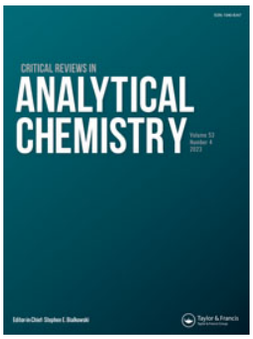

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REVIEW ARTICLE

Recent Progress in Screening of Mycotoxins in Foods and Other Commodities Using MXenes-Based Nanomaterials

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ABSTRACT

Mycotoxin pollution in agricultural food products endangers animal and human health during the supply chains, therefore the development of accurate and rapid techniques for the determination of mycotoxins is of great importance for food safety guarantee. MXenes-based nanoprobes have attracted enormous attention as a complementary analysis and promising alternative strategies to conventional diagnostic methods, because of their fascinating features, like high electrical conductivity, various surface functional groups, high surface area, superb thermal resistance, good hydrophilicity, and environmentally-friendlier characteristics. In this study, we outline the state-of-the-art research on MXenes-based probes in detecting various mycotoxins like aflatoxin, ochratoxin, deoxynivalenol, zearalenone, and other toxins as a most commonly founded mycotoxin in the agri-food supply chain. First, we present the diverse synthesis approaches and exceptional characteristics of MXenes. Afterward, based on the detecting mechanism, we divide the biosensing utilizations of MXenes into two subcategories: electrochemical, and optical biosensors. Then their performance in effective sensing of mycotoxins is comprehensively deliberated. Finally, present challenges and prospective opportunities for MXenes are debated.

KEYWORDS

Biosensing; Mycotoxins; MXenes; Nanomaterials; Synthesis

1. Introduction

Food safety issue has attracted increasing attention from scientists owing to its harmful effect on human happiness, public health, and economic losses.[1] Despite decades of efforts, billions of people throughout the world still suffer from the health hazards of food pollution such as metal ions, pesticides, antibiotics, mycotoxins, and so on.[2,3] Among them, mycotoxins, one of the most imperative toxic food risks, are secondary metabolites produced in the fungal metabolism process in a diversity of commodities comprising processed products, milk, oils, fruits, vegetables, grains, and feeds.[4–6] With the acceleration of globalization, food poisoning, and mycotoxin pollution have increasingly become a worldwide human concern. As we all know, there are over 400 mycotoxin metabolites. Among them, zearalenone (ZEA), aflatoxins (AFs), ochratoxin A (OTA), T-2 toxin (T-2), fumonisins (FMs), and deoxynivalenol (DON), are deliberated as dangerous mycotoxins owing to their high carcinogenicity and widespread distribution in foods and feedstuffs. Based on the IARC (International Agency for Research on Cancer), OTA and FB1, AFB1 and AFM1, and ZEN are classified as group 2B, 1, 3 carcinogens, respectively.[7,8] Thereinto, numerous organizations, and countries comprising the Food and Drug Administration of the USA, European Union, Japan, China, etc., have established the MRLs up to ppt points for these mycotoxins in some agricultural and food products.[9,10] Hence, it is of importance and necessity to use low-cost, accurate, rapid, simple, specific and sensitive diagnostic tactics to determine even trace amounts of mycotoxins.

Classical mycotoxins identification techniques include thin-layer chromatography (TLC), liquid chromatography-tandem mass spectrometry (LC-MS), high-performance liquid chromatography (HPLC), ELISA, and so on.[11–13] LC-MS and HPLC allow accurate quantitative/qualitative determination of mycotoxins and their derivatives. Nevertheless, the sophisticated building, bulky volume, and high cost of them restricted their use in real-time screening.[14] Even though TLC possesses the benefits of rapidity, simplicity, and relative ease of fabricating a multi-sample identification substrate, the weak quantitative ability and

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long pretreatment time limit its utilization in low-level mycotoxin sensing.[15] As a result, many of the obtainable methods are not appropriate for on-site and real-time utilization, particularly in emergency circumstances.

As an alternative to detailed yet time-consuming laboratory investigation, (bio)sensors are in an unprecedented position to fight against mycotoxins, particularly thanks to their ease of use and immediate readout.[16–18] Nevertheless, the selectivity and sensitivity to precise analytes are also desirable to enable the use of practicable bioassays.[19] Progresses in nanotechnology considerably propel the biosensor structure, especially with the progress of low-dimensional nanomaterials such as carbon-based graphene or sulfur-based TMDs (transition metal dichalcogenides).[20,21] These nanomaterials not only provide good biocompatibility to the probes by providing a favorable microenvironment but also enhance the transport capability through amazing catalyzing properties and large specific areas.[22,23] Regardless of the paramount advantages of dimensionality, two-dimensional (2D) substrates encounter restrictions without functional elements, easy aggregation, and poor electrical transport. The former two elements inhibit biorecognition loading and retention of biological activities, triggering unacceptable probe sensitivity and stability. Therefore, taking into account innovative 2D nanomaterials with plentiful fixing sites, good dispersion, and perfect biocompatibility is crucial in tracking versatile (bio)sensing nanoplatforms.[24] MXenes are deliberated relatively newfangled additions to the 2D material family. Their intriguing electrochemical performance and specific surface chemistry, together with their great biocompatibility, make them perfect as a support matrix for the establishment of state-of-the-art electrochemical sensing and biosensing tools.[25,26] Owing to its plentiful oxygen or hydroxyl-terminated interfaces, MXenes could bind with large amounts of biomolecules. Most significantly, the high hydrophilicity characteristic of MXenes could afford possibilities to regulate the interface without affecting its brilliant electrical conductivity, which is hopeful for the manufacture of high-performance electrochemical detecting substrates.[27] Affinity with the target analytes is vital to detecting, and a benefit of these materials is that, unlike graphene, which only contains carbon, numerous transition elements give MXenes to display higher affinities toward certain analyte.[28] Stable and better dispersibility is a main MXene's benefit in contrast with graphene. MXenes could preserve very high conductivity while being stably dispersed to create smooth physical coatings. Additionally, MXenes are rich in functional surface elements such as –F, –OH, and –O and the various terminal ends, which are primarily ascribed to the side responses that happen throughout the synthesis.[29] Besides, there are progresses to incorporating MXenes with other nanostructured materials to design (bio)sensors with varying abilities derived from the fascinating electrical and biological MXene properties. For instance, the nanocomposites of MXenes with polymers, metal nanoparticles, enzymes, 2D carbon materials, and so on, are extensively employed in biomedical and biosensing applications. MXene-Ag fabricated by two-step electrostatic bonding and in-situ electrostatic self-assembly is a very sensitive SERS platform.[30] In addition, MXenes modified by precious metals like gold also exhibits strong anti-cancer capabilities and low toxicity to organisms. For another instance, the microfluidic substrate using Fe_3O_4/MXene nanocomposite realized the sensitive determination of Alzheimer's biomarker.[31] Conductive polymers like polyvinyl alcohol and polyaniline with strong conductivities and low toxicity are very appropriate for MXene's functionalization. In this regard, a nanocomposite electrode containing Ti_3C_2 MXene, polyaniline, and platinum particles (Pt/PANI/MXene) is utilized to modify a screen printed carbon electrode. Currently, the emergence of molecularly imprinted polymers (MIPs), has enabled the use of polymer/MXene nanocomposites as electrochemical sensing materials, extending the applications of polymers/MXenes in the biosensing field.[32] The MIP/MXene (AN-co-MSAN/Ti_2C)-derived electrochemical probe has realized sensitive identification of c-reactive protein in human serum.[33] More recently, Fang's group reported an electrochemical sensor based on the nanoporous gold, MIPs, and Ti_3C_2Tx for the quantification of thiabendazole in actual samples. This probe shows superior reproducibility, selectivity, sensitivity, and stability.[34] In another study, Wang's team developed a rapid and simple MXene/polypyrrole-derived bacterial imprinted polymer nanoprobe for ultrasensitive detection of Salmonella.[35]

However, as far as we know, a comprehensive study on the current developments and future predictions for mycotoxins determination based upon MXenes has not been reported. Primary, the synthesis approaches of MXenes containing bottom-up and top-down strategies are discussed along with their surface functionalization and modification, where their benefits and shortcomings are emphasized. The efficient and reliable progress of these synthetic techniques considerably accelerates the practical MXene's utilization. Then, we summarize several strategies suitable for the detection of various mycotoxins in food matrices, including electrochemiluminescence (ECL), surface-enhanced Raman scattering (SERS), fluorescence, electrochemistry, and colorimetry assay by using MXenes nanomaterials with stress on the linear detection range, the limit of detection (LOD), and selectivity.

