



Recent Advances in Electrochemical and Optical Point-of-Care Testing for Marine Biotoxin Detection

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Abstract

Marine biotoxins (MBs) are harmful metabolites produced by algal species affect marine organisms and pose significant risks to marine ecosystems and human health. MBs accumulate in finfish and shellfish, resulting in over 20,000 foodborne poisoning cases annually. Rapid and sensitive MBs detection methods are urgently required to ensure food safety and protect the environment. Mouse bioassays and sophisticated testing techniques such as liquid chromatography-mass spectrometry, high-pressure liquid chromatography, and X-ray photoelectron spectroscopy are used for detecting MBs, but are limited by high cost and time consumption. Advantageously, electrochemical and optical immunoassays offer high portability, sensitivity, and potential for real-time monitoring. Advancements in point-of-care testing (POCT) systems using biosensing technologies renders ideal for detecting MBs in various food and environmental matrices. This review provides an overview of MBs, including their classification, source, and toxicity. Understanding the properties and applications of various types of MBs is essential for their effective detection via optical and electrochemical sensing. This review examines different methods of detecting MBs in seafood, including the use of enzymes, immunoassays, peptides, DNA, molecular imprinted polymers, and antigen–antibody pairs, and analysis using electrochemical and optical assays over the last five years. Sensing assays can be utilized in user-friendly tools, such as paper, microfluidic chips, smartphone-based POCT, and lateral-flow devices. Prospective directions for developing assays to facilitate the sensitive and on-site detection of MBs are proposed. This review provides a comprehensive overview of the technologies available for aiding researchers and doctors in selecting the most suitable methods of MBs detection.

Keywords Marine biotoxins · Electrochemical · Optical · POCT · Biosensor

1 Introduction

1.1 General Information

The ocean is a complex and massive aquatic system rich in both mineral and biological resources. The Earth's surface

is covered by 71% water, with oceans comprising 97% of the world's total aquatic resources. The remaining 3% consists of freshwater from glaciers, rivers, lakes, and groundwater. Oceans provide essential resources such as fish, seafood, gas, oil, rare materials, and transportation. Three billion people consume protein, with approximately 90% of these products sourced from the oceans. Coastal and marine tourism generate significant economic benefits, and rare marine materials are valuable for medical and pharmaceutical development. Pollution and climate change in ocean ecosystems influence the growth and behavior of marine species. Increased temperatures and elevated CO₂ levels lead to the large-scale production of harmful algal blooms (HABs). Consequently, marine organisms produce greater amounts of marine biotoxins (MBs) because of climate change and pollution. These MBs contaminate seafood and pose serious health risks to humans [1–4]. MBs are naturally occurring, toxic compounds that are produced by certain algal

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species, particularly diatoms, cyanobacteria, phytoplankton, and dinoflagellates. These toxins accumulate in the tissues of marine organisms, such as shellfish and finfish, through the food chain. MBs pose significant risks to marine ecosystems and human health by affecting the nervous system, increasing the risk of cancer, harming the liver, causing metabolic disorders, and leading to long-term health issues. MBs are small organic molecules with molecular weights ranging from 250 to 3000 Da. They are chemically diverse and exhibit a wide range of biological activities, often targeting the nervous and gastrointestinal systems of both humans and animals. Despite the discovery of thousands of MBs, researchers have fully elucidated only a limited number of chemical structures. Furthermore, MBs are highly resistant to common food-processing methods, including microwave cooking, air-frying, and instant cooking, making them a persistent threats. Globally, more than 20,000 food poisoning cases are linked to MBs annually, and pose ecological risks to marine mammals. Thus, sensitive and timely on-site detection methods are essential for food safety, public health, and the protection of the aquatic ecosystem [5–8].

The United States of America, New Zealand, United Kingdom, Republic of Korea, Canada, and countries of the European Union have enacted strict regulations for preventing MBs from harming the environment, aquatic ecosystems, and human health. In many countries, a mouse bioassay is the preferred method for detecting MBs, because it effectively reflects the overall toxic potential of a sample [9]. The mouse bioassay approach involves injecting MBs into mice and monitoring their ability to survive over time and during illness. However, this method has significant limitations, including being lengthy and costly, having a high false-positive rate, and lacking the ability to detect individual MBs structures at the cellular level [10]. Additionally, routine testing for MBs requires the use of a considerable number

of mice each year, which raises economic concerns within the scientific community. Common and powerful analytical methods for detecting MBs, such as enzyme-linked immunosorbent assay (ELISA), liquid chromatography mass spectrometry (LC–MS), and high-pressure liquid chromatography (HPLC), offer high effectiveness and efficiency [11–13]. Although HPLC and LC–MS require expensive instrumentation, extensive sample preparation, analytical procedures, and trained staff, these methods are not suitable for on-site applications. Although ELISA is recognized for speed and specificity, it is less effective in identifying low concentrations of MBs, mainly because of enzyme interactions. These limitations underscore the urgent need for more efficient, low-cost, sensitive, on-site, and adaptable techniques for MBs detection, particularly in resource-limited areas. Biosensors are devices designed to detect and convert substances into measurable signals by using biological components. These devices are inexpensive, straightforward, and suitable for field applications. Optical and electrochemical biosensors are particularly appealing because of cost expense. Point-of-care testing (POCT) platform utilize biosensor technology, thereby offering enhanced detection capabilities, making them ideal for monitoring MBs. Most biosensors are based on optical and electrochemical responses, which afford efficiency and user-friendliness. Figure 1 provides a summary of modern optical sensor technologies operate via colorimetric, fluorescence, and surface plasmon resonance (SPR) methods, as well as electrochemical sensors use techniques such as voltammetry and electrochemical impedance spectroscopy (EIS) for detecting MBs [14–18]. The colorimetric method utilizes probes interact with the target molecules, resulting in a measurable color change, enabling the identification of MBs through visual detection. In contrast, the fluorescence method uses materials that emit light upon excitation. In POCT platform, the surface serves as a support for the immobilized probes,

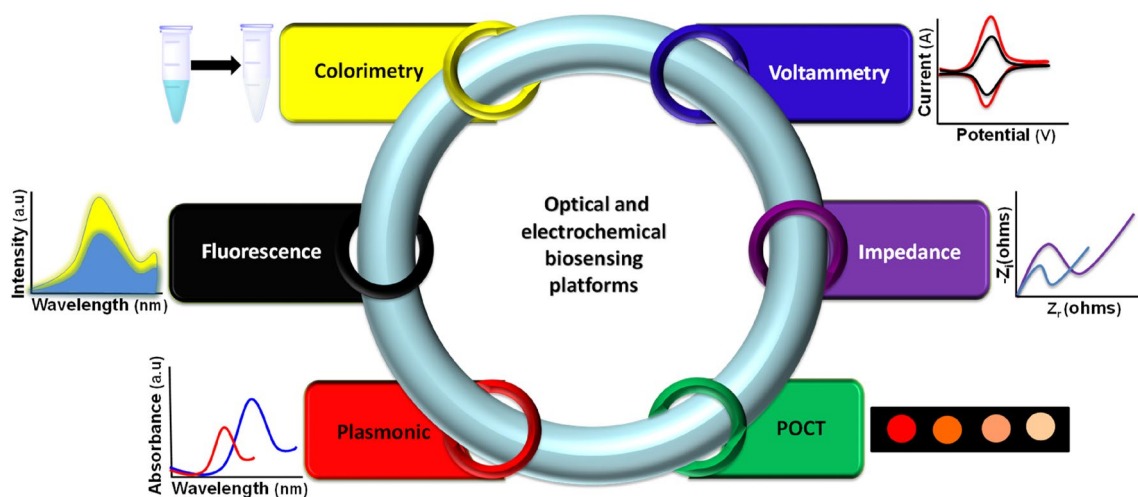


Fig. 1 Classification of optical and electrochemical biosensors for the detection of marine biotoxins (MBs)

and the probe fluorescence varies upon binding to MBs. SPR is an optical technique detects changes in the refractive index of noble-metal nanomaterials such as Ag, Au, Pt, Pd, and Cu. Plasmonic biosensors based on distinct detection principles are continually being optimized to meet the evolving requirements for MBs detection. Voltammetry monitors redox responses by recording variations in the current when a voltage is applied. In sensors, activated electrodes induce distinct changes in the current owing to their interactions with analytes. EIS techniques monitor the resistance across multiple frequencies and utilize electrodes to detect and analyze changes in the interfacial characteristics of the system, making them ideal for highly sensitive sensing [19–22].

This review examines the uses of enzymes, immunoassays, peptides, DNA, molecularly imprinted polymers (MIPs), antigen–antibody pairs, and other small chemical molecules in the detection of MBs in seafood. First, a brief introduction to the types, structures, properties, sources, and toxicity of MBs is presented. Thereafter, focus is placed on the various strategies, including electrochemical and optical assays, used in a platform of detection applications. Various POCT platforms such as paper-based POCT, microfluidic chips, smartphone-based POCT, and lateral-flow devices

are also discussed. Finally, recent advancements are summarized, significant challenges are highlighted, and future directions for developing sensitive assays for the on-site detection of MBs are proposed. This review discusses the pros and cons of biomolecular methods for detecting MBs in seafood products and synthetic assays based on enzymes, antibodies, peptides, nucleic acids, MIPs, and small chemical ligands.

1.2 Types, Source, and Toxicity of MBs

MBs are categorized based on their solubility. Hydrophilic (water-soluble) MBs, including domoic acid (DA), saxitoxins (STX), and tetrodotoxins (TTX), are easily dispersed in aquatic environments. Examples of lipophilic (fat-soluble) MBs include ciguatoxin (CTXs), okadaic acid (OA), brevetoxins (BTXs), yessotoxins (YTXs), azaspiracids (AZAs), spirolides (SPXs), and gymnodimines (GYMs). Lipophilic MBs do not dissolve in water but dissolve in organic solvents and oils. The three main classification criteria for MBs are the chemical structure, origin, and toxicity, as depicted in Fig. 2. MBs are generally categorized into three types: alkaloids, polyethers, and peptide toxins (Table 1). Peptide

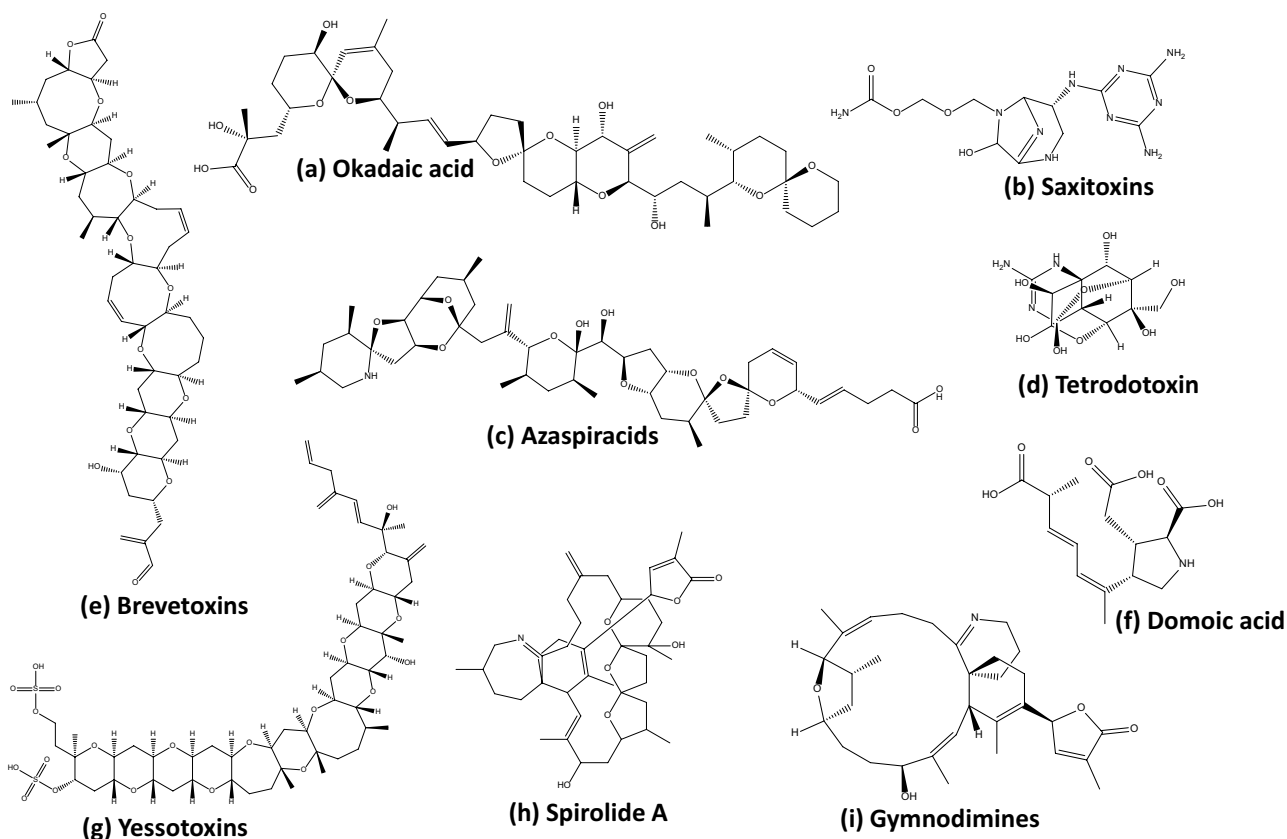


Fig. 2 Molecular structural formulae of common MBs including (a) okadaic acid (OA), (b) saxitoxin (STX), (c) azaspiracids, (d) tetrodotoxin (TTX), (e) brevetoxins, (f) domoic acid (DA), (g) yessotoxins, (h) spirolide A, and (i) gymnodimines

