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Original Research Paper

Nanozymes As Emerging Therapeutic Tools in Oxidative Stress-Mediated Ocular Diseases

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Abstract

Oxidative stress is a central pathological factor in the onset and progression of various ocular diseases, including cataract, age-related macular degeneration, diabetic retinopathy, and glaucoma. Excessive generation of reactive oxygen species (ROS) disrupts the redox homeostasis of ocular tissues, leading to lipid peroxidation, protein modification, and cellular damage. Although conventional antioxidants have been explored to counteract oxidative damage, their clinical efficacy is often limited by poor stability, rapid degradation, and insufficient bioavailability. In this context, nanozymes nanomaterials possessing intrinsic enzyme-like catalytic activities have emerged as a promising therapeutic strategy. These nanostructures can mimic natural antioxidant enzymes such as superoxide dismutase, catalase, and peroxidase, enabling sustained and efficient ROS scavenging.

This review provides a comprehensive overview of the role of oxidative stress in ocular pathophysiology and highlights the therapeutic potential of nanozymes in mitigating ROS-mediated damage. Various classes of nanozymes, including metal-based, carbon-based, and polymeric systems, are discussed with respect to their catalytic mechanisms and biomedical applications. Special emphasis is placed on their use in ocular drug delivery, where nanozymes offer advantages such as enhanced stability, prolonged activity, and improved tissue penetration. Furthermore, recent preclinical studies demonstrating the efficacy of nanozymes in different ocular disease models are critically analyzed. Despite their promising attributes, concerns related to long-term safety, biocompatibility, and clinical translation remain to be addressed. Overall, nanozymes represent a novel and versatile platform with significant potential to advance the management of oxidative stress-mediated ocular disorders.

Keywords: Nanozymes; ROS scavenging; Oxidative stress; Ocular drug delivery; Antioxidant

Introduction

Ocular diseases arise from complex and multifactorial pathological mechanisms involving oxidative stress, inflammation, mitochondrial dysfunction, and environmental as well as systemic risk factors. Recent advances in nanotechnology have highlighted the potential of nanotherapeutic approaches to overcome conventional treatment limitations, particularly in enhancing drug delivery and targeting ocular tissues[1-2]. Among the key mechanisms, mitochondrial dysfunction plays a critical role in neurodegenerative ocular conditions such as glaucoma, where impaired energy metabolism and excessive production of reactive oxygen species (ROS) contribute to retinal ganglion cell degeneration[3]. In addition, chronic exposure to ultraviolet (UV) radiation has been identified as a major environmental risk factor, inducing oxidative damage to ocular structures and contributing to diseases such as cataract and age-related macular degeneration (AMD)[4]. AMD itself is a multifaceted disorder characterized by progressive degeneration of the macula, with both genetic and biochemical factors, including altered ocular fluid biomarkers, playing a significant role in disease progression[5-6]. Furthermore, long-term use of anti-glaucoma medications is often associated with ocular surface disease, which can exacerbate patient discomfort and compromise treatment outcomes[7-8]. Systemic conditions such as diabetes further contribute to ocular complications, not only through diabetic retinopathy but also via additional ocular disorders linked to metabolic dysregulation and vascular damage[9]. Diabetic retinopathy, in particular, is now recognized as both a vascular and inflammatory disease, involving complex interactions between hyperglycemia-induced oxidative stress, inflammation, and microvascular dysfunction[10].

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Collectively, these findings underscore the intricate interplay of molecular and environmental factors in ocular diseases and highlight the need for advanced therapeutic strategies that can effectively target these underlying mechanisms. Oxidative stress is a key factor in the development of various ocular diseases, resulting from an imbalance between reactive oxygen species (ROS) production and antioxidant defense systems. Elevated ROS levels cause damage to cellular components such as lipids, proteins, and DNA, thereby affecting both anterior and posterior segments of the eye. Retinal pigment epithelial (RPE) cells are particularly susceptible to oxidative injury, where ROS can induce ferroptotic cell death and contribute to retinal degeneration[11]. In age-related macular degeneration (AMD), oxidative stress promotes inflammation and cellular dysfunction, leading to progressive vision loss[12]. Additionally, oxidative damage has been implicated in other ocular conditions such as cataract, glaucoma, and dry eye disease, where it disrupts normal cellular homeostasis and enhances disease progression [13-14].

