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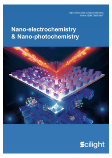

*Review*

# Non-Noble Metal SERS Substrates: From Chemical Mechanisms to Advancing Food Safety Applications

Lu Tan †, Junjun Ge † and Baokang Jin *

Department of Chemistry, Anhui University, Hefei 230601, China
* Correspondence: bkjinhf@aliyun.com
† These authors contributed equally to this work.

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**Abstract:** Food safety concerns are becoming increasingly critical, as trace contaminants such as antibiotic and pesticide residues, illicit additives, synthetic colorants, and heavy metal pollutants pose significant risks to human health. Developing rapid, sensitive, and cost-effective strategies for detecting these substances in complex food matrices has therefore become a pressing challenge in food safety monitoring. This review specifically focuses on food contaminants, including antibiotic and pesticide residues, illegal additives, synthetic colorants, and heavy-metal pollutants—that directly threaten food safety. Surface-enhanced Raman scattering (SERS), with its molecular fingerprinting capability and ultrahigh sensitivity, is widely regarded as a promising technique for this purpose. Nevertheless, the practical deployment of noble-metal substrates has been limited by high cost, poor stability, and reproducibility issues. In response, non-noble-metal SERS substrates have recently attracted substantial attention as viable alternatives. Their enhancement is dominated by chemical mechanisms (CM), where charge transfer (CT), defect-state modulation, and heterostructure coupling act synergistically to achieve signal amplification. Representative materials, including metal oxides, transition-metal chalcogenides, carbon-based systems, and emerging two-dimensional or hybrid structures, have exhibited distinct advantages in the trace detection of diverse food contaminants. This review systematically summarizes enhancement mechanisms, material categories, performance-optimization strategies, and recent advances in the field. It further highlights current challenges related to quantitative mechanistic understanding, substrate stability, matrix interference, and lack of standardized protocols. Finally, future directions are outlined, focusing on theory-guided material design, innovations in multimodal detection, and the development of portable sensing platforms, thereby offering systematic reference and scientific guidance for both fundamental research and practical translation.

**Keywords:** SERS; chemical mechanisms; charge transfer; food safety

## 1. Introduction

Food safety has become one of the most pressing global public health challenges. With the continuous expansion of the food industry, increasing complexity in processing chains, and the globalization of supply networks, the types and sources of food contaminants have grown increasingly diverse [1–4]. Trace-level pollutants, including pesticide residues, misuse of veterinary drugs and antibiotics, illicit additives, environmental toxins, and heavy metal ions, are frequently detected in food and production environments, posing serious risks to consumer health and public safety [5–8]. To clarify the focus of this review, it should be noted that our discussion is limited to contaminant-related food-safety concerns, including chemical residues and pollutants that directly threaten human health. Harmful compounds generated during thermal or other food-processing procedures (e.g., acrylamide, polycyclic aromatic hydrocarbons, heterocyclic amines), as well as biological or nutritional safety issues, are beyond the scope of this article. Conventional analytical methods, such as high-performance liquid chromatography (HPLC), gas chromatography (GC), inductively coupled plasma (ICP) and mass spectrometry–coupled techniques (HPLC–MS/MS, GC–MS), provide excellent sensitivity and precision. However, their broader application in food safety monitoring is constrained by inherent drawbacks, including long analysis times, complicated operation, high equipment costs, and limited suitability for on-site testing. These limitations restrict their ability to meet the urgent demand for rapid, low-cost, and portable detection approaches.

Surface-enhanced Raman scattering (SERS), a spectroscopic technique based on the amplification of molecular vibrational signals, has emerged as a promising alternative for food contaminant detection due to its high sensitivity, rapid response, and unique molecular fingerprinting capability [9]. Under ideal conditions, SERS can achieve detection limits down to the single-molecule level while enabling non-destructive, in situ analysis without the need for complex sample pretreatment [10,11]. Despite these advantages, the practical deployment of SERS is largely hindered by the choice and fabrication of substrate materials. For decades, high-performance SERS substrates have predominantly relied on noble-metal nanostructures, particularly gold (Au) and silver (Ag). These materials produce intense localized electromagnetic fields through localized surface plasmon resonance (LSPR), thereby significantly amplifying Raman scattering signals [12,13]. Importantly, noble-metal substrates provide exceptionally strong electromagnetic enhancement, often reaching factors of $10^6$–$10^{10}$. Thus, their enhancement efficiency remains the benchmark for high-sensitivity SERS detection. Their limitations arise not from insufficient enhancement capability but primarily from issues such as environmental degradation (e.g., Ag oxidation), insufficient long-term stability, high cost, and batch-to-batch reproducibility challenges, particularly under complex food-matrix conditions. These factors collectively impede their large-scale and routine application in food safety monitoring.

To address these challenges, non-noble-metal materials have recently emerged as an attractive research direction for SERS substrates. Examples include semiconductor metal oxides (e.g., $TiO_2$, $MoO_3$, ZnO) [14–17], transition-metal chalcogenides (e.g., $MoS_2$, $WS_2$) [18,19], carbon-based materials (e.g., graphene, graphene quantum dots) [20–22], as well as rapidly developing novel or hybrid structures such as MXenes and metal–organic frameworks (MOFs) [23,24]. Compared with noble metals, these materials offer the advantages of lower cost, environmental compatibility, and higher chemical stability. More importantly, their tunable band structures, abundant surface defects, and adjustable carrier dynamics confer unique SERS enhancement properties. Specifically, the chemical mechanisms (CM) enable non-noble-metal substrates to amplify molecular signals effectively via charge-transfer (CT) processes between analytes and substrates, even in the absence of strong electromagnetic hotspots [25,26]. Furthermore, the surface chemistry and band structures of these materials are more easily engineered, providing opportunities for selective molecular adsorption and enhancement of specific vibrational modes.

In recent years, substantial progress has been achieved through strategies such as defect engineering, doping modulation, heterostructure construction, and photonic design, which have markedly improved the enhancement performance of non-noble-metal substrates. In some cases, their signal intensities approach those of noble-metal systems [27–29]. At the same time, these substrates have demonstrated excellent capability in detecting food safety–related targets, including antibiotics, pesticides, illicit additives, food dyes, and heavy metal contaminants. Notably, beyond enabling trace-level detection, non-noble-metal substrates exhibit superior molecular selectivity and environmental adaptability in complex sample matrices. These attributes underscore their significant potential for advancing practical SERS applications in food safety monitoring.

Despite significant progress, the development of non-noble metal SERS substrates continues to face several critical challenges. A unified theoretical framework for their enhancement mechanisms has yet to be established, hindering the quantitative assessment of different enhancement pathways. Moreover, issues related to material stability and reproducibility remain unresolved, while signal interference and matrix effects are still difficult to mitigate in complex food systems. To address these challenges, it is necessary to systematically review recent advances in non-noble metal SERS substrates from four perspectives: enhancement mechanisms, material design, performance optimization strategies, and practical applications.

This review provides a comprehensive summary of the underlying enhancement mechanisms and representative pathways, categorizes different classes of materials and their structural features, analyzes key strategies for improving SERS performance, and highlights progress in food safety detection. Finally, future development directions are discussed. The overarching goal is to establish intrinsic links between material structures and electronic behaviors, elucidate structure–performance relationships governing enhancement efficiency and detection capability, and offer systematic theoretical guidance and research strategies to promote the practical application of non-noble metal SERS substrates (Figure 1).

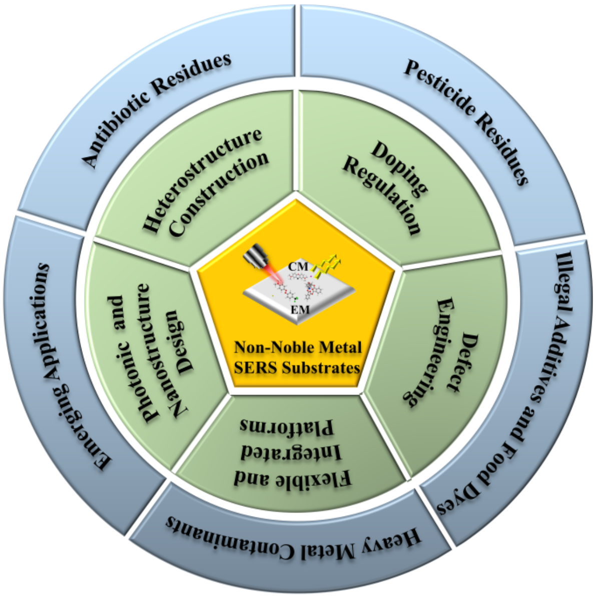

**Figure 1.** Schematic diagram of the construction strategy and application of semiconductor-based SERS for detecting food contaminants.

## 2. SERS Enhancement Mechanisms

Although certain defect-rich or doped semiconductors exhibit plasmon-like oscillations, these resonances typically lie in the mid-infrared region because of their relatively low free-carrier densities. Since SERS measurements generally employ visible or near-infrared excitation, the incident photons are far off-resonance with these semiconductor plasmons, resulting in only minimal field enhancement. Therefore, EM plays at most a weak, secondary role in non-noble metal substrates, and cannot account for the orders-of-magnitude enhancement characteristic of noble metal. The essence of SERS lies in its signal amplification mechanisms, which are generally explained by two widely accepted theories: the electromagnetic mechanism (EM) and the chemical mechanism (CM). For noble metal substrates, EM usually dominates, whereas in non-noble metal systems CM plays the primary role. A comprehensive understanding of these mechanisms and their potential synergy is crucial for the rational design of non-noble metal substrates and the optimization of their SERS performance.

### *2.1. Electromagnetic Mechanism (EM)*

EM arises from the amplification of localized electric fields induced by LSPR. In noble metal nanostructures (Au, Ag), resonance occurs when the incident light frequency matches the plasmon oscillation frequency of the nanostructure, leading to intense localized fields and the formation of "hot spots" in nanogaps or sharp tips. These hot spots can amplify Raman signals by several orders of magnitude [13,30]. In contrast, most non-noble metals, particularly wide-bandgap semiconductors and transition metal compounds, intrinsically possess low free carrier concentrations, which limits their ability to sustain strong plasmonic resonances. In fact, numerous studies have shown that even heavily doped or oxygen-deficient oxides exhibit LSPR features predominantly in the infrared region rather than in the visible range, resulting in negligible EM enhancement under common SERS excitation wavelengths. Consequently, EM should generally be considered a secondary or minor contributor in most non-noble SERS systems [9,14]. Nonetheless, their EM contribution can be substantially enhanced through deliberate material engineering. For instance, defect introduction (e.g., oxygen or sulfur vacancies) can generate localized states that increase carrier density, whereas aliovalent doping and non-stoichiometric phase regulation facilitate the formation of delocalized electrons, which may in some cases lead to weak and highly localized plasmon-like responses; however, these features often remain off-resonant with visible/NIR excitation and therefore contribute only marginally to EM enhancement [25]. In addition, rational nanostructure design, such as the construction of sharp edges, nanopores, or ordered arrays, can further concentrate localized electric fields and promote the formation of hot spots, even in systems lacking classical LSPR. collectively, these strategies endow non-noble metal substrates with appreciable EM enhancement capabilities, thereby expanding their potential for SERS applications.

### *2.2. Chemical Mechanism (CM) and Charge Transfer Pathways*

CM represents the dominant pathway in non-noble metal SERS. It originates from charge transfer (CT) between adsorbed molecules and the substrate, which modifies the molecular polarizability or introduces new optical resonance channels [31,32]. Although CM typically provides enhancement factors of only 1–100, which is far lower than EM in noble metals, it is still sufficient for trace detection in the absence of strong EM effects. The efficiency of CM is governed by several parameters: energy-level alignment between molecular frontier orbitals (HOMO/LUMO) and the substrate band edges, density of interfacial states (surface or defect states), strength of electron–vibration coupling, and the resonance condition between photon energy and the relevant transitions [33,34]. Based on Han et al., the possible CT pathways include: from the molecular HOMO to the substrate conduction band, from the CT complex to the conduction band, from the substrate valence band to the molecular LUMO, from surface states to the LUMO, and from the substrate conduction band to the molecular HOMO [35,36]. These processes rarely occur independently but typically result from the interplay of multiple mechanisms. Lombardi et al. further proposed that SERS enhancement arises from the coupling of multiple resonances within the molecule–substrate system rather than from isolated transitions [36,37]. On non-noble metal substrates, CM often exhibits selective enhancement, where certain vibrational modes are preferentially amplified due to bond-specific CT interactions. For example, nitrogen-doped carbon quantum dots (NGQDs) show pronounced enhancement with aromatic molecules owing to strong π–π interactions and favorable band alignment [38]. The apparent universality of SERS activity across many non-noble materials arises not from hidden plasmonic effects, but from CT processes enabled by favorable band alignment, defect states, and interfacial coupling. Diverse material classes, including oxides, TMDs, carbon systems, and MXenes, exhibit SERS activity because CT modifies molecular polarizability and introduces resonance channels, establishing CM as the dominant enhancement mechanism.