Table 1 Types, sources, and toxicity of marine biotoxins (MBs)

Chemical type	Toxin name	Associated poisoning	Source organisms	Toxicity
Peptide toxins	Conotoxins	Neurotoxic potential	Cone snails (<i>Conus</i> spp.)	Neurotoxic
Polyether toxins	Ciguatoxin	Ciguatera fish poisoning	Dinoflagellates	Gastrointestinal, neurological, muscle pain, and cardiovascular
	Brevetoxins	Diarrhetic shellfish poisoning (DSP)	Harmful algal blooms (red tides)	Gastrointestinal and severe neurological disturbances
	Okadaic acid	DSP	<i>Dinophysis</i> spp. and <i>Prorocentrum</i> spp.	Nausea, vomiting, diarrhea, and abdominal cramps
	Yessotoxins	DSP	<i>Protoceratium reticulatum</i> , <i>Lingulodinium polyedra</i> , and <i>Gonyaulax</i> spp.	Cardiotoxic effects
	Azaspiracids	Azaspiracid shellfish poisoning	<i>Azadinium</i> spp. (dinoflagellate)	Diarrhea, nausea, and vomiting
	Spirolides	Fast-acting neurotoxins	<i>Alexandrium</i> spp. and <i>Karenia selliformis</i>	Nicotinic acetylcholine receptors
	Gymnodimines	Neurotoxic potential	<i>Karenia brevis</i> and <i>Alexandrium</i> spp.	Cyclic imine neurotoxins
Alkaloid toxins	Tetrodotoxin	Paralysis	Pufferfish and blue-ringed octopus	Blocking nerve and muscle signals
	Saxitoxins	Paralytic shellfish poisoning	<i>Alexandrium</i> spp. <i>Gymnodinium</i> , and <i>Pyrodinium bahamense</i>	Neurotoxicity (sodium channel)
	Domoic acid	Amnesic shellfish poisoning	<i>Pseudo-nitzschia</i> spp. (diatom)	Neurotoxicity and memory impairment

toxins are small organic molecules composed of amino acids and are categorized according to their chemical structures. Conotoxins produced by cone snails (*Conus vulgaris* spp.) have many disulfide bonds and act as neurotoxins that specifically affect the neuromuscular system. Peptide toxins are classified into several categories, such as α -, μ -, ω -, σ -, κ -, and λ -conotoxins [23].

Polyether toxins contain multiple oxygenated ether rings and have high heteroatom-to-carbon ratios. Typically, these toxins are lipophilic and are categorized into three primary structural groups: macrolide, trapezoidal, and linear polyether toxins. Common polyether toxins include CTXs, BTXs, OA, YTXs, AZAs, SPXs, and GYMs. Among them, CTXs produced by the dinoflagellate *Gambierdiscus toxicus* are structurally trapezoidal and are strong toxins are present in the ocean. Diarrhetic shellfish poisoning (DSP) is caused by toxic dinoflagellates such as *Dinophysis* and *Prorocentrum* spp., which produce fat-soluble polyether toxins, including OA, BTXs, and YTXs. These dinoflagellates generate OA, which inhibits protein phosphatases 1 and 2A, resulting in gastrointestinal symptoms, such as nausea, vomiting, diarrhea, and abdominal cramps. YTXs, made by *Protoceratium reticulatum*, *Lingulodinium polyedra*, and *Gonyaulax* spp., can harm the heart but do not cause diarrhea. *Azadinium* spp. and *Amphidoma languida* can cause azaspiration shellfish poisoning, leading to serious stomach problems, and possible nerve and cell damage. BTXs, which are MBs found in *Palythoa* spp., can cause paralytic shellfish poisoning (PSP) and may accumulate in shellfish and fish. Humans are exposed to toxins by eating seafood or by

inhalation during red-tide events [24]. Both *Alexandrium ostenfeldii* and *Alexandrium peruvianum* spp. produce SPXs, which are cyclic imine toxins. These compounds function as neurotoxins by antagonizing nicotinic acetylcholine receptors, resulting in rapid toxicity. Both *Alexandrium* spp. and *Karenia selliformis* produce GYMs, which are another category of cyclic imine neurotoxins. Similar to SPXs, GYMs target nicotinic cholinergic receptors, resulting in fast-acting neurotoxic effects in animal models. However, their precise impact on human health remains under investigation (Table 1) [23, 25–28].

Alkaloid toxins are nitrogen-containing compounds with complex carbon structures often occur as secondary metabolites in marine organisms. These toxins are generally water soluble. Examples of alkaloid MBs include DA, TTX, and STX, which are the key causes of PSP and amnesic shellfish poisoning (ASP). ASP is caused by the potent neurotoxin DA, which is produced by certain diatoms, particularly those in the genus *Pseudo-nitzschia* spp. DA is highly water soluble and stable in various environments. DA primarily affects glutamate receptors, leading to neurotoxicity and memory loss when ingested through contaminated seafood [29]. TTX, a well-known neurotoxin found in pufferfish and blue-ringed octopuses, blocks nerve and muscle signaling. STX is a guanidinoamine neurotoxin initially identified in clams and mussels. Gonyautoxins, including GTX1, GTX2, GTX3, and GTX4, are hydrophilic neurotoxins that play important roles in PSP. Dinoflagellates, especially *Alexandrium* spp., *Gymnodinium catenatum*, and *Pyrodinium bahamense*, are often associated with HABs. STX primarily affects sodium

channels, resulting in neurotoxicity and posing serious health risks through the ingestion of contaminated seafood (Table 1) [30, 31].

2 Optical Immunoassay

Optical immunoassays (OIA) have emerged as prominent biosensing tools for the rapid and highly sensitive identification of MBs. These analyses employ various techniques, including SPR, colorimetric changes, and fluorescence signals, for identifying the changes in light. OIA can deliver accurate results and is cost-effective compared with traditional methods. OIA using biomolecules that interact with light causes noticeable changes in the light absorption, emission, and plasmonic properties of the system, allowing accurate optical detection. These capabilities enable the rapid and accurate detection of marine MBs, highlighting the crucial role of biosensor technology in protecting human health and preserving aquatic ecosystems [32].

2.1 Detection of Hydrophilic MBs via OIA

Harmful algal and shellfish species produce toxic compounds known as hydrophilic MBs. These highly water-soluble toxins, including DA, STX, and BTX, are easily dispersed in aquatic environments and accumulate in marine organisms, such as fish, posing risks to marine life and human health. OIA has been recognized as a quick and accurate technique for detecting these MBs by monitoring visible signals generated via the reaction between antigens and antibodies. The leading techniques are fluorescence, colorimetric, and surface-plasmon-resonance-based immunoassays. Hydrophilic MBs sensors specifically target water-soluble MBs and distinguish them from their lipophilic counterparts.

2.1.1 Colorimetric Detection of Hydrophilic MBs

Colorimetric sensors have been extensively used for the detection of hydrophilic MBs because of their potential for rapid, accurate, and cost-effective monitoring. Recent developments have significantly enhanced the sensitivity and specificity of these methods. Colorimetric immunoassays using immunoassay-based sensors have gained popularity because of their sensitivity, specificity, and applicability in food-safety monitoring. Recent advancements in the methods of detecting DA, STX, and BTXs have focused on colorimetric biosensors using ELISA, aptamers, and MIPs. ELISA is a traditional colorimetric enzyme-based immunoassay based on the specific binding of antigens and antibodies. ELISA is very sensitive and can enable the simultaneous analysis of multiple samples, making novel detection of MBs possible because of specific interactions during the

assay and the production of a colorimetric signal using a secondary antibody. ELISA is widely used in clinical diagnostics [33]. Zuki et al. (2020) developed an ELISA test using the amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) ionotropic glutamate receptor and goat anti-mouse IgG alkaline phosphatase (ALP) for detecting DA in shellfish. The limit of detection (LOD) of DA was accurately measured at concentrations as low as 0.72 ppm. The test showed recovery rates of 89.7% and 86.7% in mussels and cockles, respectively, suggesting that the method can be used for regular monitoring (Table 2) [34].

Aptamer-based colorimetric platform utilize aptamers conjugated to metal nanoparticles (NPs) for detecting MBs. Aptamers are short, single-stranded DNA or RNA sequences that selectively bind to specific targets with high stability and tunability. Upon binding to the target, the NPs undergo aggregation or dispersion, resulting in a visible color change. This competitive binding mechanism enables high sensitivity and facilitates rapid label-free MBs detection [35]. Li et al. (2021) produced an aptasensor based on terminal hybridization for stabilizing the anti-STX aptamer and strengthening the binding. This approach achieved a 145-fold improvement in the specificity compared to that of the commercial method. The detection system incorporated the anti-STX aptamer (TF-M-30f), 3,3',5,5'-tetramethylbenzidine (TMB), and a gold nanoparticles (AuNPs) nanozyme. The aptamer was linked to complementary DNA (cDNA) that was bound to STX. Movement of the cDNA initiated the catalytic activity of the AuNPs nanozyme. This enzymatic reaction led to a distinct colorimetric transition from blue to dark-blue. The assay enabled MBs detection at concentrations as low as 142.3 pM and afforded good recovery rates for the analytes in seawater and scallop samples (Fig. 3a and b) [36]. Qi et al. (2022) developed a sensor using a special molecule made of pyrimidine and purine chains for detecting STX. They created a color-sensing aptasensor functions without labels by connecting an aptamer to a special molecular switch and a AuNPs nanozyme. The aptamer-triplex molecular switch (APT-TMS) undergoes a shape change upon connecting with Plasmodium biomarkers, which causes the purine chains to stick to the surface of the AuNPs. This connection causes a color change matches the amount of Plasmodium present, increasing the peroxidase-like activity of the AuNPs toward TMB [37]. Kong et al. (2022) developed tyrosine and citrate-coated AuNPs, which were used for the effective detection of BTXs-2 and OA. Comparatively, tyrosine-coated AuNPs demonstrated better sensing performance than citrate-coated AuNPs. Tyrosine functioned as both a reducing and capping agent because the amine groups of tyrosine interacted more strongly with the AuNPs. Tyr-AuNPs exhibited superior stability compared to Cit-AuNPs because of the stronger interaction of the tyrosine amine groups with the AuNPs. The adsorbed aptamers on either Cit-AuNPs or Tyr-AuNPs

Table 2 Comparative overview of optical immunoassay (OIA) strategies for the detection of hydrophilic MBs

Sl. No	Method	Type of immuno-assay	Specific assay	Analytes	LOD	Linear range	Assay time	Real sample	Ref
1	CS	ELISA	AMPA receptor and goat anti-mouse IgG AP	DA	0.72 ppm	N.A	N.A	Mussels and cockles	[34]
2	CS	Aptamer	Anti-STX a (TF-M-30f) with AuNPs nanozyme	STX	142.3 pM	0.1457 to 37.30 nM	15 min	Scallop and seawater	[36]
3	CS	Aptamer-TMS	APT-TMS and AuNPs nanozyme with anti-STX	STX	335.6 pmol/L	0.59 to 150 nmol/L	15 min	Seawater	[37]
4	CS	Aptamer	Tyr-AuNPs with aptamer of BTXs-2	BTXs-2	2.25 ppb	0.05 to 4 ppm	5 min	Shellfish	[38]
5	CS	MIPs	Au-Pt nano-particles modified Fe ₃ O ₄ nanozyme	STX	3.1 nM	0.01 µM to 100 µM	30 min	mussels and clams	[40]
6	CS	MIPs	Dihydrokainic acid and DA glutamic acid based nano MIPs	DA	2.12 and 4.32 nmol/L	0.01 to 100,000 and 0.001 to 1000 nmol/L	N.A	Red tide	[41]
7	SPR	Antigen–antibody	Anti-DA mono-clonal with AuNPs and AuNPs with DA-BSA	DA	10 µM	N.A	30 min	N.A	[43]
8	SPR	Antigen–antibody	PAB/ AAHNFs/ AgNPs	STX	0.06 ng/mL	0.1 to 6.25 ng/mL	N.A	River water, mussel, and nassariidae	[44]
9	SPR	Aptamer	Anti-STX with AuNPs nanozyme	STX	10 fM	10 fM to 0.1 mM	30 min	Seawater	[45]
10	SPR	Aptamer	Anti-STX with AuNPs/TMP/ H ₂ O ₂ nanozyme	STX	42.46 pM	78.13 to 2500 pM	15 min	Shellfish	[46]
11	FS	RF-ELISA	CoOOH nano-flakes with anti-STX	STX	3.2 pg/mL	5.5 to 93.7 pg/mL	30 min	N.A	[48]
12	FS	Antigen–antibody	S,P-GQDs and OVA-AuNPs-Anti-STX-MAb	STX	4.9 ng/mL	1.5 to 15.9 ng/mL	60 min	Shellfish	[49]
13	FS	Aptamer -MFA	Fe ₃ O ₄ @Au-Pt nanozymes with STX aptamer	STX	0.6 nM	1 to 5000 nM	10 min	Seashell tissue	[50]
14	FS	Peptide	Zirconium-based NMOFs, TAMRA-labeled aptamer	STX	1.17 nM	0.00 to 190.52 nM	30 min	Shellfish	[51]
15	FS	MIPs	NH ₂ -MIL-101(Fe)-based MIPs with OPD	DA	8.2 nM	0.01 to 10 µM	10 min	Lake water and shellfish	[53]
16	FS	Peptide	STX-SABP1 was tagged with FAM	STX	1.5 ppb	0 to 800 ppb	10 min	N.A	[54]