Oxidative Stress in Ocular Diseases

Oxidative stress is a fundamental contributor to the pathogenesis of various ocular diseases, arising from excessive generation of reactive oxygen species (ROS) and an imbalance in antioxidant defence systems. ROS are produced through mitochondrial dysfunction, environmental exposures such as ultraviolet radiation, and metabolic processes, leading to oxidative damage of lipids, proteins, and nucleic acids in ocular tissues[15-16]. In the lens, oxidative stress induces protein aggregation and crystallin modification, ultimately resulting in cataract formation[17-18]. In the retina, elevated intraocular pressure and mitochondrial dysfunction enhance ROS production, leading to retinal ganglion cell injury and contributing to glaucoma progression[19-20]. Similarly, retinal pigment epithelial cells undergo oxidative damage and ferroptotic cell death, which plays a critical role in degenerative retinal diseases such as age-related macular degeneration[11-12]. The cornea is also highly susceptible to oxidative injury due to direct environmental exposure, where ROS disrupt epithelial integrity and alter corneal transparency [21-22]. Furthermore, oxidative stress has been implicated in inflammatory signalling pathways and epigenetic alterations, exacerbating disease progression in diabetic cataract and other ocular conditions[23]. Overall, these findings demonstrate that ROS-mediated oxidative damage affects multiple ocular structures, including the lens, retina, and cornea, highlighting oxidative stress as a central mechanism underlying diverse ocular pathologies and a critical target for therapeutic intervention.

Nanozymes: Concept and Classification

Nanozymes are a class of nanomaterials that exhibit intrinsic enzyme-like catalytic activities, enabling them to mimic the function of natural enzymes under physiological conditions. These nanostructures possess the ability to catalyse biochemical reactions similar to endogenous enzymes such as superoxide dismutase, catalase, and peroxidase, thereby facilitating the regulation of reactive oxygen species (ROS) and redox homeostasis. Unlike natural enzymes, nanozymes offer advantages including higher stability, tunable catalytic activity, cost-effective synthesis, and resistance to harsh environmental conditions[23-24]. Over the past decade, significant progress has been made in the design and functionalization of nanozymes, expanding their applications in diverse biomedical fields such as antioxidant therapy, antimicrobial activity, biosensing, and disease treatment[25-26]. Despite their well-defined catalytic functions, the classification and precise definition of nanozymes remain an evolving concept, as their properties often lie at the interface of nanotechnology and enzymology[24]. Nanozymes are classified based on their enzyme-like catalytic activities involved in reactive oxygen species (ROS) regulation. They are mainly categorized into SOD-like, catalase-like, peroxidase-like, and multi-enzyme nanozymes, along with emerging oxidase-like systems, reflecting their functional role in mimicking natural antioxidant enzymes (Figure 1 and Table 1).

Superoxide Dismutase (SOD)-like Nanozymes

SOD-like nanozymes catalyze the dismutation of superoxide radicals ($O_2^{-}\bullet$) into hydrogen peroxide and oxygen, thereby reducing oxidative stress and protecting cells from radical-induced damage. These nanozymes play a critical role in maintaining intracellular redox balance, especially in high oxidative environments. Carbon-based nanozymes and metal-based systems, including single-atom and cerium-based nanostructures, have demonstrated efficient SOD-mimicking activity with well-defined catalytic mechanisms[23, 27].

Catalase-like Nanozymes

Catalase-like nanozymes facilitate the decomposition of hydrogen peroxide into water and oxygen, preventing its toxic accumulation and subsequent cellular damage. These nanozymes are essential for maintaining oxidative homeostasis and are widely explored in therapeutic applications targeting oxidative stress-related diseases. Transition metal-based nanozymes and engineered catalytic systems exhibit significant catalase-like activity and improved stability compared to natural enzymes[28,29].

Peroxidase-like Nanozymes

Peroxidase-like nanozymes catalyze the oxidation of various substrates in the presence of hydrogen peroxide, generating reactive intermediates that are useful in biosensing, antimicrobial activity, and catalytic degradation. These nanozymes are among the most extensively studied due to their high catalytic efficiency, ease of synthesis, and versatile

applications. Several transition metal-based and bioinspired nanozymes exhibit strong peroxidase-like behaviour[30-32].

