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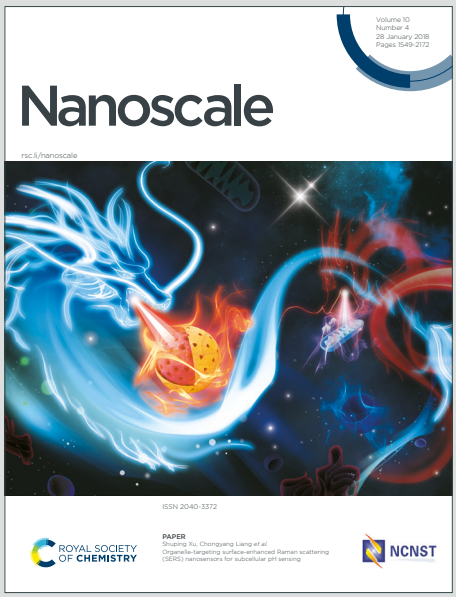

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ARTICLE

Enzymes, DNAzymes and Nanozymes for Environmental Remediation

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The escalating problem of environmental contamination requires sustainable remediation technologies. Biocatalytic systems utilizing enzymes and whole organisms have been explored for decades, although limitations such as high cost and inhibition restrict their application. Biomimetic systems, employing artificial catalysts with enzyme-like activities, such as DNAzymes and nanozymes, are generally less susceptible to these limitations and have emerged as promising alternatives. This review provides a comparative analysis of these three catalytic platforms for the remediation of various xenobiotics. By systematically comparing catalytic performance, operational robustness, and economic viability, we highlight why nanozymes could potentially outperform biological counterparts in some applications, but are unlikely to fully replace them. We conclude by outlining future directions, including the development of stimuli-responsive nanozymes, biodegradable nanozymes, and synergistic hybrid systems, to guide the rational design of next-generation remediation technologies that are efficient, sustainable, and economically viable.

Introduction

The rapid industrialization, urbanization, and intensive agriculture over the past decades have released an unprecedented volume and diversity of pollutants into the environment, especially water bodies, creating a global environmental, ecological, and health crisis. Persistent organic pollutants (dyes, phenols, pharmaceuticals, pesticides, and per- and polyfluoroalkyl substances - PFAS), antibiotic-resistant bacteria, heavy metals, and petroleum hydrocarbons accumulate in ecosystems, enter food chains, and contribute to biodiversity loss, groundwater contamination, and diseases ranging from cancer to neurological disorders.[1] These problems are compounded by climate change, creating a pressing need to develop efficient environmental remediation strategies.[2]

Traditional remediation technologies such as adsorption, membrane filtration, advanced oxidation, or incineration are often energy-intensive, generate secondary waste, or fail against recalcitrant and low-concentration contaminants.[3,4] Biotechnology-based approaches, including microbial degradation,[5] plant-based remediation,[6] enzyme catalysis,[7] and, more recently, nanozyme-catalyzed reactions,[8] offer a compelling alternative: they harness highly specific, biodegradable catalysts that operate under ambient conditions, mineralize pollutants into harmless (CO_2, H_2O) or less harmful (Cr(III), As(V)) products, and can be engineered for enhanced activity, stability, and recyclability. By mimicking or surpassing the catalytic efficiency of natural enzymes while overcoming their fragility and high cost, biomimetic remediation provides a sustainable, cost-effective, and environmentally compatible pathway toward large-scale decontamination of polluted water and soil.

Among the diverse biotechnological strategies for environmental remediation, enzyme-based catalysis has long been regarded as highly promising because of its high substrate specificity, remarkable catalytic efficiency, and ability to function under mild conditions without generating toxic byproducts. Natural enzymes, particularly oxidoreductases such as horseradish peroxidase (HRP), laccase, and cytochrome P450 enzymes, as well as hydrolases like organophosphorus hydrolase, can effectively degrade a wide spectrum of pollutants, including dyes, phenolic compounds, pesticides, and pharmaceuticals, through oxidative polymerization or hydrolytic cleavage.[9] However, their widespread practical application is restricted by intrinsic drawbacks: poor operational stability in harsh pH and temperature regimes, sensitivity to inhibitors, difficulties in recovery and reuse, and high production and purification costs.

Within the class of enzyme mimics, DNAzymes (catalytic DNA molecules selected in vitro), which emerged in the 1990s were believed to be robust, chemically stable alternatives capable of oxidizing substrates or cleaving phosphodiester bonds in the presence of specific metal ions, with notable success in heavy-metal sensing,[10,11] and peroxide-mediated degradation of model pollutants. Despite their improved stability and ease of synthesis, DNAzymes generally exhibit

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lower catalytic turnover and a narrower substrate scope compared with protein enzymes.

Since 2007,[12] nanozymes have rapidly risen as a transformative catalysis solution.[13–15] By combining the high stability and low cost of inorganic nanomaterials with enzyme-like activities (primarily peroxidase (POD), oxidase (OXD), catalase, and superoxide dismutase mimetic), nanozymes not only surpass the operational robustness of natural enzymes and DNAzymes but also offer additional advantages such as facile surface modification, magnetic recoverability, multifunctionality, and tunable activity through defect engineering and heterostructure design.[16] These attributes position nanozymes as particularly well-suited platforms for scalable, real-world environmental remediation, driving intense research interest and accelerating their transition from laboratory demonstrations to practical water-treatment technologies.[17]

This review provides a comprehensive yet high-level overview of the evolving role of biocatalytic and biomimetic systems in environmental remediation, with particular emphasis on three types of catalysts: natural enzymes, DNAzymes, and nanozymes. Whereas numerous excellent reviews have already surveyed the applications of enzymes and nanozymes individually, the present work offers a holistic comparative perspective that integrates these disparate strands into a unified narrative. We first revisit the milestones and limitations of enzymes in pollutant degradation, followed by the emergence of DNAzymes as chemically robust, programmable nucleic-acid catalysts. The final portion of the review is devoted to the explosive progress in nanozyme science, covering breakthroughs in activity modulation, multi-enzyme mimicry, and translation into practical remediation platforms. By systematically comparing catalytic efficiency, operational stability under real-world conditions, recyclability, cost-effectiveness, and scalability across the three systems, we clarify why nanozymes have begun to outperform both natural enzymes and DNAzymes in many environmental contexts. Finally, we critically assess remaining limitations, and outline promising future directions, such as stimuli-responsive and biodegradable nanozymes, and synergistic hybrid systems. This review aims to guide researchers and engineers toward the rational design of next-generation catalytic technologies that can deliver efficient, sustainable, and economically viable solutions for remediation. This review focuses on the removal and degradation of contaminants. Although detection is a critical part of remediation, it is a highly developed field that has been extensively reviewed elsewhere.[8,18]

Types of Pollutants and Remediation Pathways

Environmental pollutants amenable to enzyme-, DNAzyme-, and nanozyme-based remediation can be broadly classified into five major categories (Figure 1), each requiring distinct catalytic pathways for effective detoxification.

The first category includes small organic molecules, synthetic dyes (e.g., azo, triphenylmethane, and anthraquinone dyes), phenolic compounds (e.g., phenol, bisphenol A, chlorophenols), pharmaceuticals and personal-care products (e.g., antibiotics, β-blockers, anti-inflammatories, endocrine-disrupting chemicals), and pesticides (e.g., organophosphates, carbamates, triazines). Dyes and other chromophoric/fluorescent molecules are popular model compounds, as their degradation can be readily monitored by spectrophotometry. This group also encompasses small-molecule toxins such as aflatoxins, cyanobacterial microcystins, and bacterial endotoxins. A few representative structures are shown in Figure 1A. These pollutants are primarily degraded via oxidative pathways mediated by POD-, laccase-, or OXD-like activities, which generate reactive oxygen species (ROS, e.g., •OH, $^1O_2$, O_2•$^-$) to drive ring-opening, dehalogenation, hydroxylation, and eventual mineralization.[19] Alternatively, hydrolytic cleavage is employed for compounds like organophosphates and amide/ester-containing pesticides.

Heavy-metal ions (Hg(II), Pb(II), Cd(II), Cr(VI), As(III), Figure 1B) are particularly harmful due to their bioaccumulative properties. Long-term exposure can cause organ damage, especially in children. Remediation strategies typically involve redox transformations to less toxic and mobile states (e.g., Cr(VI) to Cr(III), As(III) to As(V)) or sequestration via adsorption onto functionalized catalyst surfaces.

PFAS and other ultra-recalcitrant halogenated organics represent an emerging frontier (Figure 1C). Their remediation is challenging due to the strength of the C–F bond. Advanced processes activated by nanozymes, such as those generating high-valent metal-oxo species or sulfate radicals (SO_4•$^-$), can achieve C–F bond activation and stepwise defluorination. This category is treated separately due to its exceptional environmental persistence, unique toxicity, and the distinct catalytic mechanisms required for their degradation.

