

Mechanism of Nitrogen-Doped Ti_3C_2 Quantum Dots for Free-Radical Scavenging and the Ultrasensitive H_2O_2 Detection Performance

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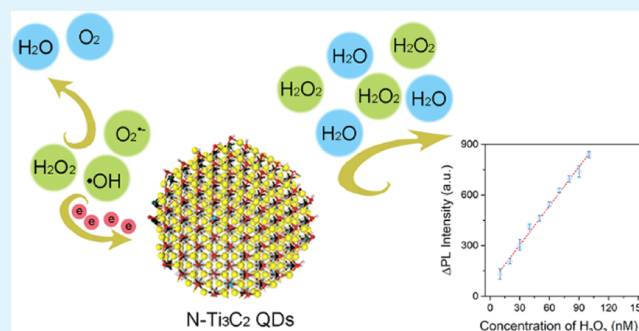
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ABSTRACT: MXene quantum dots feature favorable biological compatibility and superior optical properties, offering great potential for biomedical applications such as reactive oxygen species (ROS) scavenging and fluorescence sensing. However, the ROS scavenging mechanism is still unclear and the MXene-based materials for ROS sensing are still scarce. Here, we report a nitrogen-doped titanium carbide quantum dot ($\text{N-Ti}_3\text{C}_2$ QD) antioxidant with effective ROS scavenging ability. The doped nitrogen atoms promote the electrochemical interaction between $\text{N-Ti}_3\text{C}_2$ QDs and free radicals and thus enhance their antioxidant performance. Density functional theory (DFT) simulations reveal the hydroxyl radical quenching process and confirm that the doped N element promotes the free-radical absorption ability, especially for $-\text{F}$ and $-\text{O}$ functional groups in $\text{N-Ti}_3\text{C}_2$ QDs. Furthermore, $\text{N-Ti}_3\text{C}_2$ QDs show rapid, accurate, and remarkable sensitivity to hydrogen peroxide in the range of 5 nM–5.5 μM with a limit of detection of 1.2 nM within 15 s, which is the lowest detection limit of the existing fluorescent probes up to now. Our results provide a new category of antioxidant materials, a real-time hydrogen peroxide sensing probe, promoting the research and development of MXene in bioscience and biotechnology.

KEYWORDS: nitrogen-doped titanium carbide quantum dots, antioxidants, functional groups, fluorescence biosensor, H_2O_2



INTRODUCTION

Reactive oxygen species (ROS), including singlet oxygen, superoxide anion, hydrogen peroxide (H_2O_2), and hydroxyl radicals, play an important role in cellular life cycles such as proliferation and homeostasis.^{1,2} However, high ROS levels are detrimental to cellular components cell membranes, protein structures, and DNA, which can damage cellular functions.^{3–5} It is urgent to develop high-efficiency and low-toxicity antioxidants materials for biomedical research and clinical applications. Furthermore, disorder or accumulation of ROS could lead to several severe diseases such as cancer, Alzheimer's, central nervous system diseases, kidney disorders, and aging.^{6,7} Consequently, accurate and highly sensitive detection of the related ROS concentration (mainly H_2O_2) is critical for earlier catching and treating these diseases.

With the fast development in nanomedicine, a variety of nanomaterials with ROS scavenging activities have been reported such as metal nanoclusters,⁸ metal oxide nanoparticles,^{9,10} 2D materials (including graphene,¹¹ black phosphorus,¹² transition-metal dichalcogenides,¹³ and MXene¹⁴), and their derivatives.^{15–17} Among them, zero-dimensional QDs derived from 2D MXene have recently attracted tremendous attention in biomedical fields owing to their favorable biological compatibility and unique physico-

chemical properties.^{18,19} The strong quantum confinement, abundant active edge sites, and a high surface-to-volume ratio promote such QD materials' efficient activities and they can serve as free-radical scavengers. Ren et al. reported that niobium carbide (Nb_2C) MXene could effectively protect the cells and mice from ionizing radiation-induced ROS damage.¹⁴ Our group confirmed that Cl- and N-codoped Ti_3C_2 QDs exhibit outstanding hydroxyl radical scavenging performance.²⁰ However, the free-radical scavenging mechanism of MXene-based materials and the contribution of the functional groups and dopants are still confusing.

Apart from scavenging free radicals to suppress oxidative stress, these nanomaterials have also been widely used as ROS probes to monitor human health or diagnose ROS-related diseases.²¹ Hydrogen peroxide, as the most important marker for ROS, not only participates in several cellular processes but also connects to aging and some serious diseases.²² Until now,