### *2.3. Synergistic EM-CM Effects*

In practical systems, EM and CM are not mutually exclusive. Through defect engineering or heterostructure design, non-noble metal substrates can simultaneously promote charge transfer and induce plasmon-like responses, leading to synergistic amplification. For instance, oxygen-vacancy-rich $MoO_3$ nanorods exhibit dual enhancement arising from defect-induced plasmonic effects and interfacial charge separation, thereby achieving EM–CM synergy [26,39]. Such cooperative mechanisms significantly reduce detection limits and enhance signal stability and selectivity in food safety applications. In non-noble metal systems, EM–CM synergy may occur when defect-induced localized states slightly improve field concentration, but such effects remain modest and secondary. CM-driven charge transfer is the primary origin of enhancement, while EM contributes only weakly within these off-resonant systems.

Overall, the enhancement of non-noble metal SERS substrates primarily relies on CM, while EM contributions can also be induced through defect regulation, doping, or heterojunction engineering. Establishing a mechanistic understanding of EM–CM interactions and harnessing their synergy via rational material design are essential for advancing the performance of non-noble metal SERS platforms.

## **3. Construction and Classification of Non-Noble SERS Substrates**

Although a broad range of non-noble materials have been reported as SERS-active, their Raman enhancement ability does not arise from the material category itself. Instead, these materials become effective SERS substrates only after specific modulation or construction strategies, such as defect engineering, band-structure regulation, or heterointerface formation, create favorable conditions for molecule–substrate CT. Thus, the materials discussed in this section should not be regarded as isolated “hot materials”, but as tunable platforms whose SERS activity originates from CT-enhancing structural or electronic modification.

Building upon this principle, the SERS enhancement of non-noble-metal substrates is predominantly governed by chemical mechanisms, particularly CT processes at the molecule–substrate interface. Unlike noble metals, whose enhancement mainly relies on intrinsic plasmonic behavior, non-noble materials offer a high degree of tunability through their diverse band structures, defect chemistries, and surface functionalities. These characteristics enable engineered CT pathways and selective molecular interactions, which form the foundation for designing high-performance SERS substrates. Current studies therefore categorize non-noble SERS materials according to their compositional and structural characteristics, including metal oxides, transition-metal chalcogenides, carbon-based systems, and emerging hybrid or two-dimensional materials.

### *3.1. Semiconductor Metal Oxides*

Metal oxides, including $TiO_2$, ZnO, $MoO_{3-x}$, and $W_{18}O_{49}$, constitute the foundational class of non-noble metal SERS substrates. Their wide bandgaps and tunable surface defects enable effective charge transfer through energy-level matching with adsorbed molecules. Li et al. synthesized microscale $TiO_2$ by a flame-assisted route, enabling large-scale fabrication of SERS-active semiconductor substrates. The resulting $TiO_2$ microsphere arrays (MSAs) displayed an enhancement factor (EF) of $3.28 \times 10^7$ and enabled highly sensitive ratiometric SERS detection of $Hg^{2+}$ [40]. Liu et al. designed double-shell ZnO (ZnO-DS) hollow microspheres with outstanding SERS activity. They demonstrated LODs of $1 \times 10^{-7}$ M and EF = $1.2 \times 10^4$, attributed to Mie resonance within nanocavities and structure-induced CT. (Figure 2) [41]. Liu et al. also developed amorphous $H_xMoO_3$ quantum dots as SERS substrates, which exhibited tunable plasmonic resonance in the visible and near-infrared regions. These quantum dots achieved an ultra-high EF of $9.5 \times 10^5$ for methyl blue detection, with an LOD of $1 \times 10^{-9}$ M [42]. Cong et al. employed $W_{18}O_{49}$ nanowires to enhance interactions, resulting in LODs as low as $10^{-7}$ M and a maximum EF of $3.4 \times 10^5$ [27]. More recently, $Cu_2O$ [9], $V_2O_5$ [43], and $Ta_2O_5$ [44] have also been introduced as semiconductor oxide SERS substrates with remarkable enhancement performance. These examples indicate that the SERS activity of metal oxides stems not from the oxide composition itself but from defect-mediated band-structure tuning that enables efficient molecule–substrate charge transfer.

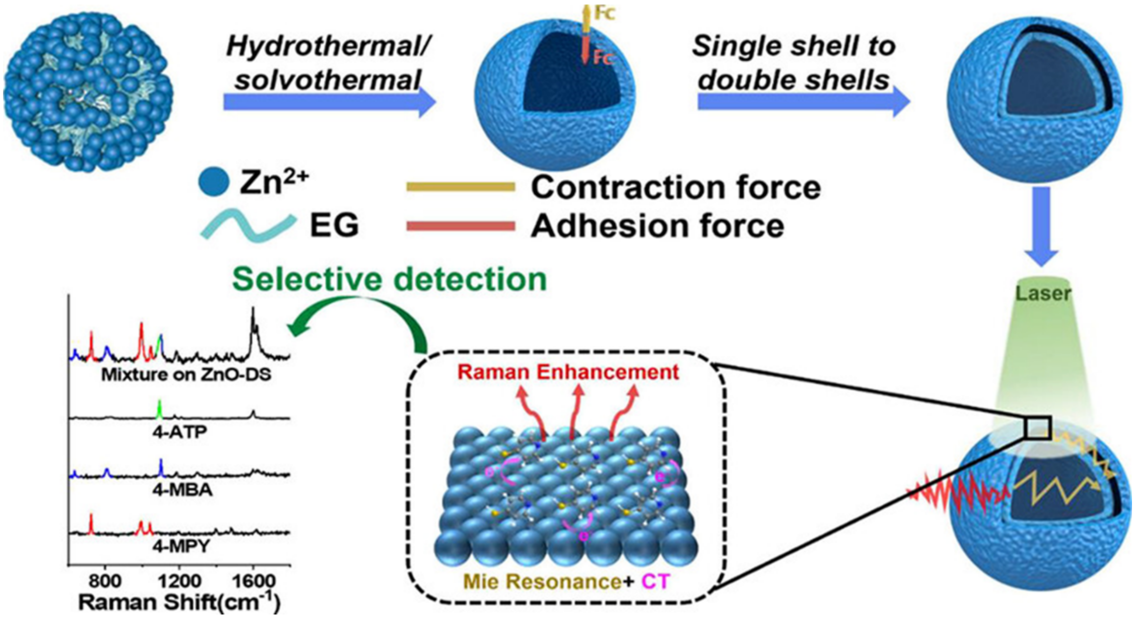

**Figure 2.** Schematic of the preparation of double-shelled ZnO hollow microspheres and their application in SERS detection. Reproduced with permission from Ref. [41]. Copyright 2024 American Chemical Society.

### *3.2. Transition-Metal Chalcogenides (TMDs)*

Two-dimensional TMDs, such as $MoS_2$, $WS_2$, $MoSe_2$, possess layered structures and tunable band gaps, facilitating superior CT dynamics [19,45]. Lv et al. synthesized Re-doped $WSe_2$, Nb atoms incorporated into 1T″ Re-$WSe_2$ further modulated its electronic structure. The resulting 1T″ Nb, Re-$WSe_2$ achieved femtomolar-level detection with a LOD ($5 \times 10^{-15}$ M) and EF = $2.0 \times 10^9$ (Figure 3A) [46]. Song et al. demonstrated that $NbS_2$ is an outstanding SERS substrate, enabling sub-attomolar detection and high EF (Figure 3B) [47]. Heterojunction TMD substrates have further enhanced photogenerated carrier separation and SERS performance. Peng et al. fabricated a WSSe/$WS_2$ heterojunction, where the built-in electric field promoted surface CT and molecular interactions, achieving a CV detection limit of $1 \times 10^{-13}$ M [48]. Importantly, TMDs often exhibit selective enhancement toward specific molecules due to their unique band structure and surface chemistry, providing advantages for trace detection in complex matrices. Overall, the high performance of TMD-based substrates arises primarily from dopant- or heterojunction-induced modulation of electronic structures that optimizes charge-transfer interactions with analyte molecules.

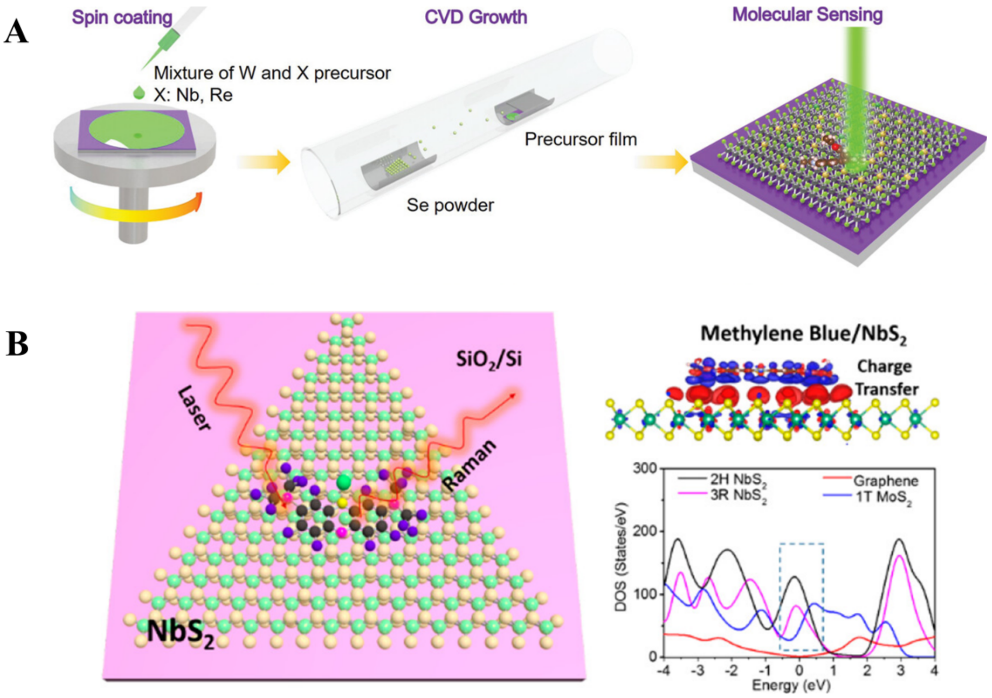

**Figure 3.** (**A**) Schematic illustration of the fabrication of X-doped monolayer $WSe_2$ (X represents Nb or Re) and their application in SERS detection. (**B**) Schematic diagram of Raman detection of MeB molecules adsorbed on $NbS_2$, electron density difference contour surfaces, and density of states near the Fermi level for different materials. (**A**) Reproduced with permission from Ref. [46]. Copyright 2022 Wiley-VCH. (**B**) Reproduced with permission from Ref. [47]. Copyright 2019 American Chemical Society.

### *3.3. Carbon-Based Substrates*

Carbon-based materials, such as graphene, reduced graphene oxide (rGO), graphene quantum dots (GQDs), and carbon nanotubes, possess high conductivity, large surface area, and structural flexibility, offering abundant adsorption sites and facilitating CT pathways [49]. Graphene and rGO can strongly adsorb aromatic molecules via $\pi$-$\pi$ interactions, enhancing molecule–substrate CT. Zhang et al. observed improved Raman enhancement on Fermi level-adjusted graphene [50]. Liu et al. built three-dimensional GO aerogels (GOAs), which delivered an EF of $3.1 \times 10^4$ and LOD of $10^{-8}$ M in dye detection (Figure 4) [21]. Graphitic carbon nitride (g-$C_3N_4$), with a band gap of ~2.7 eV and surface nitrogen coordination, has shown good sensitivity and selectivity for pesticide and antibiotic detection. Su et al. prepared hollow g-$C_3N_4$, achieving an EF of $1.84 \times 10^5$ through energy level coupling and efficient CT [20]. Moreover, carbon-based materials provide flexibility and integrability, enabling portable or paper-based SERS platforms. Meng et al. prepared flexible SERS substrates via chemical oxidation of carbon cloth, achieving an LOD below $10^{-8}$ M and three orders of magnitude enhancement in sensitivity [51]. Thus, Raman enhancement in carbon-based substrates originates mainly from engineered electronic states and $\pi$-interaction-assisted charge transfer rather than from the carbon frameworks alone.