Multi-enzyme Nanozymes

Multi-enzyme nanozymes are advanced nanostructures capable of mimicking multiple enzymatic activities simultaneously, such as combined SOD-, catalase-, and peroxidase-like functions. This multifunctionality enables enhanced catalytic efficiency and allows these nanozymes to regulate complex oxidative pathways more effectively. Recent developments include biomimetic, machine learning-assisted, and mitochondria-targeted nanozyme systems designed for improved therapeutic performance[33-35].

Oxidase-like and Other Emerging Nanozymes

In addition to classical antioxidant enzyme mimics, oxidase-like nanozymes and transition metal-based systems have been developed, expanding the functional diversity of nanozymes. These nanozymes catalyze oxidation reactions without requiring hydrogen peroxide and are widely applied in biosensing and catalytic processes. Their tunable catalytic activity and structural versatility make them promising candidates for advanced biomedical applications [36,37].

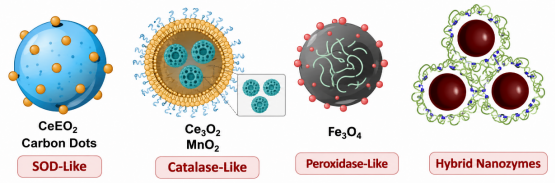

Figure 1. Types of Nanozymes

Table 1: Classification of Nanozymes

Type	Example	Activity	Application	Reference
SOD-like	CeO_2, Carbon dots	Superoxide scavenging	Antioxidant therapy	[38]
Catalase-like	CeO_2, MnO_2	H_2O_2 decomposition	Redox balance	[39]
Peroxidase-like	Fe_3O_4, Metal oxides	ROS modulation	Antimicrobial / sensing	[40]
Multi-enzyme	Hybrid nanozymes	Multiple ROS pathways	Complex disease therapy	[41]

Mechanism of Action of Nanozymes

Nanozymes exert their therapeutic effects through diverse catalytic mechanisms that mimic natural antioxidant enzymes. These mechanisms primarily involve regulation of reactive oxygen species (ROS), maintenance of redox homeostasis, and modulation of inflammation, which collectively contribute to their biomedical potential in oxidative stress-related diseases. Nanozymes exert their therapeutic effects primarily through modulation of reactive oxygen species (ROS) and restoration of cellular redox homeostasis. They mimic natural antioxidant enzymes such as superoxide dismutase (SOD), catalase, and peroxidase, thereby scavenging excess ROS and protecting cells from oxidative damage[24,42]. By catalytically converting harmful species like superoxide radicals and hydrogen peroxide into less toxic molecules, nanozymes help maintain intracellular redox balance[43,44]. Furthermore, nanozymes can regulate oxidative stress-mediated signalling pathways, thereby reducing inflammation and preventing cellular apoptosis in various disease conditions[45]. Their ability to participate in cascade catalytic reactions further enhances their efficiency in complex biological environments[46] (Shown in figure 2 and Table 2).

ROS Scavenging Activity

Nanozymes primarily function by scavenging reactive oxygen species (ROS) through enzyme-mimicking catalytic activities. Nanozymes exhibiting superoxide dismutase-, catalase-, and peroxidase-like functions convert toxic radicals such as superoxide anions and hydrogen peroxide into less harmful molecules, thereby protecting cellular components from oxidative damage[47-49]. This antioxidant capability is central to their therapeutic potential in oxidative stress-mediated diseases.

Restoration of Redox Balance

Through the regulating intracellular ROS levels, nanozymes help restore redox homeostasis, which is essential for normal cellular function. They maintain the balance between pro-oxidant and antioxidant systems, thereby preventing oxidative stress-induced cellular dysfunction. This redox-modulating property has been demonstrated in various pathological conditions, including fibrosis, metabolic disorders, and neurodegenerative diseases[50-51].

Anti-inflammatory Effects

Nanozymes also exhibit significant anti-inflammatory activity by modulating oxidative stress-related signalling pathways. Reduction in ROS levels leads to suppression of inflammatory mediators and inhibition of processes such as pyroptosis and immune cell overactivation. Consequently, nanozymes contribute to tissue protection, reduced inflammation, and enhanced healing[52-53].

Advanced Functional Mechanisms

Recent advancements have led to the development of multifunctional and responsive nanozyme systems, such as biomimetic and hydrogel-based nanozymes, which offer targeted and enhanced therapeutic effects. These systems not only scavenge ROS but also provide additional benefits such as infection control, targeted delivery, and improved tissue regeneration in complex conditions like diabetic wounds and inflammatory diseases[54-55].