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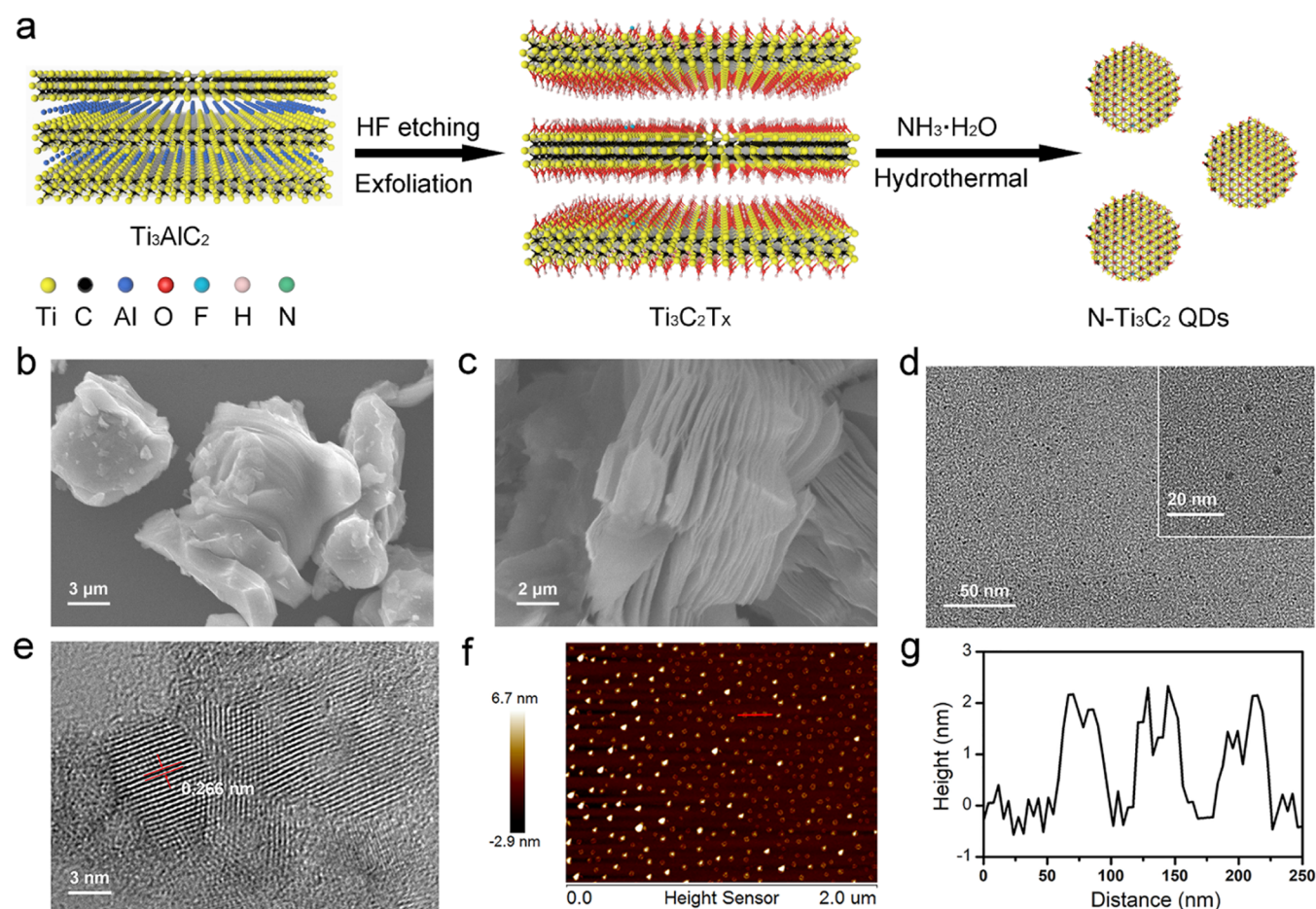


Figure 1. Schematic of synthesis and the morphology N-Ti₃C₂ QDs. (a) Schematic illustration of the preparation of N-Ti₃C₂ QDs. Typical SEM images of (b) Ti₃AlC₂ and (c) HF-etched Ti₃C₂T_x. TEM (d) and HRTEM (e) images of N-Ti₃C₂ QDs (the inset shows the high-resolution TEM image of N-Ti₃C₂ QDs). The AFM image (f) and the height profile (g) of N-Ti₃C₂ QDs.

there have been methods for detecting H₂O₂, including chemiluminescence, electrochemistry, chromatography, etc.,^{23–27} but these methods either need a complicated operation and high cost of instrumental analysis or have low sensitivity and difficulty in on-site monitoring. Therefore, fluorescence methods have gathered significant interest due to simple instruments and easy operation.²⁸ Nonetheless, the previously reported fluorescent probes exhibit unsatisfactory sensitivity. The high activity of N-Ti₃C₂ QDs to H₂O₂ and their outstanding biological compatibility as well as the intrinsic fluorescence properties show their promising potential in the H₂O₂-sensing field.

In this study, we reported an efficient antioxidant material based on MXene. The N-Ti₃C₂ QDs were synthesized by a hydrothermal method, using ammonium hydroxide as a nitrogen source. The trace level doping of nitrogen atoms could modulate the intrinsic structure of Ti₃C₂ QDs and bring about excellent ROS scavenging performance. The scavenging efficiency of N-Ti₃C₂ QDs is superior to Ti₃C₂ QDs, graphene oxide (GO), and graphene quantum dots (GQDs). In addition, with the help of readily oxidizable Ti²⁺ and small quantities of nitrogen doping, N-Ti₃C₂ QDs demonstrated superior H₂O₂ detection sensitivity with a detection limit of 1.2 nM, which is the lowest detection limit of the existing fluorescent probes for H₂O₂. Our results open a novel perspective for the application of MXene QDs in biomedical and biosensor fields.

RESULTS AND DISCUSSION

Synthesis and Characterization of N-Ti₃C₂ QDs. The synthesis procedure of N-Ti₃C₂ QDs is shown in Figure 1a. Briefly, the aluminum layers of the Ti₃AlC₂ ceramic powder is etched by HF acid and resulting multilayer Ti₃C₂T_x (T_x = OH, O, or F). After selective etching, the as-prepared Ti₃C₂T_x exhibited a loosely layered structure with an average edge length of several micrometers, as shown in the SEM image (Figure 1c). The strongest diffraction peak around 9.62° of Ti₃AlC₂ shifts toward lower angles after etching, implying that the *c*-axis lattice constantly increases and layer spacing is enlarged (Figure S1).^{29,30} Furthermore, the broadened (002) characteristic peaks in the Ti₃C₂T_x sample indicate the decrease in the crystallinity after the aluminum atoms were etched.³¹ Finally, N-Ti₃C₂ QDs could be obtained via hydrothermally cutting Ti₃C₂T_x sheets using ammonium hydroxide as a nitrogen source. TEM images (Figure 1d) show that N-Ti₃C₂ QDs are uniformly dispersed. The high-resolution TEM image (Figure 1e) exhibits the lattice fringes with an inner-plane spacing at 0.266 nm, corresponding to the (0110) crystal plane of Ti₃C₂T_x and confirms that the N-Ti₃C₂ QDs well preserved the crystal structure of pristine Ti₃C₂T_x nanosheets.¹⁸ The AFM image and the height profile of N-Ti₃C₂ QDs (Figure 1f,g) show that the N-Ti₃C₂ QDs have a similar thickness of about 2 nm, which corresponds to two layers of MXene.¹⁹

The chemical structure, composition, and functional groups of N-Ti₃C₂ QDs are explored by FT-IR and XPS spectra. As shown in Figure 2a, in addition to the similar stretching