Micro- and nanoplastics (MNPs) (plastic particles <5 mm and <1 μm, respectively) have emerged as a pervasive global pollutant due to their distribution across water and soil matrices and extreme resistance to degradation. Common polymers include polyethylene terephthalate (PET), polyurethane, polyethylene, and polystyrene (Figure 1D). While natural plastic-degrading enzymes often suffer from slow kinetics and low stability at high temperature, protein engineering has improved their performance. Nanozymes offer a complementary strategy: by generating ROS via POD- or laccase-mimetic activity, they can oxidize and embrittle polymer surfaces, facilitating subsequent microbial or enzymatic breakdown.

Pathogenic microorganisms, including bacteria, fungi, and viruses harmful to human, animal, or plant health, represent a significant class of environmental contaminants with substantial economic impacts (Figure 1E). In an industrial context, relevant challenges include biofouling and biofilm formation. Primary remediation pathways involve the use of hydrolytic enzymes (e.g., proteases, glycosidases) to degrade microbial structures and ROS-generating nanozymes for antimicrobial action.

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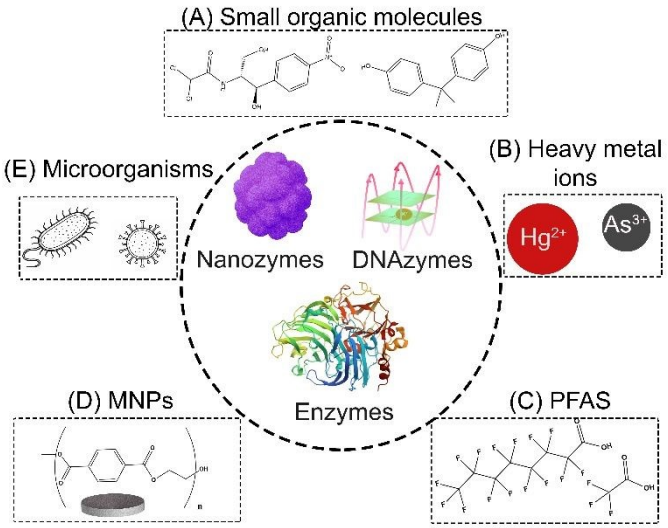

Figure 1. Representative structures of environmental contaminants: (A) small organic molecules; (B) heavy metal ions; (C) per- and polyfluoroalkyl substances (PFAS); (D) micro- and nanoplastics (MNPs); and (E) pathogenic microorganisms.

Environmental Remediation by Enzymes

Enzymes play a pivotal role in bioremediation by catalyzing the degradation, transformation, or immobilization of pollutants such as dyes, pesticides, polycyclic aromatic hydrocarbons (PAHs), heavy metals, and emerging contaminants. Key enzyme classes include oxidoreductases (e.g., laccases, PODs, oxygenases), hydrolases (e.g., esterases, amidases, lipases), and dehalogenases.[20–22] These biocatalysts are often sourced from bacteria, fungi (especially white-rot fungi), and plants, and can be deployed in free or immobilized forms for enhanced efficiency. Some representative applications are reviewed below.

Oxidoreductases are widely utilized in the bioremediation of persistent organic pollutants, ranging from industrial dyes and pharmaceuticals to pesticides by catalyzing oxidation-reduction reactions. Their mechanism involves generating highly reactive free radicals or other active intermediates that initiate chain reactions, breaking down complex molecules into simpler, often less harmful compounds, or even mineralizing them. PODs, laccases, and cytochrome P450s are the most commonly reported oxidoreductases for bioremediation. Naturally, these oxidoreductases can exhibit broad substrate specificity due to relatively large, conformationally flexible binding pockets that accommodate diverse structures.

Laccases use dissolved oxygen as their primary oxidant, while PODs require hydrogen peroxide. For substrates with high molecular weight or reduction potential, laccases require redox mediator molecules (e.g., ABTS, 1-hydroxybenzotriazole, acetosyringone).[23] Although PODs and laccases primarily catalyze the oxidation of xenobiotics and cannot directly cleave covalent bonds such as C–C or C–N, they trigger subsequent reactions that lead to deeper degradation. For example, Han et al. demonstrated the formation of multiple intermediate degradation products from tetracycline antibiotics catalyzed by laccase immobilized on $Cu_3(PO_4)_2$-based nanoflowers (Figure 2A).[24] Similarly, Ali et al. reported the formation of multiple intermediates and a proposed pathway for the degradation of the azo dye Crystal Ponceau 6R by soybean POD.[25]

Enzymes of the cytochrome P450 family are ubiquitous and typically catalyze oxidation and hydroxylation reactions. However, as summarized by Yang et al.[26], over 20 diverse reactions, including decarboxylation, epoxidation, nitration, C–S bond formation, and dehalogenation, are catalyzed by P450s. For instance, Jackson et al. reported the degradation of hexahydro-1,3,5-trinitro-1,3,5-triazine by the cytochrome P450 system XplA/B.[27] The Michaelis constant (K_M) for this abiotic molecule was 58 μM, comparable to those of natural substrates, with a turnover number (k_{cat}) of 4.44 s^{-1}, which is also high for this enzyme. The authors demonstrated that the presence of oxygen led to various degradation pathways and products. Furthermore, P450s have been reported to oxidize various polycyclic aromatic hydrocarbons, pesticides, and pharmaceuticals.[28–30] Remarkably, bacterial P450 enzymes often have K_M values in the low micromolar range, significantly lower than those of many PODs (mM range) and laccases (μM–mM range).[31,32] Bacterial P450s also possess significantly higher turnover numbers (k_{cat} > 10^3 s^{-1}) compared to mammalian P450s (5–250 min^{-1}), making them more efficient catalysts.[33] However, the operational stability of P450s remains a significant limiting factor for practical application.[26] Colosi et al. reported that HRP is able to degrade perfluorooctanoic acid in the presence of a phenolic co-substrate (4-methoxyphenol).[34] They reported 68% removal over 6 hours, with the primary products being low-molecular-weight degradation compounds with minimal fluoride release, and even some products from ring-closing reactions. Conversely, Luo et al. reported much slower degradation of perfluorooctanoic acid by laccase (50% degradation in 157 days, with a pseudo-first-order rate constant of 0.0044 day^{-1}).[35]

The substrate specificity of common remediation enzymes like PODs and laccases, while broad, is influenced by specific enzyme-substrate interactions. Glazunova et al. studied the catalytic activities of four different laccases with varying T1 copper center redox potentials against twenty monophenolic compounds and four phenolic dyes.[36] They demonstrated that the redox potential difference between the enzyme and substrate was a key activity determinant, with laccases of higher redox potential generally being more effective. For laccases with similar redox potentials, the detailed structure of the active site and substrate also played a critical role. Therefore, even chemically similar xenobiotics (e.g., different phenols) can exhibit significantly different degradation rates.

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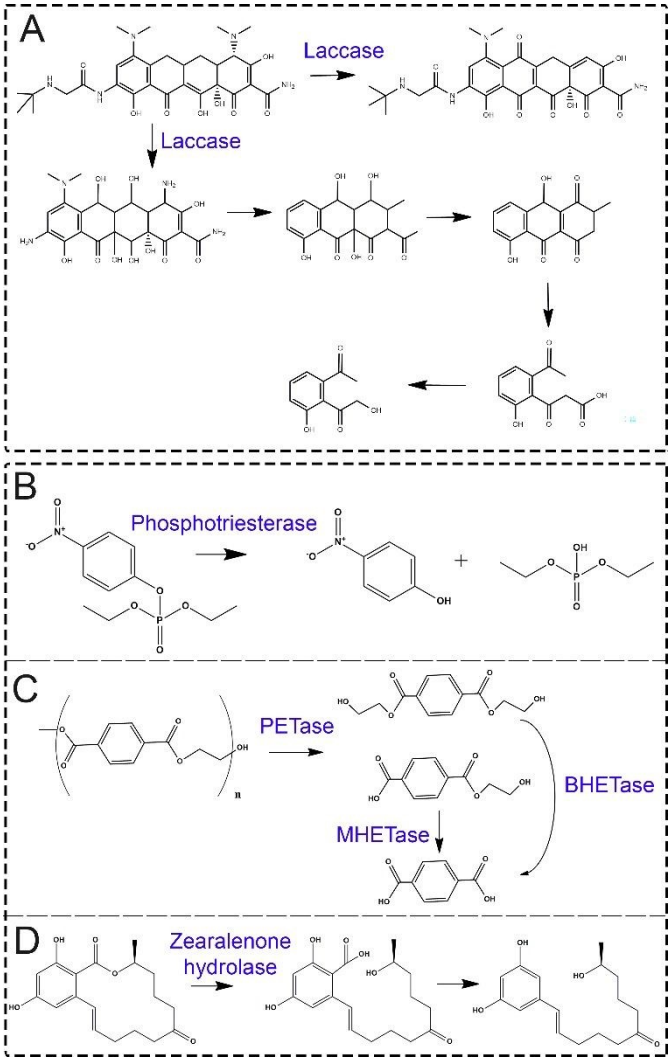