N.A., Not available

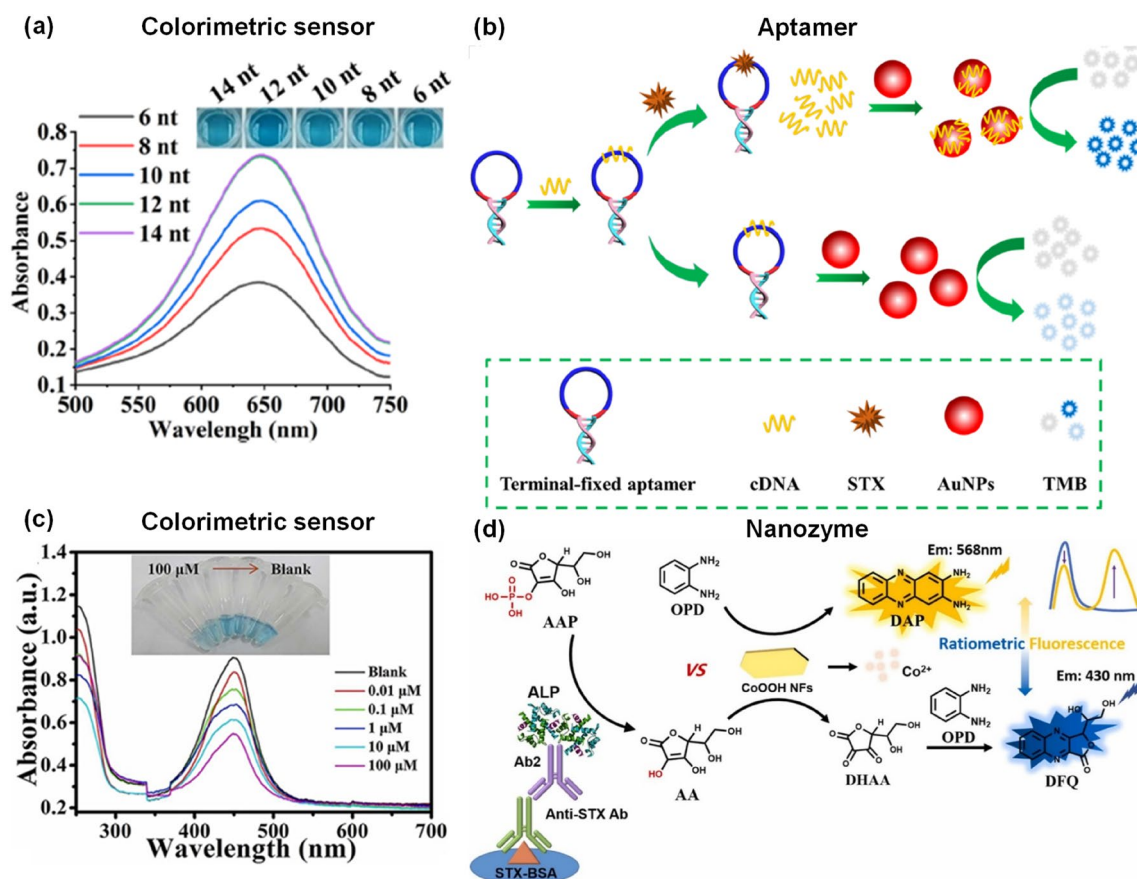


Fig. 3 **a** Colorimetric sensor-based AuNPs-aptamer-cDNA probe for STX detection. Reprinted with permission from [36]. Copyright 2022 Elsevier. **b** Schematic diagram of the terminal-fixed aptamer label-free colorimetric aptasensor (AuNPs-aptamer-cDNA) for STX. Reprinted with permission from [36]. Copyright 2022 Elsevier. **c** Col-

orimetric sensor-based MS@Au-Pt/MIP nanozyme-based sensor for STX detection. Reprinted with permission from [40]. Copyright 2024 Elsevier. **d** Mechanism of STX detection using ratiometric fluorescent sensing as a probe nanozyme. Reprinted with permission from [48]. Copyright 2023 Elsevier

helped stabilize them under high-salt conditions. Target binding reduced aptamer adsorption and enhanced target-dependent NP aggregation upon the addition of NaCl. The label-free color-changing aptamer sensor detected BTXs-2 at levels as low as 2.25 ppb and was tested using shellfish samples containing BTXs-2 (Table 2) [38].

MIPs are synthetic materials designed to selectively recognize target molecules and mimic the specificity of antibodies and aptamers. The monomers assemble around a template and are subsequently removed to create specific binding sites. These binding sites enable the MIPs to detect hydrophilic MBs with high precision, even in complex environmental and seafood samples [39]. Wu et al. (2024) developed an optical sensor for the detection of STX in shellfish. Colorimetric analysis was performed using MIPs and gold-platinum-iron oxide (Au-Pt/Fe₂O₃) nanozymes. The MIP polymer was synthesized using 3-aminopropyltriethoxysilane (APTES) and tetraethyl orthosilicate (TEOS). The binding of STX to the polymer cavities generated a blue color, blocking the catalytic sites and halting TMB oxidation.

As the concentration of STX increased, the absorbance decreased (Fig. 3c) [40]. Quezada et al. (2021) developed a molecularly imprinted nanoparticle-based assay (MINA) probe for the detection of DA. They used dihydrokainic acid (DKA) as a template for DA and glutamic acid as the imprinting component. The tests demonstrated high selectivity and the absence of cross-reactivity with structurally related drugs. Horseradish peroxidase (HRP)-labeled DA and HPP-DKA competed for the MINA-binding sites. The color intensity decreased as the DA concentration increased, indicating a decrease in the number of HRP-DKA molecules bonded to MINA (Table 2) [41].

2.1.2 SPR-Based Detection of Hydrophilic MBs

SPR is an optical sensing technique which utilizes plasmon oscillations for detecting analyte interactions in real-time. This approach is particularly effective for detecting marine toxins such as DA, STX, and TTX. This technique relies on a specific antigen adherence to the corresponding antibody or

aptamer, causing a shift in the resonance absorbance peak in proportion to the concentration of MBs. However, the small size of MBs poses a challenge for their direct detection. To overcome this problem, competitive and SPR-band-based sensors are commonly utilized (Table 2) [42].

The antigen–antibody interaction involves highly specific binding in which an antigen binds with a matching antibody to form an immune complex. This principle is crucial for detecting MBs using both plasmonic and colorimetric methods. Nelis et al. (2021a) used a plasmonic biosensor array for detecting DA. This functionality was derived from plasmon coupling between gold nanorods (AuNRs) and AuNPs. AuNRs were synthesized using the seed-mediated growth method with silver and gold by controlling the amount of cetyltrimethylammonium bromide (CTAB) and altering the acidity, which led to an SPR band at 784 nm. The nanorods were fixed onto a silica support and treated with NR-DA-bovine serum albumin (BSA), a protein connected to DA. The AuNPs were treated with anti-DA-NPs, an anti-DA monoclonal antibody. That study employed two approaches for detecting DA: one based on changes in SPR and the other using dark-field microscopy combined with pixel-based image analysis. Both methods effectively detected DA at low concentrations, highlighting their potential for food-safety applications and biosensors [43]. Wei et al. (2024) developed a nanoflower-based plasmonic immunosensor for STX detection. Artificial antibody-hybrid nanoflowers (AAHNFs) were employed to enhance the sensor stability and sensitivity. The detection mechanism of the sensor relies on SPR changes in silver nanoparticles (AgNPs), which vary with different amounts of STX. The iodine/iodide (I_2/I^-) system and ALP/ascorbic acid 2-phosphate (AAP) acted cooperatively to degrade the AgNPs. This process amplifies the signal and improves the detection accuracy. The immunosensor performed better than ELISA methods, with a LOD of 0.06 ng/mL, by enhancing factors that affect the activity of the antibody in AAHNFs (Table 2) [44].

Aptamer-based SPR sensors offer high sensitivity and selectivity for the rapid detection of MBs. Qiang et al. (2020) created a plasmonic biosensor that could quickly detect STX using anti-STX aptamers linked to AuNPs. This sensor utilizes aptamer-induced AuNPs aggregation, which results in visible plasmonic changes. When STX was added to the solution and bound to the aptamer, the AuNPs aggregated in the presence of NaCl. Changes in the absorbance of the SPR band affect the A_{680}/A_{520} ratio, which was used to quantify STX, with a LOD of 10 fM and run time of 30 min [45]. Zhao et al. (2021) developed a plasmonic sensor for STX detection by incorporating a hybridization chain reaction (HCR) to boost the signal. In this setup, AuNPs functioned as nanozymes, accelerating the reaction with TMB, whereas magnetic beads helped to minimize background noise. The anti-STX aptamer hybridizes with a complementary strand

on the magnetic beads, engaging in competitive binding with STX. Magnetic separation removes the aptamer-STX complex from the liquid, which then triggers HCR to create double-stranded DNA (dsDNA) structures, boosting the peroxidase-like activity of the AuNPs (Table 2) [46].

2.1.3 Fluorescence Detection of Hydrophilic MBs

Recent advancements in fluorescence-based detection have improved the monitoring of hydrophilic MBs such as DA and STX. Key innovations include fluorometric immunoassays, aptamer-based sensors, MIPs, and peptide-based technologies. Fluorescence sensors, in particular, utilize materials that emit light upon excitation at specific wavelengths. In assay-coated fluorescence sensors, the analyte is typically conjugated to fluorescent probes such as nanoclusters, quantum dots, or small organic molecules. The binding of hydrophilic MBs to these probes induces measurable fluorescence changes, enabling indirect detection [47]. The binding of the analyte to the antibody causes a rapid change in the fluorescence intensity that is inversely proportional to the analyte concentration. Luo et al. (2023) developed an ultrasensitive STX detection method using a ratiometric fluorescence (RF) immunoassay enhanced by an enzyme-nanozyme cascade. This RF-ELISA system uses cobalt oxyhydroxide nanoflakes (CoOOH NF) as enzymes to convert a non-fluorescent substance, *o*-phenylenediamine, into a fluorescent compound, 2,3-diaminophenazine, which emits light at 568 nm. This enabled the measurement of STX. The production of ascorbic acid mediated by ALP modulates the catalytic activity of CoOOH NF, resulting in a RF response. Anti-STX polyclonal antibodies enhance the specificity, making this method valuable for clinical diagnostics (Fig. 3d) [48]. Yin et al. (2022) developed a dual-emission fluorescence-linked immunosorbent assay (FLISA) for detecting STX in shellfish. This method uses AuNPs covered with ovalbumin (OVA-AuNPs) and sulfur–phosphorus-doped graphene quantum dots (S,P-GQDs) to generate light of two different colors from one light source. The brightness of the emission from the OVA-AuNPs-Anti-STX-MAb increased as the concentration of STX increased, but remained the same for S,P-GQDs-Anti-OA-MAb. This indicates that the two types of antibodies function independently in the photoluminescence process (Table 2) [49].