2. Synthesis of MXenes

Till now, at least twenty kinds of MXenes are found through selectively etching of preconditioning element with hydrosoluble, salt-containing fluorine ions. Even though the M-A sheet in an MXene has different mixed bonds like metallic, covalent and ionic bonds, whole of these forces are fragile than the metallic forces in the M-X sheet. This property allows us to carry out the layering MXene's operation and the selective A layer etching from the parent MAX material to acquire diverse MXenes classes.[36] The bottom-up and top-down approaches are the two major techniques to prepare novel 2D MXenes based on different mechanisms: growing from molecules and atoms, and exfoliating bulk crystals, respectively.[37]

2.1. Top-down techniques

The wet etching process and following phase exfoliation are two important stages of some present MXenes production approaches.[38] The initial MXene synthesis, as designed *via* Naguib et al., involved the soaking of Ti_3AlC_2 powder in concentrated solution of HF at ambient temperature, which could open new horizons in the synthesis of several MXene types (Figure 1a).[39]

The response is specified as follows:

$$M_{n+1}AXn + 3HF = M_{n+1}Xn + AF_3 + 1.5H_2 \quad (1)$$

$$M_{n+1}X_n(s) + 2HF = M_{n+1}X_nF_2 + H_2 \quad (2)$$

As seen in formula (1), the A sheet in the MAX parent phase bonds with fluoride ions in HF, supplying a foundation toward M-X layer stripping in reaction (2). Throughout reaction (2), in light of the mixed bond weakening in the MX sheet, –OH, –F, and –O increasingly substitute atoms; finally, the layers progressively separate, developing a loose graphite-like building called MXene.[40] Because of the presence of functional elements with negative charge on the sheet, MXene shows numerous benefits, including good dispersibility and strong hydrophilicity. Subsequently, based on this technique, the HF concentration, soaking time, and other situations are more altered to preparer MXenes like Nb_2CT_x and V_2CT_x.[41] On account of its easy operation, rapidity, and simplicity, this technique is extensively applied. For instance, Halim's team improved the technique in order to synthesize Mo_2CT_x. As revealed in Figure 1b. they employed a high-concentration solution of the HF as an etchant and a milling procedure to etch Mo_2Ga_2C powder to gain Mo_2CT_x.[42] Furthermore, novel kinds of MXenes like Cr_2TiC_2,[43] Ti_3-SiC_2,[44] and Ti_2C [45] are prepared by the same approaches containing HF as a constant etchant.

Even though this technique is rapid and simple, the corrosiveness and toxicity of high amount of the HF could not be neglected. Thereinto, an innovative synthesis strategy has been established based on low-corrosion, low-toxicity, and low-strength etchants to decrease or even substitute the application of HF. For instance, Ghidiu's group reported a technique for etching with less HF and mild situations.[46] Through a combination of hydrochloric acid and lithium fluoride to substitute high amount of HF, this strategy either reduces the HF dose or creates small flaws that improve the functions of the manufactured MXene crystals. Additionally, a new structure based on the ammonium bifluoride (an Etchant) have been designed by Wang et al. This approach not only decreases environmental contamination but also prompts greater lattice factors of the yields owing to the insertion of $–NH_3/–NH_4^+$ particles and water molecules.[47] Besides, other fluorides like ferric fluorides, tetrabutylammonium, potassium, and calcium could be utilized along with sulfuric and hydrochloric acids. The extended progress of this strategy increases new questions that the kinds of ions preinserted or molecules into the etchant might turn on the MXenes interfaces and cause their characteristics unmanageable.[48]

As a newfangled fluorine-free strategy, the hydrothermal technique is received considerable interest because of the environmental protection concept. This tactic can control the lattices or surface elements of the arranged MXene layered *via* altering the solvent. The Al layer is etched away after the Ti_3AlC_2 powder has soaked in NaOH solution around 100 h and then subjected to hydrothermal treatment in 1 M sulfuric acid about 1.5 h at 85 °C.[49] The MXenes

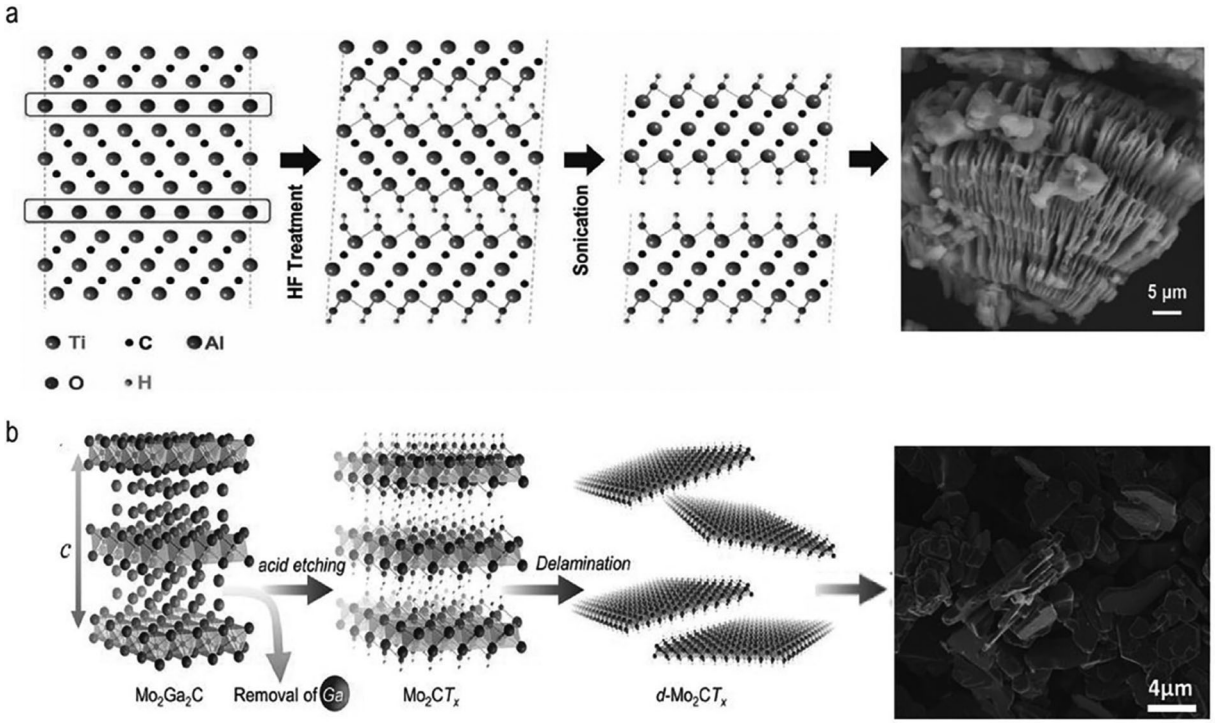

Figure 1. (a) Illustration of the exfoliation procedure toward Ti_3AlC_2. (b) Diagram displaying the delamination and synthesis of Mo_2CT_x. Reprinted with permission from ref. [39].

achieved through this technique display good interface mechanisms and the properties of strong adsorption, great lattice factors and so on. Even throughout etching, the Al sheet is etched more precisely, leading to a looser building, a higher specific surface, and a greater interlayer width. Likewise, in order to design extremely refined MXenes multilayer, scientists integrated alkali-triggered hydrothermal approach with a Baeyer's procedure, and the Tyntoll influence and the detecting interlayer of each colloid are arranged through spraying a material suspension.[50] In short, a growing amount of new fluorine-free strategies are being developed.

2.2. Bottom-up techniques

MXenes produced through the aforementioned top-down method have some shortcomings. According to the configuration, the lateral part is thermally unstable and small, and the presence of various functional units on the interface causes structural flaws in some employments, which affects the electron transmission rate. In this context, the more expansion of synthetic techniques with no interface active elements, good thermal stabilities, and well mechanical properties is sparked a new emphasis. More recently, a chemical vapor deposition (CVD) technique is used by Merve Öper's team to construct MXenes with unfunctionalized interfaces in great batches.[48]

This strategy either prevents the drawback of easy chemical detaching throughout the mass MXene fabrication or enables MXene to develop laterally in the formulation procedure, which is further favorable for preparing MXene patches with thin and high areas. The liquid Mo/Cu alloy catalytic CVD technique carried out by Zhao and coworkers is realized the similar aim. Using graphene as a platform and ion diffusion fence, MXene layers with great interfacial charge transmission capabilities could be self-grown (Figure 2).[51] The bottom-up approach overwhelms some of the drawbacks of the top-down approach, for example restricted electronic function, thermal instability, lack of environmental friendliness, and small surface area; this synthesis approach provides the benefits of high refinement degree, few defects, high lattice, and controllable surface groups, and is considered as a better synthesis technique. Unfavorably, there are limited works on the bottom-up strategy. Hence, the progress of a bottom-up strategy is highly demanded for enhancing the MXene's function or designing MXenes with predetermined characteristics.