Figure 2. Chemical transformation of xenobiotics by enzyme catalysis. (A) Degradation of tigecycline by laccase. Adapted from ref.[24] with permission from Elsevier, copyright 2023. (B) Hydrolysis of paraoxon by phosphotriesterase. Adapted from ref.[37] with permission from American Chemical Society, copyright 2004. (C) Degradation of polyethylene terephthalate (PET) by the synergistic action of polyethylene terephthalate hydrolase (PETase), mono(2-hydroxyethyl) terephthalate hydrolase (MHETase), and bis(2-hydroxyethyl) terephthalate hydrolase (BHETase). Adapted with permission from ref.[38] with permission from Elsevier, copyright 2023. (D) Hydrolysis of zearalenone. Adapted from ref.[39] with permission from Multidisciplinary Digital Publishing Institute under the terms and conditions of the Creative Commons Attribution (CC BY) license, 2022 All chemical structures were drawn using ChemDraw.

Hydrolases are another major class of enzymes used in bioremediation. In contrast to oxidoreductases, hydrolases do not achieve complete mineralization, as their function is limited to cleaving specific bonds. A typical phosphotriesterase-catalyzed reaction is shown in Figure 2B for the hydrolysis of paraoxon, a very efficient reaction (k_{cat}/K_M ≈ 10^8 $M^{-1}s^{-1}$) approaching the diffusion limit.[37] Phosphotriesterases are widely used for degrading pesticides and chemical warfare agents. Lai et al. reported that organophosphate hydrolase can hydrolyze bonds with varying efficiencies: P-O bonds (k_{cat} = 67-5000 s^{-1}), P-F bonds (k_{cat} = 0.01-500 s^{-1}), and P-S bonds (k_{cat} = 0.0067 to 167 s^{-1}) and typically has K_M ≤ 0.5 mM for P-O and P-F containing pesticides.[40] The degradation products are less toxic and can be more readily metabolized by microorganisms. Hydrolases such as cutinases and polyethylene terephthalate hydrolases (PETases) are also utilized in the bioremediation of MNPs. Cutinases primarily act on cutin but exhibit catalytic promiscuity toward synthetic polymers like PET, poly(lactic acid), and others.[38,41] PETase is an enzyme that utilizes PET as its primary substrate.[42] Complete degradation of PET also requires mono(2-hydroxyethyl) terephthalate hydrolase (MHETase) and bis(2-hydroxyethyl) terephthalate hydrolase (BHETase), which hydrolyze intermediate products (Figure 2C) for further metabolism.[43,44]

Another important hydrolase is zearalenone hydrolase, which detoxifies the highly toxic mycotoxin zearalenone by cleaving its lactone bond, leading to spontaneous decarboxylation and the formation of a non-toxic product (Figure 2D). Significant effort has been focused on engineering enzyme variants with increased thermostability and catalytic activity.[45,46] Bi et al. confirmed the practical utility of this approach, reporting 88.0–94.7% degradation of zearalenone in various food matrices.[47] Zhao et al. further confirmed high enzyme activity in degummed corn oil.[39] Notably, most studies report K_M values in the low micromolar range, making this enzyme promising for degrading trace-level zearalenone contamination.

Despite their considerable promise, the practical deployment of enzymes in environmental remediation is constrained by several critical challenges. One principal limitation is their inherent instability under real-world conditions. Unlike controlled laboratory settings, environmental matrices exhibit fluctuating pH, extreme temperatures, and inhibitory chemicals (e.g., heavy metals, solvents), which can rapidly denature enzymes and diminish catalytic activity. Furthermore, enzyme activity can be competitively or non-competitively inhibited by substrate analogues, reaction products, or co-present pollutants, leading to unpredictable performance in complex waste streams. Large-scale production and purification of enzymes remain costly, restricting industrial-scale implementation. This economic barrier is compounded by significant scalability challenges; maintaining activity, stability, and cost-effectiveness at volumes several orders of magnitude larger than bench-scale is non-trivial. Finally, most polluted environments contain complex mixtures of contaminants (e.g., coexisting pesticides, pharmaceuticals, and heavy metals). A single enzyme is typically ineffective against such diverse chemical profiles, necessitating the development of multi-enzyme cocktails or engineered microbial consortia.

Consequently, current research is intensely focused on strategies to overcome these barriers, including enzyme immobilization for enhanced stability and reusability, protein

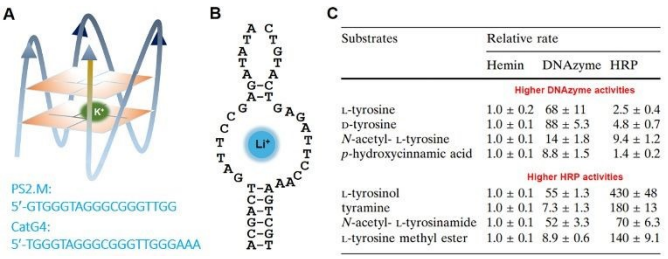
engineering to improve stability and functional properties, and the design of synergistic multi-enzymatic or biohybrid systems. For example, hydrogels are promising carriers for enzyme immobilization and stabilization.[48] Zhang et al. synthesized a cellulose-based hydrogel strengthened by montmorillonite nanosheets and doped with β-cyclodextrin to capture various persistent organic pollutants; loading this hydrogel with laccase improved pollutant oxidation.[49] The laccase-assembled hydrogel demonstrated increased enzyme stability and enhanced removal performance compared to free laccase.

An alternative approach to overcoming the limitations of natural enzymes is to use artificial catalysts with enzyme-like properties. Such catalysts should possess high catalytic efficiency (though the molecular mechanisms may differ), coupled with greater stability and lower cost. While many small molecules have been reported as artificial enzymes, their homogeneous nature presents challenges for catalyst recuperation and scalable application. In contrast, DNAzymes and nanozymes represent more promising platforms for real-world environmental applications due to their heterogeneous, recoverable nature and tunable properties.

Environmental Remediation by DNAzymes

Since enzymes are susceptible to high production costs and irreversible denaturation, efforts have been made to develop various enzyme mimics that can catalyze chemical transformations using alternative chemical frameworks. With the discovery of ribozymes in the early 1980s, efforts have been made to discover catalytic DNA or DNAzymes, since DNA is about one million-fold more stable compared to RNA.[50] The most important DNAzymes for the purpose of environmental remediation are those with POD-like activities. Those DNAzymes are based on a G-quadruplex scaffold and use hemin as a cofactor.[51,52] The most classical DNAzyme is PS2.M, although many higher-activity variants have since been reported.[53,54] Figure 3A lists a few commonly used G4-based DNAzymes along with a general G4 structure stabilized by potassium ions. Cheng et al. discovered that dimerization can further improve the catalytic activity of G4 DNAzymes.[55] Recently, the Liu lab has isolated a non-G-quadruplex DNAzyme and its structure is shown in Figure 3B.[56] As no comprehensive reviews are currently available on DNAzyme-based remediation, we herein summarize and discuss representative efforts in this emerging area.

POD DNAzymes have not been extensively investigated for pollutant degradation too much since the reaction produces incomplete degradation products. While the most popular substrates for POD DNAzymes are TMB and ABTS, other substrates were also tested. Compared with HRP, DNAzymes exhibit even higher catalytic activities against some phenolic substrates like tyrosine, although other substrates like tyramine have lower activity (Figure 3C).[57] The Shao group studied the reaction of G4 DNAzymes with cyanine dyes that have affinity to the DNAzyme complex. As such, they can react at lower concentrations. The authors obtained a K_M value of 4.6 μM, which was 560-fold lower than using ABTS and 50-fold lower than using TMB.[58] The dye was degraded to smaller fragments that absorbed at shorter wavelengths. In 2018, Kurapati and Bianco used the PS2.M DNAzyme mixed with hemin to degrade graphene oxide.[59] Transmission electron microscopy (TEM) revealed time-dependent fragmentation of GO sheets, and the experiment lasted up to 30 days, indicating relatively low reaction efficiency. From Raman spectroscopy, the G and D bands nearly fully disappeared suggesting a large extent of degradation of GO sheets after 30 days. Thus, although the 2D morphology was largely preserved, a significant fraction of the conjugated chemical structure was disrupted.