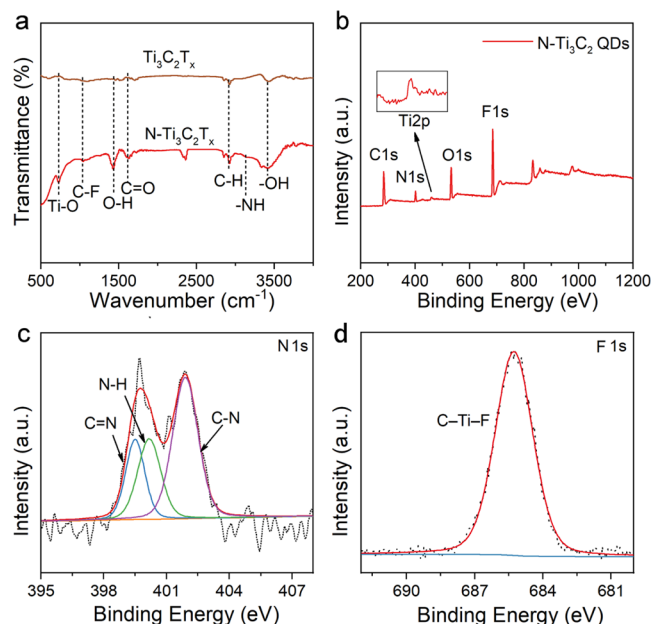


Figure 2. Chemical structure of N-Ti₃C₂ QDs. (a) FT-IR spectra of Ti₃C₂T_x and N-Ti₃C₂ QDs. (b) XPS survey of N-Ti₃C₂ QDs. (c) N 1s spectrum of N-Ti₃C₂ QDs. (d) F 1s spectrum of N-Ti₃C₂ QDs.

vibrations of Ti₃C₂T_x nanosheets and N-Ti₃C₂ QDs, including Ti–O at 665 cm^{−1}, C–F at 1100 cm^{−1}, C=O at 1650 cm^{−1}, and –OH around 3430 cm^{−1}, N-Ti₃C₂ QDs shows the –NH stretching vibration at 3120 cm^{−1}.³² The appearance of a new peak indicates that nitrogen is bonded to Ti₃C₂ QDs successfully. This result is also confirmed by the XPS spectra,

which show that the C 1s peak at 284.0 eV, the O 1s peak at 530.0 eV, the Ti 2p peak at 460.0 eV, the F 1s peak at 685.0 eV, and the N 1s peak at 400.0 eV are present, as shown in Figure 2b, demonstrating the successful doping of the nitrogen element, which is absent in the Ti₃C₂ QD sample (Figures S3 and S4). In addition, N atoms mainly bond with C atoms (Figure 2c) and F atoms attach to the Ti layer and serve as functional groups (Figure 2d).

Antioxidant Performance of N-Ti₃C₂ QDs. Next, we evaluate the antioxidant performance of N-Ti₃C₂ QDs. The way of antioxidants to scavenge free radicals could be summarized as hydrogen donation, adduct formation, and charge transfer.¹⁵ Herein, DPPH• scavenging assay was conducted to evaluate the hydrogen donation ability of N-Ti₃C₂ QDs. In the DPPH• scavenging process, DPPH• captures the hydrogen atoms from N-Ti₃C₂ QDs and is converted into a stable DPPH-H complex accompanied by the color change from deep violet to light yellow. Figure S5 reveals that N-Ti₃C₂ QDs exhibit poor DPPH• scavenging ability even with N doping, indicating that N-Ti₃C₂ QDs possess weaker hydrogen donation ability compared to the previously reported GQDs.³³ Subsequently, the adduct formation and charge-transfer free-radical scavenging models were quantitatively determined by •OH scavenging assay. Hydroxyl radicals, the most reactive chemical species, could be rapidly captured by terephthalic acid and form fluorescent product 2-hydroxyterephthalic acid, which could be monitored by fluorescence measurements. As shown in Figure 3a, N-Ti₃C₂ QDs feature the highest •OH scavenging efficiency (93.2%), which is superior to Ti₃C₂ QDs (65.9%). GO and GQDs possess favorable antioxidant performance according to previous reports.^{11,33} Under the same concentrations, the •OH scavenging ratios of GO and GQDs are 37.3 and 53.3%, respectively. The high •OH scavenging activity of N-Ti₃C₂

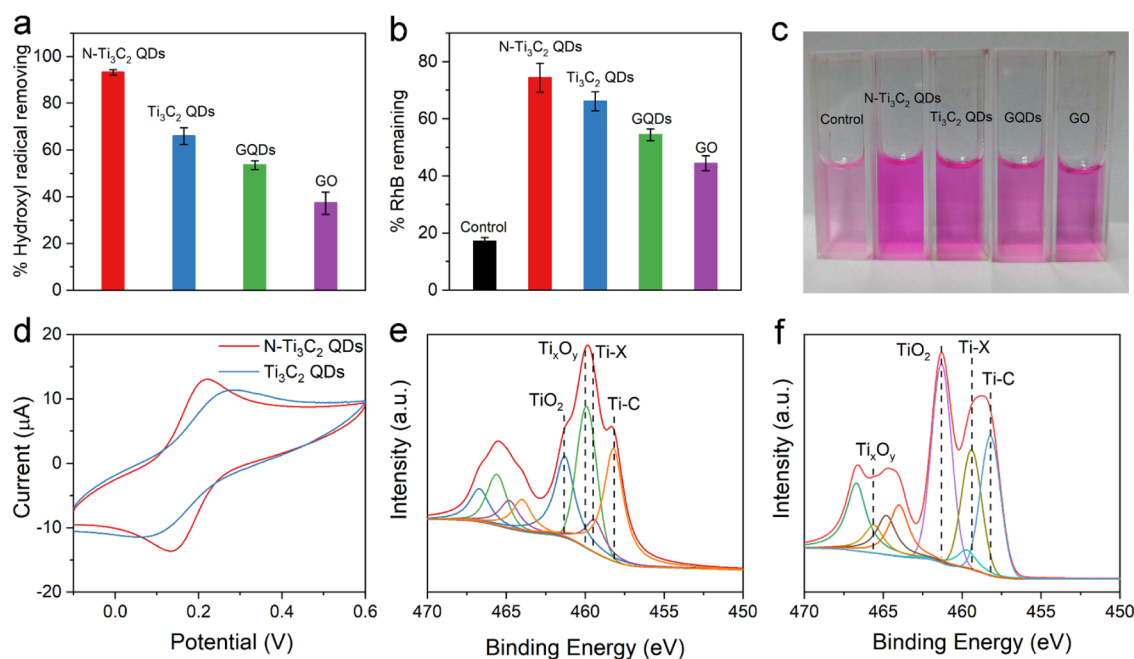


Figure 3. Antioxidant performance of N-Ti₃C₂ QDs. (a) •OH scavenging performance of N-Ti₃C₂ QDs, Ti₃C₂ QDs, GQDs, and GO. The ratio of remaining RhB (b) and the photos (c) after photocatalytic degradation with N-Ti₃C₂ QDs, Ti₃C₂ QDs, GQDs, and GO. (d) CV curves of N-Ti₃C₂ QD and Ti₃C₂ QD samples. High-resolution Ti 2p spectra of N-Ti₃C₂ QDs before (e) and after (f) reacting with •OH.

