low cost	Poor selectivity, low sensitivity
Chromatographic Analysis [23]	Thin Layer Chromatography (TLC)	Analytes are separated on a thin layer and analyzed using fluorescence compared to standard samples to determine the content.	Simple operation, convenient equipment, rapid detection, easy to popularize	Complex sample pretreatment, low accuracy, low sensitivity, poor reproducibility
	Gas Chromatography (GC)	Typically used with mass spectrometry for the analysis and determination of mycotoxins that do not contain chromophores and fluorophores or have weak absorption and fluorescence in the molecules.	High efficiency, high sensitivity, good selectivity, fast analysis speed, small sample volume required, wide application range, and simple operation	Experimental results need to be compared with the color peaks of known substances or combined with methods such as mass spectrometry.
	High Performance Liquid Chromatography (HPLC)	Solid-phase extraction columns are used to separate various mycotoxins, which then enter the detector. Finally, the content is calculated by measuring the area of each chromatographic peak in the chromatogram.	High sensitivity, high efficiency, wide application range	Expensive equipment, high cost
Immunoassay [24]	Enzyme-Linked Immunosorbent Assay (ELISA)	The analyte reacts with enzyme-labeled antigens or antibodies and the antibodies or antigens on the surface of the solid-phase carrier. Quantitative analysis is based on the amount of enzyme on the solid-phase carrier.	High safety, minimal interference, low pollution, simple operation	Not highly sensitive, prone to false positives
	Colloidal Gold Immunochromatography	The analyte moves along the test strip from the sample pad to the conjugate pad, dissolving the colloidal gold reagent on the conjugate pad and binding with antibodies to produce a color reaction. The content of the analyte is determined by observing the color change.	Convenient to use, good stability, low cost, visually measurable, and non-toxic and harmless	The accuracy of the test strip highly depends on the specificity of the antibodies.

2. Detection of Mycotoxins in Food Using MOF-based Electrochemical Sensors

2.1. Aflatoxins (AFs)

According to reports by the Food and Agriculture Organization, 25% of crops worldwide are contaminated with mycotoxins annually, including aflatoxins [25]. Aflatoxins constitute a family of fungal secondary metabolites that are structurally and chemically alike, synthesized by Aspergillus flavus and Aspergillus parasiticus. They are derivatives containing bifuran rings and coumarin structures, also known as bifuranocoumarins, commonly found in agricultural products such as corn, barley, wheat, and peanuts. Aflatoxins are highly toxic, teratogenic, stable, and carcinogenic, capable of inhibiting the immune process. More than 400 types of aflatoxins have been identified, with the most common ones being B1, B2, M1, M2, G1, and G2.

Aflatoxin B_1 (AFB_1) stands out as the most hazardous carcinogen among them and was designated as a Group 1 carcinogen by the International Agency for Research on Cancer in 1993. [26]. The molecular formula of AFB_1 is C17H12O6, with a chemical structure as shown in Figure 1, a relative molecular mass of 312.27, and a melting point range of 200°C to 300°C. AFB_1 decomposes only at its melting point, while the optimal growth temperature for AFB_1 is within the range of 28°C to 34°C, and the suitable relative humidity is between 15% to 35% [27]. AFB_1 is hepatotoxic and is one of the factors that induce primary cancer, leading to acute liver damage, cirrhosis, tumors, and teratogenic effects. It also has a strong immunosuppressive toxicity, reducing the body's resistance to secondary infections by bacteria, fungi, and parasites [28]. Therefore, aflatoxin contamination represents a major risk to food safety and the well-being of humans and animals, leading to considerable economic impacts. Consequently, swiftly and sensitively identifying aflatoxins in agricultural products like grains or dairy items, including corn, peanut oil, and milk, is crucial [29].

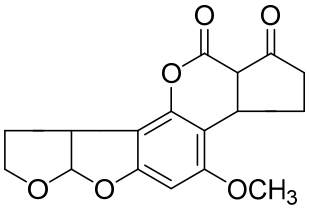

Fig 1. The structural formula of AFB_1

2.1.1. AFB_1 in Grain and Agricultural Products

AFB_1 is primarily found in grains and various nuts, commonly present in peanuts, walnuts, soybeans, rice, corn, edible oils, and other products. It directly contaminates grains, nuts, and feeds, thereby posing a direct threat to the health of humans and animals, whether consumed by humans or animals. Currently, a range of MOF-based electrochemical sensors has been engineered for the detection of AFB_1 in grain agricultural commodities.

Liao[26] and colleagues introduced a technique for crafting an aptasensor aimed at aflatoxin detection. This innovative approach incorporates the use of black phosphorus nanosheets that are embellished with gold nanoparticles to enhance the electrode. Additionally, a cerium metal-organic framework (Ce-MOF) acts as a signal marker, and electrodes are modified with prism DNA nanostructures to form the detection interface, as illustrated in Figure 2. The method capitalizes on the hybridization between prism DNA and primer probes to kickstart rolling circle amplification (RCA) on the electrode's surface. Following this, the complementary strand, adorned with AuNPs@Ce-MOF, binds to the RCA-extended strand, creating an electrochemical signal. DPV, a technique that assesses the response current by applying potential pulses of a predetermined amplitude along a linear ramp potential, is used to measure the signal. The measured response current exhibits a strong linear relationship with the logarithm of aflatoxin concentration, ranging from 24 to 10^5 pg/mL, with a detection limit reaching as low as 1.48 pg/mL. To assess the aptasensor's applicability, Liao et al. performed trials in cornmeal utilizing the standard addition technique, yielding a recovery accuracy ranging from 97.7% to 106.4%. The experimental results indicate that this aptasensor has high sensitivity and can achieve rapid detection of aflatoxin.

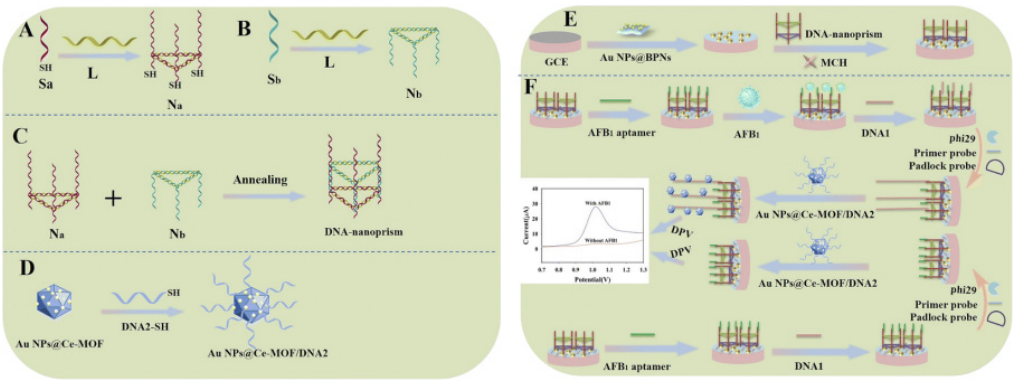

Fig 2. Schematic illustration of (A) the preparation of the lower Na structure of DNA nanoprism, (B) the preparation of the upper Nb structure of DNA nanoprism, (C) the preparation of DNA nanoprism, (D) the preparation of Au NPs@Ce-MOF-modified DNA2, (E) modification of DNA nanoprisms on electrode surfaces, (F) the aptasensor based on DNA nanoprism structure for detection of AFB_1.

Wei et al. [31] utilized ferrocene and DNA Walker for signal enhancement (as shown in Figure 3), developing a novel reagent-free aptamer sensor for the detection of AFB_1. The DNA Walker, a nanoscale automaton, propels itself along a designated pathway through the catalytic action of a DNA enzyme or a substitution reaction, transforming mechanical into chemical energy. This movement of the DNA Walker triggers the activation of numerous signal molecules, leading to substantial signal enhancement.[32] The interaction of AFB_1 with its specific aptamer triggers a DNAzyme sequence,

which in turn methodically splits the substrate chain attached to ferrocene in the presence of Mn^{2+}, causing an alteration in the electrochemical signal. Mn^{2+} is then integrated into the metal-organic framework UiO-66(Zr)-(COOH)2, which is combined with the DNA Walker mechanism. This configuration allows the sensor to commence the cleavage reaction absent Mn^{2+}, facilitating the continuous observation of AFB_1. Differential pulse voltammetry is employed for the sensor's monitoring activities. Under ideal conditions, this sensor showcases a linear response range from 0.1 pg/mL to 106 pg/mL, with a notably low detection threshold of 4.81×10^{-3} pg/mL. Impressively, the sensor has been effectively used for AFB_1 detection in peanut oil samples, achieving a recovery accuracy of 96.9 to 105.0%, which satisfies the requirements for practical applications. This investigation confirms the sensor's high specificity and sensitivity, proving its capability to accurately detect real samples and establishing a robust foundation for the effective, quick, and sensitive identification of AFB_1 in foods.

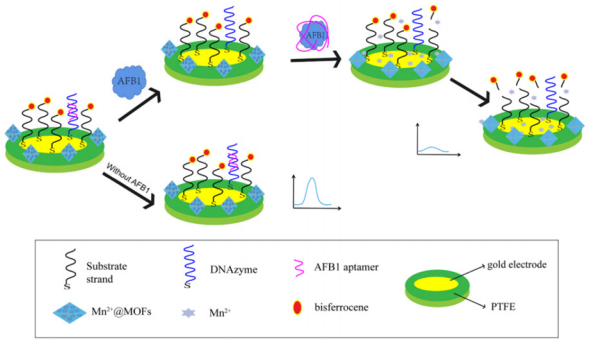

Fig 3. Schematic diagram of E-AB sensor detection based on DNAzyme-driven DNA walker signal amplification strategy

Dehaghani [33] and the team developed an innovative aptasensor for the detection of AFB1 in rice flour, utilizing gold nanoparticles synthesized on nickel-based metal-organic framework nanosheets (AuNPs/Ni-MOF) combined with the electroactive marker polybrominated biphenyl (PBP). The AFB1-specific aptamer was affixed to this composite and hybridized with its cDNA. Introducing Pyrenebutyrate (PBP) into the double-helix structure of the cDNA aptamer allowed the AFB1-altered AuNPs/Ni-MOF electrode to generate an electrochemical signal upon AFB1 contact. The performance of the aptasensor was evaluated through EIS and (CV. EIS measures the impedance at the electrode surface over various frequencies, showcasing results via the amplitude and phase shift of the signals. Conversely, CV assesses the current's reaction to voltage shifts between the working and reference electrodes. This aptasensor exhibited a linear detection range for AFB1 from 5.0 to 150,000 pg/mL, with a detection threshold of 1.0 pg/mL. Applied to rice flour samples, the sensor reported a recovery accuracy between 96% and 103%, affirming its precision and underscoring its suitability for accurate AFB1 measurements in food items.

Dehaghani [35] and their research team devised an electrochemical aptasensor with enhanced sensitivity and specificity for the detection of AFB_1 in wheat. They adopted a solvothermal approach to create Cu-MOF, later utilized to augment a Glassy Carbon Electrode (GCE), as illustrated in figure 4. The Cu-MOF's morphology, structure, and size were thoroughly examined using techniques such as Field Emission Scanning Electron Microscopy (FE-SEM), Energy Dispersive X-ray Spectroscopy (EDS), X-Ray Diffraction (XRD), and Fourier-Transform Infrared Spectroscopy (FT-IR). This detailed analysis demonstrated the pivotal role of Cu-MOF in firmly attaching the AFB_1 aptamer, largely due to its expansive surface area. The assembly of the sensor employed CV and EIS methods, with ferro/ferricyanide serving as the redox mediator. This setup demonstrated that the interaction with the AFB_1 aptamer significantly increased electron transfer resistance, underlining the sensor's effective mechanism.