Substrates	Relative rate		
	Hemin	DNAzyme	HRP
	Higher DNAzyme activities		
L-tyrosine	1.0 ± 0.2	68 ± 11	2.5 ± 0.4
D-tyrosine	1.0 ± 0.1	88 ± 5.3	4.8 ± 0.7
N-acetyl- L-tyrosine	1.0 ± 0.1	14 ± 1.8	9.4 ± 1.2
p-hydroxycinnamic acid	1.0 ± 0.1	8.8 ± 1.5	1.4 ± 0.2
	Higher HRP activities		
L-tyrosinol	1.0 ± 0.1	55 ± 1.3	430 ± 48
tyramine	1.0 ± 0.1	7.3 ± 1.3	180 ± 13
N-acetyl- L-tyrosinamide	1.0 ± 0.1	52 ± 3.3	70 ± 6.3
L-tyrosine methyl ester	1.0 ± 0.1	8.9 ± 0.6	140 ± 9.1

Figure 3. DNAzymes as catalysts. (A) Schematic illustration of a G4-based DNAzyme (hemin not shown) and two representative DNAzyme sequences. (B) Structure of a non-G4 DNAzyme. Adapted from ref.[60] with permission from John Wiley and Sons under the terms and conditions of the Creative Commons Attribution (CC BY) license,2025. (C) Comparison of the catalytic activities of the PS2.M DNAzyme and HRP for different substrates. Adapted from ref.[57] with permission from Springer Nature, Copyright 2006.

Laccases are commonly used for environmental remediation.[61] Yum et al. synthesized histidine-containing DNA and complexed it with Cu^{2+} to prepare laccase-mimicking DNAzymes.[62] The authors placed histidine modifications in various duplex, three-way junction and G-quadruplex (G4) structures and observed higher activity in one of the G4 constructs. These DNAzymes were not obtained through combinatorial selection but were rationally designed based on the coordination of copper ions.

The type of DNAzymes that can be used for environmental remediation are very limited. A major limitation of using POD DNAzymes for environmental remediation is the requirement of H_2O_2 and the poor stability of hemin under oxidative conditions. Reports have shown that hemin can be rapidly degraded under reaction conditions, leading to a short catalytic lifetime.[60,63,64] Thus, most work has remained at the proof-of-concept stage. In addition, for hydrolytic DNAzymes, their catalytic rates are still slow. Future efforts need to focus on engineering more stable and more efficient DNAzymes to enable practical applications. In addition, most DNAzymes act on nucleic acid-based substrates, and additional work is required to develop DNAzymes for substrates of environmental relevance.

The combination of functional DNA (either DNAzymes or affinity DNA binders) with nanozymes represents an actively developing approach with significant potential in analytical

chemistry,[65] biomedicine,[66] and environmental remediation. This strategy harnesses the benefits of both components: DNA serves to ensure high substrate specificity, while nanozymes act as highly stable catalysts. DNAzymes have been confirmed to be effective against bacteria and viruses for biomedical applications. Mo et al. developed a composite MOF modified with POD-like nanozymes producing hydroxyl radicals.[67] Xiong et al. developed a detection and inactivation approach for Zika virus using a G-quadruplex/hemin DNAzyme.[68] You et al. proposed using a Cu nanozyme-DNAzyme complex as a bioorthogonal catalyst for cancer therapy.[69] The complex produces reactive oxygen species (ROS) in a POD-like reaction and facilitates the accumulation of Cu^{+}, ensuring a therapeutic effect. Li et al. reported the use of such multifunctional structures for *Cronobacter sakazakii*.[70] Saranya et al. proposed an assay using a DNA structure containing a sensing part for pathogenic spirochete capture and another DNAzyme for colorimetric signal generation in a POD-like reaction.[71]

DNA is a unique building material that can be precisely assembled into various complex nanoscale motifs and can be easily modified and conjugated.[72,73] Together, they provide interesting semisynthetic bionanomaterials that leverage the strengths of biological and synthetic systems.

Environmental Remediation by Nanozymes

Nanozymes are nanomaterials that catalyze the conversion of enzyme substrates to products under physiologically relevant conditions, although their catalytic mechanisms may differ from those of their natural counterparts.[74] The most developed types of nanozymes are those with oxidoreductase-like activities, whose functionality is commonly associated with the generation of ROS in Fenton-like reactions.[75] Due to this general mechanism and the fact that nanozymes lack substrate-specific active centers, they can typically oxidize a broad spectrum of organic compounds. This property has been utilized extensively in biomedicine, where nanozymes induce oxidative stress to combat tumors, pathogens, and viruses. The same property is harnessed for environmental remediation, making nanozymes powerful tools for degrading virtually all major classes of pollutants.[76] A highly attractive aspect of nanozymes for environmental remediation is their low cost, high stability and scalable mass production.

Pioneering work utilizing the Fenton-like reaction catalyzed by Fe_3O_4 nanozymes was reported by Zhang et al. for phenol oxidation shortly after the POD-like activity of this nanomaterial was first documented.[77] The nanoparticles removed over 85% of phenol from an aqueous solution within 3 hours at 16°C, with approximately 30% mineralization. The remaining reaction products were identified by GC/MS as small organic acids, including lactic acid, tartaric acid, oxalic acid, succinic acid, maleic acid, and 1,2-propylene glycol. Since then, many types of POD-mimicking nanozymes have been used to generate ROS for the degradation of various xenobiotics.[18] In addition to ROS, Fe_3O_4 nanoparticles were reported to generate sulfate radicals ($SO_4\bullet^{-}$) from persulfate anions, which are strong oxidants with a standard redox potential (E^0 = 2.6 V), although their oxidation potential is slightly lower than that of •OH (E^0 = 2.8 V).[78] Zhao et al. reported that CeO_2 nanoparticles possess haloperoxidase-like activity and can produce HOBr from H_2O_2 and Br^- ions. This system was utilized as an antifouling agent and also shows potential as a strong oxidizing agent for various targets.[79]

Another important class of oxidoreductase nanozymes is laccase-mimicking nanozymes. These nanozymes do not require additional H_2O_2 and instead use dissolved oxygen as an oxidant. Similar to natural laccases, laccase-mimicking nanozymes are predominantly composed of copper-containing nanomaterials. We previously analyzed the K_M values reported for POD-like nanozymes and observed significant heterogeneity, spanning up to five orders of magnitude, with values typically higher than those of natural PODs (Figure 4A).[15] Interestingly, for laccase-like systems, the K_M values of nanozymes and natural enzymes are often comparable (Figure 4B).[80–91] This similarity is likely because the active sites of both natural laccases and most laccase-mimicking nanozymes involve copper ions (Cu^{+}/Cu^{2+}). Nevertheless, the nature of the organic ligands or matrices chelating the copper also significantly influences the K_M values (Figure 4C).[92–99]

Wang et al. developed a laccase-mimicking nanozyme composed of Cu^{+}/Cu^{2+} ions coordinated with a dipeptide for the oxidation of 2,4-dichlorophenol and hydroquinone.[80] The authors reported K_M values comparable to that of natural laccase, but with significantly higher k_{cat} and k_{cat}/K_M values. This enhancement in turnover is likely related to the high density of active sites on a single nanoparticle. The proposed molecular mechanism for the nanozyme was largely inspired by that of natural laccases. Although laccases naturally possess broad substrate specificity, they still exhibit preferential oxidation rates for certain substrates. In a related study, Wang et al. proposed that the remediation mechanism for chlortetracycline by a laccase-mimicking nanozyme occurs via oxidative polymerization followed by precipitation.[88]

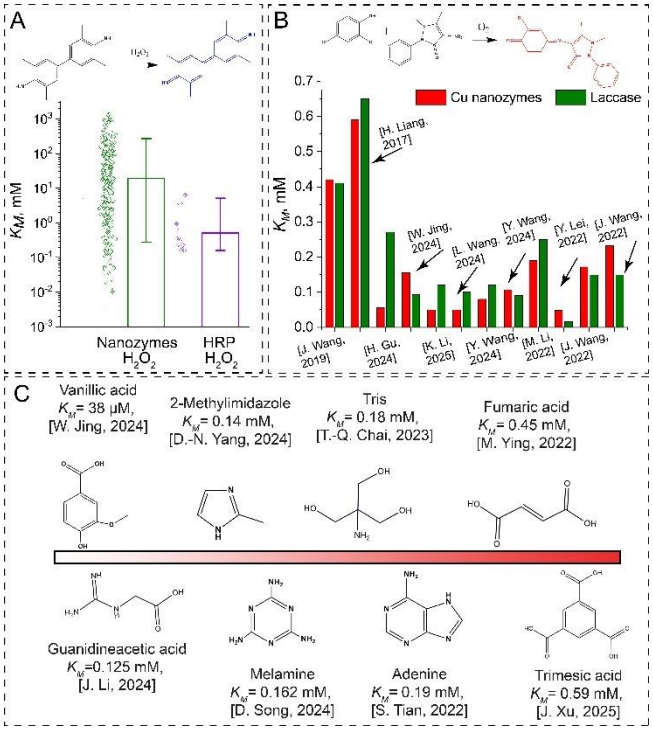


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Figure 4. Comparison of K_M values of enzymes and nanozymes. The chemical reaction is shown above the bars (A) Comparison of POD nanozymes and HRP. Adapted from ref.[15] with permission from John Wiley and Sons under the terms and conditions of the Creative Commons Attribution (CC BY) license, 2025. (B) Comparison of Cu nanozymes and natural laccases. (C) Effect of the nature of the organic ligands on K_M values for Cu nanozymes.