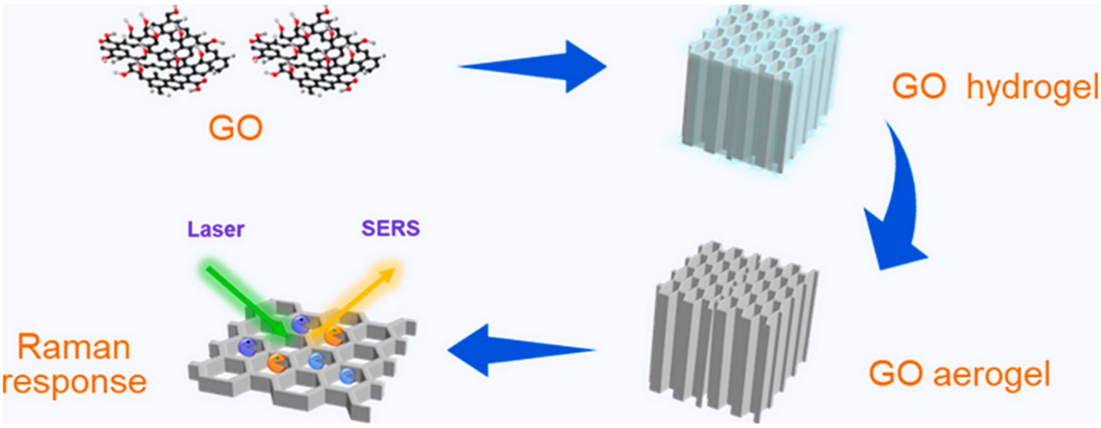

**Figure 4.** Schematic illustration of constructing three-dimensional graphene oxide aerogels via hydrothermal self-assembly and their application in SERS detection. Reproduced with permission from Ref. [21]. Copyright 2023 Elsevier.

### *3.4. Emerging Two-Dimensional and Hybrid Materials*

Emerging 2D materials and hybrid structures further expand the non-noble metal SERS landscape. MXenes (e.g., $Ti_3C_2T_x$) provide highly conductive surfaces with abundant functional groups, acting as electronic bridges to enhance CT between molecules and substrates. Qiu et al. designed a highly sensitive MXene SERS substrate via two-dimensional downsizing and molecular enrichment, yielding an LOD of $5 \times 10^{-9}$ M (Figure 5A) [52]. Metal–organic frameworks (MOFs) and covalent organic frameworks (COFs) offer highly tunable pores and molecular sieving, enabling selective adsorption and signal amplification [53–55]. Zhao et al. converted non-SERS-active MOFs into SERS-active substrates (EF = $1.0 \times 10^6$) by modulating metal centers, linkers, and framework topology (Figure 5B) [24]. Perovskite materials, due to their superior optoelectronic properties, enhance interfacial CT, as demonstrated by Guo et al. in $MAPbCl_3$-based SERS substrate [56]. Hybrid composites such as $Ti_3C_2/TiO_2$ [57], $ZnO/MAPbI_3$ [58], and $BP@MoS_2$ [59] leverage interfacial synergistic effects, promoting charge separation and enabling sensitive detection of dyes and illegal additives. These emerging materials retain the low-cost and environmentally friendly attributes of non-noble metals while enabling multifunctional integration for stable, sensitive detection in complex matrices. These studies collectively show that emerging 2D and hybrid materials function as effective SERS substrates only when interfacial engineering or structural modulation promotes favorable charge-transfer pathways.

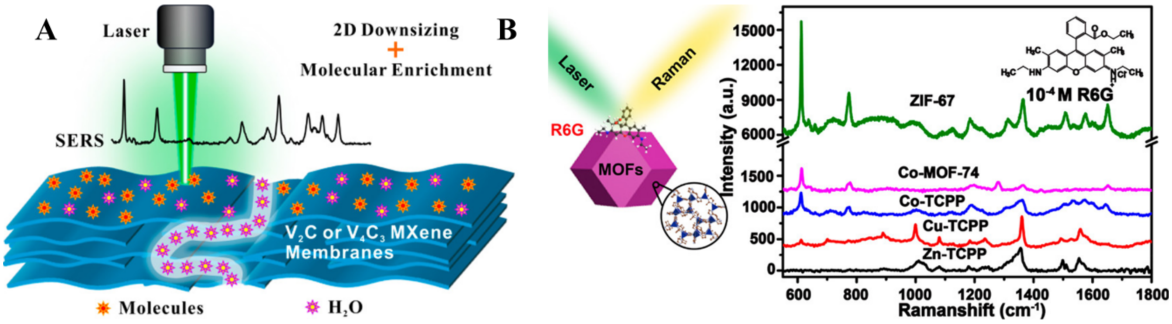

**Figure 5.** (**A**) Schematic illustration of molecular SERS detection on flexible two-dimensional vanadium carbide mxene-based membranes. (**B**) Schematic diagram of detection using different MOF SERS substrates. (**A**) Reproduced with permission from Ref. [52]. Copyright 2022 American Chemical Society. (**B**) Reproduced with permission from Ref. [24]. Copyright 2019 American Chemical Society.

Research on non-noble SERS substrates has expanded from early semiconductor oxides to TMDs, carbon-based materials, emerging 2D materials, and hybrid systems. Their diverse band structures, surface defects, and CT characteristics offer multiple pathways for SERS enhancement. These substrates facilitate trace detection of typical pollutants while providing molecular selectivity and environmental adaptability. Nevertheless, challenges such as limited signal intensity, poor reproducibility, and difficulties in large-scale fabrication remain. Therefore, integrating defect engineering, doping, heterostructure design, and photonic optimization is crucial for advancing non-noble metal SERS substrates.

## 4. Strategies for Enhancing the Performance of Non-Noble-Metal SERS Substrates

Although non-noble metal materials offer advantages such as low cost, environmental friendliness, and tunable physicochemical properties, their intrinsic SERS enhancement remains generally weaker than that of noble metals. Most non-noble systems rely predominantly on CM, typically providing EFs of only 1–100, far below the EM dominant in noble metals. To achieve the sensitivity and stability required for food safety detection, various strategies have been developed to optimize CT efficiency, enhance molecular adsorption, and improve substrate reproducibility and practicality. The Effective improvement strategies can be summarized as the following five types: defect engineering, doping regulation, heterostructure construction, photonic and nanostructure design, and flexible/integrated platforms.

### *4.1. Defect Engineering*

Defect engineering is a key approach to modulating the band structure and surface chemistry of non-noble metals. Defects, including oxygen vacancies ($O_v$), sulfur vacancies ($S_v$), and nitrogen vacancies ($N_v$), as well as edge states, introduce intermediate energy levels within the bandgap, providing additional CT pathways. By precisely controlling defect type, density, and distribution, the local density of states (DOS) can be optimized, thereby enhancing CM efficiency.

$O_v$ are the most common defects in oxide semiconductors [60–62]. Liu et al. synthesized $O_v$-rich $W_{18}O_{49}$ nanowires, achieving an EF of $2.8 \times 10^7$. The increased electron density strengthened LSPR coupling and created abundant hot spots, while defect states enhanced CT and molecular polarizability (Figure 6A) [63]. Similarly, $O_v$-rich $TiO_{2-x}$ crystal-facet heterojunctions enabled sensitive antibiotic detection with EF = $1.07 \times 10^7$ and excellent spectral reproducibility [64]. Excessive defect densities, however, may promote carrier recombination and non-radiative losses, highlighting the need for controlled generation and quantitative optimization. Methods such as plasma treatment, hydrogen reduction, and ion bombardment allow precise defect regulation [65].

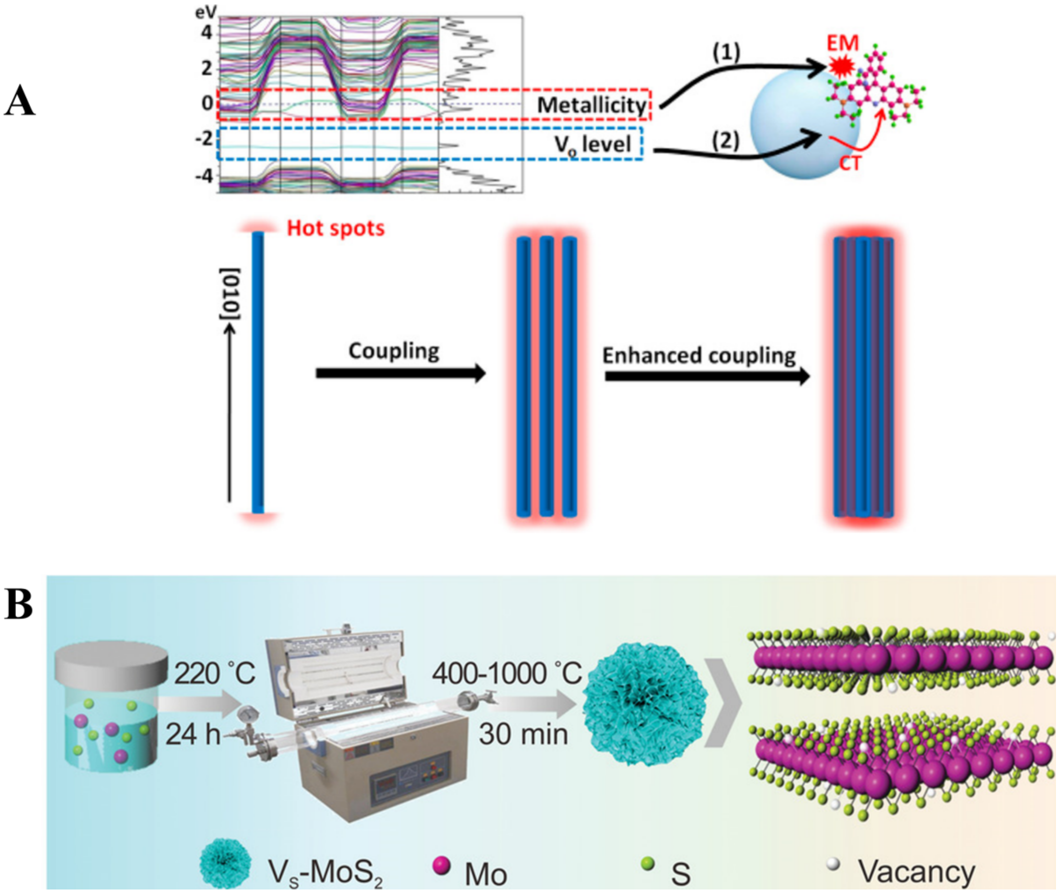

**Figure 6.** (**A**) Schematic illustration of the enhancement mechanism of $W_{18}O_{49}$ nanowires as SERS substrates. (**B**) Schematic illustration of the preparation of $MoS_2$ with abundant sulfur vacancies. (**A**) Reproduced with permission from Ref. [63]. Copyright 2018 American Chemical Society. (**B**) Reproduced with permission from Ref. [66]. Copyright 2022 Wiley-VCH.

In chalcogenides, $S_v$ also play a key role. Quan et al. developed $MoS_2$ SERS substrates, by adjusting $S_v$ density, internal carrier separation and molecular adsorption are improved, enabling ultrasensitive detection of diclofenac at nanomolar levels (Figure 6B) [66]. These examples demonstrate the central role of defect engineering in non-noble metal SERS enhancement.

### *4.2. Doping Regulation*

Doping modifies the electronic structure, Fermi level, carrier concentration, and chemical reactivity of non-noble metals, optimizing energy-level alignment with adsorbed molecules and CT efficiency.

Yang et al. prepared Ce-doped ZnO substrates, in which doping introduced surface defect levels that suppressed electron–hole recombination and facilitated CT with probe molecules, resulting in an EF of $7.3 \times 10^5$ and rapid detection of bisphenol A (LOD < 0.0001 ppm within 1 min) (Figure 7A) [67]. Song et al. reported S-doped $MnCo_2O_4$, where band-gap narrowing increased electronic transition probability, enabling sensitive detection of crystal violet (LOD = $1.0 \times 10^{-8}$ M) (Figure 7B) [68]. Doping is advantageous due to its simplicity and broad applicability, although excessive doping may induce lattice distortion or instability, necessitating a balance between performance enhancement and material stability.