3. Surface functionalization/modification of MXenes

In the structure of MXenes, the interlayer distance plays a prominent role in numerous sensing applications. Therefore, seminal attitudes have been made toward increasing the interlayer distance and producing few or single-layer buildings. A multilayer MXene structure produced by etching which is held together by van der Waals forces and or hydrogen bonding. Exfoliating or delaminating the multilayer structure of MXene can produce a single-layer configuration. The exfoliation procedure relies on the employed etchant in the primary stage. For example, Li^+ ions intercalate between the interlayers when HCl/LiF etching process produces MXenes. Subsequent sonification or shaking can exfoliate the MXenes which can result in more defects, small MXenes sheets, and low yield over ultrasonication or long time shaking.[52] Therefore, intercalating agents is suggested for delamination which increases the distance of interlayers and weakens their interaction resulting in few or single-sheet structure. Polar organic molecules and ionic materials are effective intercalating elements for MXenes exfoliation. Enormous previous synthetic methods have focused on the top-down approach in which control over structure size, morphology and is poor meanwhile bulk precursors have converted into the sole-layer construction. However, larger nanostructures are formed by assembling molecules or atoms in a bottom-up approach. Owing to their benefits over the top-down approaches comprising uniform shape/size, less flaws, and homogenous chemical composition, bottom-up approaches have been extensively adopted for the MXenes synthesis. With advances in MXene nanostructures, a diversity of detecting devices such as optical, electrochemical probes, and flexible/wearable platform have been developed.[53]

Generally, the distinctive combination of inherently abundant surface terminations and superb conductivity lead MXenes as ideal interfaces for functionalization and immobilization with other materials like metal nanoparticles (NPs), metal oxides, conducting polymers, and enzymes can be integrated with MXenes to improve their electronic, optical, and structural features.[54] The obtained nanocomposite exhibited enhanced electrochemical properties in comparison to MXene alone owing to the high surface area, excellent catalytic activity, and high conductivity of NPs. For instance, an electrochemical sensing platform was established by the introduction of Pt NPs from their aqueous solutions on the $Ti_3C_2T_x$ Mxene surface without applying any reducing element.[55] Similarly, Pd, Au, and Ag NPs were hybridized onto MXenes by in-situ reduction.[56] Alternatively, MXene demonstrates extensive tunable optoelectrical properties, containing optical absorption, transmittance, work functions, and electronic band structures. The extensive electrical and optical features of MXenes assist optoelectronic devices and sensors to be used in biomedical applications.

4. Electrochemical properties of MXenes

Electrochemical detection approaches have received significant attention owing to their promising potential applications in rapid and efficient mycotoxins analysis. Particularly, biosensors-integrated nanomaterials using an electrochemical substrate show unique selectivity and sensitivity toward many contaminants.[57–62] MXenes are widely used in the fabrication of electrochemical biosensors, not only because of their high multilayer flaky, high conductivity, and structure specific surface area, but also because of their hydrophilicity, biocompatibility, modification flexibility, surface

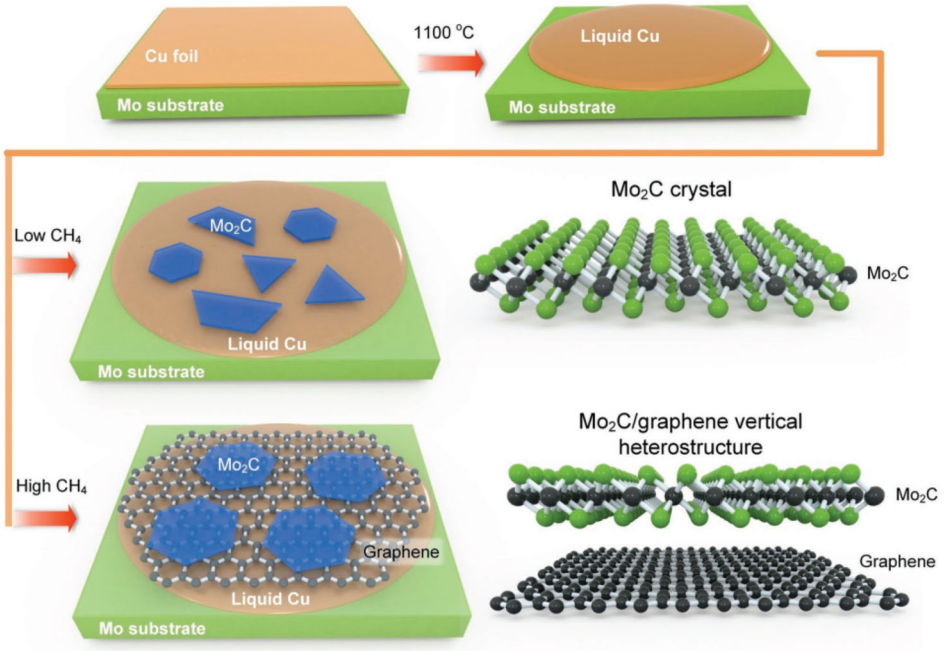

Figure 2. Illustration of the Mo_2C crystals growth under high and low flow rates of CH_4. Reprinted with permission from Reference [51].

mechanism controllability, and metal characteristics.[63] Besides, owing to their redox features, MXenes have the dual properties of a reaction catalyst and electron transfer promoter throughout the sensing.[64]

Given the DFT (density functional theory) calculation, most $Ti_{n+1}X_n$ demonstrate metallic nature with overlap between the conduction and valence bands at the Fermi level. Latest investigations by DFT calculation indicated that the electronic MXenes building is fundamentally related to their interface terminations. For instance, OH and F-terminated MXenes (with bandgaps of 0.1 and 0.05 eV) which transforms the metallic Ti_3C_2 to semiconductors exhibited reduced carrier density and thus conductivity than pristine one.[65] Furthermore, the spatial organization of -OH and -F on $Ti_3C_2T_X$ MXene can affect the electrical characteristics of the Ti_3C_2 $(OH)_2$ and $Ti_3C_2F_2$ monolayers which results in both metallic characteristic and narrow bandgap semiconductors.[66] Thus, their geometric conformation and adjusting surface groups possibly tune the electronic constructions of monolayer MXenes. Alternatively, the intercalating agents in multilayer MXenes increase the interlayer distance and therefore increase the resistance.[67] Moreover, an improved conductivity was also found by a further increase in annealing temperature by which the removal of surface terminations was accelerated. These excellent features of MXenes in comparison with other 2D materials make them be progressively employed in the manufacture of electrochemical sensors. Alongside their great electrical conductivity that accelerates the rate of heterogeneous electron transfer in MXenes, there are other characteristics of MXenes which is highly demanded in electrochemical sensors. According to the biocompatibility and high stretchability of MXenes, they are potent substrates for the construction of conductive flexible platforms for clinical analysis and health care monitoring using wearable electrochemical sensors.[68] Additionally, MXenes are effective substrate materials as inks for printing applications. The coating and printing methods are kind of eco-friendly, versatile, economic, efficient, and simple manufacturing techniques for the fabrication of powerful device tools as well as for industrialization.[69] In electrochemical probes, the modified chips are mostly designed by the drop-casting technique in which the preparation procedure needs a well-dispersed coating solution. However, the simple and feasible synthesis of MXenes with acceptable solution stability and dispersibility efficaciously resolves this issue. Benefitting from their unique surface with several chemical groups and 2D layered structure, MXenes can be adapted in the manufacture of proficient electrochemical platforms. In this regard, MXene-derived nanostructures incorporated with biomolecules or other different functional materials presented altered and colorful characteristics which are conducive to the construction of electrochemical devices or sensors.[70] Another characteristic of MXenes that enables them to be adapted in the fabrication of electrochemical sensors is their unique photothermal conversion capability. This can facilitate the dual-model detection methodology in the manufacture of electrochemical probes which extend the signal approaches of electrochemical sensors.[71]

5. Optical properties of MXenes

Along with the excellent mechanical, electronic, electrical, and properties of MXenes, their optical properties are another important aspect that should be extensively studied by tuning surface functionalization, changing elements, and lattice structures. With recent advances in MXenes, their optical characteristics like plasmon resonance, reflectivity, transmittance, and absorption have been theoretically and experimentally studied. The optical properties of MXenes are essentially affected by structural and electronic features. As well, surface terminations can meaningfully affect the

electronic band MXene's building where terminations with more electronegativity such as the –O group make a larger bandgap than others like –OH and –F terminations.[72] It was proven that the interface –O, –F, and –OH termination of MXene can adjust their optical response along with electronic properties. More in deep, O-terminated MXenes exhibited a large reflectivity and absorption efficiency in the range of visible spectrum compared to the OH- and F-terminated MXenes. Whereas, all three types of MXenes showed large absorption than pristine samples.[26] Correspondingly, it was reported that O-functionalized Ti_2CT_2 and $Ti_3C_2T_2$ have larger light absorption than the one functionalized with –OH, –F in the infrared to UV regions. The fabrication of O states nearby the Fermi energy levels is the main reason for improved absorption of O-terminated MXenes.[73] By calculating band structures and the density of states *via* DFT formulation including reflectivity, absorption, and refractivity, the optical response of diverse MXene frameworks could be investigated. For instance, it was estimated that the absorption spectrum was probably related to the involvement of interband transitions from the occupied valence band to the unfilled conduction band.[74] Despite DFT calculations, the optical performance of MXene could also be assessed by the random phase approximation method and the full-potential linearized augmented plane wave technique.[75] The layers number, flake size, thickness, and the intercalating ions in MXenes are the other factors influencing the optical response of the MXene.[76,77] Some MXenes were described to be employed in optical switching tools as they show nonlinear absorption of light from 500 to 700 nm.[74] Regarding their high electrical conductivity and great optical transparency, MXenes materials can potentially be utilized in future optoelectronic and optical sensors. They also offer superior opportunities in light-matter interactions to explore new construction methods for nanophotonic devices with exceptional optical characteristic.