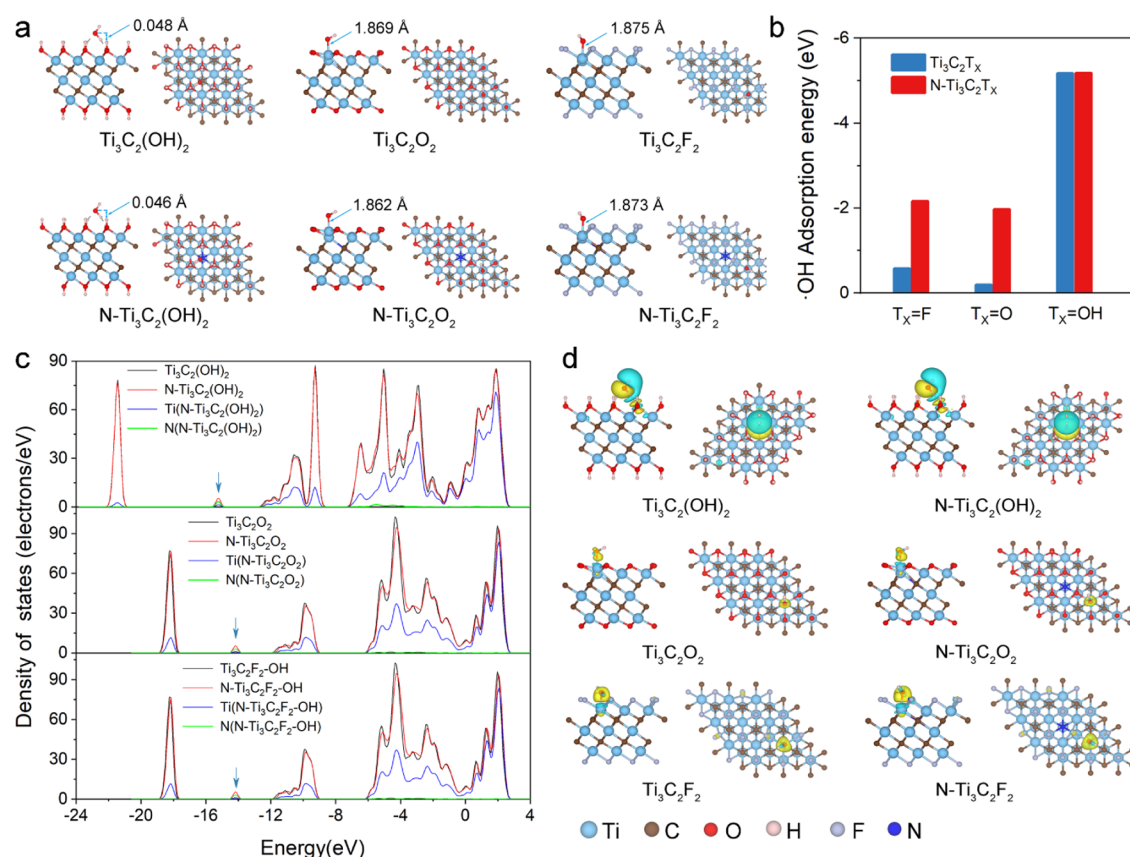


Figure 4. Interaction between $\bullet\text{OH}$ and $\text{Ti}_3\text{C}_2\text{T}_x$. The side view and the top view for the relaxed structures of $\bullet\text{OH}$ adsorbed on the $\text{Ti}_3\text{C}_2\text{T}_x$ and $\text{N-Ti}_3\text{C}_2\text{T}_x$ surfaces (a) and the corresponding adsorption energy (b). (c) Density of states for $\text{Ti}_3\text{C}_2\text{T}_x$ and $\text{N-Ti}_3\text{C}_2\text{T}_x$. (d) Side view and the top view for charge density distribution of $\text{Ti}_3\text{C}_2\text{T}_x\text{-OH}$ and $\text{N-Ti}_3\text{C}_2\text{T}_x\text{-OH}$. Charge accumulation (depletion) is represented in yellow (cyan).

QDs could be ascribed to their excellent $\bullet\text{OH}$ absorbability and high-efficiency charge-transfer ability.

Robust scavenging ability to multiple primary and secondary ROS is another standard for antioxidants.³⁴ Here, the antioxidative activities of $\text{N-Ti}_3\text{C}_2$ QDs against multiple ROS including $^1\text{O}_2$, $\bullet\text{OH}$, $\text{O}_2^{\bullet-}$, and H_2O_2 , are assessed by organic-dye-protecting experiments. To avoid the exogenous disturbance in the ROS generation process, the in situ-generated $^1\text{O}_2$, $\bullet\text{OH}$, $\text{O}_2^{\bullet-}$, and H_2O_2 via a photochemical reaction by P25 TiO_2 are used for quantitatively assessing the scavenging performance of multiple radicals of $\text{N-Ti}_3\text{C}_2$ QDs.³⁵ ROS produced by UV (365 nm)-excited TiO_2 nanoparticles could be scavenged by $\text{N-Ti}_3\text{C}_2$ QDs and inhibits the rhodamine B molecule degradation. As shown in Figure 3b, $\text{N-Ti}_3\text{C}_2$ QDs own the highest dye protection efficiency (74.3%), which is better than Ti_3C_2 QDs (66.1%), GQDs (54.4%), and GO (44.4%), suggesting that the scavenging performances of $\text{N-Ti}_3\text{C}_2$ QDs for the full range of ROS are superior to previous graphene-based antioxidants. In addition, $\text{N-Ti}_3\text{C}_2$ QDs also show (Figure S7) excellent scavenging performance for $^1\text{O}_2$ and $\text{O}_2^{\bullet-}$, respectively.