Zhang et al. demonstrated dehydrogenase-mimicking activity of an Au nanozyme in the oxidation of estradiol.[100] The authors screened several nanomaterials (CeO_2, Fe_2O_3, Fe_3O_4, MnO_2, Mn_2O_3, and Au) and confirmed that only Au could oxidize estradiol to estrone. Using mass spectrometry, they confirmed that oxidation occurred specifically at the 17β-OH position, while the phenolic hydroxyl at the C3 position remained unmodified. Using 17α-ethynylestradiol (containing an ethynyl group), a synthetic estrogen used in oral contraceptives, the authors reported significantly lower activity. Estriol and bisphenol A were not oxidized by the Au nanozyme. This is an important result clearly showing how molecular derivatization affects nanozyme activity. Derivatives of target molecules may be degraded much less efficiently by nanozymes, challenging complete pollutant clearance.

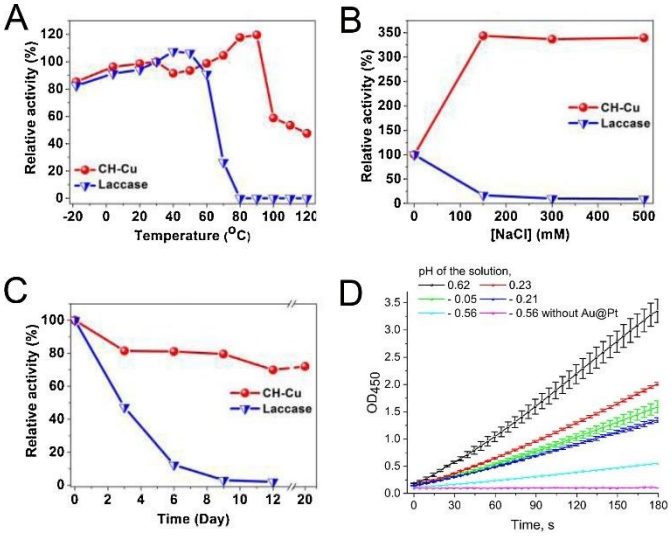

Figure 5. Comparison of the stability of nanozymes and enzymes. (A) Thermostability of a laccase-like Cu nanozyme (CH-Cu) and natural laccase. (B) Effect of NaCl concentration on catalytic activity. (C) Effect of storage time in water at 25°C. (A-C) adapted from ref.[80] with permission from Elsevier, copyright 2019. (D) Oxidation of the TMB substrate by an Au@Pt POD-mimicking nanozyme at various low pH values. Adapted from ref.[114] with permission from American Chemical Society, copyright 2025

Typically, the majority of nanozymes still have lower catalytic activity compared to natural enzymes. However, nanozymes are often reported to be more stable and robust catalysts. Wang et al. [80] demonstrated the superior operational robustness of a nanozyme compared to its natural counterpart, showing enhanced stability at high temperatures (Figure 5A), tolerance to saline conditions (Figure 5B), and sustained activity during prolonged storage in solution (Figure 5C). The superior thermostability of nanozymes is a well-documented characteristic that has found practical use in various applications.[115,116] We have demonstrated that various noble-metal POD-mimicking nanozymes (e.g., Au@Pt, Au@Pd, Au@Ir) maintain catalytic activity even at negative pH values (Figure 5D).[114]

For organic dyes such as rhodamine B, methylene blue, Congo red, and Acid Orange 7, Fe_3O_4, Co_3O_4, CeO_2, Prussian blue, and carbon-based nanozymes exhibit strong POD-like activity, rapidly activating H_2O_2 to generate •OH radicals that mineralize dyes with >95% color removal within minutes. Phenolic compounds, including phenol, 4-chlorophenol, 2,4-dichlorophenol, and bisphenol A, are effectively treated by Fe_3O_4, V_2O_5, MoS_2, Au@Pt, and Mn_3O_4 nanozymes.[8] These catalysts drive Fenton-like or POD-mimetic oxidation, converting toxic phenols into less harmful quinones or polymers, often achieving nearly complete removal at neutral pH.

Antibiotics and pharmaceuticals such as tetracycline, ciprofloxacin, sulfamethoxazole, and oxytetracycline are effectively degraded by $CoFe_2O_4$, CuO, $BiFeO_3$, and nitrogen-doped carbon nanozymes through •OH and sulfate radicals (SO_4•$^-$)-based advanced oxidation processes activated by peroxymonosulfate (PMS) or H_2O_2, routinely reaching >90% removal in 15–60 minutes.[117,118] Ghasemi et al. reported the use of a $Co_{0.5}Fe_{0.5}Fe_2O_4$ nanozyme with POD activity for the degradation of six antibiotics.[119] As the reaction is based on the generation of highly reactive ROS, the formation of multiple intermediates has been confirmed, consistent with other publications.[120,121] Huang et al. utilized an Fe-N-C single-atom nanozyme for BPA degradation and achieved 94.3% removal within 10 minutes.[122] The reaction included the formation of •OH, SO_4•$^-$, and singlet oxygen ($^1O_2$), leading to aromatic ring hydroxylation, C-C bond cleavage, ring-opening, and related pathways. Consequently, the authors reported a mixture of organic molecules that can be further mineralized (Figure 6A).

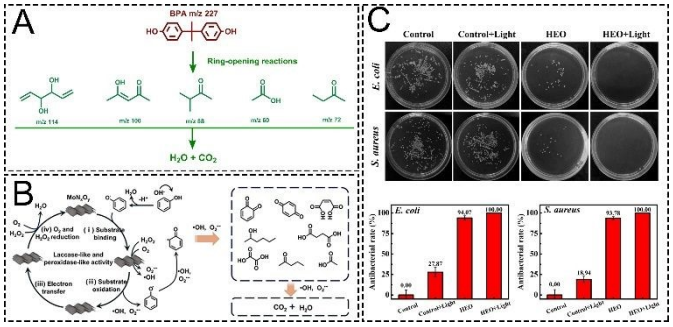

Figure 6. Nanozyme catalysis for environmental remediation. (A) Oxidation of bisphenol A by an Fe-N-C single-atom nanozyme. Adapted from ref.[122] with permission from Elsevier, copyright 2023 Elsevier. (B) Oxidation of phenol by a MoN_xO_y

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nanozyme. Adapted from ref.[123] with permission from Springer Nature under the terms and conditions of the Creative Commons Attribution (CC BY) license, 2025 (C) Antibacterial activity of a high-entropy oxide nanozyme $CrMnFeNiCuO_X$. Adapted from ref.[124] with permission from Elsevier, copyright 2025.

Rajab Ali et al. reported a POD-mimicking Fe@MoS_2 nanozyme for the detoxification of a sulfur mustard simulant. The reaction, performed in methanol, provided complete conversion within 30 minutes.[125] Zhang et al. reported a MoN_xO_y nanozyme with dual POD and laccase-like activity for phenol degradation (Figure 6B).[123] The authors confirmed the generation of $\bullet O_2^-$ (laccase-like activity) and •OH (POD-like activity), which are responsible for oxidation. Importantly, this nanozyme remains highly active at elevated temperatures, allowing its use in non-cooled wastewater streams.