With the development of 2D materials like graphene and MXenes, optical (bio)sensing substrates have experienced brilliant progress. The MXene materials can be used for the fabrication of optical assays due to their advantageous properties of colorimetry, photoluminescence, SERS, ECL, and SPR. Similar to other 2D materials, the MXenes also possess outstanding properties that shorten the advancement of high-efficiency optical assays. First, MXenes exhibit good hydrophilicity, excellent biocompatibility, and nontoxicity to living organisms, allowing them suitable for numerous (bio)-sensing applications. Their unique properties like high specific surface area, exceptional conductivity and mechanical might be hopeful in optical sensing as the SERS system, and fluorescence quenchers, together with the cargo carrier in biomedicine and imaging. As well, promising energy levels and broader absorption band causes them great value and fascinating viewpoint in optical, photothermal, and photoelectrochemical sensing. In addition, the MXenes could also be flexibly engineered through particular constituents, which donates them with new features. Due to the characteristics mentioned above, MXenes have experienced a surprising expansion in optical sensing.

6. Application of MXenes-based systems for mycotoxins detection

6.1. Aflatoxins

Till now, more than 20 subtypes are determined, comprising aflatoxin B2 (AFB2), aflatoxin B1 (AFB1), aflatoxin G2(AFG2), aflatoxin G1(AFG1), and so on. Among derivatives and analogs of aflatoxin, AFB1 is a carcinogen metabolite produced *via* filamentous fungi like *Aspergillus parasiticus* and *flavus* from cereals, nuts, stored corn, and other agricultural harvests.[78] Long-term and excessive exposure to AFB1 could trigger mutagenic, carcinogenic, and teratogenic illnesses, which poses an important menace to animals and public health. The AFB1 toxicity is 68 times that of arsenic trioxide and 10 times that of potassium cyanide.[79] As reported by Food and Agricultural Organization (FAO), around 25% of the world's farming yields have been contaminated by mycotoxins at different grades each year, causing an important economic losses to the international food production industry.[80,81] Therefore, it is of great importance to identify AFB1 pollution in food and agricultural products.

One of the most hopeful strategies for screening AFB1 at very low amounts is the SERS (surface-enhanced Raman scattering) derived probe, presenting numerous benefits including swift screening abilities, non-destructiveness, and great sensitivity.[82] The design of highly efficient SERS substrates is essential for ultrasensitive SERS detection.[83] According to substantial research, MXenes have enormous potential for Raman identifying. Like other 2D nanomaterials, MXenes could be coupled with nanomaterials like conducting polymers, metal oxides, and metal nanoparticles to further enhance their structural and electrical characteristics.[84] The benefits of MXenes-based nanostructures are their good electrical conductivity, better surface area, and excellent hydrophilicity. Indeed, MXenes using metal nanostructures not only protect metal platforms from defects but also facilitate chemical development by charge transmission with the aid of fixed biomolecules.[85] In light of this, a ratiometric SERS aptamer probe is construct for determination of AFB1. In order to construct the biosensor, AuNPs dimers were assembled through 1,2-bis(4-pyridyl) ethylene to create intense SERS "hot spots." Furthermore, these AuNPs dimers were engineered with specific aptamer (AFB1) and located onto the nanosheets of MXenes as seen in Figure 3. Throughout the sensing procedure, AFB1 attaches to the specific aptamer, which in turn its lead to the AuNPs dimers separation from MXenes nanosheets, therefore the existence of ABF1 is proved by the decrease in SERS intensity. The proposed method can detect ABF1 with LOD of a 0.6 pg/mL and a concentration range of 0.001–100 ng/mL. Besides, the designed probe was also employed in sensing of AFB1 in peanut samples, with RSD values of 4.47–8.68% and the recovery rate from 89.0% to 102.1%, which demonstrated the practicability of this technique.[86]

In another study, an aptasensor toward targeted and sensitive AFB1 was established by Shen's team.[87] To enhance the aptasensor sensitivity, the MXene/MWCNTs/$NiCo_2O_4$

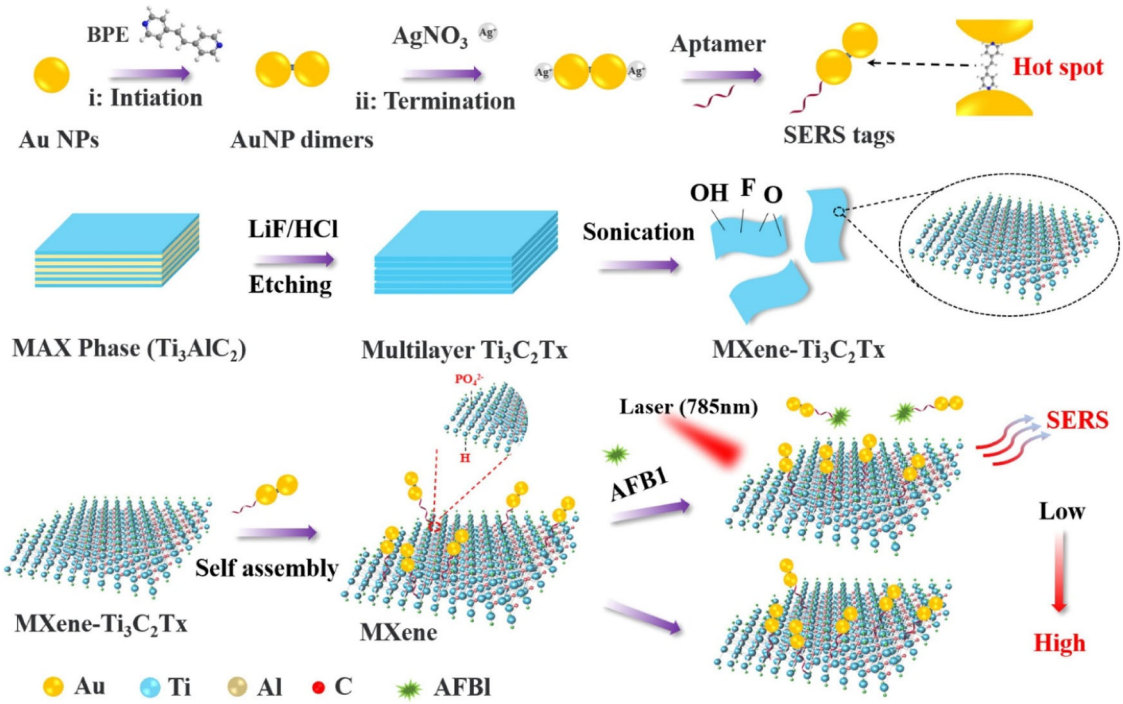

Figure 3. Schematic drawing of SERS aptamer based biosensor using AuNP dimers/MXenes assemblies toward AFB1 sensing. Reprinted with permission from ref. [86].

nanocomposite were successfully developed. The composite's surface was changed with Poly dopamine to anchor the NH_2-cDNA-aptamer system on the chip surface through the Schiff base process. The proposed strategy can identify AFB1 in actual maize flour sample with a DL of 1.890 ng/mL and linear range of a 2.5–200 ng/mL. From the literature, it could be assumed that MXene-derived aptamer probe display very low sensitivity (pg to fg) in comparison to other 2D material-derived aptamer based probes which show μg to ng sensitivity level. This can be arising from the optimum electronic band gap and brilliant electronic characteristics together with the fermi level of energy revealed *via* MXene composites. Nevertheless, the role of other elements like optimized experimental situations and transducer kind cannot be dismissed.