The EIS technique facilitated the sensor's quantitative analysis, uncovering a linear detection span from 1.0 to 2×10^5 pg/mL and a detection threshold of 0.83 pg/mL. Dehaghani and their group successfully applied this method to determine AFB_1 in wheat, resulting in a recovery efficiency of 97.8% to 105.5%. Therefore, this sensor demonstrates viable application in enhancing food quality and safety.

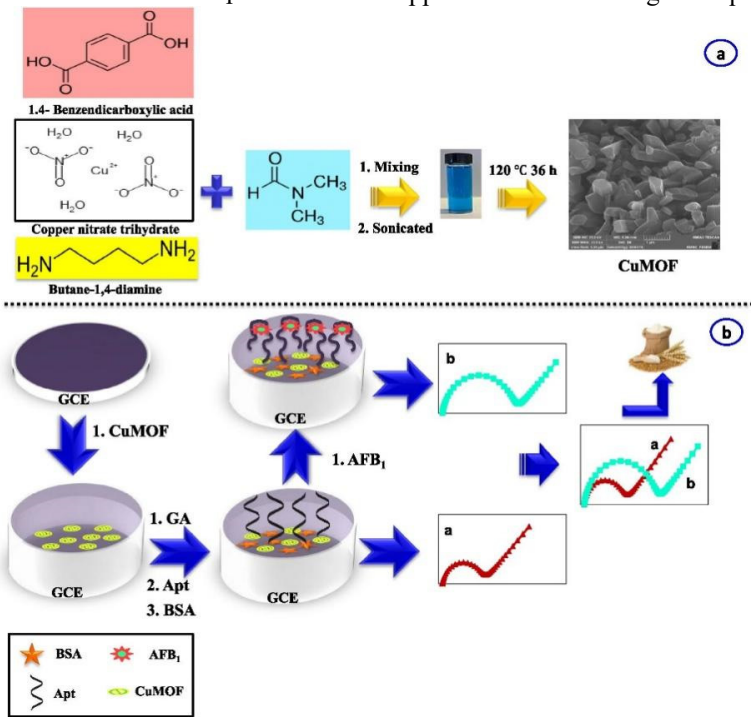

Fig 4. Schematic presentation of the preparation process of (a) CuMOF and (b) AFB_1 electrochemical aptasensor

Meng et al. [36] embedded four pyrrolic nitrogen atoms into the rigid framework of porphyrin. Through the strong interaction between the porphyrin framework and pyrrolic nitrogen atoms, they constructed a titanium-based porphyrin metal-organic framework coordinated with platinum (Ti-MOF-Pt) for the fabrication of an AFB_1 aptasensor. Ti-MOF-Pt exhibited a multi-vacancy morphology, exposing active sites on the surface and providing an effective contact interface. The high surface area of the MOF in Ti-MOF-Pt and the excellent electrochemical performance of Pt enhanced the sensing performance of the electrochemical sensor, successfully detecting AFB_1 in corn flour and rice. This method monitored the sensor using EIS and CV. The refined AFB_1 aptasensor demonstrated a linear detection scope from 100 to 7.5×10^6 pg/mL, with a detection threshold of 31 pg/mL. Meng and their team selected rice and corn flour as actual samples for evaluation, prepared in accordance with GB5009.22-2016 standards, and achieved recovery rates ranging from 96.05% to 104.45% through the application of the standard addition technique. The outcomes of these experiments indicate the electrochemical sensor's high specificity. Looking ahead, there's potential for this sensor to be adapted for the detection of additional food types in future studies.

Li et al [37] engineered an electrochemical aptasensor specifically aimed at the rapid detection of AFB_1 in corn samples. First, they synthesized Zr-MOF via solvothermal synthesis, and gold nanoparticles were doped in situ to create Au@Zr-MOF with good conductivity and uniform dispersion. The doped gold nanoparticles enhanced the conductivity of Zr-MOF without changing its crystalline morphology. Then, Au@Zr-MOF was covalently bound to a thiol-modified aptamer, and the sensor current was measured using electrochemical impedance spectroscopy. When AFB_1 was present, the aptamer recognized and bound to it, causing an increase in the electrochemical mass transfer resistance on the electrode surface. With rising AFB_1 concentrations, there was a corresponding increase in impedance values. This sensor quantitatively assessed AFB_1 by observing changes in impedance, showcasing a linear detection range from 0.1 to 10^4 ng/ml and a detection threshold of 0.19 pg/mL. The recovery rate for the corn samples tested ranged from 96% to 112%. This novel electrochemical aptasensor facilitates the quantitative analysis of AFB_1, demonstrating excellent specificity and consistency, and offers a fresh methodology for the precise and quick detection of AFB_1 in food products.

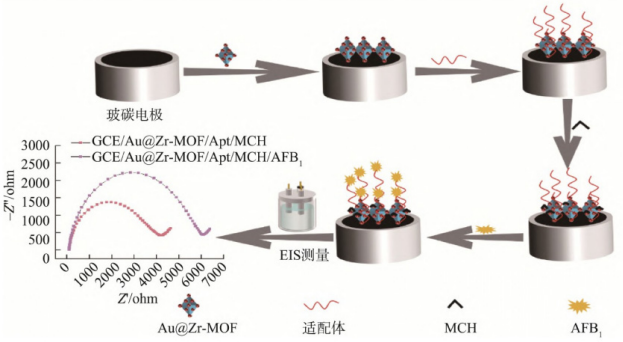

Fig 5. Construction process of electrochemical aptamer sensor

The electrochemical sensors detailed previously have all been effectively employed for identifying AFB_1 in grain-based agricultural products, evidencing extensive linear detection spans and minimal detection thresholds. These advancements represent a novel approach for the sensitive and expedited detection of AFB_1 in such products. Particularly, the technique pioneered by Wei and their team stands out for its broader detection range and lower limit of detection, a feat attributed to the adoption of an innovative signal amplification method that leverages the DNA Walker mechanism alongside a dual ferrocene configuration. This cutting-edge approach to signal amplification paves the way for further advancements in the field, inspiring ongoing research aimed at enhancing the sensitivity and speed of AFB_1 detection in cereal agricultural products.

2.1.2. AFB_1 and AFM1 in Soy and Dairy Products

When animals consume food contaminated with AFs, these toxins can be transferred to milk and dairy products and subsequently ingested by humans. As a result, aflatoxins (AFs) are often detected in soy and dairy products. However, they can also accumulate in the human body, where prolonged exposure to even low doses may increase the risk of liver cancer. Therefore, researchers such as Wang, Zhang, and others have developed MOF-based electrochemical sensors to detect AFB_1 and AFM_1 in soy and dairy products.

Wang [38] and colleagues utilized molybdenum disulfide-doped gold nanoclusters (AuNC@MoS2) as a substrate, with streptavidin-modified iron porphyrin organic porous materials loaded on AuNC@MoS2 as labels, to construct an electrochemical aptasensor based on AuNBPs@PAF-40-Fe for detecting AFB_1 in soy milk. This allowed for the quantitative detection of AFB_1. The integration of iron porphyrin with metal-organic porous materials markedly improves the catalytic efficiency of the resultant composite. Chronoamperometric analysis, which assesses the catalytic reduction current of hydrogen peroxide facilitated by AuNBPs@PAF-40-Fe, indicated that this current correlates directly with the concentration of AFB_1. Under ideal conditions, the sensor displayed a linear detection range between 50 to 8.5×10^4 pg/mL and a detection limit of 17 pg/mL. Employed for the quantitative detection of AFB_1 in real milk samples, the sensor achieved an average recovery rate of 99.28%. It exhibited remarkable selectivity, reproducibility, and stability, enhancing food safety and showing significant potential for broader applications.

Furthermore, Zheng [39] and colleagues crafted a sensor adept at the quantitative analysis of AFB_1 in authentic milk samples. To begin, they synthesized spindle-shaped, water-soluble iron-porphyrin metal-organic framework materials (PCN-223-Fe). Then, Palladium nanoparticles (PdNPs) were anchored onto the surface of PCN-223-Fe via in situ synthesis, culminating in the PdNPs/PCN-223-Fe composite. The collective action between PCN-223-Fe and PdNPs enhanced redox catalytic capabilities. Incorporating streptavidin (SA) and the PdNPs/PCN-223-Fe composite as the signal probe, the sensor employed a competitive approach for the electrochemical detection of AFB_1. It displayed a linear detection scope from 0.01 pg/mL to 10^3 pg/mL, with a notably low detection threshold of 0.018 pg/mL. Recovery rates spanned from 96.9% to 105.1%, underlining the sensor's superior selectivity, consistency, and durability.

Aflatoxin M_1 (AFM_1), which is the hydroxylated derivative of Aflatoxin B_1 (AFB_1), frequently appears in the milk of mammals that have ingested feed tainted with AFB_1. This process results in AFM_1 being a prevalent contaminant in milk and dairy products.

To enhance AFM_1 detection in milk, Kaur[40] and team

innovatively integrated molybdenum disulfide (MoS2) quantum dots (QDs) with a zirconium-based metal-organic framework (UiO-66-NH2), resulting in a novel nanocomposite material. MoS2 quantum dots are known for their substantial theoretical capacity and robust electrochemical performance, whereas MOF is characterized by their high charge transfer resistance. Consequently, the synergistic combination in the MoS2/UiO-66-NH2 composite material exhibited heightened electrochemical activity, expanded surface area, and added amine functionality. This enhanced composite was then utilized to adapt screen-printed carbon electrodes, thereby devising a straightforward, sensitive, and innovative electrochemical sensor for AFM_1 detection. The sensor demonstrated a detection capability for AFM_1 ranging from 200 to 10^4 pg/mL, with a sensitivity threshold of 60 pg/mL. The utility of this sensor was further corroborated by testing spiked milk samples, confirming its efficacy in AFM_1 analysis.

Subsequently, Yang [41] and their team crafted a Molecularly Imprinted Polymer (MIP) film through the polymerization of resorcinol, leading to the creation of an electrochemical aptasensor (Apt-Au@PEIM/AFM_1/MIP–Apt/AuNPs)/GCE) that integrates both electrochemical MIP and aptamer (Apt) technologies. The integration of cAptAu@PEIM signal amplification probes notably enhanced the sensor's current signal response, thus elevating its sensitivity towards AFM_1 detection. In the presence of AFM_1 in milk, this would hinder the signal amplification probe's ability to bind to the sensor, resulting in a significant decrease in the current signal. The performance of the sensor was assessed through cyclic voltammetry. Under optimal conditions, the system demonstrated a linear detection range spanning from 0.01 to 200 nM, achieving a detection limit of 0.07 nM (S/N=3). Spiked recovery tests in milk samples for AFM_1 indicated recovery rates ranging from 96.0% to 105.6%. Utilizing both dual recognition and signal amplification technologies, this sensor presents a new and swift method for the precise detection of AFM_1 in food products.

To identify Aflatoxin B_1 (AFB_1) in non-grain food items such as soy and dairy, experts often employ improvements to electrochemical aptasensors using organic porous materials infused with iron porphyrin. Moreover, considering that Aflatoxin M_1 (AFM_1), the hydroxylated variant of AFB_1, is typically found in milk from mammals fed AFB_1-contaminated feed, investigations extend to detecting AFM_1. This process enhances the thoroughness of the screening and analysis for such toxins.