Aptamer-based fluorescence detection is a highly sensitive and specific analytical technique for the detection of hydrophilic MBs. The magnetic fluorescence aptasensor (MFA) for detecting STX, as described by Zhu et al. (2022), uses an aptamer that specifically targets STX and $Fe_3O_4@Au$ -Pt nanozymes, leading to improved detection capabilities. The aptamer binds to STX, releasing its complementary DNA, resulting in a change in fluorescence. The nanozymes help to oxidize TMB, creating ox-TMB, which reduces the

fluorescence of graphene quantum dots (GQDs) owing to the inner-filter effect. This system achieved a LOD of 0.6 nM, demonstrating high sensitivity and accuracy [50]. Dou et al. (2023) developed a fluorescence sensor employing graphene oxide (GO) and a labeled peptide for STX detection, as illustrated in Fig. 4a and b. This sensor can detect minimal amounts of STX, with a LOD of 1.5 ppb, and uses special tiny structures made of zirconium and fluorescent materials along with labelled aptamers. Under UV light, TAMRA produces a faint red glow, which becomes stronger when bound to the toxin, allowing the detection of STX at a level of 1.17 nM [51]. The integration of MIP-based fluorescent probes enabled highly sensitive optical detection, in which fluorescence quenching or enhancement signals target binding events [52]. The RF sensor capable of detecting DA in water and shellfish. In this system, NH₂-MIL-101(Fe) was utilized as both an intrinsic fluorophore (emitting at 452 nm) and

a peroxidase-like catalyst. The sensor works via indicator displacement transduction (IDT), whereby the attachment of DA terminates the creation of hydroxyl radicals. The resulting increase in the emission intensity at 452 nm is accompanied by disappearance of the 556 nm signal of the oxidation product 2,3-diaminophenazine. To reduce the toxicity and cost of DA, 1,3,5-pentanetricarboxylic acid has been used as a substitute. The sensor displayed a broad detection range of 0.01–10 μM, with a LOD as low as 8.2 nM. The reliability of the sensor was confirmed through spike-and-recovery experiments conducted on lake water and shellfish samples [53]. Fluorescence-based sensors utilizing GO and peptide-based recognition elements have been developed for detecting STX with high sensitivity. A fluorescence sensor developed by Kim et al. (2023) used a special peptide chosen through phage display and marked with 5-carboxy-fluorescein. In this system, GO effectively diminished the

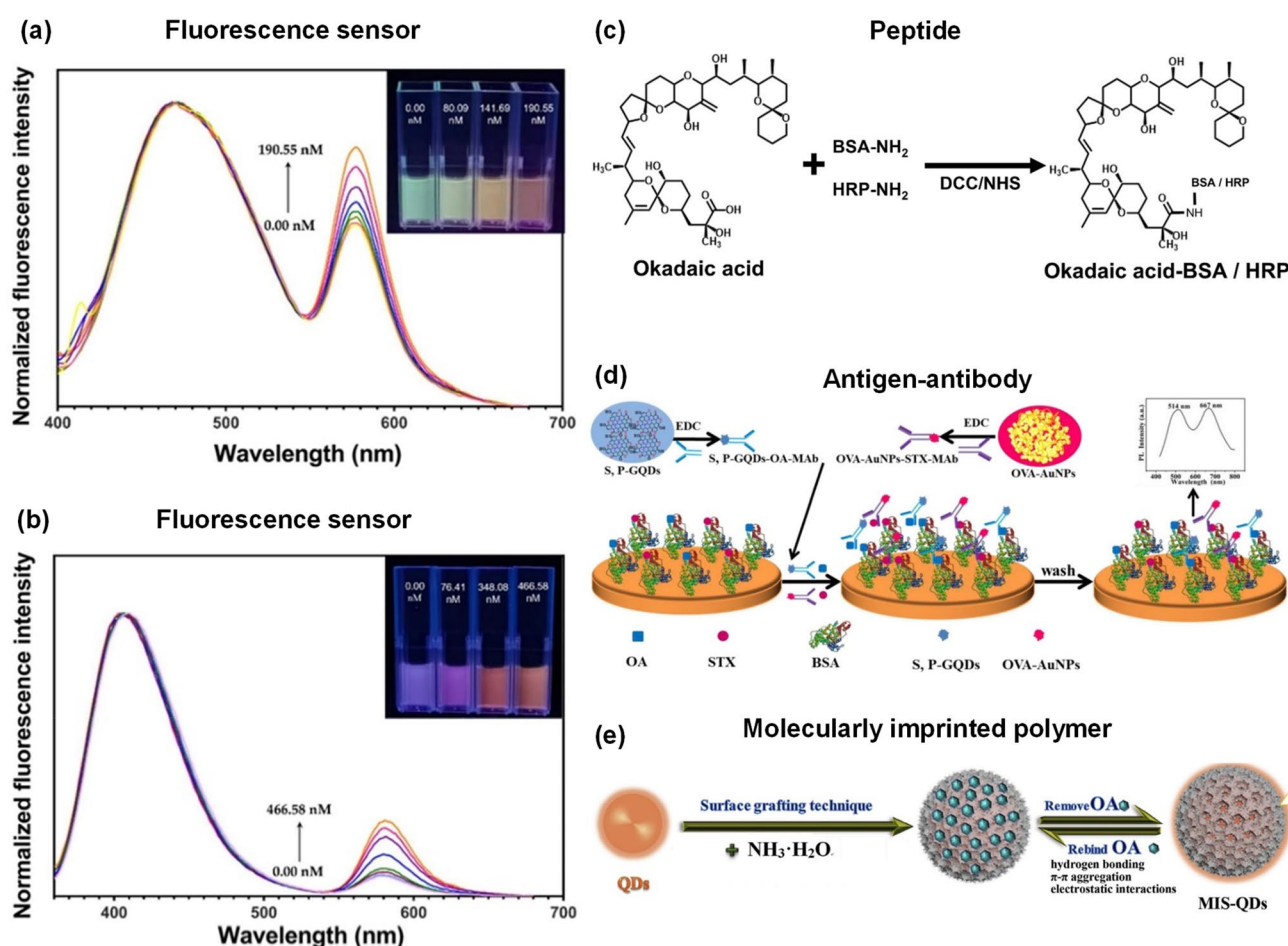


Fig. 4 **a** Normalized fluorescence spectra of NMOF-based aptasensor for STX detection. Reprinted with permission from [51]. Copyright 2023 Elsevier. **b** Fluorescence spectra of NMOF-based aptasensor for TTX detection. Reprinted with permission from [51]. Copyright 2023 Elsevier. **c** Synthesis of BSA-OA and HRP-OA peptide-based probes for OA detection. Reprinted with permission from [56]. Copy-

right 2023 Elsevier. **d** Schematic of competitive fluorescence-linked immunosorbent (antigen–antibody) assay for OA and STX detection. Reprinted with permission from [49]. Copyright 2022 Elsevier. **e** Molecularly imprinted polymer (MIPs)-functionalized, silica-coated quantum dots for OA detection. Reprinted with permission from [59]. Copyright 2020 Elsevier

fluorescence through π – π interactions. Binding of STX disrupted these interactions, leading to an increase in the fluorescence depending on the toxin concentration. This highly sensitive sensor offers a detection limit as low as 1.5 ppb, consistently works well with certified reference materials, and undergoes strong interaction with the STX-specific binding peptide (SABP1). GO was chosen because it effectively reduces the fluorescence and improves the detection performance (Table 2) [54].

2.2 Detection of Lipophilic MBs via OIA

Lipophilic MBs are toxic substances produced by marine microalgae, mainly dinoflagellates and diatoms, which are widely consumed on the food chain and can cause serious health problems. Key MBs, including OA, YTXs, AZAs, BTXs, SPXs, and GYMs, accumulate in seafood, especially shellfish, and pose considerable health risks to humans. OIA methods, such as SPR, fluorescence, and colorimetric techniques, have been developed for their detection [7].

2.2.1 Colorimetric Detection of Lipophilic MBs

Colorimetric sensors have gained popularity for detecting lipophilic MBs owing to their simplicity, cost-effectiveness, and rapid results.

Recent advancements in OA detection include the novel peptide and immunoassay-based approaches. Cho et al. (2023) developed a peptide-based ELISA method that eliminates the need for expensive antibodies and demonstrated the use of an OA-binding peptide (OA BP) as a receptor. Figure 4c illustrates the preparation of OA BPs by using dicyclohexylcarbodiimide (DCC) and N-hydroxysuccinimide (NHS) to activate the carboxyl group of OA, creating an NHS ester attached to amine-functionalized BSA. Compared to previous approaches, the newly developed direct competitive ELISA (dc-ELISA) offers a higher LOD of 5.41 ng/mL [56]. Tian et al. (2022) developed an advanced immunoassay for OA detection using gold-platinum nanoparticles (Au@Pt NPs) and HRP in a TMB–H₂O₂ colorimetric system. They created a strong monoclonal anti-OA antibody (McAb) attached to Au@Pt NPs and goat anti-mouse IgG with HRP. The optimized immunoassay achieved a LOD of 0.04 ng/mL, outperforming traditional Au/HRP-based ELISA. Validation using shellfish samples demonstrated the high accuracy and reliability of the method (Table 3) [57].

Aptamer-based devices enable the quick, precise, and specific detection of dangerous toxins such as OA, dophysistoxin-1 (DTX-1), and DTX-2. Li et al. (2022b) created a color-changing sensor that utilizes a specific aptamer to compete for binding with OA and DTXs. The aptamer acts as a tiny enzyme that attaches to toxins, causing the release of cDNA and increasing the enzyme-like activity. This

process produced a colorimetric signal at 650 nm for MBs quantification. Computer modelling has improved cDNA sequences, as well as detection methods, where molecular docking and biolayer interferometry have been used to study the interaction of aptamers with MBs. The linear detection range of the sensor in the analysis of seawater and scallop samples was 0.47–7.5 nM, with a LOD of 86.28 pM [58]. Kong et al. (2022) developed a stable, label-free colorimetric aptasensor for the detection of BTXs-2 and OA by utilizing AuNPs synthesized with tyrosine as a reducing and capping agent. Strong Au–N interactions between the amine groups of tyrosine and the AuNPs improved the stability and sensitivity of the sensor. The sensing process involved aggregation of the tyrosine-covered AuNPs upon the attachment of toxins, which caused a loss of stability and a change in the UV–visible absorbance spectrum. The sensor reliability, LOD, and usefulness for detecting marine toxins were confirmed using UV–vis spectroscopy and isothermal titration calorimetry, reaching a LOD of 5.19 ppb for OA and 2.25 ppb for BTXs-2 (Table 3) [38].

2.2.2 SPR-Based Detection of Lipophilic MBs

SPR-based sensors are important for the detection of lipophilic MBs because they are very sensitive, do not require labels, and work through interactions between the target molecules and surfaces of the NPs sensor. SPR-based spectroscopic ellipsometry (SE) and internal reflection spectroscopic ellipsometry (TIRE) have become promising label-free biosensing methods for finding BTXs. Caglayan et al. [55] reported a study that used these SPR-compatible ellipsometric methods with aptamer-based recognition elements to sensitively detect BTXs. Silico exclusion/inclusion strategy based on two previously reported aptamers, a new anti-BTXs aptamer/ Au film were fabricated as a probe. The new aptamer worked well as regular sequences for analysis, with LOD of 1.32 ng/mL in SE and 720 pg/mL in TIRE methods in the detection range (0.05–1600 nM for TIRE and 0.5–2000 nM for SE). Also, probes worked well for detecting BTXs in real samples like fish and shrimp. These results show that SPR-enhanced ellipsometric techniques could be used to monitor lipophilic BTXs in complex matrices with high sensitivity (Table 3) [55].

2.2.3 Fluorescence-Based Detection of Lipophilic MBs

A quick and sensitive method for identifying lipophilic MBs involves the use of fluorometric sensors. Various techniques have been used for fluorescence detection, including the use of small organic molecule probes, QDs, NPs, and systems using antigen–antibody, aptamers and MIPs [7]. Yin et al. (2022) created a sensor that uses light to detect OA and STX by combining special molecules called aptamers with GQDs

Table 3 Comparative overview of OIA strategies for the detection of lipophilic MBs

Sl. No	Method	Type of immunoassay	Specific assay	Analytes	LOD	Linear range	Assay time	Real sample	Ref
1	FS	Aptamer	DAIA-CuNPs	OA	1.1 ng/L	1.0 ng/L to 50.0 µg/L	30 min	Shellfish	[15]
2	CS	Aptamer	Tyr-AuNPs with aptamer (BT10)	BTXs-2 and OA	2.25 ppb and 5.19 ppb	0.05 to 4 ppm	30 min	Shellfish	[38]
3	FS	Antigen–anti-body	S, P-GQDs-Anti-OA-MAb, and OVA-AuNPs-Anti-STX-MAb	OA and STX	1.3 and 0.2 ng/mL	2.0 to 98.9 and 1.5 to 15.9 ng/mL	60 min	Alectryonella plicatula	[49]
4	SPR	aptamer	anti-BTXs-Au film	BTXs	720 pg/mL and 1.32 ng/mL	0.5 nM to 2000 nM and 0.05 nM to 1600 nM	90 min	Fish and shrimp	[55]
5	CS	dc-ELISA	OA binding peptide	OA	5.41 ng/mL	0 to 2,500 ng/mL	15 min	Shellfish	[56]
6	CS	ELISA	HRP-conjugated goat anti-mouse IgG antibody on Au@Pt/McAb	OA	0.04 ng/mL	0.12 to 10.00 ng/mL	N.A	N.A	[57]
7	CS	Aptamer	Aptamer and AuNPs@Fe ²⁺ nanozyme	OA	86.28 pM	0.4688 to 7.5 nM	20 min	Seawater and scallop	[58]
8	FS	MIPs	MIS-QDs	OA	0.25 mg/kg	10.0 to 100.0 mg/kg	6 min	Shellfish	[59]
9	FS	MIPs	CDs@SiNPs	OA	25 ng/L	100 to 1770 ng/L	10 min	Seawater and sediment	[60]
10	FS	Aptamer	Fe ₃ O ₄ @MOF@AuNPs with OA-aptamers	OA	0.015 ng/mL	0.05 to 3.00 ng/mL	20 min	Clam and mussel	[61]