MXenes-Ti_3C_2Tx could simply bind with a biomolecules majority *via* electrostatic interaction, van der Waals interactions, coordination bonds, and hydrogen bonding, making them an exceptional nanobiointerface units in biosensor fabrication. Alternatively, MXenes could facilely interact with ssDNA without chemical binding, which enhances capability of the analyte-induced ssDNA release, thus meaningfully improving the biosensor's sensitivity.[88] Meanwhile, MXenes in comparison to graphene oxide have noticeable superiority in light absorption from visible light to a near-infrared region. MXenes could adsorb ssDNA and effectively quench the fluorophore fluorescence.[89] With the benefit in visible light absorption and the robust adsorption ability on ssDNA, MXene successfully quenches the fluorescence of fluorophore-tagged ssDNA so as to considerably reduce the background signal.[90] In short, MXene can be considered as a favorable fluorescence quencher for the fabrication of fluorescent nanoprobes using CRISPR/Cas system to fulfill quantitative/qualitative trace sensing of AFB1. Inspired by these criteria, Wu and coworkers explored a novel MXene-derived fluorescence nanoprobe conjugated with the CRISPER-Cas12 method for AFB1 measurement for the first time.[91] As shown in Figure 4, initially, the front and end of the specific aptamer are supplemented with a suitable amount of bases, termed Apt-1 and Apt-2, respectively. In order to create a "locked-activator" stable complex, the designed aptamers somewhat hybridized with an activator. Meantime, the crRNA and Cas12a complex are inactivated, and the ssDNA-FAM fluorescence is quenched once immobilized on MXenes *via* hydrogen bonding. In the existence of AFB1, it binds with one ssDNA, a locked activator in the helical double-strand aptamer form releases and opens an aptamer to trigger the inactive Cas12a connected with crRNA (guide RNA) and thereby cleaves the quenched fluorophore-modified ssDNA anchored on the MXene as small fragments. Then, these fragments leave the MXene and disperse in the solution, restoring the fluorescence signal to the aqueous medium. The established fluorescent probe can detect AFB1 with a DL of 0.92 pg/mL with an acceptable linear concentration range of 0.001-80 ng/mL. Moreover, their tests were also applicable in 12 peanut samples toward AFB1 with highly accurate.

AuNPs (gold nanoparticles) are extensively recognized for their electrical conductivity and excellent biocompatibility.[92,93] AuNPs could be interaction with MXene through chelation and hydrogen bonding.[86] To further enhance the MXene's performance, Sun and coworkers engineered MXene based on gold nanoparticles for boosted biocompatibility and electrical conductivity.[94] In this study, liver microsomal can be successfully coupled with designed Au@MXene nanocomposites and anchored onto the GCE

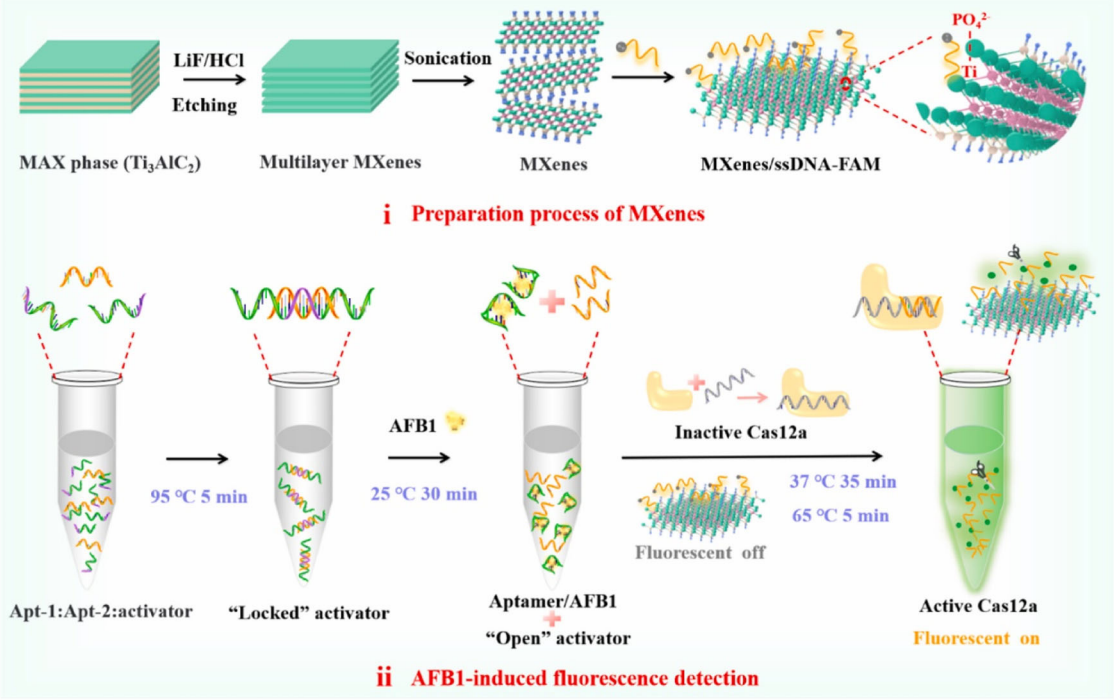

Figure 4. Representation of the MXenes-based fluorescence biosensor incorporated with CRISPR/Cas12a for specific identification of AFB1. Reprinted with permission from ref. [91].

surface for monitoring AFB1 in maize samples and phosphate buffered solutions. A current signal on the chip interface was induced due to the catalytic reaction of the fabricated liver microsomal electrochemical probe toward AFB1. In other word, the good biocompatibility, high surface area, and high conductivity of the Au@MXene complex allowed the direct electron transmission between the liver microsomal and the chip and preserved the enzyme activity in the liver microsomal to a great amount. The metabolic activities of the RLM nanoprobe that is established for the AFB1 electrocatalyst to its hydroxylation metabolite aflatoxin M1 is successfully proved. According to the alteration in the electrical signal produced *via* this metabolic actions, they can establish the association with amperometric (I – t) current signal and AFB1 content. Once the concentration of AFB1 was varied from 0.01 to 50 μM, toxin amount was linearly associated with the electrical signal with a LOD of 2.8 nM. The recovery tests analysis toward corn samples exhibited that the accuracy and recovery of constructed probe were compatible with the UPLC-MS/MS technique.

6.2. Ochratoxin A

Ochratoxin A (OTA) is created by numerous *Aspergillus* and *Penicillium* species, which pollutes a diversity of foodstuffs and feed and eventually finds its way to the human body by the skin, respiratory tract and digestive tract.[95] Accumulative proof exhibits that exposure to OTA concentrations will trigger severe toxic impacts on human body, comprising neurotoxicity, nephrotoxicity, and embryotoxicity.[96,97] Therefore, accurate identification of OTA residue is of great importance in toxicology and food safety investigation. Toward this goal, more recently, Feng's group reported a switchable signal paper-based aptasensor for the quantification of OTA using a scaffold-aptamer-signal amplifier configuration. The specific apta-cDNA hybrid with a -SH (thiol unit) is anchored *via* Au-S covalent force onto the MXene/Au composites-coated paper, utilized as the transducer platform modified on the working chip.[98] OTA aptamers combined with peroxidase mimic nanostructure using Pt@NiCo-LDH (Pt NPs doped NiCo hollow layer double hydroxides) to hybridize with their cDNA to produce a rigid dsDNA helix and create a "signal on" state. The existence of OTA allowed the apta-cDNA hybrid dissociation, releasing signal amplification labels to realize "signal off" state. Using the "signal on/off" approach, the aptamer based probe demonstrated a LOD of 8.9 fg/Ml with a broader concentration range of 20 fg/mL-100 ng/mL.

Designing nanocomposites based on MXene/polymer are nowadays at the cutting edge of study in different fields. Nevertheless, MXene tends to aggregate because of its great specific energy, which hinders the detecting function of the ending nanofiber nanocomposite. Electrospinning technology is a valuable method to construct Ti_3C_2Tx-polymeric composite as the mechanical stretching of the spinning procedure decreases the restacking and aggregation of Ti_3C_2Tx, which leads to constant dispersion inside the fiber axis and rise the electroactive part and collected charge density of the nanostructures.[99] Ti_3C_2Tx interface terminals offer the possibility to produce stable colloidal solutions with other polymers and fillers such as PVDF for processing into a diversity of composites.[99] The inserting of Ti_3C_2Tx into the PVDF fibers not only enhances the polymer's

conductivity but also improves the electrochemical, chemical stability, and hydrophilicity characteristics, which are favorable to a various utilization like actuators and sensors, supercapacitor electrodes, and wearable biosensors. Inspired by these findings, Saheed and colleagues reported an ultrasensitive electrochemical aptamer probe using electrospun Ti_3C_2Tx/PVDF composite selective/sensitive quantification of OTA.[100] The proposed aptasensor is fabricated by etching Ti_3AlC_2 using MILD (minimally intensive layer delamination) technique to create Ti_3C_2Tx, accompanied by electrospinning of the Ti_3C_2Tx at different concentrations with PVDF (Figure 5). This nanocomposite has brilliant electroactive interface places; and the electrochemical features can arise from synergetic influence between electrospun MXene with the PVDF β-phase. The dual conjugation of electrospun Ti_3C_2Tx/PVDF nanofiber works as a well-organized electrochemical redox platform that enables bulk arrangements of OTA-aptamer complexes to the chip surface. Subsequently, the constructed aptamer based probe can be able to determine OTA in a linear range of 1 fg/mL–1 ng/mL with a LOD of $\sim$ 2.15 fg/mL. The developed Ti_3C_2Tx-derived nanofiber also presented good stability, reproducibility, and applicability to quantify OTA in actual samples. In short, this study can open new horizon with MXene/polymeric electrospun hybrid nanofibers as an emerging substrate for field screening and large-scale OTA control and other mycotoxins in beverages and food.