The superior antioxidant performance of $\text{N-Ti}_3\text{C}_2$ QDs could be attributed to the doping of nitrogen atoms, which is analogous to the heteroatom-doped GQDs.¹⁶ The doped nitrogen atoms promote the electron-transfer ability between $\text{N-Ti}_3\text{C}_2$ QDs and free radicals. Cyclic voltammetry (CV) measurements are adopted to verify this assumption.³⁶ As shown in Figure 3d, the redox peak of $\text{N-Ti}_3\text{C}_2$ QDs has higher redox current than Ti_3C_2 QDs. In addition, the CV curve of $\text{N-Ti}_3\text{C}_2$ QDs shows a narrower peak-to-peak potential separation (ΔE_p) of 78 mV, which testifies that the charge-transfer kinetics of the redox reaction of $\text{K}_3[\text{Fe}(\text{CN})_6]$ and $\text{K}_4\text{Fe}(\text{CN})_6$ at $\text{N-Ti}_3\text{C}_2$ QDs is easier than the Ti_3C_2 QD-modified electrode (184 mV).³⁷ This represents that $\text{N-Ti}_3\text{C}_2$ QDs have better electron-transfer capabilities because doping of nitrogen atoms introduces more defects and provides more active sites. As demonstrated in Figure 3e, partial N atoms replace C atoms and bond with Ti atoms (462.3 eV in the Ti 2p spectrum). The results (Figures 2c and 3e) indicate that N atoms replace C atoms between the Ti atom layer or/and connect to C atoms at the edge of the MXene structure. After reacting with $\bullet\text{OH}$, XPS investigations are performed again to determine the change in $\text{N-Ti}_3\text{C}_2$ QDs. Figure S8 shows that the N atom ratio reduces to 2.52% but still exists between the Ti atom layer (Ti-X bond shown in Figure 3f) and on the edge of $\text{N-Ti}_3\text{C}_2$ QDs (C-N bond shown in Figure S8b). However, the XPS spectra of Ti 2p show that Ti^{4+} increases from 24.9 to 40.4% (Figure 3e,f) after the scavenging reaction, indicating that the ROS scavenging could be ascribed to the charge transfer from $\bullet\text{OH}$, leading to the gradual oxidation of $\text{N-Ti}_3\text{C}_2$ QDs.

DFT Simulation. To evaluate the adsorption energies of $\bullet\text{OH}$ on the $\text{Ti}_3\text{C}_2\text{T}_x$ or $\text{N-Ti}_3\text{C}_2\text{T}_x$ ($\text{T}_x = -\text{OH}$, $-\text{O}$, or F , according to the FT-IR and XPS survey shown in Figure 2a,d) nanosheets, we define the adsorption energy (E_{ads}) as

$$E_{\text{ads}} = E_{\text{total}} - E_{\text{surface}} - E_{\bullet\text{OH,isolated}} \quad (1)$$

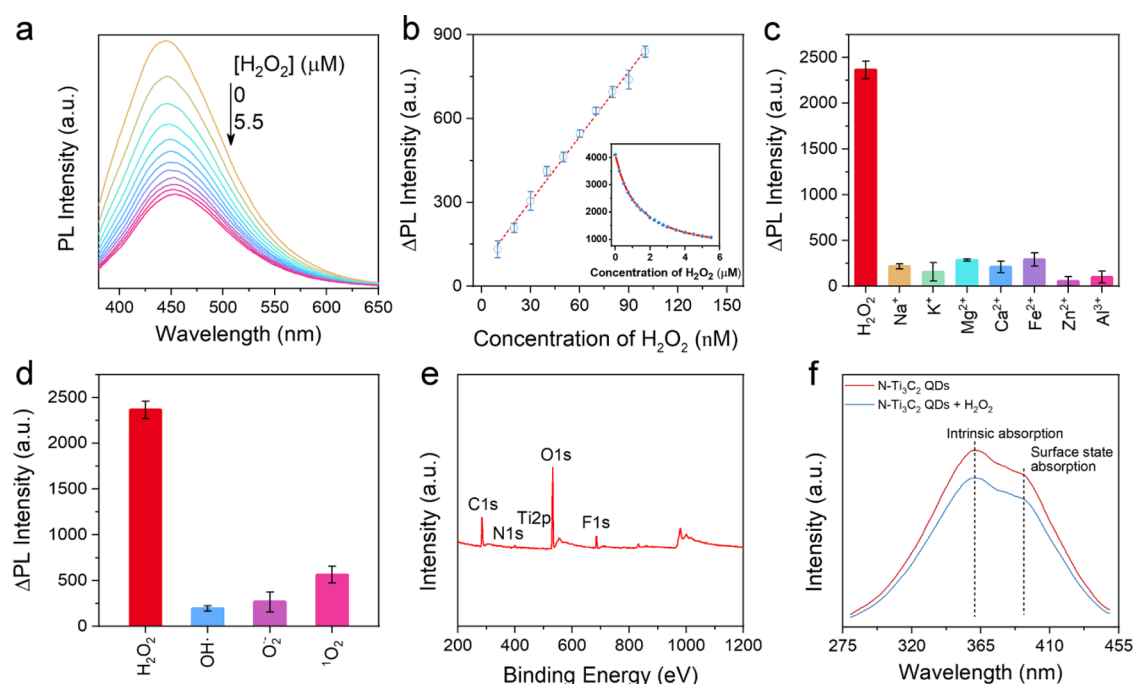


Figure 5. H₂O₂-sensing performance of N-Ti₃C₂ QDs. (a) PL intensity variation of N-Ti₃C₂ QDs with different concentrations of H₂O₂ (0–5.5 μM). (b) Linear relationship between N-Ti₃C₂ QDs and H₂O₂. (c) Selectivity of N-Ti₃C₂ QDs toward H₂O₂ and metal ions (Na⁺, K⁺, Mg²⁺, Ca²⁺, Fe²⁺, Zn²⁺, Al³⁺). (d) Selectivity of N-Ti₃C₂ QDs toward H₂O₂ and other reactive oxygen species (*OH, O₂^{•−}, ¹O₂). (e) XPS survey of N-Ti₃C₂ QDs after reacting with H₂O₂. (f) PLE spectra of N-Ti₃C₂ QDs before and after reacting with H₂O₂.