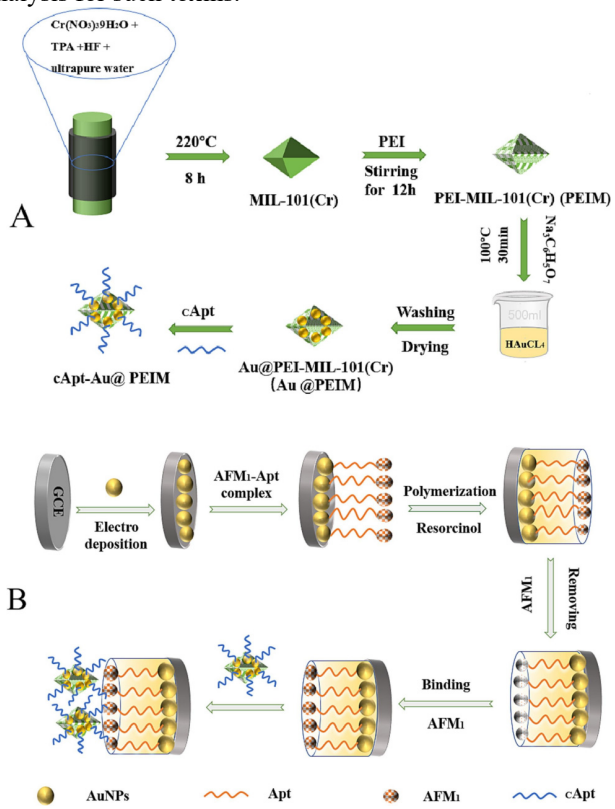

Fig 6. (A) Preparation of cApt–Au@ PEIM and (B) the sensor construction process.

Table 3. Detection of AFB_1 in Food Using MOF-Based Electrochemical Sensors

Food		Metal-Organic Framework Composites	Sensor Monitoring Method	Linear Range	Detection Limit	Recovery Rate	References
Grain agricultural products	Corn flour	AuNPs@Ce-MOF	Differential Pulse Voltammetry	24~10^5pg/mL	1.48pg/mL	97.7~106.4%	[42]
	Corn	UiO-66(Zr)-$(COOH)_2$	Differential Pulse Voltammetry	0.1~10^6pg/mL	4.81×10^{-3}pg/mL	96.9~105.0%	[31]
		Ti-MOF-Pt	Electrochemical Impedance Spectroscopy and Cyclic Voltammetry	100~7.5x10^6pg/mL	31pg/mL	96.05~104.45%	[36]
		Au@Zr-MOF	Electrochemical Impedance Spectroscopy	0.1~10^4pg/mL	0.19pg/mL	96~112%	[37]
	Rice flour	AuNPs/Ni-MOF	Electrochemical Impedance Spectroscopy and Cyclic Voltammetry	5.0~1.5x10^5×pg/mL	1.0pg/mL	96~103%	[33]
	Wheat	Cu-MOF	Electrochemical Impedance Spectroscopy and Cyclic Voltammetry	1.0~2x10^5pg/mL	0.83pg/mL	97.8~105.5%	[35]
Bean products, dairy products	Soy milk	AuNBPs@PAF-40-Fe	Chronoamperometry	50~8.5x10^4pg/mL	17pg/mL	99.28%	[38]
	Milk	UiO-66-NH2	Electrochemical Impedance Spectroscopy and Cyclic Voltammetry	200~10^4pg/mL	60pg/mL		[40]
		cAptAu@PEIM	Cyclic Voltammetry	0.01–200nM	0.07nM	96.0~105.6%	[33]
		PCN-223-Fe	Differential Pulse Voltammetry	0.01~10^3pg/mL	1.8×10^{-2}pg/ mL	96.9~105.1%	[39]

In summary, integrating MOF characterized by their high porosity, extensive surface area, and robust adsorption capabilities, with electrochemical sensors renowned for their high sensitivity and straightforward usage, has forged a novel avenue for the detection of aflatoxins in food products. This approach enhances the practicality of aflatoxin detection in food, offering good application prospects and the potential for broad application in the detection of other harmful substances.

2.2. Ochratoxins

Ochratoxin A (OTA) primarily emerges as a secondary metabolite from Aspergillus and Penicillium genera, prevalent in daily consumed foods and raw materials like coffee, wheat flour, wine, dairy products, and fruits[43, 44]. The ochratoxin family encompasses seven structurally similar toxins, including Ochratoxin A (OTA), Ochratoxin B (OTB), and Ochratoxin C (OTC), among others[3]. Of these, OTA is recognized for its potent toxicity, widespread occurrence, and extensive contamination, posing the most significant risk to agricultural produce and ranking as the top toxin producer among ochratoxins. It exists naturally as a mycotoxin, characterized as a colorless crystalline powder with a molecular formula of C20H18CINO6 and a molecular weight of 403.8. Its chemical structure is detailed with a melting point of 169°C, a molar extinction coefficient of 5550, slight solubility in water, and high solubility in polar organic solvents and dilute sodium bicarbonate solutions[44].

Found in various agricultural products and foods like cereals, nuts, dried fruits, and wines, OTA inflicts damage on human lipids, proteins, and DNA[45]. It is notorious for its nephrotoxic, carcinogenic, genotoxic, and immunotoxic properties[46]. In farm animals, OTA primarily targets the kidneys, leading to kidney diseases and is considered a causative factor of Balkan Endemic Nephropathy (BEN). The International Agency for Research on Cancer (IARC) classified OTA as a Group 2B carcinogen to humans in 1993[47], accentuating the severe health risks it poses and underlining the importance of deploying MOF-based electrochemical sensors for its swift and sensitive detection.

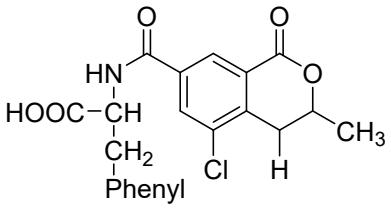

Fig 7. The chemical structure of OTA

2.2.1. Ochratoxin A in Corn

OTA is the most common, toxic, widely distributed, and significantly impactful mycotoxin contaminating agricultural products, having the closest relation to human health. OTA is commonly found in corn, representing a significant risk to both human and animal health. As a result, there has been an active pursuit in developing MOF-based electrochemical sensors aimed at the efficient and sensitive detection of OTA in corn.

Dehaghani et al. [48] established an electrochemical aptasensor capable of simultaneously determining OTA and AFB_1, two fungal toxins, in corn. Initially, the surface of the electrode was adapted by integrating a nanocomposite material, specifically AuNPs-CNDs (Gold Nanoparticles - Carbon Nanodots), which was then followed by crafting a Metal-Organic Framework known as HKUST-1-MOF, featuring copper nodes and trimesic acid. Within this framework, hemin and ferrocene were encapsulated to create hemin@HKUST-1 and ferrocene@HKUST-1, after which they were attached to aptamers designated for OTA (CDNA1) and AFB_1 (CDNA2) detection. This resulted in the formation of bioconjugated complexes. These complexes were then layered onto a Glassy Carbon Electrode (GCE), establishing a basis for the concurrent quantification of OTA and AFB_1. This sensor, modified with AuNPs-CNDs on the electrode surface, achieved the detection of fungal toxins at low concentrations with high sensitivity. Using differential pulse voltammetry, the linear detection range for OTA and AFB_1 was established at 10 to 10^5 pg/mL, with detection limits of 4.3 pg/mL for OTA and 52 pg/mL for AFB_1. The proposed dual sensor was subsequently utilized to quantify AFB_1 in corn flour, achieving a recovery rate ranging from 96.0 to 110.0%. The advantage of this electrochemical sensor is its ability to determine extremely low concentrations of OTA in actual samples with high sensitivity and accuracy, yielding satisfactory results.

Li[49] et al. engineered a dual-channel biosensor that utilizes a Zr-MOF as a signal probe, integrating fluorescence and electrochemical detection techniques for the precise identification of OTA in corn. Zr-MOFs are celebrated for their superior water, thermal, and acid-base stability, alongside their ease of synthesis and cost-effectiveness. Employing Zr-MOF as the signal probe concurrently boosts fluorescence and electrochemical signals, markedly streamlining the production process while enhancing the sensor's reusability and durability. The sensor incorporates a high-porosity gold (HPG) platform to carry DNA_1, which amplifies the electrochemical signal. The specific binding of DNA_2 with OTA prompts the release of the Zr-MOF probe into the reaction solution from the sensor surface, leading to a decrease in the electrochemical signal alongside an increase in the fluorescence response. Achieving optimal experimental conditions, the sensor demonstrates a linear OTA detection range of 0.1 to 140 pg/mL, with a sensitivity threshold of 0.024 pg/mL. This dual-channel detection strategy has been effectively employed for OTA analysis in corn samples, exhibiting rapid response, high precision, and robust anti-interference capability, signifying a forward-looking route for food safety surveillance.

Li et al. [50] developed an innovative, label-free electrochemical aptasensor for OTA detection in corn. This sensor leverages metal-organic framework nanoenzymes, specifically platinum nanoparticles embedded in manganese MOFs (PtNPs@Mn-MOF), to enhance sensitivity and specificity. First, Mn^{2+} and 2,5-dihydroxyterephthalic acid were reacted in a high-pressure autoclave to prepare Mn-MOF-74 with peroxidase enzyme activity. Then, platinum nanoparticles were loaded onto Mn-MOF-74, successfully creating the PtNPs@Mn-MOF nanocomposite material. The method characterized the stepwise modification process on the electrode surface using EIS and CV. The experiments found that the platinum nanoparticles in the composite material exhibited excellent catalytic performance, and Mn-MOF-74 could immobilize the OTA aptamer modified with a thiol group. When the target OTA is present, it specifically binds to the OTA aptamer, inhibiting the catalytic activity of PtNPs@Mn-MOF, thus reducing the nanoenzyme catalytic activity and decreasing the electrical signal, achieving

quantitative detection of OTA. The sensor exhibited a linear detection range for OTA from 10 to 3×10^5 pg/mL, with a detection limit established at 3.33 pg/mL. Investigating the sensor's effectiveness in real-world scenarios involved applying it to determine OTA recovery rates in corn, where it achieved a recovery range of 96.0 to 103.0% utilizing the standard addition method. Consequently, this sensor demonstrates its utility in the detection of OTA in actual corn samples, indicating its potential value for in-field OTA detection applications.

The aforementioned electrochemical sensors have successfully facilitated swift detection of OTA in corn, demonstrating both high sensitivity and precision, and delivering gratifying outcomes. Among them, the detection limit reported by Li and colleagues was the lowest. This is attributed to their innovative approach of employing a dual-channel method combining fluorescence and electrochemical detection. This new method leverages the individual strengths of fluorescence sensors and electrochemical sensors, resulting in higher sensitivity and better stability. It offers a novel approach for detecting other contaminants in food, illustrating the potential for broad applicability in food safety monitoring.

The contamination of wine by OTA is directly linked to its primary ingredient—grapes. Grapes, which are abundantly produced in summer and have a high sugar content, are difficult to clean and susceptible to microbial contamination. Throughout the growth, harvesting, transport, and storage phases of grapes, pathogenic microbes can infect the fruits, making OTA a common contaminant in wine.[51] OTA is primarily associated with nephrotoxicity, hepatotoxicity, teratogenicity, and immunotoxicity, posing serious health risks to humans. Consequently, Xia, Li, and others have developed MOF-based electrochemical sensors for detecting OTA in red wine.