N.A., Not available

and AuNPs such as S, P-GQDs-Anti-OA-MAb, and OVA-AuNPs-Anti-STX-MAb. This biosensor utilizes AuNPs-mediated fluorescence quenching to restore the fluorescence after the OA binds to the aptamer, with a LOD of 1.3 ng/mL (Fig. 4d) [49]. Figure 4e shows special quantum dots covered with silica for the specific identification of OA. To fabricate these quantum dots, the researchers combined CdSe/CdS/ZnS quantum dots, TEOS, and ammonium hydroxide using OA, 3-(trimethoxysilyl)propyl methacrylate, and APTES as guides. This process fabricated special binding sites that capture only OA by matching shapes and interacting with the molecules. The molecularly imprinted silica material-coated quantum dots (MIS-QDs) demonstrated strong specificity and selectivity for the fluorescence quenching of OA. Cold-plasma grafting was used to attach the analyte to 96-well microplates to facilitate direct competition. The system achieved a detection range of 10.0–100.0 mg/kg, with a LOD of 0.25 mg/kg in shellfish [59]. Lian et al. (2021) fabricated a fluorescent nanosensor for detecting OA using a

method with molecular imprinting, which allows the emission of two different colors of light. To fabricate the sensor, red-emitting carbon dots (CDs) from *Cercis gigantea* leaves were mixed with silica nanoparticles (SiNPs) using a sol–gel process, to improve their stability. Subsequently, a MIP shell was formed around the core of the CDs@SiNPs using the MIPs as the fake template, APTES as the monomer, TEOS as the crosslinker, and APTES-NBD as the fluorescent probe. The nanosensor detected OA in seawater and sediment using the light-driven electron-transfer effect between APTES and 7-nitrobenz-2-oxa-1,3-diazole (NBD). When OA binds to the sensor, it creates hydrogen bonds between the carboxyl and amino groups of the polymer, which turns off the fluorescence at 549 nm and turns it on at a different wavelength. This interaction generates a visible color shift from red to yellow-green, enabling rapid detection, as illustrated in Fig. 5a and b (Table 3) [60].

The aptamer-based fluorescence detection of lipophilic MBs employs techniques such as fluorescence quenching,

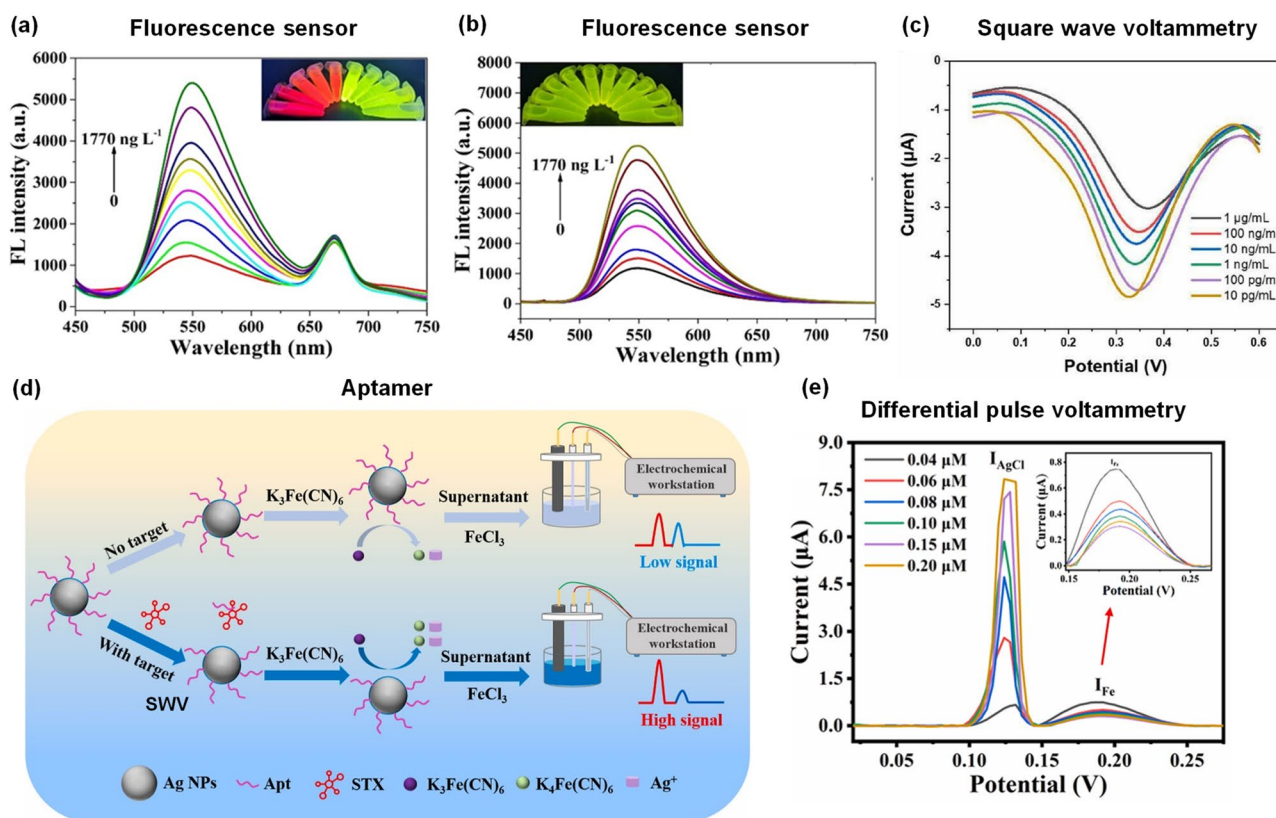


Fig. 5 **a** Fluorescence spectra of MIPs exposed to different concentrations of OA. Reprinted with permission from [60]. Copyright 2021 Elsevier. **b** Fluorescence spectra of SiO₂@NBD@MIPs exposed to different concentrations of OA. Reprinted with permission from [60]. Copyright 2021 Elsevier. **c** Square wave voltammetry spectra of the MHA/pPtNP/STX electrode for STX detection over a concentration range of 10 pg/mL to 10 µg/mL. Reprinted with permission from

[68]. Copyright 2022 Elsevier. **d** Aptamer-based electrochemical sensor for STX detection using K₃Fe(CN)₆-regulated silver nanoparticles. Reprinted with permission from [69]. Copyright 2024 Elsevier. **e** Differential pulse voltammetry (DPV) peak current for STX detection using K₃Fe(CN)₆-regulated silver nanoparticles modified with aptamer. Reprinted with permission from [69]. Copyright 2024 Elsevier

Forster resonance energy transfer (FRET), and signal transduction, which are often enhanced by nanomaterials. The diamino isophthalic acid (DAIA)-copper nanoparticle (CuNPs) system is a highly sensitive sensor uses fluorescent aptamers to detect OA by enhancing the signals with nanoparticles. In this sensor, a duplex aptamer structure is anchored onto magnetic beads. In the presence of OA, the duplex is disrupted, and the single-stranded aptamers released in the process act as a template for CuNPs formation. This process resulted in a fluorescence signal proportional to the concentration of OA. In the absence of OA, the duplex remains intact, preventing CuNPs synthesis and fluorescence emission. This method enabled detection of the analytes at low concentrations, with a LOD of 1.1 ng/L, demonstrating high specificity and trace-level detection [15]. Zhou et al. (2024) reported a magnetic aptasensor that utilized laser-induced fluorescence for detecting OA in seafood. The sensor incorporates modified Fe₃O₄@MOF@AuNPs with OA-specific aptamers, facilitating effective magnetic separation and measurement. The detection process features

an aptamer hybridized with FAM-labelled cDNA through strong Au-SH interactions. When OA is present, the aptamer changes its shape, causing the release of FAM-cDNA into the surrounding liquid and creating a fluorescence signal that reflects the amount of OA. The Fe₃O₄ magnetic nanoparticles allow for rapid separation and improved binding efficiency and specificity (Table 3) [61].

3 Electrochemical Immunoassay

Electrochemical immunoassays (EIA) are advanced bio-sensing technologies utilize various forms of electrochemical conversion for the rapid and accurate detection of MBs. The main principle of EIA is biomolecules interact with an electrode surface, leading to noticeable changes in electrical signals such as the current, voltage, and resistance. Recent advancements in biosensor technologies have facilitated the multiplex detection of MBs within a single assay, thereby reducing both the assay time and sample volume.

In addition, the integration of microfluidic platforms has enhanced the efficiency of toxin screening. These electrochemical methods are essential for the selective, sensitive, and reliable detection of microbes, underscoring their significance in public health protection and the conservation of aquatic ecosystems [62].

3.1 Detection of Hydrophilic MBs via EIA

Modern assays utilize methods such as voltammetry and EIS, which are often improved by using ELISA and aptamers. Hydrophilic MBs such as DA, STX, and TTX are essential for detecting harmful substances in the ocean that can cause serious nerve damage and health problems. These toxins are produced by harmful algal species and can trigger ASP and PSP outbreaks. The development of quick, affordable, and easily transportable electrochemical biosensors is essential for monitoring and managing MBs contamination in seafood in real time [63].

3.1.1 Voltammetric Detection of Hydrophilic MBs

Voltammetry is used to selectively target hydrophilic MBs on a redesigned working electrode surface with a biorecognition element. The target MBs affect electrochemical parameters such as the charge-transfer potential and current. Nelis et al. (2021b) developed an EIA recognizes DA and OA. The EIA employed carbon-black-modified screen-printed electrodes (CB-SPE). The sensor operates via competitive immunoassay, in which DA-mAb and OA-mAb competitively bind with toxin-protein pairs (BSA-DA and OVA-OA) instead of free MBs. A secondary antibody connected to alkaline phosphatase breaks down 1-naphthyl phosphate, producing a substance is detected by differential pulse voltammetry (DPV). The response is inversely proportional to the toxins concentration. The sensor is very accurate, stable, and sensitive to DA and OA in solution, with the ability to detect toxins at concentrations as low as 1.7 ng/mL and 1.9 ng/mL in mussel extract [64]. Electrochemical MIPs are special materials improve the precision and sensitivity of sensors using a technique called molecular imprinting, along with electrochemical detection. These polymers are formed by polymerizing the core shell to capture and release the target toxins. Jiang et al. (2022) developed a sensor for detecting DA by mixing polydopamine-reduced GO (PDA-rGO) with polyacrylamide (PAM). MIP enabled selective recognition through reversible hydrogen bonding, while PDA-rGO improved the charge transfer and sensor sensitivity. The detection mechanism employs imprinted cavities in PAM to capture DA, leading to measurable electrochemical signals. PDA-rGO accelerated the movement of electrons, facilitating the detection of DA at levels of 1–600 nM, with a LOD of 0.31 nM [65]. Liu et al. (2024) developed a peptide-based

sensor for detecting STX, a potent neurotoxin associated with paralytic shellfish poisoning. In molecular simulations, peptide S4 bound strongly to STX through hydrogen bonding and van der Waals interactions. To enhance the performance, reduced GO and AuNPs were incorporated to improve the transfer of electrons and detection sensitivity. The method was validated using seawater and oyster powder, with recovery rates ranging from 87.3% to 116.2% (Table 4) [66].