where E_{total} is total energy of the Ti₃C₂T_x or N-Ti₃C₂T_x system with the adsorbed •OH, E_{surface} is total energy of the Ti₃C₂T_x or N-Ti₃C₂T_x system alone, and $E_{\text{OH,isolated}}$ is the energy of an isolated •OH (a single •OH in a supercell), respectively. With such a scheme, negative adsorption energy means an exothermic process, while positive binding energy indicates an endothermic process. The initial height of •OH is set to be 1 Å on the Ti₃C₂T_x or N-Ti₃C₂T_x surface. After full relaxation of these configurations, adsorption energies of •OH for Ti₃C₂T_x and N-Ti₃C₂T_x systems are calculated using eq 1 and are shown in Figure 4a,b. The negative adsorption energies indicate that •OH can be spontaneously adsorbed by the Ti₃C₂T_x and N-Ti₃C₂T_x systems. Notably, the adsorption energies of •OH on the N-Ti₃C₂T_x surface are lower than that on the corresponding Ti₃C₂T_x, especially for the −F (−0.58 eV for Ti₃C₂T_x vs −2.16 eV for N-Ti₃C₂T_x) and −O (−0.19 eV for Ti₃C₂T_x vs −1.97 eV for N-Ti₃C₂T_x)-terminated modes, suggesting that N-Ti₃C₂T_x has much stronger adsorption capacity on •OH than Ti₃C₂T_x.

Next, we explore the •OH adsorption process and the corresponding charge-transfer procedure. Figure 4a shows the relaxed structures of •OH adsorbed on the Ti₃C₂T_x and N-Ti₃C₂T_x surfaces. It could be seen that following the adsorption of •OH onto the Ti₃C₂O₂H₂/N-Ti₃C₂O₂H₂ surface, the adsorbed •OH combines with a proton to form hydration water. The distance between an O atom of the adsorbed •OH and the N-Ti₃C₂O₂H₂ surface is 0.046 Å, which is shorter than the distance between the O atom and the Ti₃C₂O₂H₂ surface 0.048 Å. It implies that the bonding force for hydration water is enhanced by N atoms doping. Compared with Ti₃C₂O₂/Ti₃C₂F₂, the length of the Ti–O bond for −O and −F-terminated N-Ti₃C₂O₂/N-Ti₃C₂F₂ decreases by 0.007 and 0.002 Å, respectively. Thus, the

decrease in the distance demonstrates that the N atom makes N-Ti₃C₂T_x easier to absorb •OH.

To further study the underlying mechanism, the electronic structure is needed to be interpreted. The underlying density of states (DOS) of Ti₃C₂T_x and N-Ti₃C₂T_x are plotted in Figure 4c. For comparison of the DOS of Ti₃C₂T_x and N-Ti₃C₂T_x, a pronounced new peak located at a low energy level is emerged after doping a N atom for N-Ti₃C₂T_x. It indicates that the free-electron concentration increases. From the DOS related to the Ti atom and the N atom of N-Ti₃C₂T_x, we find that the new peaks of N-Ti₃C₂T_x are formed mostly by the Ti atom and the N atom. The Ti atom orbital hybridized with the N orbital at the site in the new peak, indicating that a chemical bond is formed between them. The enhanced reaction of the associated Ti atom leads to stronger adsorption capacity on •OH for N-Ti₃C₂T_x compared to Ti₃C₂T_x.

Figure 4d shows different charge densities. For a Ti₃C₂O₂H₂-OH/N-Ti₃C₂O₂H₂-OH system, there is obvious charge accumulation between a H atom and •OH, proving the bonding between them. There is also charge depletion of a Ti atom, demonstrating that Ti is losing electrons. In addition, for the Ti₃C₂O₂-OH/N-Ti₃C₂O₂-OH/Ti₃C₂F₂-OH/N-Ti₃C₂F₂-OH system, there is also charge accumulation between the Ti atom and the O atom of •OH, suggesting the bonding between them. It is also obvious that the Ti atom loses an electron and the accumulated charge is closer to the O atom of •OH. The redistribution of charge density gives rise to a variety of valences for the Ti atom, which corresponds to the XPS survey, as shown in Figure 3a,f.

H₂O₂ Sensing. As a typical kind of ROS, H₂O₂ is a significant oxidative stress indicator as well as a signaling molecule in biological systems. Due to the rapid and sensitive reactivity to H₂O₂, the prepared N-Ti₃C₂ QDs are used to monitor the trace amount of H₂O₂. The UV–vis spectrum of

Table 1. Comparison of the H₂O₂ Detection Performance

method	system	limit of detection	linear range	time	references
electrochemical	Au-MnO	8 nM	20 nM–15.11 mM	tens of minutes	22
electrochemical	HRP/DMSNs	0.11 μ M	0.5–103 μ M	tens of minutes	38
chemiluminescence	BPNS/GCE	0.96 nM	1 nM–1 μ M	few seconds	39
chemiluminescence	CF-CoFe ₂ O ₄ NPs-luminol-H ₂ O ₂ -GOx	500 pM	1.0 nM–4.0 μ M	tens of minutes	40
fluorescence	Eu-MOF	33.5 nM	0.05–2 μ M	tens of minutes	23
fluorescence	SWNT/collagen		12.5–400 nM	few seconds	41
fluorescence	FRET		0.7–200 μ M	few seconds	42
fluorescence	g-C ₃ N ₄	50 nM	0.1–2000 μ M	tens of minutes	43
fluorescence	TPE-HPro	100 nM	3–200 μ M	tens of minutes	44
fluorescence	PVP-AuNPs	0.8 μ M	1–100 μ M	few seconds	45
fluorescence	N-Ti ₃ C ₂ QDs	1.2 nM	5 nM–5.5 μ M	15 s	this work