Xia et al. [52] utilized a metal-organic framework CoMOF (ZIF-67) loaded with AuNPs as the electrode surface modification material. Tetrahedral nano-DNA was fixed on the electrode surface, and gold sol loaded onto CoMOF (ZIF-67) formed Au-S bonds with the DNA strand. This method used Cr-MOF as the signal probe and K3Fe (CN)6/ K4Fe (CN)6 as the reference probe, with differential pulse voltammetry to measure the response current. Additionally, the method employed the ratio of the DPV response currents of Cr MOF and potassium ferricyanide as the quantitative response signal for OTA detection, constructing a ratiometric signal amplification aptasensor for OTA in red wine. Tetrahedral DNA nanostructures bring to the table benefits such as straightforward fabrication, structural robustness, and high consistency, whereas MOF materials contribute an organized porous architecture and expansive specific surface area. Consequently, this sensor excels in the quantitative assessment of OTA, displaying a linear detection spectrum ranging from 10 pg/mL to 5×10^4 pg/mL. The real-world applicability of the sensor was appraised through recovery experiments in diluted red wine, employing the standard addition technique and attaining a recovery efficiency of 91.2% to 109.4%. Exhibiting commendable specificity, this sensor is adept at identifying minuscule concentrations of OTA in genuine samples, underscoring its potential for wide-ranging applications.

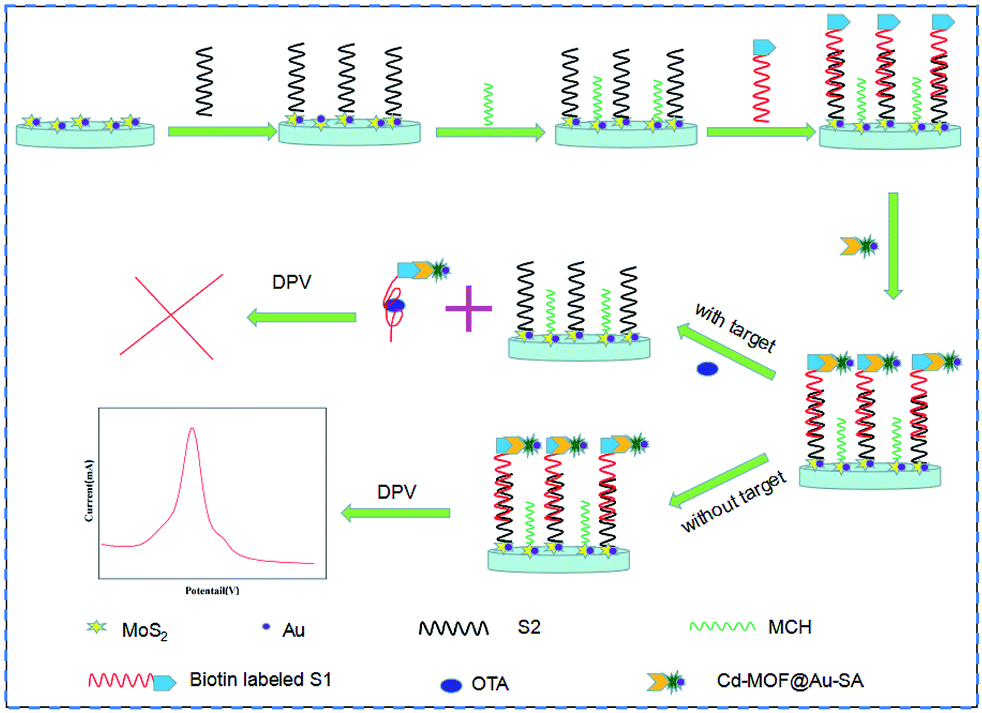

Fig 8. The stepwise procedure for the aptasensor

Li [53] and colleagues crafted an electrochemical aptasensor for OTA detection, leveraging DNA-metal nanoclusters for their operational simplicity, quick results, cost-effectiveness, and heightened sensitivity. This approach entails the pairing of DNA_1 with an OTA-specific aptamer and its immobilization on a gold electrode. Here, the OTA aptamer DNA serves as a scaffold for generating CuNCs as the signaling entity. The presence of OTA, binding specifically to its corresponding aptamer DNA, curtails the production of Cu nanoclusters, thereby diminishing the electrochemical signal's current. DPV is utilized to gauge the electrochemical signature of Cd^{2+} within the SA-AuNPs@Cd-MOF-74 complex, allowing for the quantification of OTA in red wine. Metal nanoclusters, distinguished by their diminutive size, robust stability, excellent conductivity, and fluorescence, are advantageous.

The DNA-templated synthesis of gold nanoparticles is both efficient and yields metal clusters that are markedly resilient to the complexities of environmental disruptors. The aptasensor exhibits a linear OTA detection range from 102 to 5×10^4 ng/mL, with a detection threshold of 33 pg/mL. In practical applications, Li and colleagues verified the method's efficacy in red wine testing, achieving an average OTA recovery rate of 98.3% from fortified samples. This stable, straightforward, economical, highly sensitive, and selective electrochemical aptasensor promises significant utility in food safety analysis.

Zhang[54] and others proposed a universal electrochemical aptasensor based on Cd-MOF-74, incorporating gold nanoparticles for dissolution and pre-concentration, then encapsulating the gold nanoparticles within Cd-MOF-74, and coupling with SA to form the SA-AuNPs@Cd-MOF-74 nanocomposite. MoS2 is valued for its good biocompatibility, conductivity, ease of synthesis, and low cost. The exterior of Cd-MOF-74 is rich in unsaturated metal points, offering excellent electrochemical responsiveness. This feature greatly streamlines the assay procedures and shortens the duration needed for OTA detection in red wine. It exhibits a dynamic detection scope for OTA ranging from 50 to 105 pg/mL, with the sensitivity threshold set at 10 pg/mL. The effectiveness of the suggested technique was verified through the standard addition approach, yielding an accuracy range of 91.1 to 105.2%. Due to its stability, ease of use, affordability, high sensitivity, and selectivity, this electrochemical detection sensor is poised for widespread use in the surveillance of food products.

Qiu [55] and colleagues developed a novel, sensitive, and reusable electrochemical aptasensor using the metal-organic framework UiO-66, which was assembled in situ as a signal amplification platform. This design uniquely leverages Zr^{4+} ions' specific coordination with phosphate groups (-PO43-) to enhance the sensor's target recognition capability. The binding aptamer (OBA) for OTA was hybridized with a thiol-modified complementary sequence (TSS) fixed on the gold electrode surface. Then, UiO-66 was attached to the terminal end of OBA via Zr-O-P coordination bonds, allowing for the assembly of a large number of methylene blue (MB) signal probes, which possess -PO43-, onto the surface of UiO-66 through Zr-O-P coordination bonds. When OTA competes for binding with OBA, OBA detaches from the electrode surface, causing the signal probe to fall off and the electrochemical signal to weaken. The sensor's electrochemical signal was measured using cyclic voltammetry, achieving a linear detection range for OTA in red wine from 0.1 to 2.0 μM, with a detection limit of 0.079 fM (S/N=3). To demonstrate the sensor's applicability in real samples, it was used to determine the recovery rate for various concentrations of OTA in red wine samples, achieving 95.8~104%. This aptasensor features a wide range, ultra-low detection limit, and excellent specificity, holding broad application prospects in food safety monitoring.

Wang and colleagues [56] developed a novel electrochemical aptasensor for the rapid and sensitive detection of OTA in red wine, employing a nano-gold modified electrode as the fixed substrate and DNA-modified Au-MOF as the signal probe (Figure 9). The electrode modification process was characterized using cyclic voltammetry. The nano-gold modified electrode enhances the sensor's conductivity and the quantity of biomolecules that can be fixed, while the DNA-modified MOF acts as a signal probe to generate and amplify the detection signal. In the presence of OTA, the OTA aptamer detaches from the MOF and specifically binds to OTA, preventing the capture of the signal probe and reducing the electrochemical signal. The electrochemical signal of Cu^{2+} in MOF was detected using DPV, revealing that the sensor has a linear detection range for OTA from 0.1 to 5.0 nmol/L, with a detection limit of 0.03 nmol/L (S/N=3). The feasibility of its practical application was evaluated by determining OTA in red wine using the standard addition method, achieving recovery rates of 98.6~105.0%. Therefore, this method can successfully be used for detecting OTA in red wine and has the potential for real-time detection of various harmful substances in food.

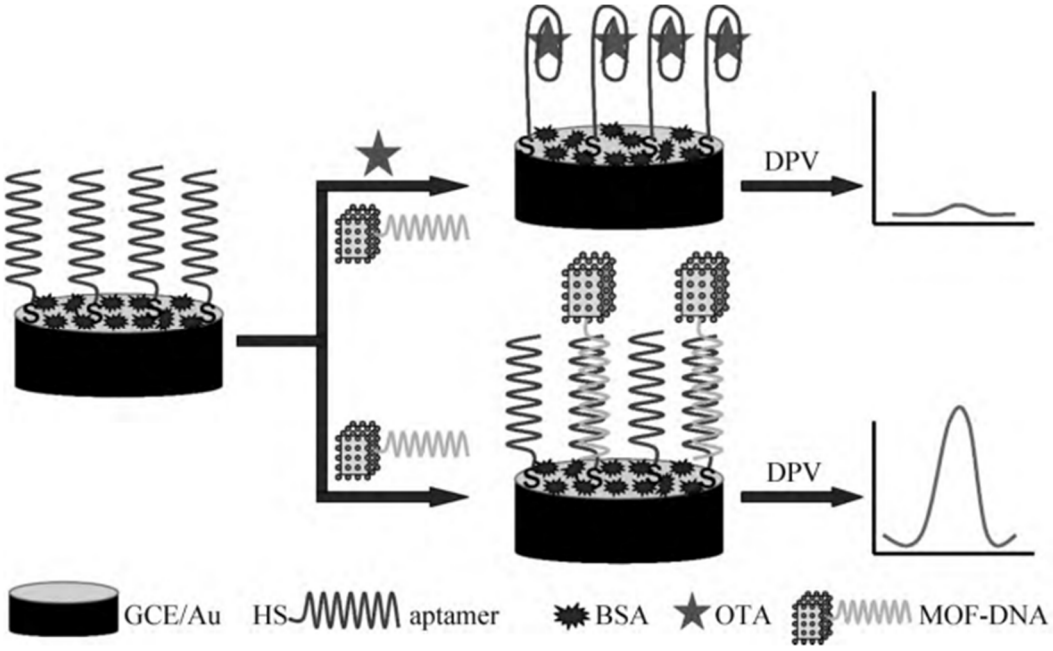

Fig 9. Schematic diagram of the electrochemical biosensor for OTA detection

The aforementioned electrochemical sensors have effectively and sensitively detected OTA in red wine,

showcasing potential value for OTA detection with broad application prospects. Notably, both Zhang and Li employed Cd-MOF-74 as electrode material, attributed to cadmium's excellent conductivity and strong electrochemical activity, making it widely used in electrodes. This high-quality material, Cd-MOF-74, is also expected to be widely used for detecting other food contaminants.

2.2.2. Ochratoxin A in Juice

Improper handling during fruit and vegetable processing can lead to the use of rotten or spoiled fruits for juice production, resulting in the presence of OTA in various juices and posing a potential health risk to humans. Thus, Qiao, Song, and others have developed MOF-based electrochemical sensors for detecting OTA in juice.

Qiao and colleagues [57] developed a novel label-free OTA electrochemical aptasensor based on two-dimensional MOF nanosheets (Cu-TCPP-MOF), designed for detecting OTA in apple and orange juices. The porphyrin in Cu-TCPP-MOF, with its π-electron system and electron-donating properties, accelerates the rate of electron transfer. Additionally, they employed the DNA Walker strategy, methylene blue (Mb), and silver nanoparticles to amplify the sensor signal, thereby enhancing the sensor's detection sensitivity. In the presence of OTA, it binds with the aptamer of complementary sequences, leading to the subsequent binding of complementary bases and causing DNA Walker to bind with 1-ssDNA, resulting in a structural change in 1-ssDNA and a weakened Mb signal. EIS was used to monitor the sensor, which exhibited a linear detection range for OTA from 104 pg/mL to 106 pg/mL, with a detection limit of 8×10-5 pg/mL. To evaluate the reliability and feasibility of the aptasensor in real applications, it was utilized for OTA detection in fresh apple and orange juices, achieving recovery rates of 99.27%~101.20%. The sensor's high sensitivity and good selectivity make it suitable for OTA detection.