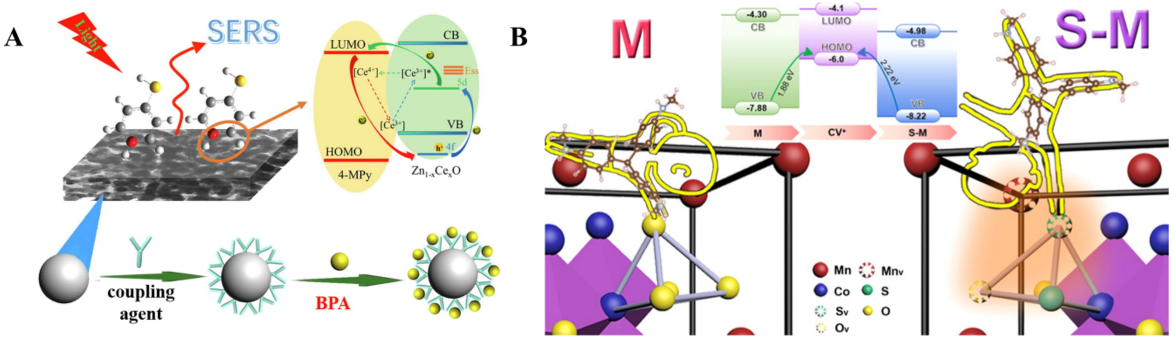

**Figure 7.** (**A**) Schematic diagram of SERS detection of bisphenol A using Ce-doped ZnO. (**B**) Schematic diagram of the SERS detection principle for sulfur-doped Co-Mn oxide nanotubes. (**A**) Reproduced with permission from Ref. [67]. Copyright 2021 Elsevier. (**B**) Reproduced with permission from Ref. [68]. Copyright 2022 American Chemical Society.

### *4.3. Heterostructure Construction*

Heterostructures, including semiconductor–semiconductor, semiconductor–carbon, and semiconductor–2D material, promote electron-hole separation, extend carrier lifetime, and enhance CT efficiency.

Xie et al. constructed $TiO_2/MoO_x$ heterojunctions with staggered band alignment, facilitating electron transfer to adsorbed molecules, achieving a detection limit of $10^{-8}$ M and EF of $1.445 \times 10^8$ (Figure 8A) [69]. Chen et al. developed *Z*-type $MoO_{3-x}/CuS$ heterojunctions, which not only catalyzed conversion of leucomalachite green to the SERS-active malachite green but also amplified the Raman signal, demonstrating superior activity compared to individual components (Figure 8B) [70]. Beyond electronic modulation, heterostructures offer additional functionality; for example, TMD/carbon composites enhance adsorption via π-π interactions [38,71,72], while MOF/oxide composites combine molecular sieving with selective enhancement [73–75]. Such multifunctional coupling has made heterostructure design a key focus in non-noble SERS research.

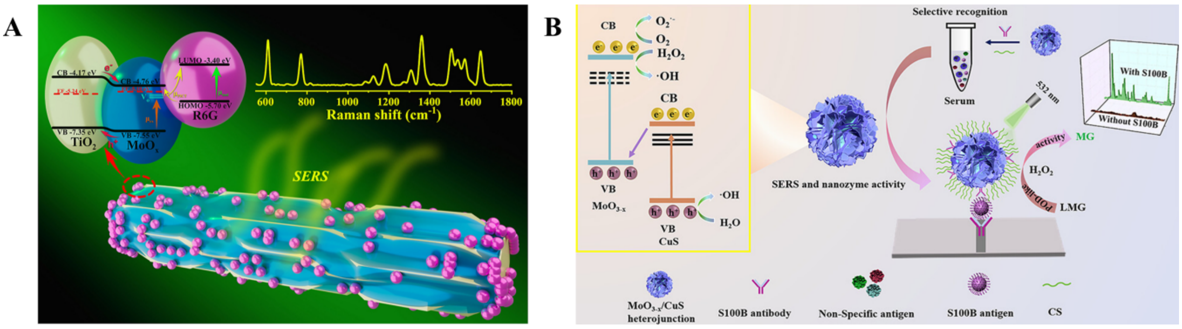

**Figure 8.** (**A**) Schematic of SERS detection principle for $TiO_2/MoO_x$ heterojunctions. (**B**) Schematic of SERS detection with *Z*-type $MoO_{3-x}/CuS$ heterojunctions and its mechanism. (**A**) Reproduced with permission from Ref. [69]. Copyright 2022 Elsevier. (**B**) Reproduced with permission from Ref. [70]. Copyright 2024 American Chemical Society.

### *4.4. Photonic and Nanostructure Design*

Manipulating light–matter interactions provide additional enhancement pathways. Photonic crystals, ordered nanostructures, and hollow/cavity structures can amplify local fields and increase molecular enrichment [41,76,77].

Qi et al. fabricated $TiO_2$ inverse opal photonic crystals, where multiple scattering enhanced light–matter interactions, boosting sensitivity [78]. Zhao et al. developed Co-doped $TiO_2$/GO photonic crystals, achieving a detection limit of $10^{-12}$ M for 4-MBA (Figure 9) [79]. Feng et al. prepared self-assembled $Cu_2O$ nanoarrays, where plasmon-induced hot-electron transfer (PIHET) facilitated highly sensitive and selective SERS detection, enabling rapid on-site monitoring of emerging viral variants [9]. Hollow and multilayer structures similarly improve molecular enrichment and local field intensity, as demonstrated by Ji et al. using hollow $V_2O_5$ microspheres [43]. These strategies rely on geometric and optical manipulation rather than intrinsic material properties, broadening substrate applicability.

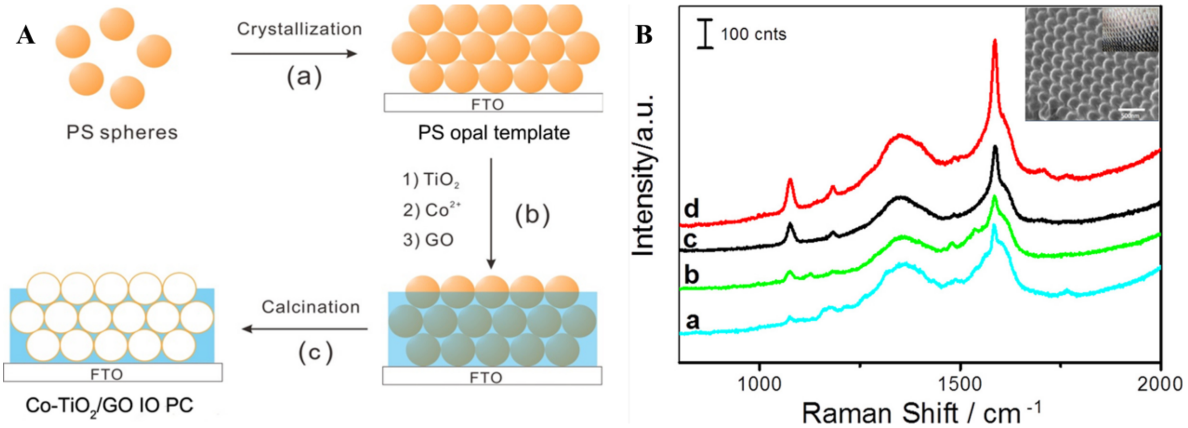

**Figure 9.** (**A**) Schematic of preparation for Co-doped $TiO_2$/graphene oxide SERS substrates based on anti-opalescent structured photonic crystals and (**B**) SERS spectra of 4-MBA at different concentration. Reproduced with permission from Ref. [79]. Copyright 2021 Elsevier.

### *4.5. Flexible and Integrated Platforms*

For practical applications, substrates must combine sensitivity with portability, low cost, and convenience. Flexible carriers, including paper, cellulose, and polymer films, support on-site and point-of-care detection.

Liu et al. fabricated $Ti_3C_2$ MXene/ZnO quantum dot heterostructure films, combining high sensitivity (LOD = $1 \times 10^{-7}$ M for 4-MPY) with excellent flexibility, uniformity, and stability (RSD = 10.7% over 60 days) (Figure 10A) [80]. Jiang et al. integrated Ca-doped $TiO_2$ with cotton fabrics, where dual defects (oxygen vacancies and $Ti^{3+}$ states) promoted multi-channel CT and efficient carrier separation, enabling in situ detection of antibiotics in fish surfaces and aquaculture water (Figure 10B) [81]. These platforms demonstrate that flexible SERS substrates can meet both sensitivity and practical usability requirements. Integration with wearable or smart devices may further enable real-time, dynamic monitoring for food safety regulation.

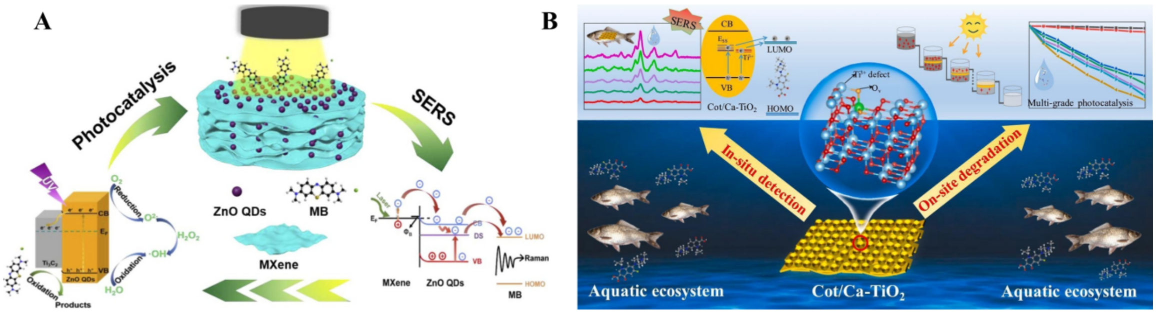

**Figure 10.** (**A**) SERS Detection Process and Recyclability Principle of Flexible MXene/ZnO Films. (**B**) Cot/Ca-$TiO_2$ Flexible SERS Substrates for In Situ Detection and Degradation of Quinolone Drug Residues on Fish Surfaces and in Pond Water. (**A**) Reproduced with permission from Ref. [80]. Copyright 2025 Elsevier. (**B**) Reproduced with permission from Ref. [81]. Copyright 2024 Elsevier.

In summary, the five complementary strategies—defect engineering, doping regulation, heterostructure construction, photonic/nanostructure design, and flexible platforms—collectively enhance CT dynamics, optical responsiveness, and practical applicability of non-noble metal SERS substrates, establishing a robust foundation for their deployment in food safety detection.

To provide a clearer performance overview, the representative non-noble-metal SERS substrates discussed in this section, including metal oxides, TMDs, carbon-based materials, and heterostructure systems, are summarized in Table 1. The table lists enhancement factors, detection limits, structural features, and analyte categories, enabling direct comparison of different material classes and optimization strategies.

**Table 1.** Representative non-noble-metal SERS substrates.

| Materials | Strategy | Analyte | EF | LOD | Ref. |
|---|---|---|---|---|---|
| $W_{18}O_{49}$ | Oxygen vacancies | R6G | $2.8 \times 10^7$ | 100 nM | [63] |
| $TiO_{2-x}$ | Oxygen vacancies | Antibiotics | $1.07 \times 10^7$ | 6.4 nM | [64] |
| $MoS_2$ | Sulfur vacancies | Diclofenac | $5.85 \times 10^3$ | 1.0 nM | [66] |

**Table 1.** *Cont.*

| Materials | Strategy | Analyte | EF | LOD | Ref. |
|---|---|---|---|---|---|
| Ce-doped ZnO | Doping | BPA | 7.3 × $10^5$ | $10^{-4}$ ppm | [67] |
| $TiO_2/MoO_x$ | Heterostructure | R6G | 1.45 × $10^8$ | 10 nM | [69] |
| $MoO_{3-x}/CuS$ | Heterostructure | LMG | 1.75 × $10^7$ | 0.47 pg/mL | [70] |
| Graphene/$MoS_2$ | Heterostructure | R6G | -- | 1.0 nM | [71] |
| $TiO_2$ | Photonic | 4-MBA | 2.0 × $10^4$ | 6.0 nM | [78] |
| MXene/ZnO | Flexible | 4-MPY | 4.6 × $10^4$ | 100 nM | [80] |

## 5. Applications of Non-Noble Metal SERS Substrates in Food Safety Detection

Food safety monitoring represents a significant application of SERS technology. With increasing demands for trace-level detection, non-noble metal SERS substrates have attracted growing attention due to their low cost, chemical stability, and molecular selectivity. These substrates have been successfully applied for the detection of antibiotics, pesticide residues, illegal additives, and heavy metals, demonstrating excellent sensitivity, selectivity, and adaptability.