It is noteworthy that the Ti_3C_2 MXene nanomaterial has a high fraction of Ti group, which is simply partially changed into TiO_2 throughout oxidation.[101,102] In this regard, Ti_3C_2 MXene can be used for modification of the TiO_2 NPs. In the MXene-based TiO_2, MXene could be applied as a carrier or cocatalyst to increase the photocatalytic functions. Concerning the above strategies, Chen's group reported a photocatalytic fuel cell-based nanoprobe for the quantification of OTA residue.[103] To achieve the high-efficiency of OTA determination, MSNs are utilized as nanocontainers for glucose loading, and specific aptamers are immobilized on the MSNs interface as dual-gated molecules to develop signal nanoprobes. The binding affinity of target toxin with specific aptamer was higher than the force between MSN and aptamer, which leads to the glucose release from MSNs. Under visible light illumination, the detached glucose is photo-oxidized *via* Ti_3C_2-TiO_2 and engaged as an electron acceptor to decrease Prussian blue, causing a great cell output signal with a maximum output power (23.516 μW cm^{-2}). Meantime, the electrochromic Prussian blue facilitated colorimetric OTA sensing. The Ti_3C_2-TiO_2-derived probe revealed excellent diagnostic function toward OTA in beer samples with a linear range of 0.2 ppb-20 ppb and a LOD of 0.0587 ppb. Besides, noble metals (Ag, Pt and Au) acting as electron sinks can enhance charge transmission capability of Ti_3C_2-TiO_2 through storing and trapping electrons.[104] Given that fabricating inspired Schottky junction through combination Ti_3C_2-TiO_2 with noble metals affords a superb surface contact to enable electron-hole migration and separation, which is estimated to achieve a high-efficient photoelectrochemical (PEC) probe even in the sacrificial agent's absence. In this context, Au@PtAg core-shell NPs were engineered on the Ti_3C_2-TiO_2 interface to create Schottky junction, which transmits photo-generated electrons and prevents electron-hole pairs recombination, thereby meaningfully improving the PEC signal. Chen's group integrate a DNAzyme cascade enhancement approach to further increase the sensitivity toward OTA as a result of its more flexible functionalization and better stability.[105] As seen in Figure 6, Au@PtAg/Ti_3C_2-TiO_2 can be successfully immobilized onto the chip surface

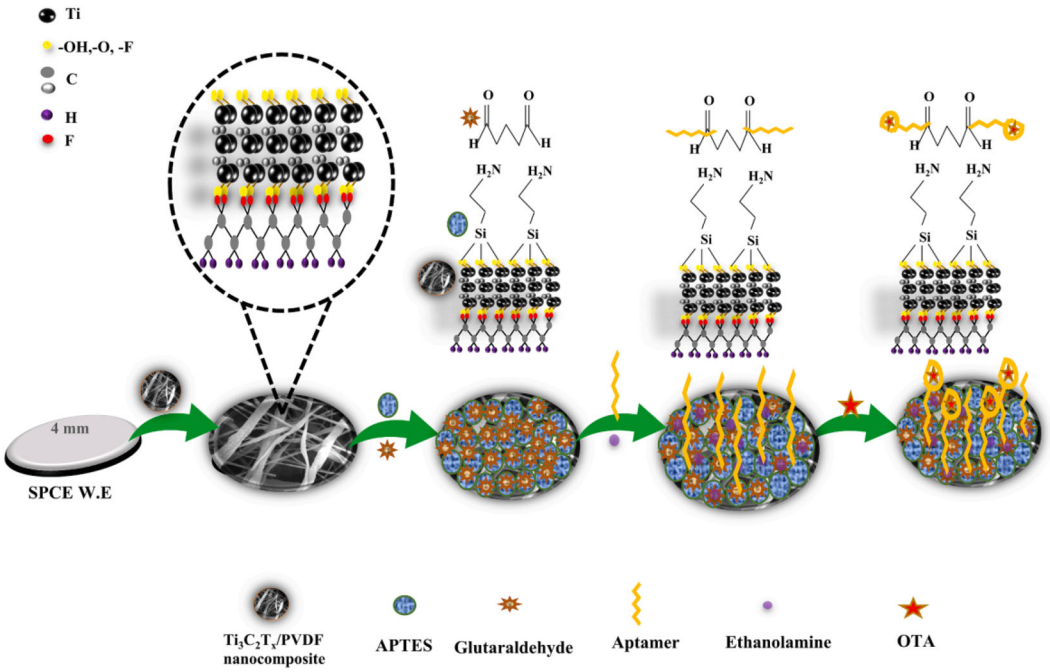

Figure 5. Schematic drawing of an ultrasensitive electrochemical aptasensor using Ti_3C_2Tx/PVDF hybrid nanofiber toward OTA sensing. Reprinted with permission from ref. [100].

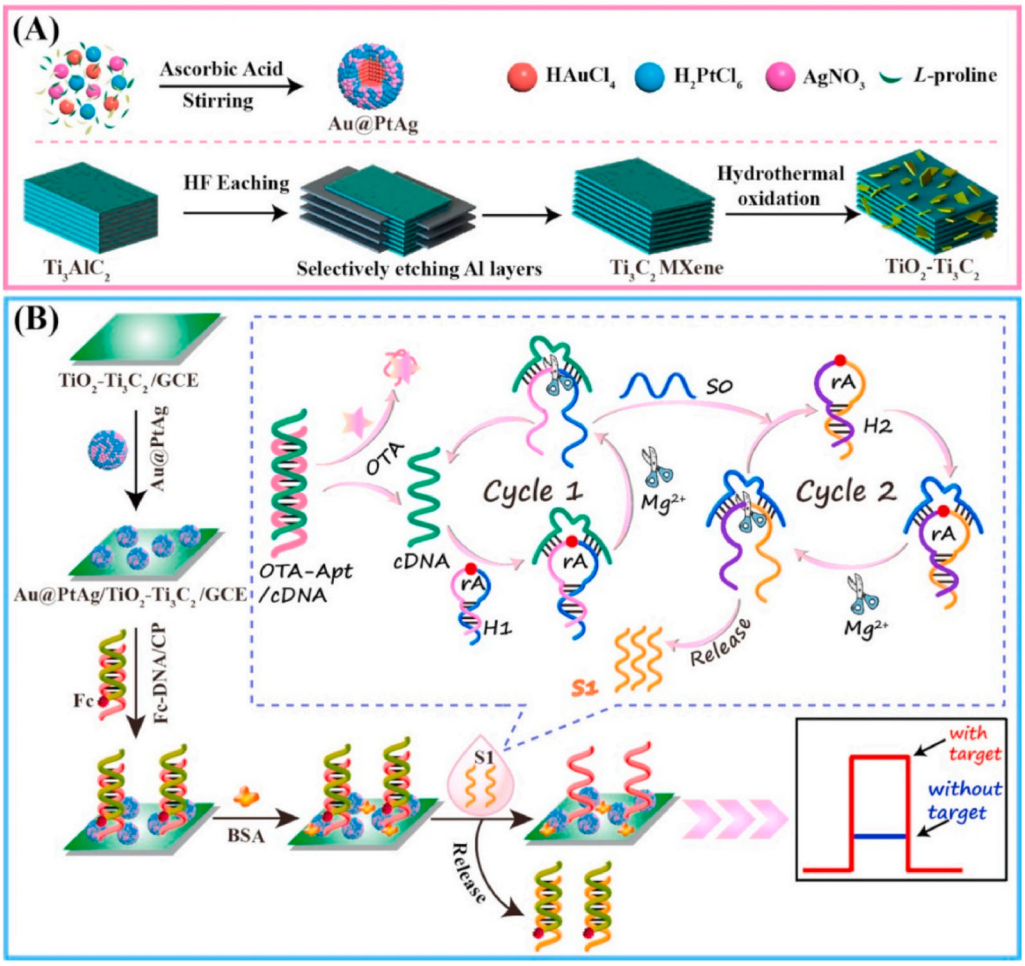

Figure 6. Diagram of (A) Ti_3C_2-TiO_2 and Au@PtAg construction. (B) The PEC aptamer probe manufacture procedure and Mg^{2+}-reliant DNAzyme cascade amplification toward determination of OTA. Reprinted with permission from ref. [105].