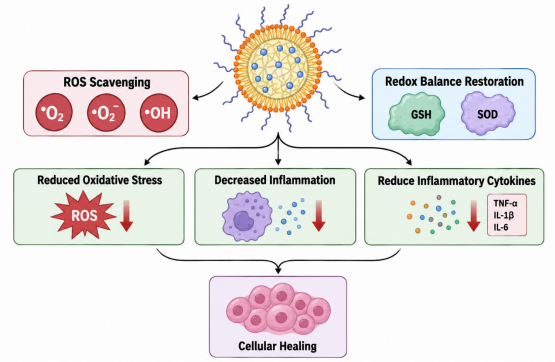

Figure 2. Mechanism of Action Nanozymes

Table 2: Mechanism of Nanozymes

Mechanism	Description	Outcome	Reference
ROS scavenging	Neutralization of superoxide & H_2O_2	Reduced oxidative stress	[38]
Redox balance restoration	Regulation of ROS/antioxidant levels	Cellular protection	[39]
Anti-inflammatory effect	Inhibition of cytokines & pathways	Reduced inflammation	[56]

Types of Nanozymes Used in Ocular Therapy

Metal-Based Nanozymes (CeO_2, Au, Fe_3O_4, etc.)

Metal-based nanozymes are the most extensively studied class in ocular therapy due to their strong catalytic activity and excellent redox properties. Cerium oxide (CeO_2) nanozymes, in particular, exhibit reversible redox cycling between Ce^{3+}/Ce^{4+} states, enabling efficient scavenging of reactive oxygen species (ROS) and restoration of redox balance in ocular tissues. These nanozymes have demonstrated significant therapeutic potential in conditions such as dry eye disease, cataract, glaucoma, and keratitis[38,39,57]. Additionally, iron-based and other transition metal nanozymes (e.g., Fe_3O_4, FeCoOx) show peroxidase-like and antibacterial activities, making them useful in treating infectious ocular diseases such as bacterial keratitis [58,59].

Carbon-Based Nanozymes

Carbon-based nanozymes, including carbon dots and graphene-derived nanomaterials, are widely explored due to their high biocompatibility, tunable surface properties, and intrinsic antioxidant activity. These nanozymes exhibit SOD- and catalase-like activities, enabling efficient ROS scavenging and anti-inflammatory effects. In ocular applications, carbon dot-based nanozymes have been successfully incorporated into hydrogels and eye-drop formulations to enhance ocular retention and therapeutic efficacy in diseases such as dry eye syndrome and retinal disorders[58-59,46]. Their favourable safety profile makes them particularly suitable for sensitive ocular environments.

Polymer-Based and Hybrid Nanozymes

Polymer-based and hybrid nanozymes combine nanomaterials with polymers or biomimetic coatings to improve stability, bioavailability, and targeted delivery. These systems often include nanozyme-loaded hydrogels, membrane-coated nanozymes, or multifunctional composites that enhance ocular surface retention and controlled drug release. Such nanozymes have shown promising results in treating dry eye disease, corneal injuries, and inflammatory ocular conditions by providing sustained ROS scavenging and anti-inflammatory effects[37, 54-55]. Additionally, hybrid nanozymes with multifunctional properties (e.g., anti-fungal, anti-MMP activity) have been developed for complex ocular infections such as fungal keratitis[60] (Table 4).

Table 3: Nanozymes in Ocular Diseases

Disease	Nanozyme	Mechanism	Outcome	Reference

Cataract	Fe-curcumin nanozyme	ROS scavenging	Anti-apoptotic effect	[57]
AMD	Rhodium nanozyme	Antioxidant + anti-inflammatory	Retinal protection	[61]
Glaucoma	CeMOF nanozyme	IOP regulation + redox balance	Neuroprotection	[62]
Dry eye	Cerium oxide nanozyme	ROS scavenging	Tear film stabilization	[38]
Retinal disease	Mitochondria-targeted nanozyme	Oxidative damage removal	Retinal recovery	[39]
Keratitis	Multi-enzyme nanozyme hydrogel	Antibacterial + ROS control	Corneal healing	[63]