an N-Ti₃C₂ QD aqueous solution (Figure S9) exhibits two absorption peaks at 260 and 320 nm, respectively. Under 365 nm UV irradiation, N-Ti₃C₂ QDs emit a strong blue fluorescence with a corresponding emission position of 445 nm in the photoluminescence (PL) spectra. The fluorescence is steady under 360 nm light excitation in the pH range of 2.0–12.0 (Figure S10). Compared to Ti₃C₂ QDs, N-Ti₃C₂ QDs exhibit enhanced fluorescence performance, which could be ascribed to an increased carrier lifetime after N doping.⁴⁶ This outstanding fluorescence property makes N-Ti₃C₂ QDs to be served as fluorescent probes. As shown in Figure 5a, the H₂O₂ detection assay was carried out by adding different amounts of H₂O₂ to an N-Ti₃C₂ QD aqueous solution. With the increase in the H₂O₂ concentration, the PL intensity of solutions decreases accordingly (Figure 5a). Figure 5b shows great linearity from 5 to 100 nM of the H₂O₂ concentration with a high *R*-square value (0.9882). The fluorescence intensity of N-Ti₃C₂ QDs continues to decrease with the H₂O₂ concentration between 0.1 and 5.5 μ M (inset of Figure 5b). The limit of detection based on $3\sigma/k$ (where σ is the standard deviation of the blank measurement and k is the slope of the calibration graph) is 1.2 nM, which is the lowest detection limit till now (Table 1).

To further verify the selectivity of an N-Ti₃C₂ QD probe to H₂O₂, the PL intensity in response to various ions, including Na⁺, K⁺, Mg²⁺, Ca²⁺, Fe²⁺, Zn²⁺, Al³⁺ ions, and ROS, are investigated. As shown in Figure 5c, N-Ti₃C₂ QDs exhibit a low response to metal ions because their fluorescence property is dominated by the intrinsic structure and surface states of N-Ti₃C₂ QDs. Furthermore, N-Ti₃C₂ QDs show a 5-fold higher fluorescence quenching ratio response to H₂O₂ over similar ROS, including $\cdot$ OH, O₂ $\cdot^-$, and ¹O₂, as shown in Figure 5d. This indicates that N-Ti₃C₂ QDs have excellent selectivity for detecting H₂O₂ and show promising potential to be applied in complex biological environments. XPS measurement was carried out after the reaction of N-Ti₃C₂ QDs with H₂O₂ (Figure 5e and Table S1). Compared with original N-Ti₃C₂ QDs (Figure 2c), the element ratio of F, N, and Ti in N-Ti₃C₂ QDs significantly reduced while the oxygen content increased, indicating that N-Ti₃C₂ QDs are oxidized to a certain extent after sensing for H₂O₂. This oxidation process could not only destroy the intrinsic structure of N-Ti₃C₂ QDs but also change the surface defect states and functional group composition. As shown in Figure 5f (PLE spectra), two electronic transitions of N-Ti₃C₂ QDs at 358 and 400 nm are regarded as intrinsic absorption and the trapping of the excited-state energy by the surface states, respectively.^{46,47} The intrinsic absorption at 358 nm decreased by 14.8% and the functional groups' absorption

at 400 nm decreased by 15.7% after reacting with H₂O₂. The decrease in the intrinsic absorption is attributed to the gradual oxidation of the MXene structure. The decrease in functional groups' absorption is owing to the oxidation of Ti, which breaks the surface Ti–OH and Ti–F bonds. The change in the intrinsic structure and surface defect states cause a gradual reduction in the PL intensity.

CONCLUSIONS

In this work, N-Ti₃C₂ QDs were successfully synthesized by a hydrothermal method using ammonium hydroxide as a nitrogen source. The as-prepared N-Ti₃C₂ QDs exhibit superior free-radical scavenging ability than Ti₃C₂ QDs. CV tests demonstrate that the doped N atoms promote the electronic transport between N-Ti₃C₂ QDs and free radicals, which is further confirmed by DFT simulations. DFT calculations show that N doping efficiently promotes the $\cdot$ OH adsorption ability of –F and –O functional groups. $\cdot$ OH is scavenged through the $\cdot$ OH adsorption in the functional groups and further charge transfer from $\cdot$ OH to a Ti element in N-Ti₃C₂ QDs. In addition, the DFT results indicate that –OH exhibits the highest $\cdot$ OH adsorption activity among the functional groups in N-Ti₃C₂ QDs. Moreover, after the addition of H₂O₂, the fluorescence of N-Ti₃C₂ QDs gradually decreased. As a real-time fluorescent probe, the detection limit of the fluorescence response of an N-Ti₃C₂ QD sensor to H₂O₂ is as low as 1.2 nM. Our work facilitates the understanding of the antioxidant mechanism of MXene-based materials and provides a potential candidate for H₂O₂ sensing in the biology field.

EXPERIMENTAL SECTION

Preparation of N-Ti₃C₂ QDs. The Ti₃AlC₂ powder was purchased from the Laizhou Kai Kai Ceramic Materials Company Limited. First of all, the Ti₃AlC₂ (10 g) powder was dissolved in 100 mL of HF (50%) and etched at room temperature for 18 h. After centrifugation (3500 rpm), the sediment was washed five to six times with deionized water until the pH reached 6. The Ti₃C₂T_x powder was obtained by drying at room temperature for 24 h. Then, the Ti₃C₂T_x (0.3 g) powder was dissolved in deionized water (20 mL) by ultrasonication. The pH of the solution was adjusted to 9 with ammonia water and the solution was transferred into a 100 mL Teflon-lined stainless steel autoclave at 120 °C for 6 h to obtain N-Ti₃C₂ QDs. Ti₃C₂ QDs were prepared without ammonia water added by hydrothermal treatment at 150 °C. GQDs were prepared by the electrochemical method, as reported in our previous work.⁴⁸ GO was prepared by the modified Hummers method.⁴⁹

Scavenging DPPH and Hydroxyl Radicals. As a stable radical, 2,2-diphenyl-1-picrylhydrazyl radical (DPPH $\cdot$) is commonly used to

test the antioxidant properties of antioxidants. It can combine with the hydrogen atoms of the antioxidant to form a stable H-DPPH complex along with the color change. The concentration of DPPH[•] can be monitored by its characteristic absorption peak at 517 nm. A total of 1 mL of DPPH[•] alcohol (100 μ M) solutions was mixed with 1 mL of an N-Ti₃C₂ QD (100 μ g/mL) aqueous solution and incubated 1 h in the dark. The residual DPPH[•] was detected by its characteristic absorption peak (517 nm). TiO₂ can generate a hydroxyl radical in the UV light (365 nm) and *p*-phthalic acid (PTA) captures it to form fluorescent product 2-hydroxyterephthalic acid (excitation wavelength: 315 nm, emission peak: 430 nm). The activity of antioxidants to scavenge hydroxyl radicals was represented by detecting the intensity of the fluorescence after the reaction.