offering the great primary PEC signal. Thereafter, ferrocene-tagged duplex system is fixed on modified electrode, causing considerably reduced PEC signal because of the quenching impact of quenched ferrocene. In the OTA existence, it can specifically and rapidly couple to OTA-Apt and freedom cDNA from OTA-Apt/cDNA. Consequently, cDNA could hybridize with H1 integrated at the rA-cleavage location to trigger the DNAzyme, which then cleaves H1 at a precise rA place supported by Mg^{2+} to run cycle I (S0). At the same time, the resulting cycle I could instantly activate the cycle II amplification mode. Particularly, S0 hybridizes with H2 that having the rA cleavage site, and then Mg^{2+} catalyzes the cleavage of H2 to departure S0 and S1, releasing S0 able to initiate the following cycle. Plentiful S1 could be produced after multiple cycles, which in turn can be employed to attach and removed Fc-DNA from the interface chip, leading to a substantial rise in the photocurrent signal. Hence, through merging Au@PtAg/Ti_3C_2-TiO_2 with Mg^{2+}-reliant DNAzyme-supported cascade enhancement approach, an ultrasensitive PEC aptamer nanoprobe was successfully established toward OTA sensing. Under optimal conditions, the well-developed aptasensor displays outstanding photocurrent function in the linear range of 5 fg/mL-10 ng/mL with a LOD down 1.73 fg/mL, presenting high sensitivity, selectivity as well as stability.

6.3. Deoxynivalenol

Deoxynivalenol (DON), also recognized as vomitoxin, belongs to the type B group of trichothecene substances produced by fungi species in the genus Fusarium. Besides, DON renders the stable chemical and high solubility characteristics, donating its long-term existence in cereals and cooked foods.[106] All in all, humans being exposed to DON by foodstuff, mucous membrane, skin, and respiratory tract, which might cause hemorrhage, diarrhea, emesis, anorexia, and other symptoms.[107] Both the World Health Organization and the Food and Agriculture Organization have recognized DON as one of the most hazardous pollutants. To realize efficient and convenient screening of DON in foodstuff and feed, progresses of highly sensitive determination strategy are in urgent need. Sangu's group reported an electrochemical aptamer probe for the highly sensitive identification of DON *via* anchoring DON aptamer on Ti_3AlC_2 as detecting interface. This strategy revealed potential to determine mycotoxin in foodstuff and feed because of its cost effective, stable nature, greatly selective, and sensitive.[108]

The MXenes derived dots (0D), also called as Ti_3C_2 dots, inherits the biocompatibility, conductivity, and hydrophilicity of MXenes and possess distinctive photoelectrochemical and optical properties. In comparison to layered Ti_3C_2,

Ti_3C_2 dots have a greater specific surface area and a small size, well environmental friendliness and high sensitivity.[109] Nevertheless, quantum dots can aggregate in ECL environments owing to the small size, which can quench or attenuate light radiation, restricting their utilization. To solve this problem, researchers have developed various approaches. Homojunction impact is deliberated as an impressive technique to increase the chemical and physical properties of MXenes. Homojunctions, which are composed of materials with the same crystal and/or composition building, could offer continuity of band bonding and efficient promote the charge transmission at the interface.[110] Using these inspirations, Wang's team introduced an ECL "on-off-on" aptasensor using Ti_3C_2 dots/Ti_3C_2 nanosheet (TDTN) for sensitive detection of DON in milk samples.[111] In comparison to Ti_3C_2 nanosheet and Ti_3C_2 dots, the ECL-TDTN intensity was 2 times of Ti_3C_2 nanosheet and 4 times of Ti_3C_2 dots as emitters. Indeed, this can be arising from homojunction influence which can afford continuity of band bonding and efficiently promote charge transmission at the interface. According to ECL signal variations produced by DON and aptamer immobilized the chip interface, the aptamer based probe exhibited "on-off-on" functions and precisely sensed DON in the actual milk sample, with a LOD of 0.3 pg/mL and a linear range of 0.001–20 ng/mL.

In another study, Lin et al. intoduced a CRISPR-Cas12a-mediated LRET aptasensor based on the Au NPs/Ti_3C_2Tx MXene as the boosted quencher toward DON determination (Figure 7).[112] Specific DON aptamer is configured to induce the trans-cleavage Cas12a activity. Au NPs/Ti_3C_2Tx MXene and ssDNA-UCNPs (ssDNA functionalized upconversion nanoparticles) were designed as quenchers and probes, respectively. In the absence of DON, aptamer induced Cas12a to cleave the probes' ssDNA, inhibiting the probes from attaching onto MXene-Au, continuing the upconversion luminescence. Otherwise, DON be able to bind with specific aptamer and Cas12a is inactivated. Then, ssDNA-UCNPs are fixed through MXene-Au and quenched UCL *via* LRET. Given this technique, a linear range of 1–500 ng/mL and a LOD as low as 0.64 ng/mL were realized toward DON. Furthermore, the developed sensor is effectively employed to quantify DON in Tai Lake water and corn flour with recoveries of 95.2–104% and 96.2–105%, respectively. This scaffold realizes a specific and sensitive exploration of DON and significantly extends the quantification range of CRISPR-Cas probes for non-nucleic acids contaminants in the foodstuff and environment.

6.4. Zearalenone

Zearalenone (ZEN), also termed as the F-2 mycotoxin, is secreted through Fusarium krukowii, Fusarium xylinum, and Fusarium oxysporum that broadly found in moldy grains. Hence, it is also dispensed to a certain amount in agro-food products like dairy products, beer, and flour. Furthermore, it is thermostable and not degraded *via* heating, extrusion, and milling.[113] ZEN is an endocrine disrupting substance that could disorder the digestive and reproductive organization of human bodies, which might carry excessive economic burden to food industry and agriculture.[114] Thereinto, an ultrasensitive, accurate, and quick diagnostic technique that helps in timely screening is of utmost significance. Sangu and cowerkers established an ultrasensitive thin layer on screen-printed electrode based on the MXene/Chitosan composite for ZEN sensing in corn and cow milk samples.[115] Chitosan is an appropriate

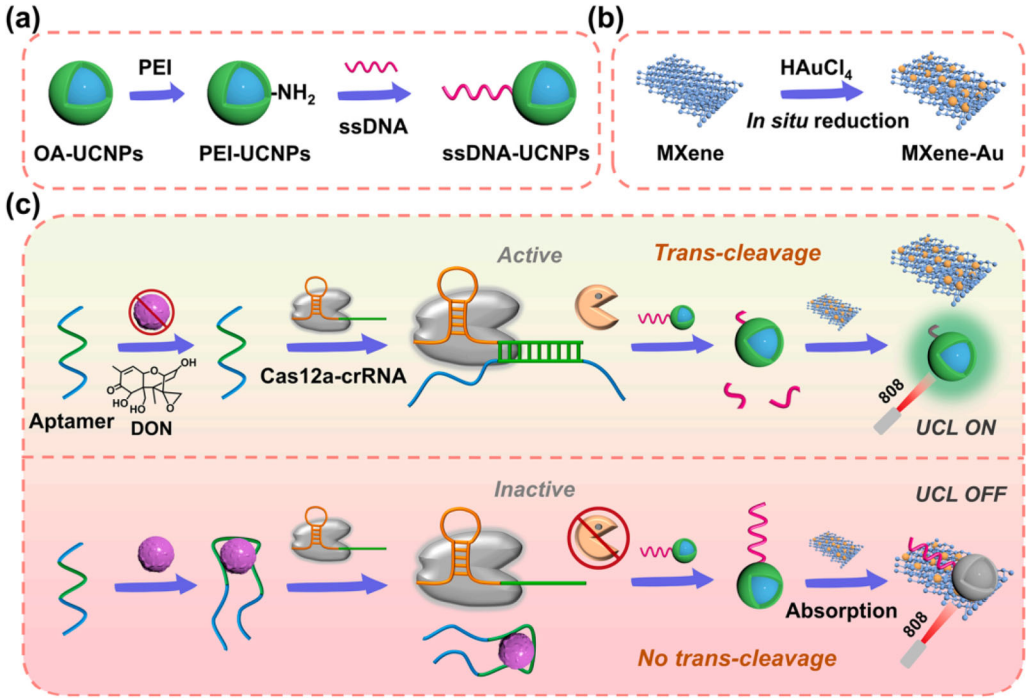

Figure 7. Schematic drawing of the construction procedure of (a) ssDNA-UCNPs and (b) MXene-Au and (c) the outline of CRISPR-Cas12a-assisted aptasensor to identify DON. Reprinted with permission from ref. [112].

Table 1. Characteristics of MXene-based nanomaterials for (bio)sensing of mycotoxins.