Li et al. (2024) described a novel sensor used a small pillar structure on a Au electrode to accurately detect small amounts of STX. The sensor was constructed by forming a PAN nanopillar film and sputtering it with AuNPs. MB-tagged anti-STX aptamers (MB-Apt) were immobilized on the electrode via Au–S interactions. DNA strand with 5 thymine bases (T5) was introduced to prevent structural collapse. When attached to STX, MB-Apt changes its shape, which improves electron transfer and raises the oxidation current, allowing for the detection of STX across a wide range with high sensitivity and selectivity [67]. Figure 5c shows a highly sensitive biosensor created by Park et al. (2022) that uses electrochemical aptamers to detect STX in water. The sensitivity of the sensor was enhanced by incorporating a gold electrode modified with porous platinum nanoparticles (pPtNPs). The thiol-modified STX aptamer was treated with tris(2-carboxyethyl)phosphine. This was subsequently attached to pPtNPs and an STX-coated gold electrode to facilitate selective detection. Square-wave voltammetry (SWV) confirmed the high sensitivity and ability of the sensor to distinguish STX from toxins, similar to DA [68]. Chwan et al. (2024) developed a biosensor able to low cost detect STX in MBs at on-site. Microfluidic technology using a DNA-based aptamer sensor enabled rapid on-site detection. To enhance the surface area and conductivity, they created, filtered, and dried a nanocomposite of polyaniline (PANI) and rGO. This nanocomposite was coated onto a SPE, allowing the attachment of a DNA probe. A probe targeting the STX-4 gene was electrochemically linked to DNA from algal cultures or environmental samples. The electrochemical signal was altered upon hybridization with STX-specific DNA, as measured by DPV. Sensitivity tests indicated high specificity, with a detection sensitivity of 10–10,000,000 cells/mL, meaning the probe did not react to unrelated sequences [62]. Figure 5d and e show a highly sensitive electrochemical aptasensor for detecting STX. Zeng et al. (2024) modified AgNPs with an STX-specific aptamer using potassium ferricyanide ($K_3Fe(CN)_6$). In the absence of STX, $K_3Fe(CN)_6$ partially dissolves the AgNPs, generating Ag^+ and reducing Fe^{3+} to Fe^{2+} . The DPV signal is weak because $Fe[Fe(CN)_6]^-$ is formed by $FeCl_0$, and $AgCl$ precipitates with Cl^+ . The attachment of STX causes the aptamer the break apart, revealing the AgNPs and accelerating the etching process. This aptasensor uses ratiometric signals to

Table 4 Comparative overview of EIA strategies for the detection of hydrophilic MBs

Sl.No	Method	Type of immuno-assay	Specific assay	Analytes	LOD	Linear range	Assay time	Real sample	Ref
1	DPV	Aptamer	Polyaniline/rGO SPCE	STX	10 cells/mL	10 to 10,000,000 cells/mL	30 min	N.A	[62]
2	DPV	Antigen–anti-body	CB-modified SPEs with DA-mAb/OA-mAb	OA and DA	1.7 and 1.9 ng/mL	4 to 34 and 0.35 to 3.9 ng/mL	30 min	Mussel	[64]
3	DPV	MIPs	MIPs-SPEs with PDA-rGO/PAM	DA	0.31 nM	1 to 600 nM	10 min	Mussel	[65]
4	DPV	Peptide	Specific peptides and rGO-AuNP composites	STX	6.9×10^{-4} µg/L	10 to 1000 ng/L	90 min	Seawater, artificial seawater, and oyster powder	[66]
5	DPV	Aptamer	T5/MB-Apt/Au@PAN nanopillar array	STX	1 pM	3 to 100 nM	30 min	Shellfish	[67]
6	SWV	Aptamer	pPtNP/STX aptamer complex	STX	4.669 pg/mL	10 pg/mL to 1 µg/mL	20 min	Freshwater	[68]
7	DPV	Aptamer	K ₃ Fe(CN) ₆ , Ag nanoparticles with STX aptamer	STX	1 nM	0.04 to 0.15 µM	90 min	Clams and mantis shrimps	[69]
9	EIS	Antigen–anti-body	CB-,SPE, AuNPs, and GNST with anti-DA	DA	0.4 ng/mL	5 to 62 ng/mL	2 min	Shellfish	[70]
10	EIS	Aptamer	Au/APT-STX/6-mercaptophexanol	STX	0.3 µg/L	0.3 to 30 µg/L	60 min	Lake water	[71]

N.A., Not available

detect STX in water and seafood, reducing the background noise while maintaining the binding ability of the aptamer and sensitivity. A label-free design and streamlined system enhanced the accuracy of the sensor by eliminating the need for complex electrode modifications (Table 4) [69].

3.1.2 Impedance Detection of Hydrophilic MBs

EIS is used to monitor changes in the capacitance and charge transfer resistance at electrode–electrolyte interfaces. Target-induced changes in impedance at the sensor interface allow aptamer-based EIS sensors to detect MBs with high specificity and sensitivity [92]. Nelis et al. (2020) reported the addition of gold nanostars (GNST), AuNPs, and CB-SPE for detecting DA. The cost-effectiveness and exceptional electrochemical properties of CB-SPE render it ideal for DA detection. To prepare CB-SPE, layers of CB, AuNPs, and GNST were individually added to the electrodes one at a time. Functionalized magnetic beads covered with anti-DA antibodies were added to improve the accuracy and flow of electrons, facilitating magnetic separation

of the immunocomplex. The biosensor was designed to improve the flow of electrons and detect electrical signals when a magnetic field was used to pull the immunocomplex, which helps reduce interference from other materials in complicated samples, such as shellfish. The biosensor also showed strong ability to specifically detect DA with very tiny interference from other substances, reaching a LOD of 0.4 ng/mL, which is better than that achieved with regular electrodes [70]. Serrano et al. (2021) developed a sensor using EIS and magnetic beads for detecting STX, which is a strong toxin found in some algae. In this sensor, a special DNA piece (M-30f) is attached to a gold electrode via strong bonds to ensure the stability of the sensor. The detection process depends on important factors: when the aptamer attaches to STX, it changes its shape, which affects the charge transfer resistance (R_{ct}). This alteration disrupts electron flow at the electrode–electrolyte interface, resulting in enhanced impedance changes. Additionally, when the aptamer folds after connecting with STX, the repulsion between the charges is reduced, which increases the signal intensity. The biosensor was used to accurately check water

safety, with a LOD of 0.3 µg/L, showing strong accuracy and reliability (Table 4) [71].

3.2 Detection of Lipophilic MBs via EIA

Lipophilic MBs from HABs present significant risks to marine organisms, resulting in foodborne illnesses such as ASP and PSP. EIA provides a quicker and more cost-effective alternative for detecting toxins, including OA, YTXs, AZAs, SPXs, and GYMs, owing to advancements in nanomaterials, label-free detection methods, and multiplex assay designs. Nevertheless, challenges persist regarding standardization, field applicability, cross-reactivity, and biosensor stability [84].

3.2.1 Voltammetry Detection of Lipophilic MBs

Voltammetric sensors effectively detect MBs such as OA using redox reactions. Recent advances in nanomaterials have significantly enhanced the sensitivity of sensors employing various techniques, including EIS and electro-generated chemiluminescence (ECL). These advancements have enabled the detection of ultra-trace levels of MBs using photoelectrochemical immunosensors (PECIA). PECIA have garnered attention owing to exceptional sensitivity and specificity. Zheng et al. (2021) developed competitive Near-Infrared (cNIR)-PECIA for OA detection, achieving good detection with the help of antibodies, even at very low levels of 0.007 ng/mL. The sensor worked effectively within the range of 0.01–60 ng/mL, using a special electrode made with tungsten oxide and upconversion nanophosphors (UCNPs). Adding chitosan made the electrode more stable, and monoclonal antibodies attached to NaYF₄:Yb,Tm UCNPs facilitated signal transmission when activated by 980 nm NIR light, boosting the photocurrent (Fig. 6a, b and, Table 5) [72].

Three-dimensional gold nanoelectrode ensembles (3d-GNEES), fabricated via electrodeposition, afford significantly enhanced surface areas and electrochemical properties. By adding polythionine, electrodes improved electron transfer and offered many amino groups for attaching glutaraldehyde and anti-OA antibodies. The detection method, which uses EIS and SWV, had an extremely low LOD of 3.20×10^{-15} g/mL and 2.65×10^{-12} g/mL across a wide range of measurements (Fig. 6c) [73]. To enhance both the sensitivity and specificity, a two-dimensional C₃N₄-based electrochemical aptasensor was developed for OA detection, as reported by Chen et al. (2024). The sensor uses g-C₃N₄ nanosheets with amino groups and special anti-OA aptamers possessing a thiol group to improve its ability to conduct electricity and send signals. Reverse amplification is triggered when free aptamers bind to the matching ssDNA-coated g-C₃N₄, which slows the movement of electrons and

enhances the sensitivity of the sensor. Upon connecting to the aptamer, OA separates from ssDNA, reestablishing charge transfer and causing clear changes in the DPV signal. This method enables ultrasensitive OA detection with a LOD of 0.080 pg/mL (Table 5) [74].

In addition to electrochemical voltammetry, impedance, ECL, and microfluidic sensors provide additional detection strategies. Peng et al. (2020) developed an ECL immunosensor for the detection of OA using S,P-GQDs as effective light-emitting materials. A sensor electrode modified with CMCNT-PDDA-AuNCs exhibited enhanced electron transfer, surface area, and optimized performance. Figure 6d shows the method of measuring free and attached OA using an indirect competitive ECL immunoassay, which produced a weaker ECL signal as the amount of OA increased, with a LOD of 0.005 ng/mL and a range of 0.01–20 ng/mL [75]. The piezoelectric aptasensor utilized AuNPs on a quartz crystal microbalance (QCM) platform for label-free OA detection. When OA attaches to aptamer, it stops the aptamer from linking with capture DNA, which reduces the mass and changes the frequency, enabling a LOD as 0.32 nM over a broad range of 0.5–200 nM [76]. Kim et al. (2024) developed a novel EIA for detecting TTX. This sensor uses a special binding peptide fabricated from a phage display, where the screen-printed electrode is replaced with polypyrrole and AuNPs. This peptide offers enhanced specificity, simple synthesis, and stable performance. Cysteine facilitates strong binding of the peptide with gold, and changing both electrodes improves how well the peptide conducts electricity and holds receptors. The sensor demonstrated a rapid response time of 2 min, a LOD of 2.80 ppb, and high selectivity for similar marine toxins (Table 5) [77].

3.2.2 Impedance Detection of Lipophilic MBs

Lipophilic MBs accumulate in shellfish and pose health risks owing to their high fat solubility and membrane permeability, in addition to resistance to heat and digestion. EIS has emerged as a powerful tool for the real-time detection of MBs, enhancing both the process sensitivity and specificity. Aptamers, which represent special and stable DNA/RNA sequences, are generally considered superior to antibodies, thereby producing more effective biosensors and allowing the low-cost monitoring of MBs. Aptamers can be easily synthesized and modified to target a wide range of MBs, thereby rendering them versatile tools for biosensor development. Their high affinities and selectivity significantly contribute to the development of accurate EIS-based detection systems for use in seafood screening. Building on these principles, Nai et al. (2021) developed a highly sensitive EIA method for the detection of OA. This method employed 3d-NEE groups modified with (*p*-aminobenzoic acid), which were created by coating with gold and subsequent careful

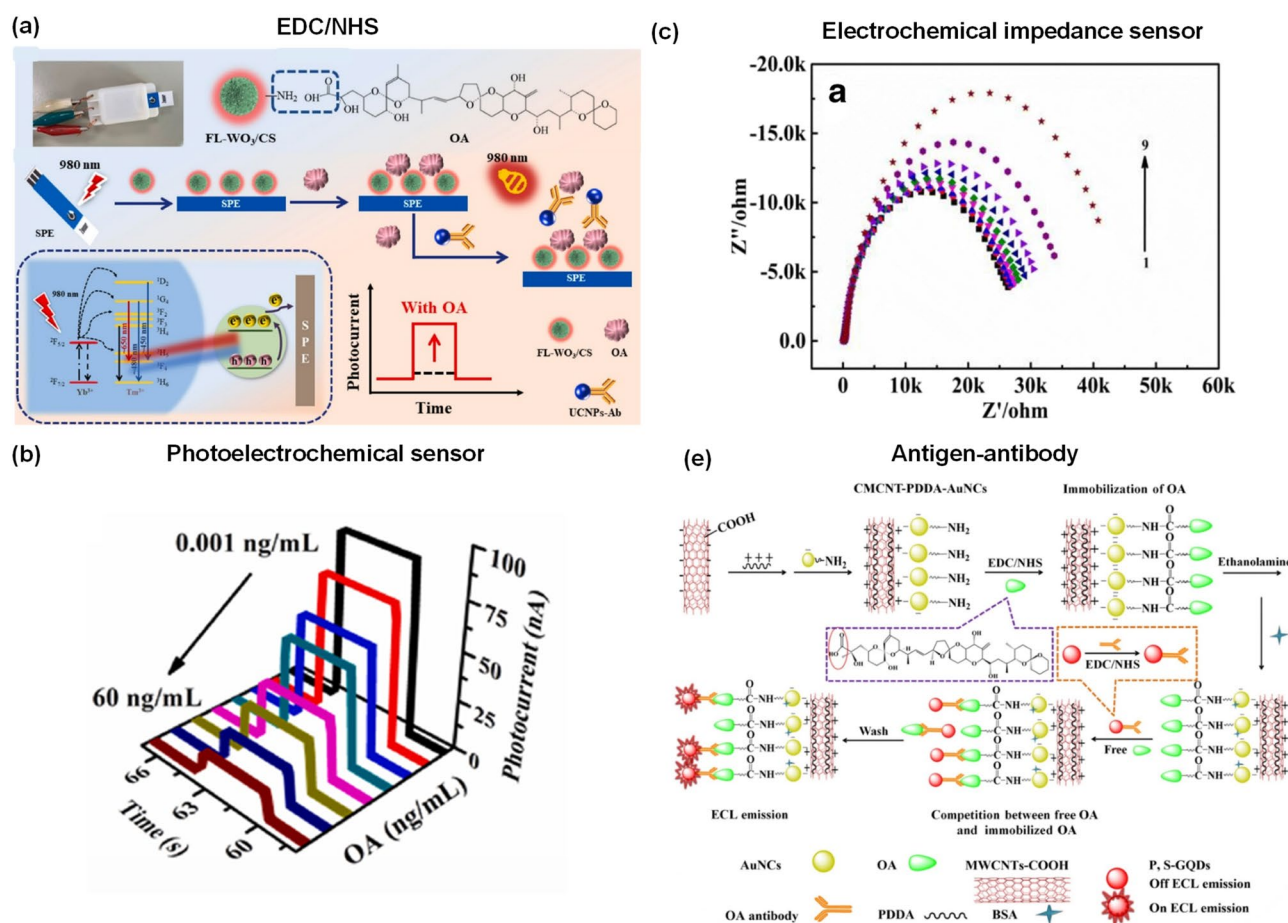


Fig. 6 **a** Near-infrared-mediated photoelectrochemical (PEC) based EDC/NHS assay for OA detection using NaYF₄:Yb. Reprinted with permission from [72]. Copyright 2021 Elsevier. **b** PEC responses for OA detection using NaYF₄:Yb-based sensing system. Reprinted with permission from [72]. Copyright 2021 Elsevier. **c** Electrochemical impedance spectrum for OA detection using polythionine-modified