Phosphatase-like activity is reported less commonly than oxidoreductase mimicry. Zhou et al. reported a Zr-metal-organic framework (MOF) nanozyme modified with an aptamer for the degradation of paraoxon and profenofos.[126] Immobilized aptamers ensure specific binding, localizing the substrate near the active sites. Wang et al. reported the hydrolytic remediation of paraoxon using a Cr-MOF nanozyme, achieving 100% conversion in 24 hours in water/acetonitrile mixtures.[127] Emerging persistent contaminants such as PFAS have higher reduction potentials than •OH, making direct oxidation inefficient. This necessitates alternative approaches, such as photocatalytic degradation. While this method also employs nanoparticles, it operates via fundamentally different reaction mechanisms.[128]

The ability to generate diffusing ROS is a unique property of POD nanozymes, allowing their use against viruses and bacteria. This capability, widely used in biomedical research, is being adapted to treat pathogenic and opportunistic microorganisms. Haloperoxidase-mimicking nanozymes are often utilized against marine biofouling.[112,129] Yu et al. reported a nanozyme with multiple activities, including ROS and HOBr formation, catalytic glutathione depletion, and photothermal heating.[124] As a result of this complex action, the authors achieved remarkable antibacterial activity (Figure 6C). The nanozyme alone facilitated significant antibacterial activity against *E. coli* and *S. aureus* (≈94%), while additional light irradiation resulted in complete inhibition of bacterial growth. In such applications, nanozymes may demonstrate multiple antibacterial mechanisms beyond ROS generation, including ion release (Cu^{2+}, Zn^{2+}), photothermal heating, or hydrolytic activity.[124,130–132]

Specificity of Nanozymes for Environmental Remediation

Since nanozymes are heterogeneous catalysts, their catalytic activity and specificity can be tuned by surface modifications.[101] As discussed by Fan et al., nanozymes cannot typically compete with enzymes in terms of substrate specificity, reaction specificity, and stereo- and regiospecificity of catalysis.[147] For remediation applications, reaction and substrate specificity are of primary importance, as they determine the efficiency of xenobiotic degradation. Presence of multiple catalytic activities (i.e., low reaction specificity) is well-known for various nanozymes.[148,149] Reaction specificity (e.g., peroxidase or catalase degradation pathway) is commonly reported to be a function of pH.[150,151] Therefore, potential side reactions due to low reaction specificity should be considered during technology development and, if necessary, suppressed by selecting appropriate reaction conditions.

Sun et al. reported Zn(II)-coordinated β-cyclodextrin and azobenzene-modified 1,4,7,10- tetrazazcyclodecane Au nanoparticles as highly effective hydrolytic nanozymes for methyl paraoxon and p-nitrophenyl diphenyl phosphate.[102] The authors reported UV/visible light-induced structural reorganization of the surface layers, allowing them to turn off and on nanozyme activity. Lyu et al. demonstrated that the nature of the immobilized organic ligands and metal ions significantly affects the k_{cat} and K_M of the catalytic hydrolysis of organophosphorus compounds by Au nanoparticles.[103] Chen and Willner recently summarized the main surface-modification strategies for increasing the specificity of nanozyme catalysis.[104] These include conjugation of aptamers, cyclodextrins, amino acids/peptides, and molecularly imprinted polymers. Such modifications ensure accumulation of the target substrate near the catalytically active surface, thereby enhancing catalytic transformation through spatial proximity. For example, conjugation of an antidopamine aptamer to Cu^{2+}-modified carbon dots facilitated a 50-fold enhanced oxidation of dopamine compared to the non-modified catalyst.[105] The same strategy has proven effective for oxygenation of L-tyrosinamide to the catechol product.

An unusual effect of surface modifications on chiral selectivity was reported by Zhan et al.[106] The authors demonstrated that bare Au nanoparticles oxidized D- and L-glucose isomers identically. However, after coating the surface with single-stranded DNA, the nanozymes preferentially oxidized the L-isomer (selectivity factors around 1.33), whereas coating with double-stranded DNA led to preferential oxidation of the D-isomer. This effect was attributed to the differential affinity of DNA structures for the glucose isomers. Liu et al. utilized protamine (an arginine-rich peptide) coating on Rh nanoclusters deposited on reduced graphene oxide to achieve 40-fold higher activity compared to the peptide-free composite.[107]

Zhou et al. reported stereospecificity for D/L-3,4-dihydroxyphenylalanine (DOPA) oxidation using D- or L-cysteine-modified Au-mesoporous silica nanoparticles.[108] Specifically, D-cysteine-modified nanozymes showed higher specificity for L-DOPA oxidation, while L-cysteine-modified ones preferred D-DOPA. Molecular dynamics simulations explained this effect by differences in the number and strength of hydrogen bonds between DOPA and cysteine, which determine substrate binding affinity.

Yin et al. prepared a single-atom Fe nanozyme embedded within mesoporous SiO_2 to restrict enzymatic substrate channels.[109] They reported high catalytic activity and reaction specificity due to enhanced substrate transport and shortened

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radical migration pathways compared to traditional nanozymes. An enzyme-inspired structural approach was used by Qileng et al. to develop a nanozyme for specific Cu^{2+} binding.[110] The authors performed dealloying of Ni_2Pt nanoparticles to create Pt nanostructures that function as substrate channels and specifically recognize Cu^{2+}.

Reaction specificity is also largely determined by the morphology of nanozymes. As demonstrated by Wang et al., CeO_2 nanozymes of different shapes show opposite effects: cubic particles enclosed by (100) facets exhibited high catalase-like activity and antioxidant properties, whereas CeO_2 octahedral nanozymes enclosed by (111) facets facilitated high ROS production and showed pro-oxidant properties.[111] Similarly, Yuan et al. reported varying levels of POD/CAT and haloperoxidase activity for different morphologies of CeO_2.[112]

Thus, beyond molecular imprinting[113]) strategies such as surface ligand engineering (with aptamers, peptides, or DNA), channel confinement, and morphology control offer viable routes to enhance substrate selectivity in nanozymes for practical applications in complex environmental matrices. These approaches can increase local substrate concentration, modulate binding affinity (including chiral selectivity), or alter reaction pathways, thereby improving preferential degradation of target pollutants.

There are also a few emerging approaches for increasing specificity, which, although have been demonstrated on other applications, may be adapted for remediation purposes. O'Mara et al. developed a cascade nanozyme for carbon dioxide reduction via multiple consecutive reactions in nanoconfined volumes.[142] In such a cascade system, specificity would be determined by the size of the channels, and the first reactions of the cascade would guide the whole process to a specific product among possible others. The same group proposed analytical assays for the specific electrochemical detection of various biomolecules using nanochannels that prevent active surface shielding and allow diffusion of small target molecules toward active centers.[143,144] Such an approach fits the requirements of environmental remediation, which utilizes multicomponent solutions with high concentrations of high-molecular-weight interfering biomolecules.

Challenges and Perspectives of Nanozymes for Environmental Remediation

Taken together, the versatility, stability, reusability, and low cost of nanozymes make them highly promising for the real-world treatment of diverse pollutants in wastewater, groundwater, and surface water. Moreover, nanozymes can play multiple roles beyond catalysis. Due to their high surface area, materials like MOFs can adsorb xenobiotics. For example, Prussian blue-modified biochar demonstrated high removal efficiency for thallium ions (Tl^+) from water and soil across a broad pH range and in the presence of competing cations.[133] Surface modification with affinity receptors (antibodies, aptamers, carbohydrates, synthetic receptors) allows nanozymes to capture target analytes, increasing the degradation rate through proximity effects.[126] Nevertheless, the incorporation of such biomolecules would diminish the cost and stability advantages of nanozymes. In this regard, using molecular imprinting to improve specificity might be a more practically viable route.[134,135] Although the literature primarily highlights analytical uses for molecularly imprinted nanozymes [136], the technique has also proven effective for imprinting pollutants like antibiotics, toxins, and pesticides,[113] and has been successfully applied in the photocatalytic remediation of ciprofloxacin,[137] paracetamol,[138] and methylene blue[139]. Furthermore, a large group of light-activated nanozymes, whose activity can be switched on/off by light exposure, provide a useful tool for precise spatiotemporal control over catalytic degradation.[140] Aside from imprinting,[113] using cost-effective affinity ligands such as aptamers,[141] may also be an interesting approach.

While nanozymes show immense promise for environmental remediation, several significant limitations must be addressed to transition from laboratory proof-of-concept to field-scale application. These challenges primarily arise from the nanoscale nature of nanozymes and the differences between idealized experimental conditions and complex real-world matrices.

The conditions in contaminated environments (e.g., soil, groundwater, industrial effluent) differ drastically from the controlled buffers used in kinetic studies. A primary concern is the matrix effect, which is particularly dramatic for nanozymes due to their high surface area. Upon introduction into a complex medium, proteins, natural organic matter, polysaccharides, and other biomolecules rapidly adsorb onto the nanozyme surface, forming a biomolecular corona. This well-characterized phenomenon, extensively studied in biomedical contexts, effectively shields the active sites, leading to a significant decrease in catalytic activity.[145,146] Although the quantitative impact in environmental settings is not fully characterized, this surface fouling inevitably diminishes the benefits of nanozymes' inherent stability. Furthermore, while laboratory-scale recovery methods (e.g., chemical washing, UV-ozone treatment) exist, they are often too complex or expensive for large-scale, in-situ applications. The current literature must evolve to include rigorous testing in representative environmental matrices.