Detection readout	Sensing scheme	Food matrix	Target	Analytical characteristics	References
SERS	Ti_3C_2Tx MXenes loaded with Au nanoparticle dimers.	Peanut samples	AFB1	DL= 0.6 pg·mL^{-1} LR= 0.001–100 ng·mL^{-1}	[86]
Electrochemical	Nanocomposite fabricated based on the MXene/MWCNTs/$NiCo_2O_4$	Maize flour	AFB1	DL= 1.890 ng·mL^{-1} LR= 2.5–200 ng·mL^{-1}	[87]
Fluorescence	Aptasensor based on CRISPR/Cas12a and MXenes	Peanut samples	AFB1	DL= 0.92 pg. mL^{-1} LR= 0.001–80 ng·mL^{-1}	[91]
Electrochemical	Nanocomposite constructed based on the poly 4-vinyl pyridine, Ti_3C_2Tx, and GO-COOH.	Grape juice	AFB1	DL= 3 pg. mL^{-1} LR= 0.01–50 ng mL^{-1}	[122]
Electrochemical	aptasensor was developed using MXene-Au and Pt@NiCo-LDH-catalyzed signal amplification	–	OTA	DL= 8.9 fg. mL^{-1} LR= 20 fg. mL^{-1} –100 ng mL^{-1}	[98]
Electrochemical	Aptasensor based on the electrospun MXene/polyvinylidene fluoride nanofiber	Grape juice samples	OTA	DL= 2.15 fg. mL^{-1} LR= 1 fg mL^{-1}–1 ng mL^{-1}	[100]
SERS	Au-Ag Janus NPs are successfully assembled with Mxenes nanosheets.	Red wine samples	OTA	DL= 1.28 pM LR= 0.01–50 ng mL^{-1}	[123]
Electrochemiluminescence	Aptasensor was proposed using Ti_3C_2 dots/Ti_3C_2 nanosheet	Milk samples	DON	DL= 0.3 pg mL^{-1} LR= 0.001–20 ng. mL^{-1}	[111]
LRET	Aptasensor was developed using the combination of CRISPR-Cas12a with MXene-Au	Corn flour and Tai Lake water	DON	DL= 0.64 ng L^{-1} LR= 1–500 ng. mL^{-1}	[112]
Electrochemical	The prepared Ti_3AlC_2-MAX surface is immobilized with a tailor-made DON aptamer.	Plant samples	DON	DL= 1 fg mL^{-1} LR= 1fg mL^{-1} to 1 ng mL^{-1}	[108]
Electrochemical	Screen-printed electrode was developed based on the MXene/Chitosan composite.		ZEA	DL= 0.4 pg mL^{-1}	[115]
Electrochemical	Heterostructure was designed based on the MoS_2 QDs and the Ti_3C_2Tx/ MWCNT	Corn and flour	ZEA	DL= 0.32 ng. mL^{-1} LR= 3.00–300 ng. mL^{-1}	[121]

binder of MXene because of its superb electrical, thermal, and mechanical characteristics, along with nontoxic since it is a biopolymer. Effective etching of aluminum creates intercalated MXene layers which offers large surface area toward biomolecules immobilization. The proposed aptasensor using MXene/Chitosan has LOD of 0.4 pg/ml and displays a good determination of ZEN in spiked commodity.

In recent years, different functional materials such as carbon nanotubes (CNTs), graphene, boron nitride, and Pt NPs, have been advanced to modify MXenes to inhibit self-restacking and boost electrochemical function.[70,116,117] Among them, CNTs could be favorably incorporated into MXene and impede the aggregation of MXene, resulting in improved electrochemical activity.[118] In (bio)sensors, the integrating with MWCNTs to produce MXene-derived heterostructure also shows a great synergetic electrocatalytic impact on analyte, causing an excellent electrochemical sensing performance.[119] Besides, the progress of novel technologies and materials has donated desirable opportunities for the employment of heterojunction constructions to (bio)-sensing. For example, Chandran and coworkers found that an amalgamation of Ti_3C_2Tx MXene with MoS_2 render a highly conductive MXene/MoS_2 heterostructure, leading to a favorable electrode material.[120] According to these inspirations, Huang et al. exploited an innovative electrode using a MoS_2QDs and Ti_3C_2Tx-modified MWCNTs heterostructure for the electrochemical quantification ZEA in food samples.[121] The common MXene's modification excellently suppresses the components aggregation, fulfills a perfect porous building, and meaningfully rises the electrocatalytic activity and effective surface area. The exceptional heterostructure takes benefit of MoS_2 QDs to simply align with atoms and decline the shortcomings of its low conductivity. The outcomes reveal that the designed probe be able to detect ZEA as low as 0.32 ng/mL, which is far below the maximum residue value listed *via* the European Union (EU) (75 μg/kg). Hence, this material could be applied for quantification in actual samples. In summary, the biosensing applications of MXenes for various mycotoxins are listed in Table 1.

7. Conclusion and future prospective

Although many efforts have been made to inhibit mycotoxins, contamination with them is often unavoidable. Hence, rapid and specific diagnostic approaches for mycotoxins quantification can have an imperative function in food safety guarantee. So, as described in this literature update, novel available methods and approaches which engaged MXenes and their composites enable the highly sensitive identification of various mycotoxin, providing promising and important characteristics. Obviously, MXenes-derived (bio)sensors exhibit lower detection limits and greater sensitivity than various classical 2D materials like graphene, and their nanohybrid constituent materials are more suitable for analysis. Furthermore, MXene guarantees the biomolecule's activity *via* modifying and combining them with other materials. Even though MXenes have several features, there are some challenges in the signal-to-noise ratios and the biosensor's stabilities and clinical biomaterials transformations.

MXene is still at the beginning of development. Till now, the most broadly applied MXene types is Ti_3C_2Tx, whereas

there are very few studies on MXenes using other transition metals. Even though various types are estimated in theory, only a segment of them are experimentally produced.

Although, extensive endeavors are devoted to the construction of MXenes-derived optical scaffolds, compared to electrochemical devices the number of studies is quite low. It can be favorable to explore the MXenes with specific features like 3D MXene foams, MQDs, magnetic MXenes and suitable fluorescent quenching can extend their utilizations in fluorescence imaging, therapy, immunoassays, and other related fields. MXenes suffer from severe oxidative degradation once exposed to moisture, thereby impairing their sensing properties. Hence, under ambient conditions, the oxidative stability of MXene should be determined before developing a (bio)-sensor. Although significant efforts have been made to increase the oxidative stability of MXene through designing hybrids with metal oxides and CNTs to tune its shape, oxidation of MXene is challenging to achieve signal reproducibility in electrochemical biosensors. It should be noted that for the MXene's synthesis, no synthetic technique is established to precisely control the spatial distribution, surface end, structure, size, and yield. It is problematic to prevent the use of toxic substances throughout synthesis, which more limits their feasible utilization. Therefore, further effectual engineering strategies with manageable characteristics must be advanced for their production. It is desirable to functionalize MXenes using surface engineering to give greater catalytic activity and specific adsorption, for instance, selective hybrid of polymers, metal oxides, metals, and other materials with change the nanostructure and electronic conformation of MXenes. It is well known that the well structure design prompts great diagnosis sensitivity. Besides, incorporating the (bio)sensors within miniaturization devices using the suggested tests with the easiness of operation for wearable, flexible, and portable probes are important.

To sum up, the most of the studies have been dedicated to evaluating the detecting function of MXenes despite the large variety of advanced 2D-materials of phases, stoichiometry, and structures. This creates a significant gap between real-world application, theoretical predictions, in-lab technology, and commercial progress. The use of ab-initio simulations, machine learning, and deep learning are effective approaches for investigators pursuing the stoichiometry, phases, and structures of MXenes with perspectives of next-generation assays. For continuing development of MXenes-derived sensors, experimental and simulation calculations must work simultaneously. Additionally, the effective production of free-standing films of MXenes has proposed their successful incorporation in flexible, wearable, and portable tools. Eco-friendly, economical, reproducible, energy-efficient, diversified, and scalable sensor architecture strategies are the keys to technology integration to produce next-generation (bio)sensors using MXenes.

CRediT authorship contribution statement

Sulieman Ibraheem Shelash Al-Hawary: Writing e review, Investigation, Visualization, Conceptualization. **I. B. Sapaev:** Visualization, Investigation, Writing - original draft. **Raed H. Althomali:** Writing e review, Conceptualization. **Ebraheem Abdu Musad Saleh:** Writing - original draft, Visualization. **Kamran Qadir:** Writing - original draft. **Rosario Mireya Romero-Parra:** Conceptualization, Writing - original draft, Writing - review & editing, Supervision, Project administration, Funding acquisition. **Gailany Ismael ouda:** Writing - original draft. **Beneen M. Hussien:** Writing - original draft. **Montather F. Ramadan:** Writing - original draft. All authors contributed to writing of the reviewing and editing of this review.

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