Table 4: Types Used in Ocular Therapy

Type	Example	Advantage	Limitation	Reference
Metal-based	CeO_2, Fe_3O_4	High catalytic activity	Toxicity risk	[64]
Carbon-based	Carbon dots	Good biocompatibility	Lower activity	[9]
Polymer-based	Hydrogel nanozymes	Sustained release	Complex synthesis	[8]

Ocular Drug Delivery Challenges and Advantages of Nanozymes

Ocular drug delivery is inherently challenging due to the presence of multiple anatomical and physiological barriers that restrict drug absorption and reduce therapeutic efficacy. Structural barriers such as the corneal epithelium, conjunctiva, and blood-retinal barrier significantly limit drug permeability into both anterior and posterior segments of the eye[66-67]. In addition, dynamic precorneal factors including tear turnover, blinking, and nasolacrimal drainage rapidly eliminate administered formulations, resulting in low ocular bioavailability, particularly for conventional dosage forms such as eye drops[68-69]. Delivery to the posterior segment remains especially difficult, as drugs must overcome tightly regulated barriers, often necessitating invasive techniques such as intravitreal injections[70-71]. Furthermore, formulation-related challenges such as poor drug solubility, instability, and limited residence time further compromise therapeutic outcomes[72-73]. Recent advances in nanotechnology-based delivery systems, including nanoparticles, nanoemulsions, and nanosuspensions, have shown promise in improving drug penetration and retention; however, challenges related to long-term safety, scalability, and clinical translation still remain[74-78]. Nanozymes offer significant advantages over natural enzymes due to their enhanced stability, cost-effectiveness, and tunable catalytic properties. They remain active under harsh physiological conditions such as varying pH and temperature, unlike natural enzymes

which are prone to denaturation[24]. Additionally, nanozymes possess high surface area and modifiable structures, enabling improved catalytic efficiency and multifunctional activity in biomedical applications[42-43]. Their ability to mimic multiple enzyme activities and participate in cascade reactions further enhances their therapeutic and diagnostic potential[44-45]. These features make nanozymes promising candidates for advanced disease treatment and biosensing applications.

Therapeutic Applications

Nanozymes have emerged as promising therapeutic agents in ocular diseases primarily due to their potent antioxidant, anti-inflammatory, and catalytic properties, which enable effective modulation of oxidative stress a key factor in most eye disorders[38].

Cataract

Cataract formation is strongly associated with oxidative damage to lens proteins and epithelial cells. Nanozymes, particularly ROS-scavenging systems such as Fe-curcumin nanozymes, have demonstrated the ability to reduce oxidative stress and inhibit apoptosis in lens epithelial cells, thereby delaying cataract progression[57]. Additionally, antioxidant nanozyme systems help maintain lens transparency by restoring redox balance and preventing protein aggregation [38].

Age-Related Macular Degeneration (AMD)

In AMD, oxidative stress-induced damage to retinal pigment epithelial (RPE) cells plays a central role. Nanozymes such as rhodium-based systems have shown significant protective effects by reducing ROS levels, suppressing inflammation, and preserving retinal structure and function[37]. Furthermore, mitochondria-targeted nanozymes effectively eliminate oxidative damage in retinal tissues, thereby preventing neovascularization and disease progression[61].

Diabetic Retinopathy (DR)

Diabetic retinopathy involves chronic oxidative stress, inflammation, and vascular dysfunction. Nanozyme-based therapies, including selenium-based nanomedicines, have demonstrated potential in regulating ROS levels and improving retinal microenvironment under diabetic conditions[79]. Moreover, advanced nano-in-micro platforms provide sustained drug delivery and enhanced therapeutic efficacy in retinal disorders, suggesting promising applications in DR management 5.

Glaucoma

Glaucoma is characterized by increased intraocular pressure (IOP) and oxidative damage to retinal ganglion cells. Nanozymes, particularly cerium-based systems, have shown the ability to regulate redox balance and modulate NAD^+ metabolism, thereby reducing IOP and providing neuroprotection[36].Additionally, antioxidant nanozyme strategies help mitigate oxidative stress-mediated damage in glaucoma progression[38].

Dry Eye Disease

Dry eye disease is associated with oxidative stress, inflammation, and tear film instability. Multiple nanozyme-based systems, including cerium oxide nanozymes, carbon dot nanozyme hydrogels, and virus-inspired nanozymes, have demonstrated effective ROS scavenging, anti-inflammatory activity, and improved ocular surface retention[6,56, 39]. These systems also inhibit ferroptosis and enhance tissue repair, leading to significant therapeutic outcomes.