### *5.1. Detection of Antibiotic Residues*

Antibiotics are widely used in livestock and aquaculture, and their residues can enter the human body through the food chain, posing risks of antibiotic resistance and health hazards. Non-noble metal SERS substrates, with tunable structures and molecular recognition capabilities, offer a promising approach for sensitive detection of antibiotic residues.

We employed $WO_3/W_{18}O_{49}$ heterojunction substrates with an internal Raman standard to achieve high sensitivity and stability for trace antibiotics. The abundant oxygen vacancies and built-in electric fields synergistically promoted interfacial charge transfer, enhancing the SERS effect. In real milk samples, detection limits (LODs) for doxycycline hydrochloride (DCH) and enrofloxacin (ENR) were $1.023 \times 10^{-8}$ M and $1.014 \times 10^{-7}$ M, respectively, well below regulatory maximum residue limits (Figure 11A) [17]. Furthermore, nitrogen-doped graphene quantum dots (NGQDs) combined with $WO_3$ nanosheets ($WO_3$ NSs) formed a heterostructured SERS substrate, where enhanced CT and strong π-π interactions between NGQDs and target molecules resulted in ultrasensitive detection of norfloxacin (NOR) in drinking water, with a LOD of $8.76 \times 10^{-9}$ M (Figure 11B) [38]. Zhang et al. fabricated $TiO_2$/ZnO heterojunction substrates using interface engineering strategies. Efficient carrier separation and strong interfacial coupling facilitated CT between substrate and analytes, enabling detection of enrofloxacin in eggs with a LOD of only 13.1 μg/kg, outperforming both EU standards and conventional noble-metal-based methods [82].

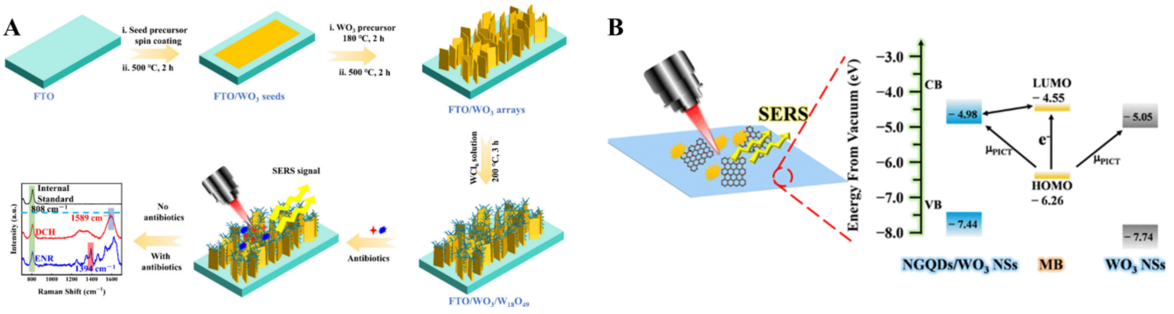

**Figure 11.** (**A**) Schematic diagram of the preparation steps for the $WO_3/W_{18}O_{49}$ heterojunction substrate and its ratio-based detection of ENR and DCH using the internal standard method. (**B**) Schematic diagram of the detection principle for molecules on NGQDs/$WO_3$ nanostructures and the corresponding charge transfer mechanism. (**A**) Reproduced with permission from Ref. [17]. Copyright 2025 American Chemical Society. (**B**) Reproduced with permission from Ref. [38]. Copyright 2023 Royal Society of Chemistry.

These studies demonstrate that non-noble substrates can achieve high sensitivity while selectively enhancing different classes of antibiotics, offering feasible solutions for monitoring residues in dairy, eggs, and aquatic products. Notably, the LODs achieved by these non-noble substrates ($10^{-9}$–$10^{-7}$ M) are comparable to or even lower than many Au- or Ag-based SERS substrates reported for the same antibiotics (typically $10^{-8}$–$10^{-6}$ M), underscoring their potential as cost-effective alternatives.

### *5.2. Detection of Pesticide Residues*

Pesticide residues remain a major concern due to their structural diversity and potential health risks. Non-noble metal substrates offer tunable bandgap properties and selective adsorption for efficient detection.

Zhang et al. synthesized $MoO_2$ nanospheres exhibiting strong surface plasmon resonance and chemical stability, enabling detection of clenbuterol and methyl parathion with LODs of $1.0 \times 10^{-8}$ M (Figure 12A) [83]. Quan et al. developed a $MoS_2/TiO_2$ heterostructure ($MTi_{20}$), achieving enhanced SERS sensitivity and stability for α-endosulfan with LODs of $1.0 \times 10^{-8}$ M (Figure 12B) [84]. Liang et al. utilized CuO to detect paraquat in food with a LOD of 0.3 mg $L^{-1}$ [85]. These results confirm the feasibility of non-noble substrates for pesticide residue monitoring.

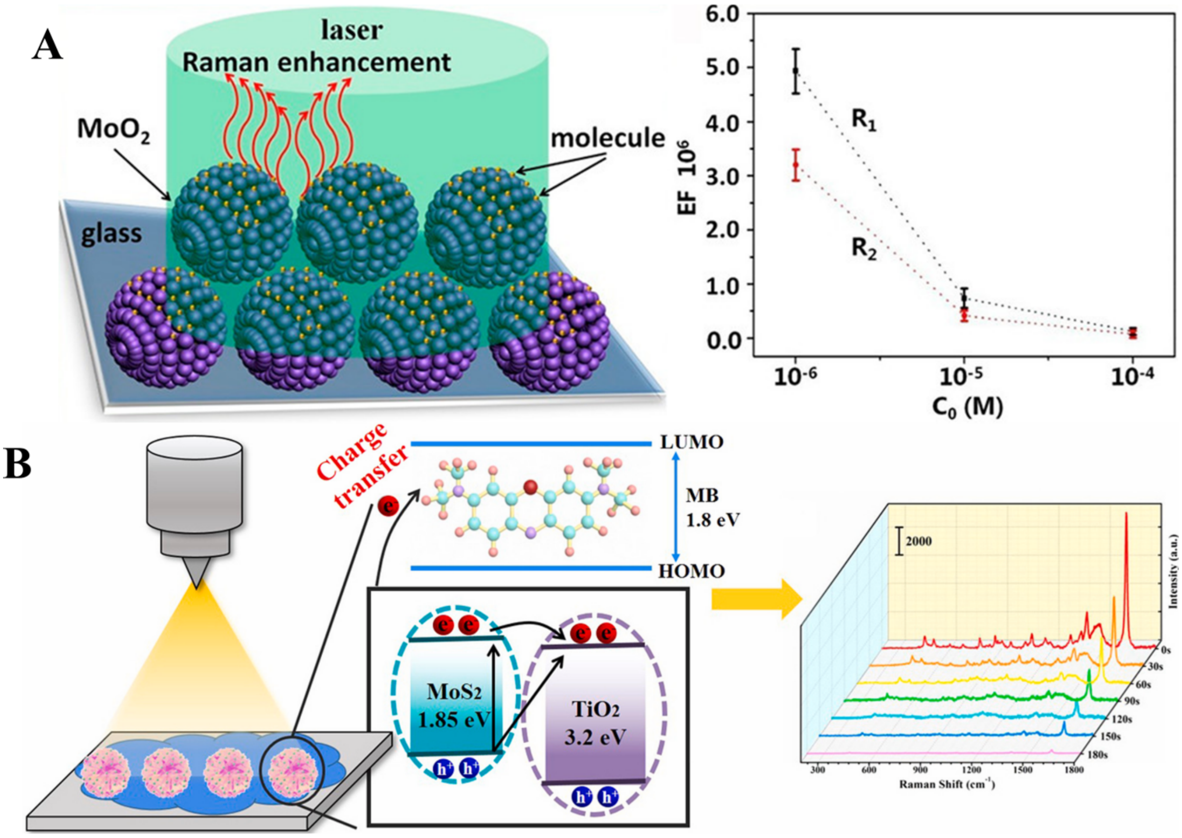

**Figure 12.** (**A**) Schematic of SERS detection principle and SERS enhancement performance on $MoO_2$ substrates (**B**) Schematic of enhancement mechanism for SERS detection on $MTi_{20}$ and detection of different concentrations of α-endosulfan. (**A**) Reproduced with permission from Ref. [83]. Copyright 2017 American Chemical Society. (**B**) Reproduced with permission from Ref. [84]. Copyright 2021 Elsevier.

### *5.3. Detection of Illegal Additives and Food Dyes*

Illegal additives and food dyes, such as aspartame, melamine, malachite green, and Sudan red, are strictly regulated due to toxicity and carcinogenicity. SERS, with its molecular fingerprint specificity and rapid response, offers an ideal detection approach.

Xu et al. employed Sc-doped 1T-$MoS_2$, retaining the metallic conductivity while enhancing interactions, reducing LODs for aspartame (APM) and thiabendazole (TBZ) to $5.3 \times 10^{-5}$ M and $5.0 \times 10^{-9}$ M, respectively (Figure 13A) [86]. Nisa et al. combined molecularly imprinted polymers (MIPs) with GO for melamine detection in milk, achieving sensitive and selective analysis (Figure 13B) [87]. Recently, we designed a g-$C_3N_4/W_{18}O_{49}$ heterostructure (WCN) on flexible membrane, integrating defect regulation and bandgap matching, and detected malachite green in fish skin with an LOD of $1.9 \times 10^{-10}$ M (Figure 13C) [29]. These examples illustrate the effectiveness of heterojunction non-noble metal substrates in detecting illegal additives, even in complex matrices.

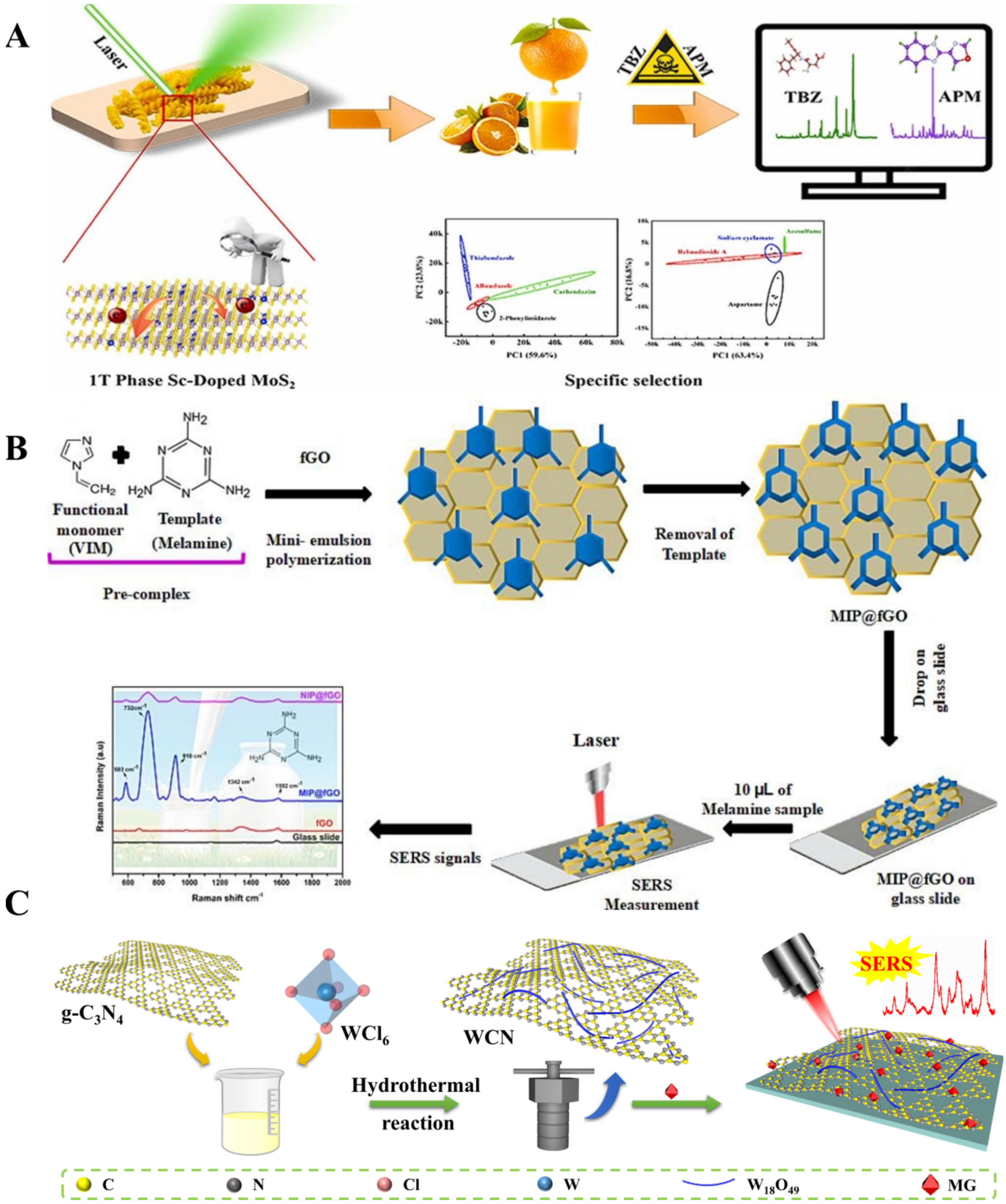

**Figure 13.** (**A**) Schematic of Sc-doped 1T-MoS$_2$ for precise identification and detection of AMP and TBZ in fruit juices. (**B**) Preparation of MIP-functionalized GO and its principle diagram for melamine detection. (**C**) Schematic diagram of WCN SERS substrate preparation and its application in MG detection. (**A**) Reproduced with permission from Ref. [86]. Copyright 2025 Elsevier. (**B**) Reproduced with permission from Ref. [87]. Copyright 2025 Elsevier. (**C**) Reproduced with permission from Ref. [29]. Copyright 2023 Royal Society of Chemistry.