Dye Protect Assay. Overall, 2 mL of a solution containing PBS (25 mM), *p*-phthalic acid (0.5 mM), TiO₂ (50 μ g/mL), and 50 μ g/mL N-Ti₃C₂ QDs, Ti₃C₂ QDs, GO, or GQDs was irradiated by ultraviolet light (8 W, 365 nm) for 1 h. Then, the fluorescence intensity (430 nm) of 2-hydroxyterephthalic acid was detected by PL spectra. The control sample was conducted in the same condition except that no N-Ti₃C₂ QDs were added. Rhodamine B (RhB) was used as a model target molecule for an oxidant attack. Overall, 2 mL of the solution containing TiO₂ (P25, 50 μ g/mL), RhB (10 μ M), and antioxidants (250 μ g/mL) was irradiated by the UV light (8 W, 365 nm) for 1 h. The concentration of the remaining RhB was monitored by its absorption spectra (552 nm).

H₂O₂-Sensing Assay. H₂O₂ was diluted with deionized water and (was) added to 2 mL of an N-Ti₃C₂ QD solution (50 μ g/mL) according to a series of concentration gradients (0–5.5 μ M), and then was slowly shaken and allowed to stand still for 15 s. The fluorescence spectra were obtained for the mixture solution under 360 nm excitation. In selective experiments, ¹O₂ was generated from the on-line reaction of a NaClO solution with H₂O₂.⁵⁰ •OH was produced by the Fenton reaction (Fe²⁺–EDTA/H₂O₂ = 1:1).⁵¹ O₂^{•−} was generated from a hypoxanthine/xanthine oxidase system.⁵² Considering the reaction rate of different ROS and the fluctuation of PL intensity as time, the fluorescence intensity change of N-Ti₃C₂ QD solutions to H₂O₂, •OH, and ¹O₂ sensing were recorded after 15 s of the reaction. As for O₂^{•−} sensing, the intensity change was recorded after 1800 s of the reaction. Metal ions (Na⁺, K⁺, Mg²⁺, Ca²⁺, Fe²⁺, Zn²⁺, and Al³⁺) and free radicals with a concentration of 2 μ M as an interference were determined.

DFT Calculations. All DFT calculations in this work are carried out using the Vienna Ab initio Simulation Program (VASP). The electron–ion interaction is described by the projector augmented wave (PAW) method;⁵³ the generalized gradient approximation (GGA) functional of Perdew, Burke, and Ernzerhof (PBE)⁵⁴ is used to describe the electron exchange–correlation. The energy cutoff for the planewave basis is set to 500 eV to ensure the convergence of the calculations. The Brillouin zone integration is performed within the Monkhorst–Pack scheme using a 3 × 3 × 1 mesh for the geometry optimizations.⁵⁵ Systematic calculations presented here have been performed in a 3 × 3 × 1 supercell with a periodic boundary condition. For an N-Ti₃C₂T_x system, the composition is one C atom replaced by one N atom. To avoid interactions between neighboring slabs along the *z*-axis, a vacuum layer of 20 Å is included. Both the supercell size and atomic positions are relaxed to equilibrium, and energy minimization is continued until the forces on all atoms are converged to smaller than 10^{−3} eV/Å. The total energy of each system is relaxed until the difference value is smaller than 10^{−7} eV.

Characterization. Scanning electron microscopy (SEM) images were obtained using a JSM-7401 electron microscope. Transmission electron microscopy (TEM) was measured using a JEM-2010 electron microscope. Atomic force microscopy (AFM) images were performed with a Bruker Dimension Icon microscope in ambient air. The XRD patterns of the QDs were measured using a D/MAX 2500H X-ray diffractometer with Cu K α radiation. Ultraviolet–visible spectroscopy was performed using a TU-1900 spectrophotometer and photoluminescence spectra of samples were obtained using a 4500 Fluorimeter. Fourier transform infrared spectra (FT-IR) were recorded using a NEXUS spectrometer 670. X-ray photoelectron

spectroscopy (XPS) was recorded using an ESCALAB 250Xi electron spectrometer with an Al monochromatic K α radiation ($h\nu$ = 1486.6 eV) source. XPS survey was conducted before and after N-Ti₃C₂ QDs reacted with H₂O₂. Raman spectra were carried out using an RM 2000 Microscopic Confocal Raman Spectrometer (Renishaw PLC, England) under a He–Ne laser with an excitation wavelength of 632.8 nm. The electrochemical cyclic voltammetry was tested at a CHI 660D working station with N-Ti₃C₂ QDs or Ti₃C₂ QDs modified glassy carbon electrode (GCE) as a working electrode, a Pt plate as a counter electrode, and Ag/AgCl as a reference electrode. The GCE electrode was burnished with alumina powder before the experiment, and then ultrasonicated 20 min in ethanol and deionized water, respectively. The electrolyte was KCl (0.1 M) containing potassium ferricyanide (0.5 mM K₃[Fe(CN)₆]) and potassium ferrocyanide (0.5 mM K₄[Fe(CN)₆·3H₂O]). The data were recorded after about four cycles under steady-state conditions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acsami.1c11242>.

XRD patterns of Ti₃AlC₂ and Ti₃C₂T_x, TEM image, FT-IR spectrum, XPS survey of Ti₃C₂ QDs, DPPH[•] scavenging efficiency of N-Ti₃C₂ QDs and Ti₃C₂ QDs, Raman spectra of N-Ti₃C₂ QDs before and after reacting with DPPH[•]. UV–vis spectrum of N-Ti₃C₂ QDs, and PL spectra (Ex = 380 nm) of Ti₃C₂ QDs and N-Ti₃C₂ QDs (PDF)

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Notes

The authors declare no competing financial interest.

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