The second challenge is lower specificity of nanozyme catalysis due to the absence of well-defined active sites. The low substrate specificity (e.g., the ability to catalyze reactions with a broad range of substrates) is a common inherent characteristic of nanozymes. Although high substrate specificity is reported in some studies,[152] generally, nanozymes are able to non-specifically utilize a broad range of substrates. On the other hand, the broader specificity of nanozymes could be useful as it allows the degradation of a broad range of molecules with various structures. Therefore, practical solutions should consider whether broad specificity is detrimental or useful for the specific case. Unlike natural enzymes with precise substrate-binding pockets, most nanozymes operate through surface-mediated reactions or the generation of ROS, resulting in largely indiscriminate catalysis. In multicomponent environmental samples, this can lead to

uncontrolled reactions. For example, using a POD-mimic nanozyme to generate •OH for degrading a target dye in sewage will concurrently oxidize non-target organic matter and beneficial microbial communities. This not only reduces the efficiency of the target reaction by consuming ROS but may also produce unknown and potentially harmful transformation by-products. As mentioned above, molecularly imprinted polymers and other surface modification strategies may provide viable approaches to partially address this limitation.

A critical research gap involves the environmental fate and behavior of nanozymes post-application.[153] Their potential aggregation, dissolution, or interaction with environmental colloids can hinder mobility, preventing them from reaching contaminated zones. Furthermore, the long-term ecological impact of persistent nano-catalysts in ecosystems remains largely unknown, raising concerns about nanotoxicity. Their greatest strength, chemical inertness and robustness, can become a liability if they accumulate as non-biodegradable nanoscale pollutants. Without a clear understanding these factors, predicting the efficacy and safety of long-term applications remains challenging.

The synthesis and functionalization of many high-performance nanozymes often involve complex, multi-step procedures or expensive precursors, posing challenges for cost-effective, large-scale production. Very few studies explicitly analyze the cost of nanozyme preparation.[79,154] There exists a pronounced trade-off between catalytic performance and ease of manufacture. For instance, Prussian blue analogs and iron oxide nanozymes are promising due to their low cost, straightforward synthesis, and proven environmental compatibility. Conversely, single-atom nanozymes, while exhibiting exceptional activity, often require complex preparation protocols involving high-temperature pyrolysis or precise atomic deposition. However, this high efficiency (typically demonstrated in model systems such as pure buffers) comes at the cost of poor stability. The high surface free energy of isolated metal atoms promotes migration and aggregation during prolonged operation, while harsh environmental conditions (variable pH, high ionic strength, complex organic matrices) can accelerate ligand bond degradation and carrier corrosion. Guo et al. recently reviewed the major stability challenges and potential strategies to overcome them.[155] Since aggregation of isolated atoms into nanoparticles is a common problem for SANs, potential solutions include strengthening interactions between single atoms and coordination atoms of the support, locating atoms into pores that act as molecular cages, and other defect engineering strategies. These methods are challenging to scale and dramatically increase production costs. Therefore, the marginally higher activity of a complex nanozyme may not justify its use if a simpler, more robust analog can achieve the required remediation threshold at a fraction of the cost. Additionally, effective recovery and reuse of nanozymes from treated environmental media (e.g., soil or turbid water) remain significant engineering hurdles. Without efficient recovery strategies, the technology risks becoming a pollutant itself and may be economically unviable. There are a few reports claiming scalable SAN synthesis that confirm the principal feasibility of mass production. For instance, Pei et al. performed high-throughput screening of more than 19,000 structures and selected 22 SANs with area coverage up to 200 cm^2 per 1 hour of synthesis.[156] The authors identified Pt-Ni-Ti-Cu and Co-Ti-Ni-V composites with antioxidant activities. They also performed a techno-economic analysis that clearly demonstrates the benefits of using SAN-embedded stents over drug-eluting and exosome-eluting stents. Such analyses are vital for developments targeting practical applications and should be routinely reported to justify new developments.

Finally, very few studies focus on the operational stability of nanozymes and their biodegradation. The Liu lab has reported that oxidative etching of Ag materials during catalysis with H2O2 substrate leads to low chemical stability, making such nanozymes single-use (one-turnover) materials.[148] While this limited stability may be acceptable for certain analytical applications,[157] it would restrict their practical use in bioremediation. The Zhang group has published several studies on the long-term catalytic performance of various nanozymes.[158,159] In these works, the authors repeatedly observe increased activity during prolonged catalysis for Prussian Blue nanozymes. In contrast, for other materials (Fe_3O_4, Pt, Au), activity either remains stable or declines. Sun et al. reported an SAN Mn nanozyme for the elimination of pharmaceuticals (removal efficiency 93–100%) and for antibacterial activity in water using a continuous-flow operating reactor.[160] Importantly, the authors confirmed the recycling performance of the catalyst under backwashing conditions, achieving 99% removal efficiency toward tetracycline over 24 successive cycles of backwash and filtration. Chen et al. reported a Co-SAN nanozyme for degradation of meropenem in wastewater with high efficiency (>97%), confirming functionality in both dispersed catalyst suspension and membrane filtration reactor modes.[161] Such studies are crucial for translating nanozymes from bench scale to industrial use.

Understanding the degradation pathways of nanozymes is crucial for practical applications. On one hand, it ensures high functional stability, as some nanozymes may degrade during catalysis. On the other hand, it helps assess potential ecotoxicity risks.[153,162,163] Many studies have successfully utilized nanozymes for in vivo applications with minimal toxic effects, which confirms their potential for environmental remediation purposes[164–166] Li et al. systematically reviewed stimuli-responsive degradation mechanisms of biodegradable nanozymes, identifying pH variations, redox agents, and chelating agents as primary triggers for nanozyme breakdown in environmental matrices.[167] Generally, three major pathways for degradation are physical (aggregation, sorption), chemical (dissolution, oxidation/reduction), and biological (microbial or enzymatic degradation).[168] For example, ZnO, MnO_2, and Ag nanoparticles have been reported to release metallic cations in low-pH media.[169,170] In contrast to dissolution, aggregation of nanoparticles is commonly reported due to their high surface area, which leads to their sedimentation.[171] Although there are

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no universal recommendations, the assessment of risks should be performed individually for each case, taking into account the properties of the nanozyme and the surrounding medium. Risk assessment could be performed in accordance with existing regulatory documents and guidance.[172,173]

Comparative Evaluation of Enzymes, DNAzymes and Nanozymes for Remediation

Table 1 summarizes the primary remediation pathways and representative catalysts for various xenobiotics. The main degradation mechanisms are hydrolysis and oxidation, the latter often initiating further breakdown reactions. Enzymes offer a broad spectrum of highly specific catalysts, often tailored to particular pollutant classes (e.g., phosphoesterases for organophosphates) or specific chemical bonds. In contrast, nanozymes function primarily as versatile, broad-spectrum oxidants. Their strength lies not in specificity, but in the application of powerful, generalized oxidative stress capable of damaging a wide array of contaminants, from recalcitrant organic molecules to living cells.[174–176] Consequently, POD and OXD mimicking nanozymes are used for the remediation of diverse targets, ranging from small organic molecules to bacteria. The catalytic repertoire of DNAzymes remains limited, primarily to POD-like reactions demonstrated in proof-of-concept studies, confining their current primary role largely to biosensing rather than bulk degradation.[177]

Table 1. Commonly used remediation pathways and catalysts for various xenobiotics

Xenobiotics	Primary reactions	Enzymes	DNAzyme activities	Nanozyme activities
Dyes	Oxidation	Laccases POD	POD Laccase	POD OXD
Pesticides	Oxidation, Hydrolysis, Dehalogenation	Laccases, POD, P450s, Dehalogenase, Phosphoesterase	Laccase	Hydrolase POD OXD
Pharmaceutical	Oxidation, Hydroxylation	Laccases, POD, P450s, Tyrosinase	Laccase	POD OXD
PAH	Oxidative Ring Cleavage	Laccases, POD, P450s Dioxygenases	Laccase	POD OXD
PFAS	Hydrolysis of F-C bond, Oxidation	Dehalogenases, POD, Laccases	Laccase	POD OXD
Heavy metals	Reduction, Complexation, Adsorption	Metal reductases Phytochelatin synthases		MOF POD OXD
MNP	Hydrolysis	Cutinases PETase		POD OXD
Microorganims	Lysis, Oxidative stress	Catalase Hydrolase		Halo peroxidase POD, OXD

Having reviewed the mechanisms and applications of each catalyst class, a quantitative comparison of their kinetic and operational parameters is essential to assess practical viability. Catalyst selection is determined not only by the pollutant type but also by the need to maximize reaction rates and minimize catalyst consumption. The following kinetic framework, while discussed using enzymes as an example, is applicable to all catalytic systems.

Key kinetic parameters include K_M and k_{cat}. K_M measures the catalyst's affinity to its substrate. A lower K_M indicates stronger binding, making the catalyst suitable for treating dilute environmental plumes. For concentrated waste streams, a higher K_M may be acceptable. The turnover rate (k_{cat}) dictates the intrinsic degradation speed. A higher k_{cat} is desirable, enabling faster processing and lower catalyst loading. Catalytic efficiency (k_{cat}/K_M) combines affinity and speed into a single value describing performance under realistic conditions. A high k_{cat}/K_M indicates effectiveness even against trace pollutants.