removal of the material. This study, an immunosensor based on 3d-NEEs is considered to enhance the surface area and conductivity, with the incorporation of a polydimer film to retain the biomolecules in place. Staphylococcal protein A is used to arrange the antibodies, and BA is incorporated to prevent unwanted sticking. The resulting sensor exhibited LODs of 6.47×10^{-3} ng/mL (EIS) and 9.15×10^{-3} ng/mL (SWV), thereby demonstrating a broad dynamic range. The exceptional recovery of the sensor from the oyster samples validated its real-world applicability [78]. Additionally, Chen et al. [79] created an extremely sensitive EIA for the label-free detection of OA used by probe g-C₃N₄. This sensor detected extremely low quantities of OA (i.e., 1×10^{-14} mol/L), and worked effectively across a broad concentration range of 1×10^{-14} to 1×10^{-8} mol/L, thereby demonstrating its strong ability to distinguish OA from similar MBs, such as DTX and pectenotoxins (PTX). The sensor was immobilized on a GCE to enhance its electrochemical

three-dimensional gold nanoelectrode ensembles. Reprinted with permission from [73]. Copyright 2020 Springer Nature. **d** Electrode fabrication using anti-OA-Mab, CMCNT-PDDA-AuNCs, and competitive indirect electrochemiluminescence for OA quantification. Reprinted with permission from [75]. Copyright 2020 Elsevier

performance, and an EIS detection method was employed, wherein the binding of OA altered the aptamer shape, which in turn affected the charge-transfer resistance to ensure a precise measurement. Notably, both aptasensor methods and the use of nanomaterials enhance the detection ability for this toxin (Table 5) [79].

4 POCT Platforms for Detection of MBs

Several cutting-edge technologies are being investigated for the detection of MBs, including advanced adaptations of existing methods. In our fast-paced world, substantial breakthroughs in POCT platform have been driven by the continuously expanding demand. The POCT platform market is expected to reach USD 70.8 billion by 2030, driven by several key factors such as advanced diagnostic technologies in laboratories, the growing demand for rapid and

Table 5 Comparative overview of EIA strategies for the detection of lipophilic MBs

Sl.No	Method	Type of immuno-assay	Specific assay	Analytes	LOD	Linear range	Assay time	Real sample	Ref
1	PECIA	Antibody	cNIR-PECIA and FL-WO ₃ with NaYF ₄ :Yb, Tm	OA	0.007 ng/mL	0.01 to 60 ng/mL	60 min	Mussel	[72]
2	SWV, EIS	Antigen–antibody	BSA/anti-OA/GA/PTh/3d-GNEEs	OA	3.20×10^{-15} g/mL	1×10^{-12} to 1×10^{-7} g/mL	40 min	Scallop	[73]
3	DPV	Aptamers	g-C ₃ N ₄ nanosheets, thionine, ssDNA	OA	0.080 pg/mL	10^{-13} M to 10^{-10} M	90 min	Mussel	[74]
4	ECL	Antigen–antibody	S, P-GQDs and CMCNT-PDDA-AuNCs with anti-OA	OA	0.005 ng/mL	0.01 to 20 ng/mL	50 min	Ostrea plicatula	[75]
5	QCM	Aptamers	AuNPs-DNA aptamer	OA	0.32 nM	0.5 to 200 nM	60 min	Mussel	[76]
6	CV	Peptide	Polypyrrole/AuNPs	TTX	2.80 ppb	2 to 1000 ppb	2 min	N.A	[77]
7	EIS	Immunoassay	pPABA-3DNEEs and BSA with anti-OA	OA	6.47×10^{-3} ng/mL	0.01 to 1.0 ng/mL	N.A	Oyster	[78]
8	EIS	Aptamers	g-C ₃ N ₄ with S-aptamer	OA	1×10^{-14} mol/L	1×10^{-14} to 1×10^{-8} mol/L	60 min	Mussel	[79]

N.A. Not available

reliable diagnostic solutions, the increasing global problem of chronic diseases, and the critical need for on-site and accurate detection of diseases and toxins. Various technological advancements such as miniaturized devices for POCT including glucose meters and pregnancy test kit are driving the growth of the market. Examples of these improvements include paper-based assays, smartphone-integrated systems, microfluidic platforms, and lateral flow immunoassays (LFIA). These technologies offer high sensitivity, cost-effectiveness, ease of use, and quick on-site results. Notably, POCT platform function as compact and portable diagnostic systems by detecting changes in the probe color, viscosity, and flow parameters. Interactions with MBs result in changes induced by probes, indicating the presence of MBs and enabling on-site detection [93].

4.1 Lateral Flow Immunoassays

The LFIA is a paper-based POCT kit uses the binding between antigens and antibodies to identify specific substances and presents the result as a colored line. Capillary action allows the sample to flow along the membrane via capillary forces. In the presence of a target analyte, antibody binding occurs, creating detectable complexes along the test line [17, 94]. Hendrickson et al. (2022a) introduced a dual EIA method using monoclonal antibodies (mAbs)

conjugated with AuNPs for the detection of DA. DA reacts with mAbs and the GAMI-AuNP conjugate to produce a DA-mAbs-GAMI-AuNPs complex. When this complex moves along the membrane to the test area, DA fills the mAbs binding spots, creating a visible line in the T region. The LFIA was able to detect DA with an LOD of 1.4 ng/mL, rendering it sufficient for regulatory use in seawater, mussels, shrimp, and octopus samples [80]. Another study used a different method wherein the antibodies were linked to AuNPs, achieving LODs of 1.2 and 0.1 ng/mL for DA and OA, respectively. The specific antibody and a GAMI-AuNPs combination to process the sample on a test strip. In the absence of DA, an mAb-GAMI-AuNPs complex is formed and binds to the DA-protein conjugate immobilized in the T zone. The immobilized DAGI captures the excess conjugate in Zone C, producing a second line. In the presence of DA, the DA-mAb-GAMI-AuNPs complex prevents mAbs from attaching to the T zone, leading to a weaker or non-existent signal [81]. Additionally, Wang et al. (2022a) developed an immunoassay based on colloidal gold to detect OA and its derivatives analogs in shellfish. Their mAb-2D7 system accurately identified OA-group toxins, and their DC-ELISA exhibited an extremely low LOD of 0.023 ng/mL [82]. Furthermore, a quantum dot nanobead-based ICA was fabricated for direct OA detection in shellfish. The QDNB-mAb system was tested using OA-BSA, while goat anti-mouse

IgG was incorporated into the control line. Upon the addition of OA, competition reduced the T-line fluorescence, indicating contamination. Notably, it was found that fluorescence quenching with an increasing OA concentration was the underlying mechanism for quantitative detection. Moreover, the QDNBs enhanced the detection intensity, leading to an improved sensitivity, with the sensor detecting 20 ng/mL of OA [83]. In another study, Mills et al. (2022) developed a portable multiplex LFIA for the simple on-site testing of three important MBs present in shellfish. Consequently, the simultaneous detection of these MBs with low LODs (0.1 ng/mL OA; 1.1 ng/mL STX; 4.4 ng/mL DA) and extended working ranges was achieved. A compact battery-powered Cube Reader was used to read the results of a straightforward ethanol-based extraction protocol with high recoveries. Based on the competitive immunoassay principle, mAb-conjugated AuNPs were able to target free toxins within the sample. In addition, anti-mouse IgG to keep track of the process, while the Cube Reader identifies the toxins by comparing them to toxin–OVA conjugates that are known to adhere to the membrane (Table 6 and Fig. 7a) [84].

4.2 Microfluidic Device

A microfluidic device (MFD) employs tiny channels to quickly analyze chemicals on-site while using extremely small sample volumes. Consequently, MFD rely on capillary-driven flow to detect changes (such as color shifts, viscosity, or electrical signals) when the target substance interacts with the sensing material on the chip. This technology has revolutionized POCT diagnostics and environmental monitoring by enabling rapid, sensitive, and portable testing [95]. For example, the microfluidic OA sensor developed by Ji et al. (2023) was fabricated using a 3D-printed PDMS chip and plasma treatment. This sensor featured a serpentine mixer, magnets, a washing chamber, and a detection chamber prefilled with mineral oil, wash buffer, and the TMB substrate. The obtained sensor competes with OA-HRP to adhere to MBs bearing OA-specific mAbs on their surfaces. The complexes were retained in the magnetic chamber, washed, and transported to the detection chamber. Subsequently, the detected HRP produces a brown/yellow signal in the TMB, which is inversely proportional to the OA concentration. This system allowed for detection within 1 h, rendering it an efficient diagnostic screening tool for DSP [85]. Additionally, Mao et al. (2022) fabricated a microfluidic aptasensor to facilitate the sensitive detection of OA. This sensor was based on OA-HRP and was firmly attached to tiny polystyrene beads bearing carboxyl groups. The microspheres were packed in a microdam and a Y-shaped microfluidic glass chip. The sensor detection range was 12.4 pg/mL, and the light intensity was found to be inversely proportional to the OA concentration. Notably, the sensor

effectiveness was demonstrated using a photomultiplier tube (Table 6) [87].

Both MFDs and LFIA offer distinct benefits in POCT for MBs, but their practical applications and operational mechanisms are similar. LFIA is particularly advantageous due to its affordability, ease of use, rapid results, and portability. LFIA is ideal for the preliminary detection of MBs in real samples due to its on-site capability, low sample volume requirement, and lack of need for a skilled operator. However, it has some drawbacks, such as low sensitivity and difficulty in performing quantitative analysis without spectrum. On the other hand, MFD offers analytical control with factors following sensitivity, flow rate, and the incorporation of an assay. Using optical or electrochemical outputs, MFD can produce quantifiable signals and detect lower MBs concentrations. A disadvantage is that these systems often require additional components, such as pumps, a flow injector, and photodetectors. Comparatively, MFD is the standard platform for quantitative analysis, while LFIA is well-suited for preliminary rapid on-site POCT sensors for MBs (Table 6).

4.3 Paper-Based Assays

Paper-based assays use a porous paper or membrane to detect small volumes of samples based on color change and capillary action, making them cost-effective. Common papers used in POCT sensors include cellulose, nylon, Whatman filter paper, chromatography sheets, and polyvinylidene fluoride sheets. Paper-based assays use color, fluorescence-based reagents, and nanomaterials for biomarker detection owing to their compact, portable, and require minimal sample volumes. Paper-based assays are easy to fabricate and cost-effective, making them good for places with little resources. Figure 7b shows the miniaturized cNIR-PECIA system developed for the simultaneous detection of TTX and OA. This system incorporates a small paper electrode with multiple AuNPs and Ag–S QD channels. The electrode array, which contains six channels, was fabricated by printing carbon and Ag/AgCl inks onto filter paper and then adding AuNPs via electrodeposition. Two immunoassay formats were employed, namely a sandwich technique for TTX detection, which used Ag₂S QD-labeled secondary antibodies, and a competitive format for the detection of OA, which used BiOI@UCNPs-labeled anti-OA antibodies. When exposed to 980 nm NIR light, the Ag₂S QDs and BiOI@UCNPs created different electrical signals by converting light energy into electrical energy through the photovoltaic effect. The TTX assay resulted in an increased signal intensity, whereas the OA assay produced decreased signal intensity, allowing for accurate dual quantification through photocurrent readings. The obtained sensor demonstrated a great ability to detect low quantities of TTX and OA (5 and 7 pg/mL,