Song and colleagues [58] introduced cobalt phthalocyanine nanoparticles (CoPc) into the iron-based metal-organic framework NH2-MIL-101(Fe), resulting in the formation of a novel nanocomposite material NH2-MIL-101(Fe)@CoPc. They developed a new type of electrochemical impedance sensing sensor for detecting OTA in watermelon juice using this nanocomposite. The CoPc nanoparticles demonstrated excellent catalytic activity, capable of redox reactions, substituting functional groups, and enhancing electron delocalization effects. When combined with the high porosity of NH2-MIL-101(Fe), the electrochemical signal was significantly amplified, thereby enhancing the sensor's detection sensitivity. The sensor was monitored using EIS and CV. The linear detection range for OTA was found to be 0.0001–100 pg/mL, with a detection limit of 6.3×10-5 pg/mL. To validate the sensor's practicality for OTA detection, it was tested on watermelon and apple juice samples, exhibiting recovery rates of 98.2~102.4%. Thus, the sensor, characterized by high selectivity, reproducibility, stability, and regenerability, is suitable for a variety of fruit juices.

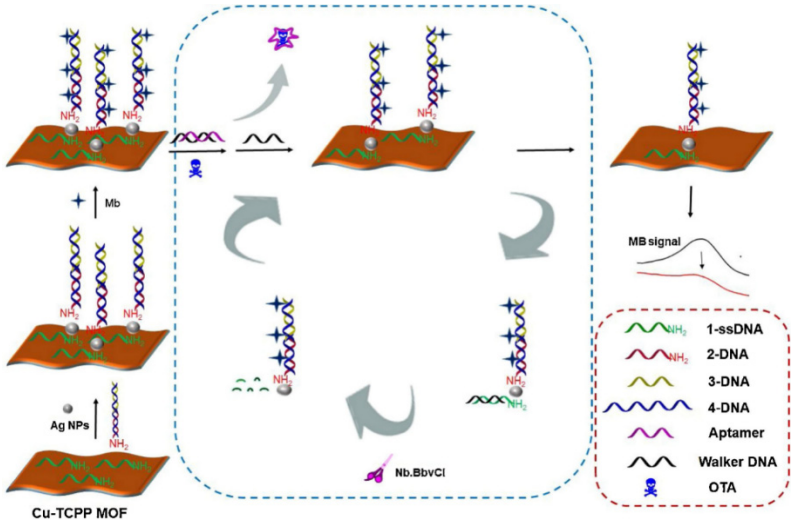

Fig 10. The illustration of the proposed aptasensor based on DNA walkers and 2D Cu-TCPP MOF sheets.

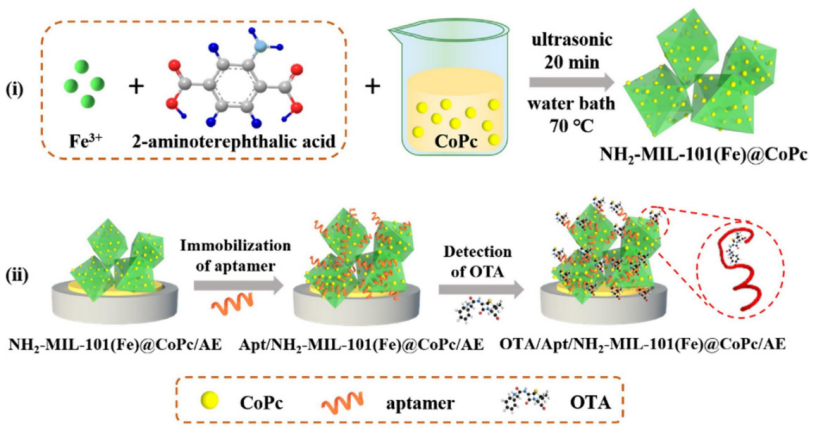

Fig 11. Schematic diagram of (i) the preparation of NH2-MIL-101(Fe)@CoPc nanocomposite and (ii) the fabrication of NH2-MIL-101(Fe)@CoPc-based aptasensor for detecting OTA

The electrochemical sensors discussed above all demonstrate outstanding electrochemical performance and biosensing capabilities for OTA, proving successful in detecting OTA in food. These developments hold potential value for future analyses of OTA in food, with Qiao et al.'s method exhibiting a particularly broad detection range. This is attributed to the amplification of the electrochemical signal using the DNA Walker strategy and the acceleration of electron transfer rates through the use of porphyrin with a π-electron system. Such advancements are promising for further application in detecting harmful fungal toxin residues in food, addressing food safety concerns effectively.

Table 4. Detection of OTA in Food Using MOF-Based Electrochemical Sensors

Food		Metal-Organic Framework Composites	Sensor Monitoring Method	Linear Range	Detection Limit	Recovery Rate	References
Corn		HKUST-1-MOF	Differential Pulse Voltammetry	10~10^5pg/mL	4.3pg/mL	96.0~110.0%	[48]
		PtNPs@Mn-MOF	Electrochemical Impedance Spectroscopy and Cyclic Voltammetry	10~3x10^5pg/mL	3.33pg/mL	96.~103.%	[50]
		Zr-MOF	Differential Pulse Voltammetry	0.1~140pg/mL	2.4×10^{-2}pg/mL		[49]
Red wine		CoMOF(ZIF-67)	Differential Pulse Voltammetry	10~5x10^4pg/mL		91.2~109.4%	[52]
		Cd-MOF-74	Differential Pulse Voltammetry	10^2~5x10^4ng/mL	33pg/mL	98.3%	[53]
		Cd-MOF-74	Differential Pulse Voltammetry	50~10^5pg/mL	10pg/mL	91.1~105.2%	[59]
		UiO-66	Cyclic Voltammetry	0.1~2.0Mm	7.9×10^{-2}fM	95.8~104%	[55]
		Au-MOF	Cyclic Voltammetry	0.1-5.0nmol /L	0.03nmol/L	98..6-105. 0%	[56]
Fruit juice	Apple juice	Cu-TCPP-MOF	Electrochemical Impedance Spectroscopy	10^{-4}~10^6pg/mL	8×10^{-5}pg/mL	99.27~101.20%	[57]
	Watermelon juice, Apple juice	NH2-MIL-101(Fe)	Electrochemical Impedance Spectroscopy and Cyclic Voltammetry	1×10^{-4}~100pg · mL^{-1}	6.3×10^{-5}pg/mL	98.2~102.4%	[58]

2.3. Zearalenone

Zearalenone (ZEN), which thrives in temperate or warm climates, is a toxic secondary metabolite produced by Fusarium species, including Fusarium graminearum and Fusarium culmorum. Renowned for its high estrogenic activity both in vitro and in vivo, ZEN primarily contaminates grains such as wheat, corn, oats, rice, sorghum, and rye, or foods containing these grains, also known as F-2 toxin. Naturally occurring ZEN and its derivatives include α-zearalenol (α-ZAL), α-zearalanol (α-ZOL), β-zearalenol (β-ZAL), and β-zearalanol (β-ZOL) [60]. ZEN appears as a white crystalline substance with a molecular weight of 318.364 g/mol and the formula C18H22O5. It possesses a melting point of 164-165°C and is insoluble in water but soluble in various organic solvents such as benzene, acetonitrile, acetone, or alcohol [61].

ZEN and its metabolites share a similar biological structure with estradiol, allowing them to bind to animal estrogen receptors, influencing chromosome structure and the transcription and translation of related genes, leading to decreased levels of animal estrogens.[62] Moreover, ZEN exhibits hepatotoxicity, reproductive toxicity, and immunotoxicity, reducing the nutritional value of crops and feed, affecting the healthy growth of livestock and poultry, and causing significant economic losses to the livestock industry.[63] ZEN also poses a serious threat to global food security. For instance, in the United States, approximately 10 million tons of crops such as corn and wheat flour are contaminated with ZEN annually, also resulting in substantial economic losses. Hence, there is a pressing demand for efficient and sensitive detection methods for ZEN in crops and food to safeguard global public health and mitigate economic losses in the livestock and agricultural industries [64].

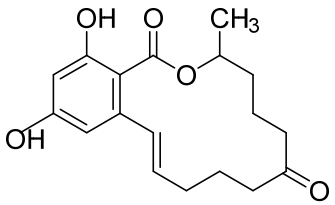

Fig 12. The chemical structure of ZEN

2.3.1. Zearalenone in Agricultural Products

Zearalenone (ZEN) is primarily found in moldy corn, wheat, barley, and other grains and their by-products, with the highest frequency of contamination occurring in corn and corn-derived plants. ZEN can be absorbed by animals through the consumption of moldy grains and by-products, leading to mainly subacute and chronic poisoning in these animals. Furthermore, ZEN can enter the human body directly or indirectly through contaminated grains and animal-derived food products, posing significant risks to human health [65]. Hence, He, Zeng, and their colleagues devised an electrochemical sensor utilizing MOF for detecting ZEN in agricultural products.

He and colleagues [66] devised an electrochemical aptasensor for detecting ZEN in corn, employing CoSe2/AuNRs, a 3dsDNA-PtNi@Co-MOF network, and nicking enzymes as a signal amplification system (as depicted in Figure 13). The 3dsDNA-PtNi@Co-MOF network facilitates the attachment of abundant signal labels (Thi) and provides numerous signal amplifiers (PtNi@Co-MOF). Additionally, CoSe2/AuNRs function as an excellent electrode material when coated on gold electrodes, thereby enhancing the electrochemical signal for rapid, efficient, and sensitive detection of ZEN. In the presence of ZEN, a substantial Thi signal is observed. The sensor exhibited a linear detection range for ZEN from 5×10^8 to 2.5×10^9 pg/mL, with a detection limit of 1.37×10^{-6} pg/mL (S/N=3). To investigate the practical application of the proposed ZEN aptasensor, various concentrations of ZEN were added to corn

samples, resulting in recovery rates ranging from 93.6% to 103.4%. Thus, the sensor exhibited good electrochemical response in the analysis of ZEN in corn samples.