Keratitis (Bacterial/Fungal)

Nanozymes have shown strong antimicrobial and anti-inflammatory potential in keratitis treatment. Multi-enzyme mimicking nanozyme hydrogels and metal-based nanozymes exhibit antibacterial and antifungal activities while promoting corneal healing[63,80]. These systems also help in reducing oxidative damage and preventing infection-induced tissue destruction.

Uveitis and Retinal Inflammatory Disorders

In inflammatory ocular diseases such as uveitis, nanozyme-loaded nanogels have demonstrated targeted immunomodulatory effects along with ROS scavenging, leading to reduced inflammation and improved retinal protection[81].

Toxicity and Safety Concerns

Nanozymes, despite their promising catalytic and antioxidant properties, present certain toxicity and safety concerns that must be carefully evaluated before clinical application. One major issue is metal-induced toxicity, as many nanozymes are composed of transition metals that can generate excess reactive oxygen species (ROS) under certain conditions, leading to cellular damage instead of protection[64]. Additionally, dose-dependent cytotoxicity and long-term accumulation in biological systems remain critical challenges, particularly due to their non-biodegradable nature, which may result in organ toxicity and inflammatory responses[82]. Furthermore, advanced nanozyme systems such as multi-metallic and single-atom nanozymes may enhance catalytic efficiency but can also increase toxicity risks due to altered surface reactivity and bio-interactions[83-84]. Another important concern is biocompatibility and off-target effects, especially in biomedical applications, where improper targeting may affect healthy tissues[82]. Overall, while nanozymes offer significant therapeutic potential, balancing catalytic activity with biosafety, biodegradability, and controlled reactivity is essential for their safe clinical translation.

Challenges and Future Perspectives

Nanozymes have emerged as promising alternatives to natural enzymes; however, several limitations continue to hinder their widespread application. A primary challenge lies in their limited catalytic specificity and selectivity, as nanozymes often lack the precise substrate recognition exhibited by natural enzymes, thereby restricting their efficiency in complex biological and environmental systems [40, 64].

In addition, the catalytic activity of nanozymes is highly influenced by environmental conditions, including pH, temperature, and ionic strength, which may result in variability and reduced reproducibility across different applications[85]. Another significant concern involves biosafety and long-term toxicity, particularly for metal-based nanozymes, which may induce oxidative stress, unintended cellular damage, or bioaccumulation within tissues[64]. Furthermore, challenges related to scalable synthesis, structural heterogeneity, and batch-to-batch reproducibility remain critical barriers to their industrial and clinical translation[41]. These factors collectively limit the consistency and reliability required for regulatory approval and real-world applications. From a future perspective, the development of highly selective, biocompatible, and multifunctional nanozymes represents a key research direction. Advanced strategies such as single-atom nanozymes, biomimetic surface engineering, and hybrid nanoplatforms are expected to enhance catalytic precision and reduce toxicity. Moreover, the integration of nanozymes with targeted drug delivery systems and stimuli-responsive platforms holds significant potential for improving therapeutic efficacy and minimizing off-target effects[84,41]. Overall, addressing these challenges through rational design and interdisciplinary approaches will be essential to fully realize the potential of nanozymes in biomedical, environmental, and analytical applications.

Conclusion

Nanozymes have emerged as a transformative class of enzyme-mimicking nanomaterials, offering significant advantages over natural enzymes, including enhanced stability, cost-effectiveness, and tunable catalytic properties. Their ability to mimic multiple enzymatic activities and efficiently regulate reactive oxygen species (ROS) has positioned them as promising candidates in diverse fields such as biomedicine, environmental remediation, and biosensing. In particular, their application in managing oxidative stress has demonstrated considerable potential in the treatment of various diseases, including ocular disorders such as cataract, glaucoma, and retinal degeneration. Despite these advancements, several critical challenges remain to be addressed. The relatively low substrate specificity compared to natural enzymes, along with sensitivity to environmental conditions such as pH and temperature, can limit their catalytic efficiency and reproducibility. Additionally, concerns related to long-term biocompatibility, potential toxicity, and bioaccumulation especially in metal-based nanozymes pose significant barriers to their clinical translation. Issues related to scalable synthesis, structural uniformity, and batch-to-batch consistency further complicate their industrial and therapeutic applications. To overcome these limitations, current research is increasingly focused on the rational design and engineering of next-generation nanozymes. Strategies such as the development of single-atom nanozymes, biomimetic surface modifications, and multifunctional hybrid nanostructures are being explored to enhance catalytic specificity, reduce toxicity, and improve overall performance. Furthermore, the integration of nanozymes with targeted drug delivery systems and stimuli-responsive platforms offers new opportunities for achieving controlled and site-specific therapeutic effects. In conclusion, while challenges persist, the continuous evolution of nanozyme design, supported by interdisciplinary approaches, is expected to unlock their full potential. With further optimization in terms of safety, efficiency, and precision, nanozymes are poised to play a pivotal role in the development of advanced therapeutic and diagnostic technologies in the near future.