### *5.4. Detection of Heavy Metal Contaminants*

Heavy metal ions (e.g., $Hg^{2+}$, $Pb^{2+}$) are usually Raman inactive, requiring indirect detection strategies using functionalized molecular probes. Non-noble metal substrates enable signal modulation via on/off mechanisms or product-enhanced SERS.

Zhang et al. employed ZnO submicron flower (ZnO SFs) for $Pb^{2+}$detection in drinking water. Calcined ZnO SFs exhibited narrowed bandgaps and enhanced CT, achieving a LOD of 3.55 pM over a linear range of 10 pM–100 μM (Figure 14) [88]. Kamal used $Ag_3PO_4$ microcubes modified with 4,4′-bipyridine for ultra-sensitive detection of $Hg^{2+}$ and $Pb^{2+}$, reaching an ultrasensitive LOD of $10^{-15}$ M, with reusability over four cycles [89]. Parveen et al. developed 3D ZnO@SWCNTs composites, enhancing plasmonic coverage and interparticle coupling, enabling sensitive $Pb^{2+}$ detection at 0.225 nM [90]. These approaches highlight the potential of non-noble metal SERS substrates for heavy metal monitoring via chemical recognition and indirect signal amplification.

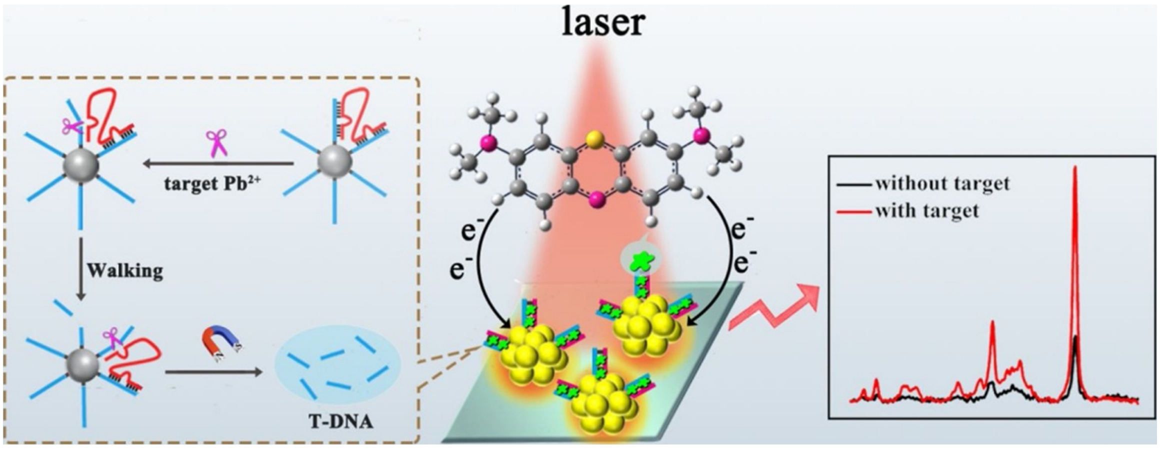

**Figure 14.** Schematic diagram of SERS detection principle and signal changes for $Pb^{2+}$ on ZnO SFs. Reproduced with permission from Ref. [88]. Copyright 2021 Elsevier.

### *5.5. Emerging Applications*

Beyond conventional pollutants, non-noble SERS substrates show promise for emerging pollutants. Han et al. fabricated $Ti_3C_2T_x/TiO_2/W_{18}O_{49}$ heterojunctions for rapid detection of micro/nanoplastics in environmental samples (Figure 15) [91]. Quan et al. employed $ZnO/MoS_2$ to detect bisphenol A with a LOD of 1 nM [92]. Zhang et al. demonstrated $Mo_{4/3}B_2$ MBene as a stable, highly sensitive SERS substrate for portable detection of ricin in river water, achieving a LOD of 0.01 μg/mL [93]. These studies extend the applicability of non-noble metal SERS substrates to emerging contaminants, supporting food quality control, safety traceability, and comprehensive monitoring across the food supply chain.

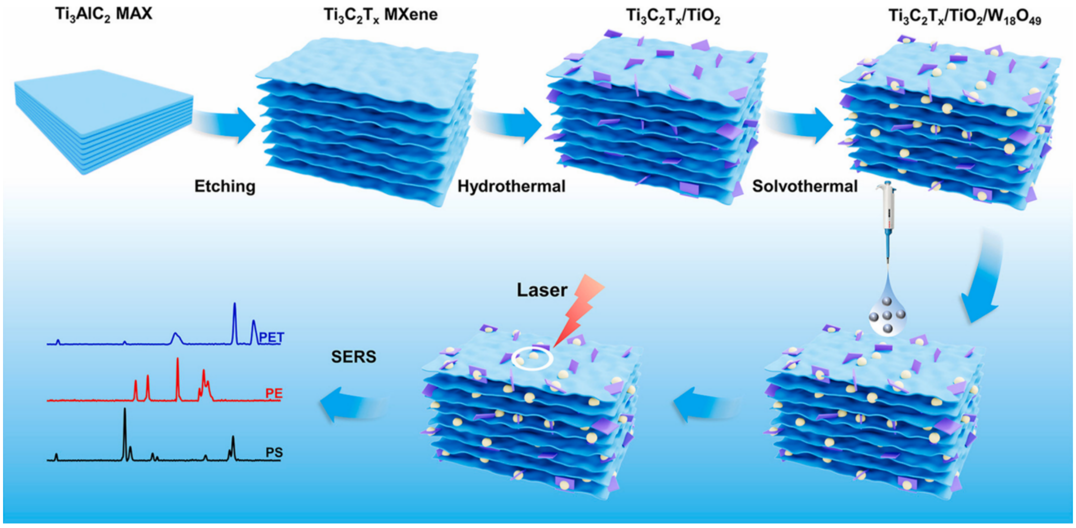

**Figure 15.** Schematic of the construction of a 3D $Ti_3C_2T_x/TiO_2/W_{18}O_{49}$ SERS Substrate and Detection of Micro/Nano Plastics. Reproduced with permission from Ref. [91]. Copyright 2025 Elsevier.

Non-noble SERS substrates exhibit excellent performance for detecting antibiotics, pesticides, illegal additives, food dyes, and heavy metals, and are expanding into microplastics, endocrine disruptors, and toxins. Their low cost, chemical stability, and molecular selectivity confer distinct advantages. Remaining challenges include signal interference in complex matrices, lack of quantitative standards, and scalability of substrate production. The next chapter addresses these challenges and future directions.

## 6. Conclusions and Outlook

In recent years, non-noble metal SERS substrates have emerged as an important direction in surface-enhanced Raman scattering research, owing to their advantages of low cost, tunable structural features, and environmental friendliness. From the perspective of enhancement mechanisms, their core lies in chemical enhancement, particularly CT processes between analyte molecules and substrates, which are further reinforced by synergistic contributions from defect states, band structure engineering, and photonic effects. Systematic studies on metal oxides, TMDs, carbon-based materials, emerging two-dimensional systems, and hybrid structures have not only elucidated how band structures and surface chemical features influence SERS activity but also broadened their applicability to complex food matrices. Performance optimization strategies such as defect engineering, heterostructure construction, doping modulation, and flexible substrate design have significantly improved the sensitivity, selectivity, and stability of non-noble metal SERS substrates, thereby expanding their prospects in food safety detection.

On the application side, non-noble metal SERS substrates have been successfully employed for trace detection of antibiotics, pesticides, illegal additives, food dyes, and heavy metals, and their scope has further extended to emerging targets such as microplastics, biotoxins, nutrient adulteration, pathogenic microorganisms, and contaminants from packaging materials. These studies have not only demonstrated their feasibility under laboratory conditions but also provided new insights into constructing practical food safety monitoring platforms. In particular, when integrated with flexible supports, molecular imprinting, ratiometric signal analysis, and multimodal detection strategies, non-noble metal SERS substrates exhibit remarkable potential for practical deployment.

Nevertheless, significant challenges remain before their transition from laboratory prototypes to real-world applications can be achieved. First, the contributions of CT, defect states, and localized photonic effects are often entangled, making quantitative evaluation difficult and hindering the establishment of a unified theoretical framework. Second, the structural stability and reproducibility of substrates remain insufficient, and their performance is susceptible to interference from multicomponent food matrices. Third, most studies are still limited to model molecules or spiked samples, leaving a gap with large-scale, standardized, and industrial applications.

Future research is expected to advance along the following directions:

(1) Mechanistic insights: Establishing a unified theoretical framework of chemical enhancement by combining first-principles calculations with time-resolved spectroscopic techniques to unravel the synergistic effects of CT, defect states, and photonic contributions.
(2) Material design: Achieving predictive and controllable performance optimization through multiscale defect regulation, bandgap engineering, and multi-heterostructure coupling.
(3) Methodological expansion: Developing ratiometric analysis, internal standard strategies, and machine learning-assisted spectral interpretation to enhance quantification accuracy and anti-interference capability.
(4) Practical applications: Designing low-cost, flexible, and scalable non-noble metal substrates in combination with portable Raman devices to enable rapid screening, on-site detection, and intelligent supervision of food safety.
(5) Interdisciplinary integration: Coupling with electrochemistry, fluorescence, photothermal, and other analytical techniques to construct multimodal detection platforms that overcome the limitations of single-signal readouts and improve detection reliability.
(6) Extension to processing-derived toxicants: Although not covered in this review, compounds generated during thermal or other food-processing procedures (e.g., acrylamide, polycyclic aromatic hydrocarbons, heterocyclic amines) represent an important yet underexplored class of analytes. Future studies should investigate SERS-active substrate designs, sample-pretreatment workflows, and chemometric strategies tailored to these thermally induced toxicants and benchmark their detection performance against established analytical methods.

In conclusion, while substantial progress has been made in both mechanistic understanding and application exploration, further efforts are required to address theoretical unification, substrate standardization, and translational feasibility. With the deep integration of materials science, spectroscopy, and food safety research, non-noble metal SERS substrates are expected to bridge the gap from fundamental studies to real-world applications, ultimately becoming a powerful tool for safeguarding food safety.

## Author Contributions

L.T.: conceptualization, data curation, writing—original draft preparation; J.G.: data curation, writing—original draft preparation, investigation; B.J.: supervision, writing—reviewing and editing, funding acquisition. All authors have read and agreed to the published version of the manuscript.

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## Conflicts of Interest

The authors declare no conflict of interest.

## Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

## References

1. Dincer, C.; Bruch, R.; Costa-Rama, E.; et al. Disposable Sensors in Diagnostics, Food, and Environmental Monitoring. *Adv. Mater.* **2019**, *31*, 1806739.
2. Yosri, N.; Gao, S.; Zhou, R.; et al. Innovative Quantum Dots-based SERS for Ultrasensitive Reporting of Contaminants in Food: Fundamental Concepts and Practical Implementations. *Food Chem.* **2024**, *467*, 142395.
3. Xu, J.; Zhang, S.; Luo, S.-H.; et al. Rapid Sample Pretreatment Facilitating SERS Detection of Trace Weak Organic Acids/Bases in Complex Matrices. *Anal. Chem.* **2024**, *96*, 9399–9407.
4. Chen, Y.; Gu, W.; Zhu, C.; et al. Recent Advances in Photoelectrochemical Sensing for Food Safety. *Anal. Chem.* **2024**, *96*, 8855–8867.
5. Tang, X.; Ji, C.; Zeng, W.; et al. Development of an Integrated EC–SPME–SERS Platform with the pAg-rGO-Au Substrate for Ultrasensitive Detection of Fenthion. *ACS Sens.* **2025**, *10*, 6206–6217.
6. Mahmood Khan, I.; Niazi, S.; Akhtar, W.; et al. Surface Functionalized AuNCs Optical Biosensor as an Emerging Food Safety Indicator: Fundamental Mechanism to Future Prospects. *Coord. Chem. Rev.* **2023**, *474*, 214842.
7. Han, T.; Cui, C.; Xing, Y.; et al. Advances of Signal Amplification Strategies and Sensing Formats in Electrochemiluminescence Sensors for Mycotoxins. *TrAC Trends Anal. Chem.* **2024**, *180*, 117961.
8. Xie, X.; Pu, H.; Sun, D.W. Recent Advances in Nanofabrication Techniques for SERS Substrates and Their Applications in Food Safety Analysis. *Crit. Rev. Food Sci. Nutr.* **2018**, *58*, 2800–2813.
9. Feng, E.; Zheng, T.; He, X.; et al. Plasmon-Induced Charge Transfer-Enhanced Raman Scattering on a Semiconductor: Toward Amplification-Free Quantification of SARS-CoV-2. *Angew. Chem. Int. Ed.* **2023**, *62*, e202309249.
10. Lin, C.; Liang, S.; Peng, Y.; et al. Visualized SERS Imaging of Single Molecule by Ag/Black Phosphorus Nanosheets. *Nano Micro Lett.* **2022**, *14*, 75.
11. Su, Y.; Wen, S.; Luo, X.; et al. Highly Biocompatible Plasmonically Encoded Raman Scattering Nanoparticles Aid Ultrabright and Accurate Bioimaging. *ACS Appl. Mater. Interfaces* **2021**, *13*, 135–147.
12. Zhao, M.; Sikdar, D.; Zhao, M.; et al. 3D Self-Assembly of a Bilayer Nanoparticle Metasurface for Surface-Enhanced Raman Scattering (SERS) Sensing. *Nano Lett.* **2025**, *25*, 8251–8257.
13. Tan, L.; Lou, Y.; Zhu, J.-J. High-performance SERS Chips for Sensitive Identification and Detection of Antibiotic Residues with Self-assembled Hollow Ag Octahedra. *Chem. Commun.* **2023**, *59*, 14443–14446.
14. Glass, D.; Cortes, E.; Ben-Jaber, S.; et al. Dynamics of Photo-Induced Surface Oxygen Vacancies in Metal-Oxide Semiconductors Studied Under Ambient Conditions. *Adv. Sci.* **2019**, *6*, 1901841.
15. Fujisawa, J.-I.; Kaneko, N.; Hanaya, M. Interfacial Charge-transfer Transitions in ZnO Induced Exclusively by Adsorption of Aromatic Thiols. *Chem. Commun.* **2020**, *56*, 4090–4093.
16. Yang, J.; Dang, T.; Ma, S.; et al. Plasmon-Free Surface-Enhanced Raman Spectroscopy Using α-Type $MoO_3$ Semiconductor Nanorods with Strong Light Scattering in the Visible Regime. *ACS Appl. Mater. Interfaces* **2024**, *16*, 41257–41270.
17. Tan, L.; Zhao, Y.; Zhou, P.; et al. A Ratiometric SERS Strategy Based on a $WO_3/W_{18}O_{49}$ Homojunction Substrate with Built-In Raman Internal Standard for Accurate Trace Antibiotic Detection. *Anal. Chem.* **2025**, *93*, 17275–17284.
18. Jena, T.; Choudhary, G.; Hossain, M.T.; et al. Salt-Catalyzed Directed Growth of Bilayer Palladium Diselenide ($PdSe_2$) Dendrites and Pd Nanoparticle-Decorated $PdSe_2$–$Pd_2Se_3$ Junction Exhibiting Very High Surface Enhanced Raman Scattering Sensitivity. *Chem. Mater.* **2024**, *36*, 5922–5934.
19. Tang, X.; Hao, Q.; Hou, X.; et al. Exploring and Engineering 2D Transition Metal Dichalcogenides toward Ultimate SERS Performance. *Adv. Mater.* **2024**, *36*, e2312348.
20. Su, Y.; Yuan, B.; Jiang, Y.; et al. A Bioinspired Hollow g-$C_3N_4$–CuPc Heterostructure with Remarkable SERS Enhancement and Photosynthesis-mimicking Properties for Theranostic Applications. *Chem. Sci.* **2022**, *13*, 6573–6582.
21. Liu, W.; Wang, Z.; Yan, W.; et al. Construction of Ultra-sensitive Surface-enhanced Raman Scattering Substrates Based on 3D Graphene Oxide Aerogels. *Carbon* **2023**, *202*, 389–397.
22. Chen, N.; Xiao, T.-H.; Luo, Z.; et al. Porous Carbon Nanowire Array for Surface-enhanced Raman Spectroscopy. *Nat. Commun.* **2020**, *11*, 4772.
23. Liu, X.; Li, T.; Lee, T.-C.; et al. Wearable Plasmonic Sensors Engineered via Active-Site Maximization of TiVC MXene for Universal Physiological Monitoring at the Molecular Level. *ACS Sens.* **2024**, *9*, 483–493.
24. Sun, H.; Cong, S.; Zheng, Z.; et al. Metal–Organic Frameworks as Surface Enhanced Raman Scattering Substrates with

High Tailorability. *J. Am. Chem. Soc.* **2019**, *141*, 870–878.

25. Meng, X.; Yu, J.; Shi, W.; et al. SERS Detection of Trace Carcinogenic Aromatic Amines Based on Amorphous $MoO_3$ Monolayers. *Angew. Chem. Int. Ed.* **2024**, *63*, e202407597.
26. Zhou, Y.; Gu, Q.; Qiu, T.; et al. Ultrasensitive Sensing of Volatile Organic Compounds Using a Cu-Doped $SnO_2$-NiO p-n Heterostructure That Shows Significant Raman Enhancement. *Angew. Chem. Int. Ed.* **2021**, *60*, 26260–26267.
27. Cong, S.; Yuan, Y.; Chen, Z.; et al. Noble Metal-comparable SERS Enhancement from Semiconducting Metal Oxides by Making Oxygen Vacancies. *Nat. Commun.* **2015**, *6*, 7800.
28. Yang, L.; Sang, Q.; Du, J.; et al. A Ag Synchronously Deposited and Doped $TiO_2$ Hybrid as an Ultrasensitive SERS Substrate: A Multifunctional Platform for SERS Detection and Photocatalytic Degradation. *Phys. Chem. Chem. Phys.* **2018**, *20*, 15149–15157.
29. Tan, L.; Yue, S.; Lou, Y.; et al. Enhancing Charge Transfer in $W_{18}O_{49}$/g-$C_3N_4$ Heterostructure via Band Structure Engineering for Effective SERS Detection and Flexible Substrate Applications. *Analyst* **2023**, *149*, 180–187.
30. Kim, N.H.; Hwang, W.; Baek, K.; et al. Smart SERS Hot Spots: Single Molecules Can Be Positioned in a Plasmonic Nanojunction Using Host-Guest Chemistry. *J. Am. Chem. Soc.* **2018**, *140*, 4705–4711.
31. Jiang, X.; Wang, R.; Tang, Y.; et al. Sulfur Vacancy-Rich $MoS_2$ Flower-Like Microsphere with Synchronously Tunable Electromagnetic and Chemical Effects for Boosting Semiconductor SERS. *Adv. Funct. Mater.* **2025**, *35*, 2418412.
32. Yoon, J.; Kim, S.-H. Plasmonic–Photonic Hybrid Hydrogels for Slow-Light-Amplified Surface-Enhanced Raman Scattering Detection of Small Molecules. *ACS Nano* **2025**, *19*, 29531–29542.
33. Wang, X.; Guo, L. SERS Activity of Semiconductors: Crystalline and Amorphous Nanomaterials. *Angew. Chem. Int. Ed.* **2020**, *59*, 4231–4239.
34. Chaudhry, I.; Hu, G.; Ye, H.; et al. Toward Modeling the Complexity of the Chemical Mechanism in SERS. *ACS Nano* **2024**, *18*, 20835–20850.
35. Han, X.X.; Ji, W.; Zhao, B.; et al. Semiconductor-enhanced Raman Scattering: Active Nanomaterials and Applications. *Nanoscale* **2017**, *9*, 4847–4861.
36. Lombardi, J.R.; Birke, R.L. Theory of Surface-Enhanced Raman Scattering in Semiconductors. *J. Phys. Chem. C* **2014**, *118*, 11120–11130.
37. Yang, L.; Peng, Y.; Yang, Y.; et al. A Novel Ultra-Sensitive Semiconductor SERS Substrate Boosted by the Coupled Resonance Effect. *Adv. Sci.* **2019**, *6*, 1900310.
38. Tan, L.; Lu, X.; Yue, S.; et al. Nitrogen-doped Graphene Quantum Dot-intensified Tungsten Oxide Nanosheets as a SERS Substrate for Antibiotics Detection. *Chem. Commun.* **2024**, *60*, 13360–13363.
39. Vo, T.H.; Le, H.T.T.; Nguyen, L.H.; et al. Nanorod Structure Tuning and Defect Engineering of $MoO_x$ for High Performance SERS Substrates. *Nanoscale* **2024**, *16*, 22297–22311.
40. Li, J.; Xie, Q.; Li, J.; et al. Macroscale $TiO_2$ Microspherical Arrays with Multiple Synergistic Effect for Highly Sensitive Surface-Enhanced Raman Scattering. *Adv. Funct. Mater.* **2024**, *34*, 2400523.
41. Liu, Y.; Dang, A.; Liu, X.; et al. Synergistic Resonances and Charge Transfer in Double-Shelled ZnO Hollow Microspheres for High-Performance Semiconductor-Based SERS Substrates. *ACS Appl. Nano Mater.* **2024**, *7*, 10104–10113.
42. Li, H.; Xu, Q.; Wang, X.; et al. Ultrasensitive Surface-Enhanced Raman Spectroscopy Detection Based on Amorphous Molybdenum Oxide Quantum Dots. *Small* **2018**, *14*, e1801523.
43. Ji, W.; Li, L.; Guan, J.; et al. Hollow Multi-Shelled $V_2O_5$ Microstructures Integrating Multiple Synergistic Resonances for Enhanced Semiconductor SERS. *Adv. Opt. Mater.* **2021**, *9*, 2101866.
44. Yang, L.; Yang, Y.; Lombardi, J.R.; et al. Charge Transfer Enhancement in the Surface-enhanced Raman Scattering of $Ta_2O_5$ Superstructures. *Appl. Surf. Sci.* **2020**, *520*, 146325.
45. Lv, Q.; Wu, X.; Tan, J.; et al. Ultrasensitive Molecular Sensing of Few-layer Niobium Diselenide. *J. Mater. Chem. A* **2021**, *9*, 2725–2733.
46. Lv, Q.; Tan, J.; Wang, Z.; et al. Femtomolar-Level Molecular Sensing of Monolayer Tungsten Diselenide Induced by Heteroatom Doping with Long-Term Stability. *Adv. Funct. Mater.* **2022**, *32*, 2200273.
47. Song, X.; Wang, Y.; Zhao, F.; et al. Plasmon-Free Surface-Enhanced Raman Spectroscopy Using Metallic 2D Materials. *ACS Nano* **2019**, *13*, 8312–8319.
48. Peng, Y.-R.; Zhang, T.; Yang, T.H.; et al. Scalable Fabrication of Janus WSSe/$WS_2$ Heterostructures as Ultrasensitive Detection Platform for Electrochemical Ammonia Products by Surface-enhanced Raman Spectroscopy (SERS). *Chem. Eng. J.* **2025**, *522*, 166830.
49. Liang, X.; Li, N.; Zhang, R.; et al. Carbon-based SERS Biosensor: From Substrate Design to Sensing and Bioapplication. *NPG Asia Mater.* **2021**, *13*, 8.
50. Zhang, N.; Zhang, K.; Zou, M.; et al. Tuning the Fermi Level of Graphene by Two-Dimensional Metals for Raman Detection of Molecules. *ACS Nano* **2024**, *18*, 8876–8884.
51. Meng, S.; Liang, J.; Jia, W.; et al. Metal-free and Flexible Surface-enhanced Raman Scattering Substrate Based on

Oxidized Carbon Cloth. *Carbon* **2022**, *189*, 152–161.