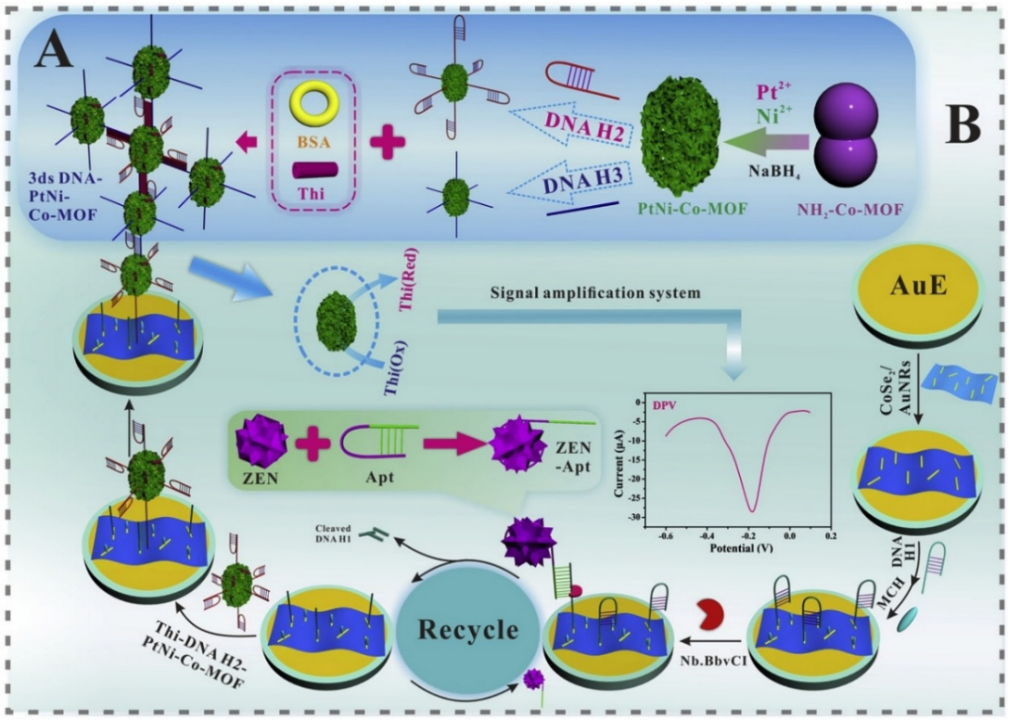

Fig 13. Illustration of the fabricated Thi labeled 3 ds DNA-PtNi@Co-MOF networks (A), the fabricated aptasensor for ZEN detection (B)

Zeng and colleagues[67] introduced an electrochemical sensor based on a copper-based metal-organic framework (Cu-MOF) and magnetic Fe3O4-graphene oxide (Fe3O4-GO) for detecting ZEN in corn. Initially, Cu (II) ions were synthesized with H3BTC ligands at room temperature to form Cu-MOF, which was then combined with magnetic Fe3O4-GO to create the Cu-MOF/Fe3O4-GO nanohybrid. Cu-MOF's high porosity enhances the analytical performance of the nanohybrid sensing electrode, while Cu-MOF/Fe3O4-GO offers improved current response signal, a large effective surface area, high electron transfer rate, and good reproducibility and repeatability. Differential pulse adsorptive stripping voltammetry (DPASV) facilitated electrochemical quantitative analysis. This sensor demonstrated a lower detection limit and wider linear detection range, spanning from 1.592×10^5 to 2.8562×10^6 pg/mL, with a detection limit of 2.314×10^4 pg/mL. To assess the feasibility and applicability of the Cu-MOF/Fe3O4-GO nanocomposite sensor, voltammetric detection of ZEN in corn flour was carried out using the standard addition method, resulting in recovery rates ranging from 95.8% to 97.3%. Thus, the sensor enables rapid, efficient, and sensitive detection of ZEN in corn.

Previously, Li [68] prepared an electrochemical sensor based on Cu-MOF/Fe3O4-GO using a similar method. DPV was employed to measure various concentrations of ZEN under 0.1M PBS (pH=7.0) conditions using Cu-MOF/Fe3O4-GO/GCE, revealing a favorable linear relationship within a concentration range of 0.03 to 9μM and a detection limit of 0.0255μM (S/N=3). The sensor was utilized for detecting ZEN in corn flour, yielding recovery rates ranging from 92.5% to 95.7%. Thus, this sensor offers advantages such as low cost, ease of operation, and short analysis time, rendering it suitable for the electrochemical detection of ZEN in food.

Lai and colleagues[69] developed a highly sensitive, selective, and stable electrochemical sensor for detecting ZEN in Coix seed, employing a nanocomposite material, Ce-MOF@MWCNTs, as the electrode substrate. Ce-MOF offers excellent biosensing capabilities and a large surface area, while MWCNTs provide good conductivity. Toluidine Blue (TB), an aromatic heterocyclic alkaline biodye with redox electrochemical activity and stability, was utilized as a signal probe. Through electrophoretic deposition, TB was immobilized onto the electrode, followed by fixing the Zearalenone aptamer (ZEA) onto the electrode via Au-S and Pt-S bonds. Upon interaction with ZEN, ZEA formed a complex with ZEN, resulting in a change in the electrochemical signal of TB. The construction of the electrochemical sensor was confirmed by measuring the current using CV. The linear detection range for Coix seed was found to be 5.0×10^{-2} to 5×10^4 pg/mL, with a detection limit of 1.0×10^8 pg/mL (S/N=3). To further assess its practical applicability, the fabricated aptamer sensor was employed for detecting ZEN in Coix seed using the standard addition method, yielding recovery rates ranging from 97.0% to 103.0%.

Compared to traditional detection methods, this sensor offers higher efficiency, convenience, sensitivity, and specificity in electrochemical detection.

The aforementioned sensors demonstrate excellent reproducibility, repeatability, and selectivity, enabling the detection of Zearalenone in various agricultural products. This provides more reliable technical support for the detection of ZEN in food.

2.3.2. Zearalenone in Beer

Due to Zearalenone (ZEN) being highly prone to contaminating grains such as barley, wheat, and corn, which are the primary raw materials for beer produced through liquid fermentation, the use of ZEN-contaminated crops can lead to the presence of ZEN contaminants in beer. Hence, Duan and colleagues developed an electrochemical sensor utilizing MOF to detect ZEN in beer.

Duan and colleagues [70] initially prepared MTV polyMOF (Ti) using polyether polymer, 1,4-benzenedicarboxylic acid, and titanium butoxide. Utilizing the multivariate titanium metal-organic framework (MTV polyMOF(Ti)), a novel electrochemical sensor was established for detecting ZEN in beer. The synthesized MTV polyMOF(Ti) showcased an ultrathin nanosheet structure comprising TiO2 nanocrystals and polymer layers. In contrast to the single-ligand Ti-MOF, MTV polyMOF(Ti) exhibited high porosity, excellent electrochemical activity, and strong biocompatibility towards aptamers, enabling efficient and sensitive detection of ZEN. The sensor's response current was evaluated using EIS and DPV, revealing a linear detection range for ZEN in beer spanning from 1×10^{-2} pg/mL to 10^{4} pg/mL, with a detection limit of 7×10^{-3} pg/mL. Application of the proposed aptasensor for ZEN determination in beer demonstrated recovery rates ranging from 95.72% to 104.50%, highlighting the sensor's good selectivity, reproducibility, stability, reusability, and applicability.

2.3.3. Zearalenone in Milk

When animals consume agricultural products contaminated with ZEN, the resulting milk or dairy products can also contain ZEN, making it a contaminant in substances like milk, seriously endangering human health. Hence, Lai and colleagues devised an electrochemical sensor utilizing MOF to detect ZEN in milk.

Lai and colleagues[71] synthesized a lanthanide metal-organic framework (PTCA-La-MOF, PLM) modified with polycyclic aromatic hydrocarbon (PAH) derivative perylene-3,4,9,10-tetracarboxylic acid (PTCA), establishing a ECL immunosensor for detecting ZEN in milk (illustrated in Figure 14). The functional nanomaterial NG-PEI-NiZnMOF, acting as the sensing platform for the ECL sensor, leveraged its substantial specific surface area to enhance the loading of AuNPs, facilitating the capture of numerous antibodies through Au-N bonds. The construction process of the immunosensor was characterized using CV and EIS, affirming the successful development of the immunosensor. The sensor exhibited a linear detection range for ZEN in milk from 10^{4} to 10^{5} pg/mL, with a detection limit of 2.1×10^{-4} pg/mL. Recovery experiments in milk, employing the standard addition method, yielded recovery rates ranging from 90.7% to 103.40%. This sensor not only detects ZEN in milk but also has broader applicability for other harmful substances in food.

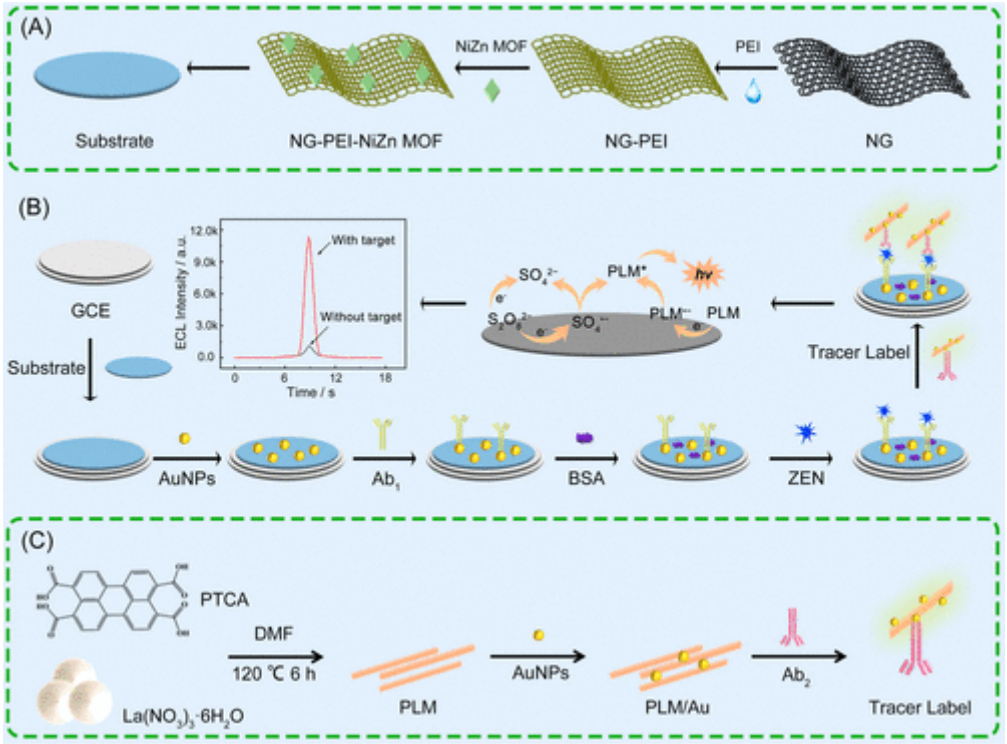

Fig 14. (A) The synthesis process of the NG-PEI-NiZn MOF. (B) The fabrication process of the ZEN immunosensor. (C) The synthesis process of the tracer label

The aforementioned sensors offer advantages including low cost, simplicity of operation, and rapid analysis time. They have demonstrated rapid and sensitive detection of ZEN in agricultural products, milk, and beer, suggesting a promising application outlook. Furthermore, these sensors can function as electrochemical sensors for detecting additional mycotoxins in food, indicating their broad applicability and potential in ensuring food safety and public health.

2.4. Deoxynivalenol

Deoxynivalenol (DON), commonly referred to as vomitoxin, is categorized as a type B trichothecene mycotoxin generated by Fusarium species, including Fusarium graminearum, Fusarium culmorum, and Fusarium roseum, predominantly found in grains and their products, like wheat, corn, rye, barley, and oats. Among these, wheat and corn are the most affected, with the highest concentrations of DON [72]. The chemical designation for DON is 3,7,15-trihydroxy-12,13-epoxytrichothec-9-en-8-one, with the formula C15H20O6 and a molecular weight of 296.3. Under standard conditions, pure DON manifests as a colorless crystalline solid with a melting point ranging from 151 to 152°C [73]. The molecular structure of DON is illustrated in the figure. This toxin has the propensity to leach from contaminated grains into water and soil, leading to significant

harm to agricultural resources and the environment in proximity[74]. Moreover, DON not only contaminates crops and food products but also affects the immune function of humans and animals, leading to symptoms such as vomiting, reduced appetite, digestive disorders, weight loss, and reproductive damage[3]. Epidemiological studies have suggested a correlation between the high incidence of Kashin-Beck disease (KBD) and skeletal abnormalities with high exposure to DON in water and food in regions like Henan and Gansu [75]. As a result, the International Agency for Research on Cancer (IARC) under the World Health Organization (WHO) has categorized DON as a Group 3 carcinogen. Electrochemical sensors utilizing MOF have found extensive application in the sensitive detection of DON.