For natural enzymes, superior catalytic efficiency is critically dependent on a narrow window of optimal pH, temperature, and medium composition. Their operational instability leads to rapid deactivation in non-ideal environmental conditions, rendering high intrinsic rates ineffective in real-world settings. Nanozymes redefine the kinetic-stability paradigm. While their intrinsic k_{cat}/K_M for a specific substrate may be lower than that of natural enzymes, their true advantage emerges under operational conditions. Their robustness across extreme pH, temperature, and inhibitory matrices ensures that a consistent and substantial reaction rate is maintained over extended periods.

A significant issue in the field is that kinetic parameters for nanozymes are often established using standard chromogenic substrates (e.g., TMB for PODs, 2,4-DCP with 4-AAP for laccases) and then extrapolated to actual pollutants, an approach that is frequently inaccurate. Enzymes and nanozymes can demonstrate vastly different activities toward various substances.[178] For accurate quantitative evaluation, kinetic studies should therefore be performed directly on the target contaminant. Examples of this good practice include Wang et al. reporting K_M for 17β-estradiol oxidation by a Tb^{3+} nanozyme,[179] Shams et al. for epinephrine oxidation by a

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laccase-mimicking nanozyme,[180] and Zhou et al. for paraoxon hydrolysis by a phosphatase-mimicking MOF.[126]

Reaction rates can be estimated using the Michaelis-Menten model. A critical challenge is that typical environmental concentrations ([S]) of micropollutants like antibiotics, PFAS, and endocrine disruptors are very low (often nanomolar range or even lower).[181–183] In a homogeneous system, with a typical enzyme $K_M \approx$ 0.2 mM and assuming [*S*] = 10 nM, the reaction rate is less than 1% of V_{max}, making the process extremely slow. Several strategies exist to overcome this limitation. One intuitive approach is to use catalysts with lower K_M. Some enzymes, such as certain cytochrome P450s, have K_M values in the micromolar range. However, even with K_M = 1 µM, the reaction rate remains near 1% of V_{max}, and K_M can vary significantly among structural analogues. Immobilizing enzymes onto carriers at high loadings (10–100 mg/g) creates local catalyst concentrations orders of magnitude higher than those achievable in homogeneous solution.[184] This allows even intrinsically slow reactions to process contaminants over extended time in flow-through systems. Carriers can also concentrate substrates, further enhancing reaction rates. Crucially, immobilization enables catalyst reuse. For example, Lloret et al. used immobilized laccase to achieve >90% removal of estrogens over 16 days in a continuous system.[185] However, immobilization can induce enzyme denaturation, diffusion limitations, and steric hindrance, negatively affecting catalytic activity.[186] While these effects have been extensively studied for enzymes, they have not yet been systematically evaluated for nanozyme or DNAzyme systems and require further investigation.

We summarize the comparative analysis of the three catalyst classes in terms of catalytic performance, operational stability, practicality, and environmental compatibility in Table 2. High substrate specificity is usually considered as one of the main advantages of enzymes, whereas the broad-spectrum activity of nanozymes (consequence of their low substrate specificity) can be viewed as an advantage for treating complex, multicomponent waste streams.

Table 2. Comparative performance analysis of catalysts

Characteristics	Parameter	Type of the catalyst		
		Enzyme	DNAzyme	Nanozyme
Catalytic performance	Substrate specificity	High	Low	Low
	Activity (k_{cat}, s^{-1})	High	Low/Medium	Medium
	Affinity to the substrate (K_M, mM)	High	Medium	Medium/High
Operational stability	Stability to abiotic environmental factors (stability to pH, inhibitors, extreme temperatures)	Low	Medium	High
	Stability to environmental factors (inhibitors, degrading enzymes, matrixes)	Low	Medium	Medium
Practical factors	Recovery	Medium	Medium	High
	Cost	High/Medium	High	Low
	Scalability	High	Medium	High
	Integration into technologies	High	Low	Medium
	Multifunctionality	Low	Medium	High
Environmental compatibility	Eco-Toxicity Potential	Low	Low	High
	Biodegradation	High	Medium	Low
Summary		High-efficient catalysts for degradation of wide ranges of xenobiotics, ready for practical applications.	Applicability limited to sensing and proof-of-concept studies	High-efficient artificial catalyst for degradation of wide range of xenobiotics

The comparison reveals that while natural enzymes lead in intrinsic catalytic performance, nanozymes achieve a comparable overall score by excelling in operational stability and practical factors. DNAzymes, though stable, are limited by their catalytic scope and scalability. This highlights the fundamental trade-off: enzymes are kinetically superior but fragile, while nanozymes are operationally robust but less specific and raise questions regarding their environmental fate. To date, biotechnological approaches using enzymes and microorganisms remain the dominant strategies for environmental remediation, as living systems contain cascades of enzymes facilitating complete pollutant mineralization. It is clear that artificial catalysts cannot wholly replace biocatalysts at this time. Rather than competing, these systems are complementary. The selection criterion must therefore shift from asking 'Which catalyst has the highest activity?' to 'Which catalyst system delivers the greatest cumulative degradation over time, meeting real-world requirements for cost, stability, and environmental safety?' The next grand challenge is to move beyond standalone catalysts and engineer integrated

nano-bio hybrid systems. Such systems would unify the high specificity and catalytic power of biology with the robustness and tunability of nanotechnology, paving the way for truly sustainable and efficient next-generation remediation technologies.

Conclusions and Future Directions

This review has systematically analyzed the catalytic mechanisms, kinetic efficiency, operational stability, and practical viability of three platforms for environmental remediation: natural enzymes, DNAzymes, and nanozymes. While enzymes remain the most developed and widely useful catalysts, nanozymes represent a highly promising technology for specific applications where robustness is paramount. Although enhancing nanozyme activity and specificity is a general research trend, driven largely by advances in functional materials design,[187] our analysis for bioremediation points toward several more impactful pathways for future research.

First, building synergistic hybrid enzyme-nanozyme systems, where a robust nanozyme performs an initial oxidation or pre-treatment (e.g., polymer degradation), can generate intermediates that are more susceptible to complete mineralization by a co-immobilized enzyme. Beyond cascading reactions, the nanozyme component can also serve as a protective scaffold, shielding the enzyme from pH extremes, proteolysis, or environmental inhibitors. Research should focus on sophisticated immobilization strategies (e.g., within metal-organic frameworks or multi-compartment hydrogels) that ensure efficient substrate channelling between catalytic sites while maintaining the stability of both components. Incorporating enzyme-functionalized particles into recoverable hydrogel bead matrices may further improve stability and reuse while enabling proximity-driven substrate channeling.[48,188]

Second, the development of biodegradable nanozymes is essential for practical implementation. For sustainable deployment, catalysts must be designed to perform their intended function and subsequently undergo safe decomposition under specific environmental conditions. The key challenge is to engineer such a controlled lifecycle without compromising the catalytic robustness required during the active remediation phase.

Third, the unique properties of nanozymes can be exploited to create multifunctional "all-in-one" platforms capable of capturing target pollutants and enhancing effective local concentrations and reaction rates. By functionalizing nanozyme surfaces with high-affinity biological agents or selective chelators, degradation rates may be accelerated beyond diffusion-limited kinetics. This strategy is particularly valuable for contaminants present at ng/L to µg/L levels.

Fourth, the research needs to move from proof-of-concept to real-life validations. Despite great promise at the laboratory benchmark scale, translation into practical utilization could be limited by high cost, cumbersome preparation, and poor stability. Some interesting strategies are very inspiring. For example, Farha's group developed a technology for the hydrolysis of organophosphorus nerve agents using MOFs integrated onto a fiber for potential applications such as protective masks and clothing.[189,190]

Finally, stimuli-responsive nanozymes activated by specific environmental triggers (e.g., a target pollutant, pH, or light) would enable precise spatial and temporal control over catalytic activity. Such on-demand functionality minimizes unnecessary ROS generation, reduces non-specific reactions, and enhances both the precision and safety of remediation.

The intelligent design of smart, responsive, and sustainable hybrid catalysts therefore represents a key pathway toward efficient and environmentally compatible remediation technologies capable of addressing complex present and future pollution challenges.

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Author contributions

Vasily Panferov: writing - original draft, visualization and conceptualization. Jung Heon Lee – writing - original draft, conceptualization. Juewen Liu: writing - original draft, conceptualization and supervision.

Conflicts of interest

There are no conflicts to declare".

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

Notes and references

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No primary research results, software or code have been included and no new data were generated or analysed as part of this review.