52. Lan, L.; Fan, X.; Yu, S.; et al. Flexible Two-Dimensional Vanadium Carbide MXene-Based Membranes with Ultra-Rapid Molecular Enrichment for Surface-Enhanced Raman Scattering. *ACS Appl. Mater. Interfaces* **2022**, *14*, 40427–40436.
53. Xiong, Y.; Chen, S.; Ye, F.; et al. Synthesis of a Mixed Valence State Ce-MOF as an Oxidase Mimetic for the Colorimetric Detection of Biothiols. *Chem. Commun.* **2015**, *51*, 4635–4638.
54. Ma, Y.; Li, X.; Li, A.; et al. $H_2S$-Activable MOF Nanoparticle Photosensitizer for Effective Photodynamic Therapy against Cancer with Controllable Singlet-Oxygen Release. *Angew. Chem. Int. Ed.* **2017**, *56*, 13752–13756.
55. Zhou, N.; Su, F.; Guo, C.; et al. Two-dimensional Oriented Growth of Zn-MOF-on-Zr-MOF Architecture: A Highly Sensitive and Selective Platform for Detecting Cancer Markers. *Biosens. Bioelectron.* **2019**, *123*, 51–58.
56. Yu, Z.; Yu, W.; Xing, J.; et al. Charge Transfer Effects on Resonance-Enhanced Raman Scattering for Molecules Adsorbed on Single-Crystalline Perovskite. *ACS Photonics* **2018**, *5*, 1619–1627.
57. Li, R.; Chen, Q.; Shi, W.; et al. Microstructure Evolution of $Ti_3C_2/TiO_2$ Quasi-dynamic Heterostructures with high SERS sensitivity. *Ceram. Int.* **2024**, *51*, 9877–9883.
58. Yan, L.; Zhang, X.; Lv, D.; et al. Charge Transfer Process in ZnO/$MAPbI_3$ Heterojunctions of Perovskite Solar Cells (PSCs) Sensing by Surface-Enhanced Raman Scattering. *J. Mater. Chem. C* **2023**, *11*, 9179–9188.
59. Liu, X.; Dai, Y.; Yao, W.; et al. Development of Multifunctional BP@$MoS_2$ Two-dimensional Hybrid Nanomaterials for Label-free Surface-enhanced Raman Spectroscopy Detection and Synergistic Light-conversion Depredation of Pathogenic Bacteria. *Talanta* **2026**, *297*, 128700.
60. Li, H.; Sun, B.; Xu, Y.; et al. Surface Defect-mediated Efficient Electron-hole Separation in Hierarchical Flower-like Bismuth Molybdate Hollow Spheres for Enhanced Visible-light-driven Photocatalytic Performance. *J. Colloid Interface Sci.* **2018**, *531*, 664–671.
61. Gu, Z.; Yang, N.; Han, P.; et al. Oxygen Vacancy Tuning toward Efficient Electrocatalytic $CO_2$ Reduction to $C_2H_4$. *Small Methods* **2019**, *3*, 1800449.
62. Sachs, M.; Park, J.S.; Pastor, E.; et al. Effect of Oxygen Deficiency on the Excited State Kinetics of $WO_3$ and Implications for Photocatalysis. *Chem. Sci.* **2019**, *10*, 5667–5677.
63. Liu, W.; Bai, H.; Li, X.; et al. Improved Surface-Enhanced Raman Spectroscopy Sensitivity on Metallic Tungsten Oxide by the Synergistic Effect of Surface Plasmon Resonance Coupling and Charge Transfer. *J. Phys. Chem. Lett.* **2018**, *9*, 4096–4100.
64. Jiang, X.; He, S.; Tang, Y.; et al. High Energy Facet-dominated $TiO_{2-X}$ Facet Heterojunction with Excellent Carrier Utilization for Ultrasensitive SERS Sensing and Efficient Degradation of Antibiotic Residues. *Sens. Actuators B: Chem.* **2024**, *403*, 135241.
65. Tan, L.; Yuan, B.; Lou, Y.; et al. An Oxygen Vacancy-Engineered $Bi_2MoO_6$ Light Collector with Prominent SERS Enhancement for Ultrasensitive Detection and Degradation of Organic Contaminants. *J. Alloys Compd.* **2023**, *945*, 169233.
66. Quan, Y.; Tang, X.H.; Shen, W.; et al. Sulfur Vacancies-Triggered High SERS Activity of Molybdenum Disulfide for Ultrasensitive Detection of Trace Diclofenac. *Adv. Opt. Mater.* **2022**, *10*, 2201395.
67. Gao, M.; Yao, J.; Li, J.; et al. A Novel Strategy for Improving SERS Activity by Cerium Ion f→d Transitions for Rapid Detection of Endocrine Disruptor. *Chem. Eng. J.* **2021**, *430*, 131467.
68. Wen, S.; Mu, M.; Xie, Q.; et al. Investigation of Sulfur Doping in Mn–Co Oxide Nanotubes on Surface-Enhanced Raman Scattering Properties. *Anal. Chem.* **2022**, *94*, 5987–5995.
69. Xie, S.; Lai, K.; Gu, C.; et al. Fine Fabrication of $TiO_2/MoO_x$ Nano-heterojunctions and Investigating on the Improved Charge Transfer for SERS Application. *Mater. Today Nano* **2022**, *18*, 100179.
70. Chen, Y.; Zhang, J.; Li, Y.; et al. Bifunctional $MoO_{3-x}$/CuS Heterojunction Nanozyme-Driven “Turn-On” SERS Signal for the Sensitive Detection of Cerebral Infarction Biomarker S100B. *Anal. Chem.* **2024**, *96*, 17711–17719.
71. Sun, T.; Wu, Y.; Ma, H.; et al. The Design of $WTe_2$/Graphene/Ag NPs Heterostructure for the Improvement of the Chemical Enhancement in SERS. *Nano Lett.* **2024**, *24*, 15324–15330.
72. Pei, J.; Yang, F.; Zhao, H. Plasma-induced Enhancement of Light–matter Interaction on Graphene–$MoS_2$ Heterostructure for Sensitive SERS Sensing. *Nano Res.* **2025**, *18*, 94907376.
73. Yuan, W.; Jiao, K.; Yuan, H.; et al. Metal–Organic Frameworks/Heterojunction Structures for Surface-Enhanced Raman Scattering with Enhanced Sensitivity and Tailorability. *ACS Appl. Mater. Interfaces* **2024**, *16*, 26374–26385.
74. Sun, H.; Gong, W.; Cong, S.; et al. Ultrathin Two-Dimensional Metal–Organic Framework Nanosheets with Activated Ligand-Cluster Units for Enhanced SERS. *ACS Appl. Mater. Interfaces* **2022**, *14*, 2326–2334.
75. Fu, J.-H.; Zhong, Z.; Xie, D.; et al. SERS-Active MIL-100(Fe) Sensory Array for Ultrasensitive and Multiplex Detection of VOCs. *Angew. Chem. Int. Ed.* **2020**, *59*, 20489–20498.
76. Song, X.; Li, Y.; Yin, M.; et al. Multilayered Hollow Transition Metal Nitride Spheres Made from Single-source Precursors for SERS Analytics. *Nat. Commun.* **2025**, *16*, 2678.
77. Gao, C.; Yang, Y.; Chen, H.; et al. 3D Hollow $MoS_2$ Architecture Enabled Highly Sensitive SERS Detection. *Adv. Mater.*

*Interfaces* **2024**, *8*, 2400734.

78. Qi, D.; Lu, L.; Wang, L.; et al. Improved SERS Sensitivity on Plasmon-Free $TiO_2$ Photonic Microarray by Enhancing Light-Matter Coupling. *J. Am. Chem. Soc.* **2014**, *136*, 9886–9889.
79. Zhao, Z.; He, H.; Zhu, Y.; et al. An Ordered Fish Scale-like Co-$TiO_2$/GO Inverse Opal Photonic Crystal as the Multifunctional SERS Substrate. *J. Alloys Compd.* **2021**, *858*, 158356.
80. Liu, Y.; Dang, A.; Liu, X.; et al. Recyclable MXene Film as SERS Sensor with High Sensitivity and Flexibility Adjusted with ZnO Quantum Dots. *Sens. Actuators B Chem.* **2025**, *422*, 136685.
81. Jiang, X.; Li, K.; Tang, Y.; et al. A Double Defects-dominated Flexible $TiO_2$ Matrix for in-situ SERS Sensing of Antibiotic Residues in Aquatic Ecosystem (Fish & Fishpond Water) and Their on-site Degradation in Flowing Water. *Sci. Total Environ.* **2024**, *921*, 171154.
82. Zhang, H.; Tang, Y.; Wang, W.; et al. A New Semiconductor Heterojunction SERS Substrate for Ultra-sensitive Detection of Antibiotic Residues in Egg. *Food Chem.* **2023**, *431*, 137163.
83. Zhang, Q.; Li, X.; Yi, W.; et al. Plasmonic $MoO_2$ Nanospheres as a Highly Sensitive and Stable Non-Noble Metal Substrate for Multicomponent Surface-Enhanced Raman Analysis. *Anal. Chem.* **2017**, *89*, 11765–11771.
84. Quan, Y.; Su, R.; Yang, S.; et al. *In-situ* Surface-enhanced Raman Scattering based on $MTi_{20}$ Nanoflowers: Monitoring and Degradation of Contaminants. *J. Hazard. Mater.* **2021**, *412*, 125209.
85. Liang, P.; Cao, Y.; Dong, Q.; et al. A Balsam Pear-shaped CuO SERS Substrate with Highly Chemical Enhancement for Pesticide Residue Detection. *Microchim. Acta* **2020**, *187*, 335.
86. Xu, H.; Li, B.; Wang, Z.; et al. Pure Metallic 1T Phase Sc-Doped $MoS_2$ Fusilli Morphology for Ultra-Sensitive SERS Detection. *J. Hazard. Mater.* **2025**, *491*, 138043.
87. Liman, G.; Aylaz, G.; Shaikh, H.; et al. Graphene Oxide Decorated with Melamine-imprinted Nanobeads for SERS Detection of Melamine in Milk. *Spectrochim. Acta Part A Mol. Biomol. Spectrosc.* **2025**, *338*, 126156.
88. Zhang, H.; Huang, S.; Yang, X.; et al. A SERS Biosensor Constructed by Calcined ZnO Substrate with High-efficiency Charge Transfer for Sensitive Detection of $Pb^{2+}$. *Sens. Actuators B Chem.* **2021**, *343*, 130142.
89. Kamal, S.; Yang, T.C.-K. Silver Enriched Silver Phosphate Microcubes as an Efficient Recyclable SERS Substrate for the Detection of Heavy Metal Ions. *J. Colloid Interface Sci.* **2022**, *605*, 173–181.
90. Parveen, S.; Saifi, S.; Akram, S.; et al. ZnO Nanoparticles Functionalized SWCNTs as Highly Sensitive SERS Substrate for Heavy Metal Ions Detection. *Mater. Sci. Semicond. Process.* **2022**, *149*, 106852.
91. Han, K.; Yan, Z.; Ding, Z.; et al. High-sensitivity SERS Sensor Leveraging Three-dimensional $Ti_3C_2T_x/TiO_2/W_{18}O_{49}$ Semiconductor Heterostructures for Reliable Detection of Trace Micro/Nanoplastics in Environmental Matrices. *Talanta* **2025**, *286*, 127474.
92. Quan, Y.; Yao, J.; Yang, S.; et al. ZnO Nanoparticles on $MoS_2$ Microflowers for Ultrasensitive SERS Detection of Bisphenol A. *Microchim. Acta* **2019**, *186*, 593.
93. Zhang, W.; Peng, Y.; Wang, C.; et al. Molybdenum Boride MBene with an Ultraclean Surface for Stable and Portable Detection of Environment Toxins. *ACS Sens.* **2025**, *10*, 6950–6961.