Conflict of Interest:

The authors declare no conflict of interest

References

1. Reimondez-Troitino S, Csaba N, Alonso MJ, de la Fuente M. Nanotherapies for the treatment of ocular diseases. *Eur J Pharm Biopharm.* 2015; 95:279–293. doi: 10.1016/j.ejpb.2015.02.019
2. Fangueiro JF, Silva AM, Garcia ML, Souto EB. Current nanotechnology approaches for the treatment and management of diabetic retinopathy. *Eur J Pharm Biopharm.* 2015;95(Pt B):307–322. doi: 10.1016/j.ejpb.2014.12.023
3. Kamel K, Farrell M, O'Brien C. Mitochondrial dysfunction in ocular disease: Focus on glaucoma. *Mitochondrion.* 2017; 36:44–53. doi: 10.1016/j.mito.2017.05.004
4. Yam JCS, Kwok AKH. Ultraviolet light and ocular diseases. *Int Ophthalmol.* 2014; 34:383–400. doi:10.1007/s10792-013-9791-x
5. Kersten E, Paun CC, Schellevis RL, Hoyng CB, Delcourt C, Lengyel I, et al. Systemic and ocular fluid compounds as potential biomarkers in age-related macular degeneration. *Surv Ophthalmol.* 2017;62(1):9–39. doi: 10.1016/j.survophthal.2017.05.003
6. Mitchell P, Liew G, Gopinath B, Wong TY. Age-related macular degeneration. *Lancet.* 2018;392(10153):1147–1159. doi:10.1016/S0140-6736(18)31550-2
7. Boso ALM, Gasperi E, Fernandes L, Costa VP, Alves M. Impact of ocular surface disease treatment in patients with glaucoma. *Clin Ophthalmol.* 2020; 14:103–111. doi:10.2147/OPTH.S229815
8. Andole S, Senthil S. Ocular surface disease and anti-glaucoma medications: Various features, diagnosis, and management guidelines. *Semin Ophthalmol.* 2023;38(2):158–166. doi:10.1080/08820538.2022.2094714