Table 5. Detection of ZEN in Food Using MOF-Based Electrochemical Sensors

Food		Metal-Organic Framework Composites	Sensor Monitoring Method	Linear Range	Detection Limit	Recovery Rate	References
Agricultural products	Corn	PtNi@Co-MOF	Differential Pulse Voltammetry	5×10^{8}~2.5×10^{9}pg/mL	1.37×10^{-6} pg/mL	93.6~103.4%	[66]
		Cu-MOF	Differential Pulse Voltammetry	1.592×10^{5}~2.8562×10^{6}pg/mL	2.314×10^{4}pg/mL	95.8~97.3%	[67]
		Cu-MOF	Differential Pulse Voltammetry	0.03~9μM	2.55×10^{-2}μM	92.5~95.7%	[68]
	Coix seed	Ce-MOF	Cyclic Voltammetry	5.0×10^{-2}~5×10^{4}pg/mL	1.0×10^{8}pg/mL	97.0~103.0%	[69]
Beer		MTVpolyMOF(Ti)	Electrochemical Impedance Spectroscopy and Cyclic Voltammetry	1×10^{-2}~10^{4}pg/mL	7×10^{-3}pg /mL	95.72~104.50%	[70]
Milk		PTCA-la-MOF	Electrochemical Impedance Spectroscopy and Cyclic Voltammetry	10^{4}~10^{5}pg/mL	2.1×10^{-4}pg/mL	90.7~103.40%	[71]

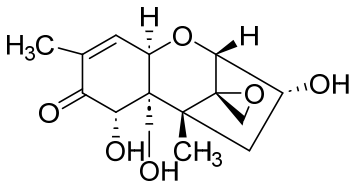

Fig 15. The chemical structure of DON

2.4.1. Deoxynivalenol in Milk

Due to animals consuming crops or poultry feed contaminated with DON, the resulting milk may contain DON contaminants, making it a common pollutant in milk. Consumption of such contaminated milk can lead to acute poisoning symptoms in humans, such as anorexia, vomiting, diarrhea, fever, instability in standing, sluggish reaction, and in severe cases, damage to the hematopoietic system, affecting individuals' health and well-being. Thus, Song and colleagues have successfully devised an electrochemical sensor based on MOF for detecting DON in milk.

Song et al. [76] utilized 4-(1H-tetrazol-5-yl) benzoic acid (H2TZB) and 2,4,6-tri(4-pyridyl)-1,3,5-triazine (TPT) as organic linkers, combined with Co^{2+} and Ni^{2+}, to form a nickel-based bimetallic MOF framework (CoNi-MOF). This framework was employed to construct an electrochemical label-free impedimetric immunosensor for detecting DON in milk. Compared to individual Co-MOF and Ni-MOF, CoNi-MOF demonstrated enhanced affinity towards antibodies, resulting in heightened detection sensitivity. The CoNi-MOF-based sensor demonstrated good biocompatibility compared to conventional electrochemical sensors. The sensor was monitored via electrochemical impedance spectroscopy, revealing a linear detection range for DON in milk spanning from 1 to 50 pg/mL, with a detection limit of 0.30 pg/mL. To affirm the applicability of the developed electrochemical immunosensor for real samples, milk was selected for recovery rate experiments, resulting in recovery rates ranging from 95.7% to 102.6%. This method boasts advantages such as high sensitivity, good selectivity, and simplicity of operation, holding great potential for detecting toxic and harmful residues in food.

2.4.2. Deoxynivalenol in Crops

Deoxynivalenol (DON) is a common contaminant in crops, often detected in corn, peanuts, wheat, and other agricultural products due to factors such as growth conditions and improper storage, threatening the health of both humans and animals. To safeguard food safety, researchers like Cui, Wen, and others have developed electrochemical sensors based on MOF for detecting DON in crops.

Cui et al. [77] developed a unique hierarchical CoCo PBA@PCN-221 nanohybrid through an innovative in-situ MOF-on-MOF strategy, enabling the creation of an electrochemical impedimetric immunosensor for the highly sensitive detection of DON in peanuts (illustrated in Figure 16). The CoCoPBA@PCN-221 nanohybrid, characterized by diverse metal valence states and oxygen vacancies, demonstrates enhanced electrochemical activity, thereby boosting the conductivity of the nanohybrid. Moreover, owing to the nano-layered structure of CoCoPBA@PCN-221, its extensive specific surface area, and the synergistic interaction between Co^{2+}/Co^{3+} and Zr clusters, CoCoPBA@PCN-221 achieves high binding affinity with DON antibodies, enhancing the sensor's sensitivity and efficiency, thus improving sensor performance. Cui and colleagues conducted electrochemical impedance spectroscopy measurements on real peanut samples, revealing a linear detection range of 1×10^{-3} pg/mL to 10^{3} pg/mL and a detection limit of 50 pg/mL. To assess the sensor's practicality, real peanut samples were tested, with recovery rates ranging from 96.2 to 108.0%. Therefore, this sensor exhibits high selectivity, repeatability, stability, and applicability for food.

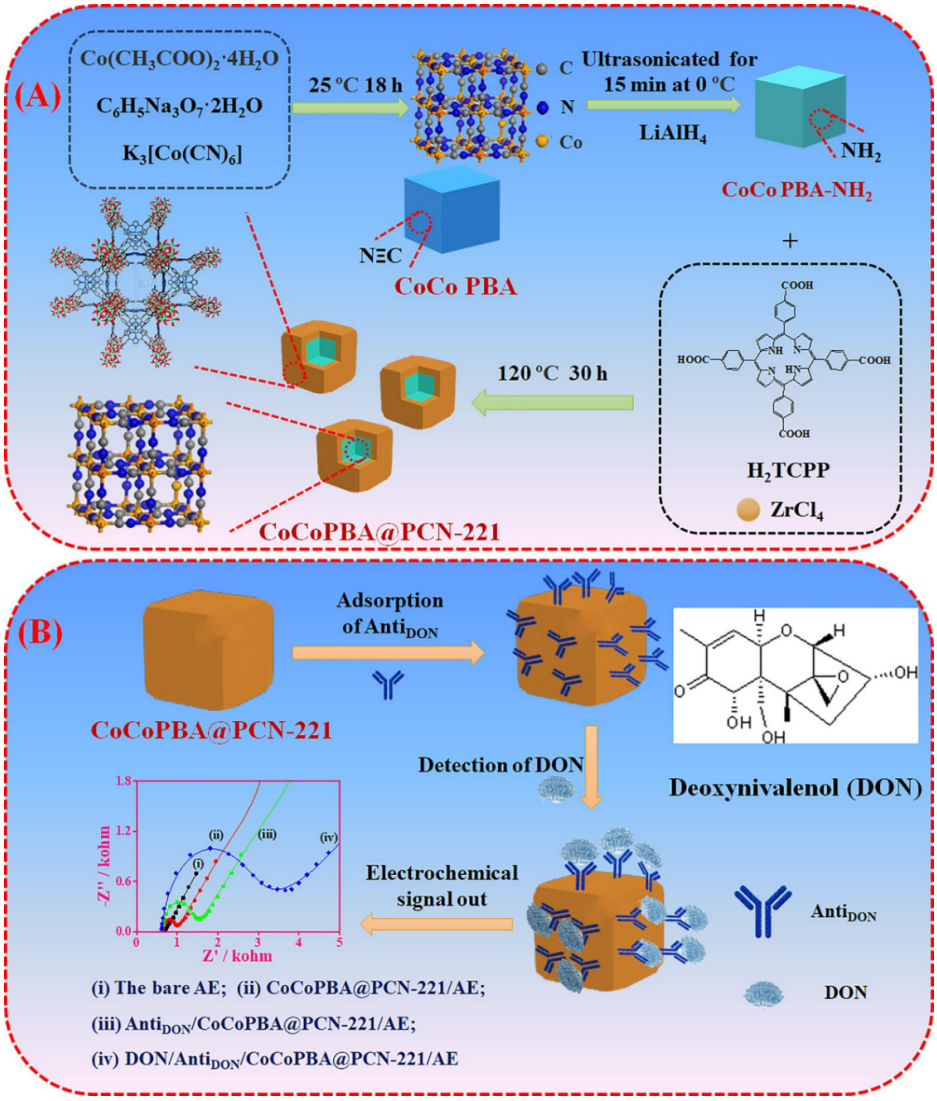

Fig 16. (A) Schematic diagrams of the preparation of the CoCoPBA@PCN-221 nanohybrid and (B) the development of the CoCoPBA@PCN-221-based immunosensor for DON detection, including (i) the bare AE, (ii) coating of electrode with CoCoPBA@PCN-221 nanohybrid (CoCoPBA@PCN-221/AE), (iii) adsorption of AntiDON (AntiDON/CoCoPBA@PCN-221/AE), and (iv) detection of DON by electrochemical technique (DON/AntiDON/CoCoPBA@PCN-221/AE)

Wen and colleagues [78] devised a simple electrochemical sensor for the rapid, efficient, and sensitive detection of DON in wheat, leveraging multifunctional nitrogen-doped Cu-MOF nanomaterials (N-Cu-MOF). With its large specific surface area and excellent conductivity, N-Cu-MOF emerges as an ideal electrochemical signal probe. Additionally, the interaction between amino groups and copper enhances the stability of the aptamer, endowing the sensor with high sensitivity, low detection limits, and good selectivity. Differential pulse voltammetry demonstrated the sensor's excellent reproducibility and repeatability, with a linear detection range for DON in wheat from 20 to 2×10^4 pg/mL and a detection limit of 8 pg/mL. Recovery rate experiments conducted on wheat samples revealed rates ranging from 95.6% to 105.9%, providing a versatile method for the rapid and sensitive analysis of highly toxic DON in food samples.

Furthermore, Wang and others [79] synthesized an amino-modified porous MOF, namely Calcined-PA-NH2-MIL-101 (CPNM), to create an electrochemical immunosensor for rapid and sensitive DON detection in wheat. PA stands for palmitic acid. The induction of defects through the properties of monocarboxylic acids resulted in a highly stable porous structure, which increased the catalytic active sites and promoted biomolecule modification, thereby enhancing electrochemical analytical performance. The amino functionalization also facilitated CPNM to become an excellent carrier for the covalent fixation of DON antibodies. The potential of employing CPNM as a DON sensing nanomaterial was investigated through cyclic voltammetry. Under optimized conditions, the electrochemical immunosensor displayed a detection range for DON spanning from 10 to 10^7 pg/mL, with a detection limit of 9.6 pg/mL. Recovery rate experiments conducted on wheat samples yielded rates ranging from 90.7% to 105.3%, offering a fresh perspective for DON detection utilizing electrochemical aptasensor technology.

Xia et al. [80] introduced a novel electrochemiluminescence (ECL) sensor for DON detection in corn. Illustrated in Figure 17, the sensor employs Ru-MOF as the receptor, incorporating the organic ligand 4,4'-dicarboxylic acid-2,2'-bipyridine ruthenium (II) rich in carboxyl groups, combined with Zn^{2+} to synthesize functionalized Ru-MOF containing a substantial amount of Ru^{2+}. In this setup, Ru-MOF functions as the energy donor, while Bi2S3 serves as the energy acceptor. The successful construction of the sensor was validated using

electrochemical impedance spectroscopy. The sensor exhibited a linear detection range for DON spanning from 10^4 to 5×10^8 pg/mL, with a detection limit of 9×10^3 pg/mL, thereby offering an effective analytical tool for ensuring food safety.