Table 6 Comparative analysis of POCT platforms for the detection of MBs

Sl.No	Method	Type of POCT platform	Specific assay	Analytes	LOD	Linear range	Assay time	Real sample	Ref
1	CS	Smartphone-based POCT	HRP, B-SA-HRP, GO composite	OA	0.02 ng/mL	0.02 to 33.6 ng/mL	15 min	Mussels	[14]
2	CS	LFIA	MAbs-AuNPs	DA	1.4 ng/mL	2.9 to 35.8 ng/mL	10–20 min	Seawater, mussels, shrimps, and octopuses	[80]
3	CS	LFIA	AuNPs with anti-species OA and DA	OA and DA	0.1 and 1.2 ng/mL	2.5 and 100 ng/mL	18 min	Seawater, octopuses, mussels, tiger shrimps, crabs, whelks, and scallops	[81]
4	CS	LFIA	Anti-OA mAb-2D7 with AuNPs	OA	0.023 ng/mL	0.036 to 0.932 ng/mL	10 min	Mussel	[82]
5	FS	LFIA	QDNBs-McAb	OA	20 ng/mL	0.62 to 20 ng mL ⁻¹	20 min	<i>Glossaulax didyma</i> , <i>Rapana venosa</i> , and <i>haliotis</i>	[83]
6	CS	LFIA	Toxin–OVA conjugate (OA–OVA, STX–OVA, DA–OVA)	OA, STX, and DA	0.1, 1.1 and 4.4 ng/mL	0.2 to 1.5, 2.5 to 65.0, and 8.2 to 140.3 ng/mL	35 min	Mussel tissue	[84]
7	CS	MFD	MBs-mAbs probes and OA-HRP with microfluidic chamber	OA	0.49 ng/mL	0.49 to 36.46 ng/mL	60 min	Shellfish	[85]
8	CV	Paper-based POCT	Ab ₂ -Ag ₂ S QDs/ AuNPs and NaYF ₄	TTX and OA	5 and 7 pg/mL	0.001 to 100 and 0.001 to 80 ng/mL	45 min	Shellfish	[86]
9	ECL	MFD	Polystyrene microspheres, HRP, OA34 aptamer	OA	12.4 pg/mL	41.3 to 4.02 ng/mL	80 min	Mussel and shellfish	[87]
10	FS	Paper-based POCT	B-CDs@MIPs	DA	10 nM	0.05 to 5 mM	10 min	Shellfish and lake water	[88]
11	FS	Smartphone-based POCT	DAIA and G-quadruplex	OA	3.1 × 10 ⁻³ ng/mL	1.0 × 10 ⁻³ to 1.0 × 10 ³ ng/mL	20 min	Shellfish	[89]
12	SPR	Smartphone-based POCT	AuNPs with aptamer-OA34	OA	1.80 mg/L	20 to 10 000 mg/L	30 s	Shellfish	[90]
13	FS	Smartphone-based POCT	B-CDs@SiO ₂ /CdTe MIPs	DA	18 nM	0.03 to 1 μM	10 min	N.A	[91]

N.A. Not available

respectively), working well over a wide range of concentrations, demonstrating a high specificity results [86]. Figure 7c shows a paper-based fluorescent sensor for the detection of DA in seafood. This sensor is based on a combination of MIPs with CDs. The sensor was constructed using a sol–gel process with APTES, TEOS, and PTA as dummy templates. The MIPs form special binding spaces

in silica-based materials, reducing the brightness of the B-CDs. When DA binds to the imprinted cavities, this earlier suppression is lifted, allowing the fluorescence to return based on the amount of DA present. The LOD was determined to be 10 nM, and the improved analytical ability was attributed to dual emissions (Table 6) [88].

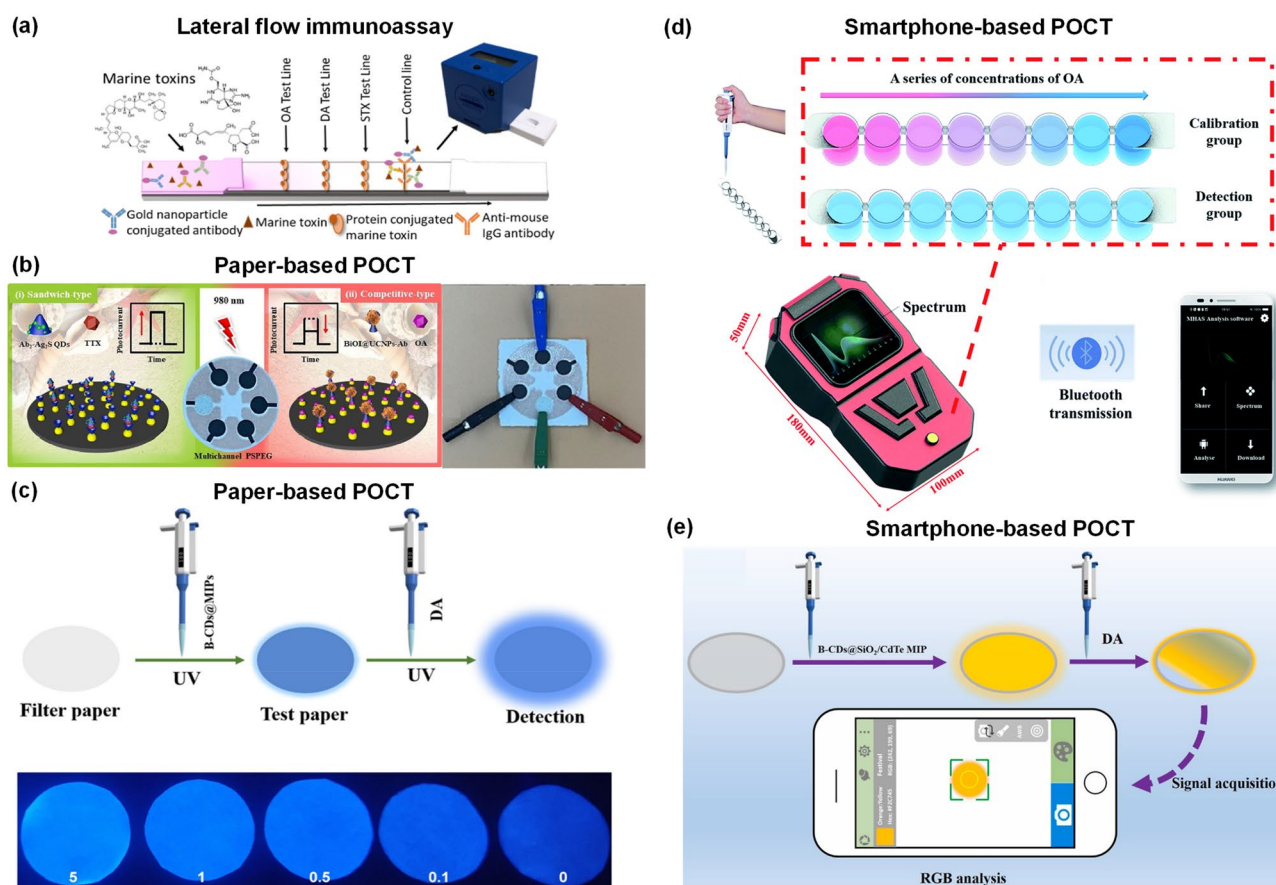


Fig. 7 **a** Lateral-flow immunoassay for OA, STX, DA sensing based on probe antigen–antibody binding. Reprinted with permission from [84]. Copyright 2022 American Chemical Society (licensed under CC-BY 4.0). **b** Schematic diagram showing a paper-based PEC immunosensor integrated into a POCT platform for the detection of TTX and OA. Reprinted with permission from [86]. Copyright 2024 Elsevier. **c** Paper-based POCT kit for DA analysis. Reprinted with

permission from [88]. Copyright 2022 Elsevier. **d** Colorimetric and multi-channel handheld automatic spectrometer based on spectral detection of OA. Reprinted with permission from [90]. Copyright 2021 Royal Society of Chemistry. **e** Schematic of a smartphone-based test strip system for DA sensing. Reprinted with permission from [91]. Copyright 2022 Elsevier

4.4 Smartphone-Based POCT Applications

POCT refers to the performance of on-site detection at the point of sample collection, enabling rapid results without reliance on centralized laboratory facilities. POCT is designed to be simple, rapid, portable, and user-friendly, which makes it an ultimate platform for sensors in clinical and environmental analysis. Colorimetric, electrochemical, and fluorescence-based detection techniques are frequently used in portable multimodal POCT platform that are integrated with smartphones. The smartphone-integrated POCT platform facilitates the recording and analysis of results through its camera, light source, and calculation capabilities. These integrations operate effectively and work well in the marine field for the sensitive on-site detection of MBs without requiring complex instrumentation. For example, Shan et al. (2023) developed a highly sensitive fluorescent aptasensor for the detection of OA. The sensor uses a special

aptamer attached to magnetic beads while also employing G-quadruplex pre-coding rolling circle amplification to render it more sensitive. The fluorescence intensity increased in proportion to the OA concentration, facilitating portable on-site detection. This method employed thioflavin T for fluorescence detection and achieved an ultralow LOD of 3.1×10^{-3} ng/mL, enabling rapid and high-throughput seafood screening. Notably, this approach has been validated in spiked shellfish samples with high recoveries [89]. Figure 7d shows a colorimetric and multichannel handheld automatic spectrometer developed for the rapid detection of OA. This device consists of an eight-well microplate, a broadband LED light source, and a microspectral sensor. A 3D-printed bracket was used to align the light path to minimize interference. Designed using SolidWorks software and produced via 3D printing, this device incorporated an LED driver and a control module to ensure its efficient operation. Powered by an Arduino UNO and a lithium battery, a touchscreen

was incorporated for user interaction. The sensitivity was enhanced using AuNPs and OA-specific aptamers, achieving an LOD of 1.80 mg/L within the concentration range of 20–10,000 mg/L. The data were processed using an Arduino microcontroller and transmitted to a smartphone application via Bluetooth, which performed real-time data analysis and displayed the results. Notably, the results were obtained within 30 s, rendering this a faster alternative to conventional microplate readers [90]. Additionally, Li et al. (2022a) reported a smartphone-assisted microarray immunosensor for the detection of OA. Their sensor employs a method that boosts the signal in several steps by using GO to enhance the OA detection performance. This approach combines an indirect ELISA with smartphone imaging, rendering it a quick and sensitive detection approach. A color change was observed upon the HRP-promoted oxidation of the TMB substrate, creating a blue color. The smartphone camera was used to capture the corresponding images, and Image J software was employed to convert the color intensity into a grayscale value, which was inversely correlated with the OA concentration [14]. The QD-containing MIPs were used to generate a selective sensor for DA detection, as shown in Fig. 7e. This sensor was fabricated using a sol–gel method by incorporating CDs embedded in silica with CdTe QDs. APTES-modified CdTe QDs were pre-assembled with a pseudo-template through strong interactions, and MIPs were prepared by combining PTA, APTES, TEOS, ammonia, and B-CDs@SiO₂. The amino groups present in the APTES and PTA components formed hydrogen bonds, thereby creating MIP cavities. This system emits blue light from B-CDs@SiO₂ and red light from the CdTe QDs, thereby allowing for the specific detection of DA. Upon DA binding to the sensor, bonding interactions lead to electron transfer from the CdTe QDs to DA, leading to reduced light intensity at 610 nm. This sensor was tested using circular filter paper discs illuminated by 365 nm UV light, and the results were recorded using a smartphone camera. The resulting linear relationship between the log of the B value and the DA concentration allows for the facile, rough, and on-site detection of DA (Table 6) [91].

5 Conclusions and Future Perspectives

This review provides a comparative overview of marine biotoxins and highlights their types, sources, properties, toxicological effects, and real-world concerns. The impacts of climate change and ocean pollution on MBs levels underscore the urgent requirement for sensitive, selective, rapid, and on-site detection technologies. Immunoassay-based biosensors represent novel, versatile, and highly specific devices for MBs detection. A number of recent methods were explored herein for the detection of MBs, including

colorimetric, fluorescence, SPR, voltammetry, and electrochemical impedance platforms, along with cutting-edge recognition strategies involving antigen–antibody systems, aptamers, nanozymes, and MIPs. Recent advancements in POCT, such as lateral flow chromatography, microfluidic devices, and paper-based and smartphone-based sensors, have significantly improved the assay sensitivity, speed, and portability. Moreover, smartphone-integrated devices are revolutionizing the on-site detection of MBs with real-time readouts and user-friendly interfaces, thereby facilitating decentralized testing. Nevertheless, a few key concerns remain unresolved, namely the lack of certified reference materials, which difficulty assay standardization and validation, and the occurrence of matrix interference from seafood and environmental samples, which compromises the detection accuracy. The reported methodology inability to simultaneously detect multiple analytes limits its practical applicability, while full integration with smart analytics, the Internet of Things (IoT), and data platforms remains in its early stages.

Future research should prioritize the development of next-generation biorecognition assays, including nanoparticles and hybrid aptamers with MIPs systems to offer enhanced sensitivities and selectivity. In addition, smart diagnostics based on a combination of POCT devices with smartphone applications, wireless communication, IoT, artificial Intelligence, and data analytics is essential for achieving on-site and field-ready results. Furthermore, regulatory standardization with cross-laboratory validation and the global organization of assay protocols is necessary for accurate monitoring MB, and translational development should focus on the device affordability, ease of production, and strength for real-world applications. Ultimately, the evolution of sophisticated biosensors for MBs detection will be driven by addressing the current limitations and welcoming technical innovations to improve marine ecosystem monitoring and public health protection.

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Data availability Data are contained within the article.

Declarations

Conflict of interest The authors declare no competing financial interest.

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