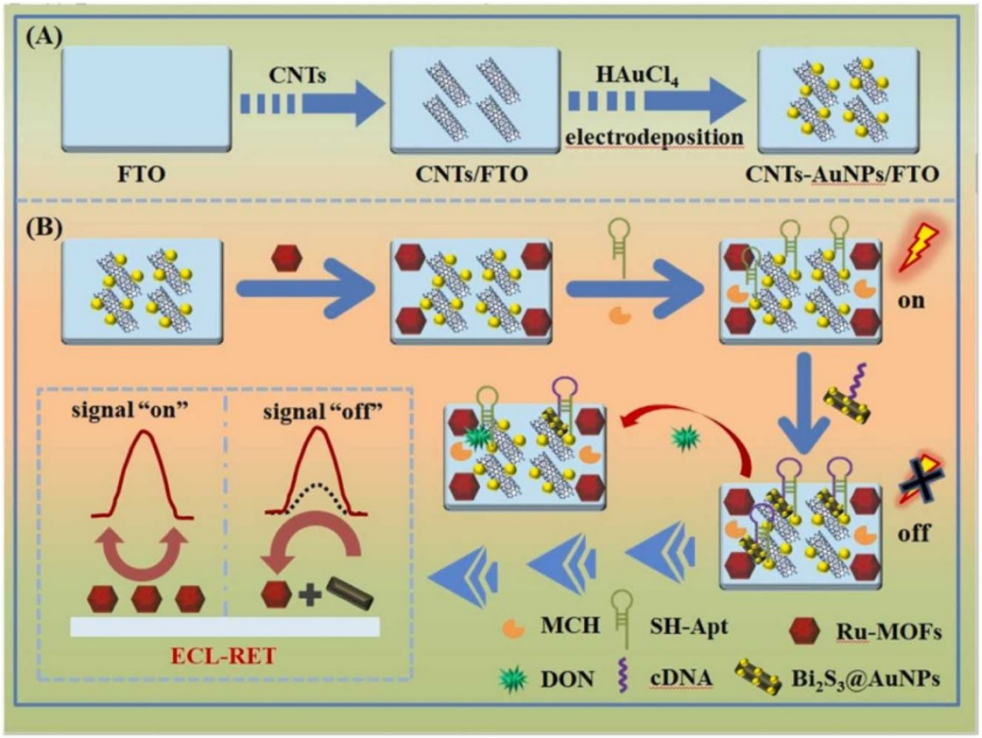

Fig 17. Schematic illustration of the construction of the ECL-RET system for DON detection

Wang and colleagues [81] aimed to enhance the detection performance and simplify the operation steps of sensors by constructing a signal amplification type label-free electrochemical aptasensor for detecting DON in corn flour. The sensor used CeMOF@Au as the base material, incorporating magnetic separation technology to reduce matrix interference. Magnetic separation technology relies on magnetic force to physically separate substances based on their magnetic properties. The remarkable conductivity of CeMOF@Au significantly enhanced the electrode's responsiveness, while its extensive specific surface area and high porosity provided ample space and numerous active sites for DNA loading. CeMOF@Au's excellent conductivity significantly enhanced the electrode's responsiveness, while its large specific surface area and high porosity provided ample space and numerous active sites for DNA loading. Electrochemical detection using impedance spectroscopy, cyclic voltammetry, and differential pulse voltammetry demonstrated a linear detection range for DON from 10 to 5×10^5 pg/mL, with a detection limit of 1.79 pg/mL. Recovery rate experiments conducted on corn flour showed rates between 94.38% and 98.68%, confirming the sensor's successful application in detecting DON in food.

The sensors described offer a wide linear detection range and low detection limits, each displaying unique advantages in the detection of DON in crops, providing new perspectives for the detection of DON in other foods. Among the researchers, Wang and colleagues accomplished the broadest linear detection range by employing palmitic acid (PA) as the electrode material. PA facilitated an increase in the number of catalytic active sites, thereby enhancing the electrochemical performance. This also proves the feasibility of using monocarboxylic acids like PA as electrode modification materials.

2.4.3. Deoxynivalenol in Rice Flour and Wheat Flour

Agricultural products processed from crops contaminated with DON, such as rice flour and wheat flour, frequently consumed by people, can easily introduce DON into the human body. To minimize human consumption of agricultural products containing DON, Yuan and colleagues developed a new type of MOF-based electrochemical sensor to ensure food safety.

Yuan et al. [82] devised an MOF-based electrochemical immunosensor to detect DON in rice flour and wheat flour. To tackle the issue of poor stability in electrochemical signal probes, they employed a biomimetic mineralization technique to encapsulate Prussian Blue (PB) within highly porous ZIF-8, yielding the composite material PB@ZIF-8. A polydopamine (PDA) coating was then applied to the surface of PB@ZIF-8 to furnish binding sites for IgG, resulting in the PB@ZIF-8/PDA/IgG electrochemical probe. An indirect competition approach was utilized, wherein DON antibodies affixed on the modified electrode captured PB@ZIF-8/PDA/IgG, generating a signal. A robust electrochemical signal was detectable in the absence of DON, diminishing as the concentration of DON increased. Thus, they established an indirect competitive electrochemical immunosensor for the sensitive detection of DON. The linear detection range for DON spanned from 0.1 to 5000 pg/mL, with a detection limit of 0.0186 pg/mL. Differential pulse voltammetry determined DON concentration in spiked rice flour and wheat flour samples, yielding recovery rates ranging from 90.51% to 118.00% and from 85.67% to 107.26%, respectively. Hence, the immunosensor can detect DON with heightened sensitivity and rapidity, offering a more efficient and reliable analytical approach for DON detection.

To mitigate the influence of environmental factors on the performance of electrochemical sensors, Yuan et al.[82]

devised a ratiometric electrochemical immunosensor. They synthesized Fe-MOF material via solvothermal synthesis, incorporating AuNPs to bolster the stability and conductivity of Fe-MOF/AuNPs. Subsequently, PDA and IgG were introduced and modified on its surface to generate the signal probe (Fe-MOF/AuNPs/PDA/IgG, SP). The electrical signal of the signal probe (ISP) decreased proportionally with increasing DON concentration, as measured by differential pulse voltammetry. The sensor exhibited a linear detection range from 0.5 pg/mL to 5000 pg/mL during electrochemical detection, with a limit of detection (LOD) of 0.0166 pg/mL. The recovery rates for DON detection in rice flour and wheat flour samples ranged from 88.95% to 114.20% and from 82.47% to 96.29%, respectively. These results underscore the high efficacy of the developed immunosensor for detecting DON in real grain matrices.

In a sum, Yuan and colleagues developed two different MOF-based electrochemical sensors for detecting DON in food, where the ratiometric electrochemical sensor showed a lower detection limit. This was due to the incorporation of gold nanoparticles as electrode material, which enhanced the electrode's stability and conductivity, facilitating rapid and sensitive detection of DON in food with promising application prospects.

Table 6. Monitoring of DON in Food Using MOF-Based Electrochemical Sensors

Food		Metal-Organic Framework Composites	Sensor Monitoring Method	Linear Range	Detection Limit	Recovery Rate	References
Milk		CoNi-MOF	Electrochemical Impedance Spectroscopy	1~50pg/mL	0.30pg/mL	95.7~102.6%	[76]
Crops	Peanuts	CoCoPBA@PCN-221	Electrochemical Impedance Spectroscopy	1×10^{-3}~10^{3}pg/mL	50pg/mL	96.2~108%	[77]
	Wheat	N-Cu-MOF	Differential Pulse Voltammetry	0.02~20ng/mL	8pg/mL	95.6~105.9%	[78]
		NH_2-MIL-101	Cyclic Voltammetry	10~10^{7}pg/mL	9.6pg/mL	90.7~105.3%	[79]
	Corn	Ru-MOF	Electrochemical Impedance Spectroscopy	10^{4}~5×10^{8}pg/mL	9×10^{3}pg/mL		[80]
		CeMOF@Au	Electrochemical Impedance Spectroscopy, Cyclic Voltammetry, Differential Pulse Voltammetry	10~5×10^{5}pg/mL	1.79pg/mL	94.38~98.68%	[81]
Rice flour, Wheat flour		PB@ZIF-8	Differential Pulse Voltammetry	0.1~5×10^{3}pg/mL	1.86×10^{-2}pg/mL	90.51~118.00%, 85.67~107.26%	[82]
		Fe-MOF	Differential Pulse Voltammetry	0.5~5000pg/mL	1.66×10^{-2}pg/mL	88.95%~114.20% 82.47%~96.29%	[82]

3. Conclusion

Mycotoxins are highly toxic and pose teratogenic, carcinogenic, and mutagenic hazards, constituting a severe threat to food safety, socio-economic development, and human health. Mycotoxins, commonly present in grain crops, are difficult to detect due to their low concentrations, necessitating rapid and sensitive detection methods. To date, electrochemical sensors are predominantly utilized for identifying mycotoxins in food, demonstrating extensive applications across agriculture, the food and petroleum sectors, and extending into environmental and biomedical research areas. Compared to traditional detection methods, electrochemical detection offers advantages such as fast analysis speed, low detection cost, and ease of miniaturization.

MOF represents a category of materials and offers high specific surface areas, high porosity, structural tunability, good conductivity, and stability, making them widely used as excellent metallic materials. The exceptional structural characteristics and large surface area of MOF composites provide recognition spaces for target molecule detection and show great potential in enhancing the catalytic performance of electrocatalysts, often serving as electrode materials. For instance, UiO-66, mentioned in this paper, leverages its unique adsorption properties and semiconductor performance, combined with Zr, NH2, and other materials as electrode materials, for the detection of AFB_1; metal nanoparticles such as Fe, Au, etc., forming octahedral nanostructures through covalent bonds with porphyrins and MOF, serve as ideal electrochemical sensing media. Electrochemical sensors based on MOF, when paired with electrochemical signal amplification methods, provide effective and sensitive detection of various mycotoxins. For AFB_1, they exhibit a linear detection range from 0.1 to 10^4 pg/mL, achieving the lowest detection limit at 4.81×10^{-3} pg/mL. For OTA, the linear detection range extends from 10^{-4} to 10^6 pg/mL, with a minimum detection limit of 6.3×10^{-5} pg/mL. For ZEN, the sensors can detect concentrations ranging from 5×10^{-2} to 5×10^4 pg/mL, with the lowest detection threshold at 1.37×10^{-6} pg/mL. Lastly, for DON, they cover a range from 1×10^{-3} to 10^3 pg/mL, with the lowest detection limit marked at 1.66×10^{-2} pg/mL.

These detection ranges and limits have achieved satisfactory results in practical sample applications.

4. Challenges and Future Perspectives

Despite the outstanding electrochemical detection capabilities of MOF, MOF composites are constrained by high costs, complex synthesis processes, and the lack of large-scale production capabilities. Furthermore, MOF materials often suffer from lower structural stability and low electrical conductivity, where the catalytic active sites nearly fail to rapidly bind with reactants, leading to suboptimal detection outcomes for mycotoxins. Therefore, developing MOF composites with high stability, high conductivity, and enhanced electrochemical responses for detecting mycotoxins

in food remains a challenge. Specific challenges include:

1. The extremely low concentrations of mycotoxins in food make successful detection difficult, and a single grain type often contains multiple mycotoxins, making it challenging for MOF-based sensors to simultaneously detect multiple mycotoxins in food.

2. The diversity of mycotoxin forms, where a category of mycotoxin often includes several variants, such as aflatoxins that include B1, M1, G1, and more. Whether MOF-based sensors can successfully detect all forms within a category of mycotoxin requires further investigation.

3. Mycotoxins are predominantly found in crops and agricultural products, which are often grown in fields and subject to extreme weather conditions, potentially making practical detection difficult. There is a need to develop rapid and convenient MOF-based methods for real-time detection of mycotoxins in crops.

In the future, MOF composites could be integrated with paper-based devices, smartphones, and the internet to develop sensitive, accurate, rapid, and portable electrochemical sensing methods. This integration could facilitate the detection of other contaminants in food, leveraging the advancements in technology and connectivity to enhance food safety monitoring and ensuring public health.

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