9. Feldman-Billard S, Dupas B. Eye disorders other than diabetic retinopathy in patients with diabetes. *Diabetes Metab.* 2021;47(3):101279. doi: 10.1016/j.diabet.2021.101279
10. Semeraro F, Morescalchi F, Cancarini A, Russo A, Rezzola S, Costagliola C. Diabetic retinopathy, a vascular and inflammatory disease: Therapeutic implications. *Diabetes Metab.* 2019;45(6):517–527. doi: 10.1016/j.diabet.2019.04.002
11. Totsuka K, Ueta T, Uchida T, Roggia MF, Nakagawa S, Vavvas DG, et al. Oxidative stress induces ferroptotic cell death in retinal pigment epithelial cells. *Exp Eye Res.* 2019; 181:316–324. doi: 10.1016/j.exer.2018.08.019
12. Abokyi S, To CH, Lam TT. Central role of oxidative stress in age-related macular degeneration: Evidence from molecular mechanisms and animal models. *Oxid Med Cell Longev.* 2020; 2020:7901270. doi:10.1155/2020/7901270
13. Nita M, Grzybowski A. The role of reactive oxygen species and oxidative stress in the pathomechanism of age-related ocular diseases and other pathologies of the anterior and posterior eye segments in adults. *Oxid Med Cell Longev.* 2016; 2016:3164734. doi:10.1155/2016/3164734
14. Seen S, Tong L. Dry eye disease and oxidative stress. *Acta Ophthalmol.* 2018;96(4):e412–e420. doi:10.1111/aos.13526
15. Pinazo-Duran MD, Gallego-Pinazo R, García-Medina JJ, Zanón-Moreno V, Nucci C, Dolz-Marco R, et al. Oxidative stress and its downstream signaling in aging eyes. *Clin Interv Aging.* 2014; 9:637–652. doi:10.2147/CIA.S52662
16. Ahmad A, Ahsan H. Biomarkers of inflammation and oxidative stress in ophthalmic disorders. *J Immunoassay Immunochem.* 2020. doi:10.1080/15321819.2020.1726774
17. Ho MC, Peng YJ, Chen SJ, Chiou SH. Senile cataracts and oxidative stress. *J Chin Med Assoc.* 2010;73(6):295–301. doi: 10.1016/j.jcgg.2010.10.006
18. Marsili S, Salganik RI, Albright CD, Freel CD, Johnsen S, Peiffer RL, et al. Cataract formation in a strain of rats selected for high oxidative stress. *Exp Eye Res.* 2004;79(5):595–612. doi: 10.1016/j.exer.2004.06.008
19. Moreno MC, Campanelli J, Sande P, Sáenz DA, Keller Sarmiento MI, Rosenstein RE. Retinal oxidative stress induced by high intraocular pressure. *Free Radic Biol Med.* 2004;37(6):803–812. doi: 10.1016/j.freeradbiomed.2004.06.001
20. Ferreira SM, Lerner SF, Brunzini R, Evelson PA, Llesuy SF. Oxidative stress markers in aqueous humor of glaucoma patients. *Am J Ophthalmol.* 2004;137(1):62–69. doi:10.1016/S0002-9394(03)00788-8
21. Shoham A, Hadziahmetovic M, Dunaief JL, Mydlarski MB, Schipper HM. Oxidative stress in diseases of the human cornea. *Free Radic Biol Med.* 2008;45(8):1047–1055. doi: 10.1016/j.freeradbiomed.2008.07.021
22. Cejka C, Cejkova J. Oxidative stress to the cornea and advances in treatment of corneal oxidative injuries. *Oxid Med Cell Longev.* 2015; 2015:591530. doi:10.1155/2015/591530
23. Guo Z, Ma X, Zhang RX, Yan H. Oxidative stress, epigenetic regulation and pathological processes of lens epithelial cells underlying diabetic cataract. *Ann Eye Sci.* 2023. doi: 10.1016/j.aopr.2023.10.001
24. Wei H, Gao L, Fan K, Liu J, He J, Qu X, Wang E, et al. Nanozymes: A clear definition with fuzzy edges. Nano Today. 2021; 40:101269. doi: 10.1016/j.nantod.2021.101269
25. Ren X, Chen D, Wang Y, Li H, Zhang Y, Chen H, Li X, Huo M. Nanozymes: recent development and biomedical applications. J Nanobiotechnol. 2022; 20:92. doi:10.1186/s12951-022-01295-y
26. Yang D, Chen Z, Gao Z, Tammina SK, Yang Y. Nanozymes used for antimicrobials and their applications. Colloids Surf B Biointerfaces. 2020; 195:111252. doi: 10.1016/j.colsurfb.2020.111252
27. Hamed EM, Fung FM, Li SFY. Bimetallic Cu/Zn single-atom nanozyme with superoxide dismutase-like activity. Mater Chem. 2023:101809. doi: 10.1016/j.mtchem.2023.101809
28. Xu D, Wu L, Yao H, Zhao L. Catalase-like nanozymes: Classification, catalytic mechanisms, and their applications. Small. 2022; 18:2203400. doi:10.1002/smll.20220340
29. Zhang W, Zhao M, Chu D, Chen H, Cui B, Ning Q, et al. Dual-ROS-scavenging and dual-lingering nanozyme-based eye drops alleviate dry eye disease. *J Nanobiotechnol.* 2024; 22:229. doi:10.1186/s12951-024-02499-0
30. Bilal M, Khaliq N, Ashraf M, Hussain N, Baqar Z, Zdarta J, et al. Enzyme mimic nanomaterials as nanozymes with catalytic attributes. Colloids Surf B Biointerfaces. 2022; 214:112950. doi: 10.1016/j.colsurfb.2022.112950
31. Yang D, Chen Z, Gao Z, Tammina SK, Yang Y. Nanozymes used for antimicrobials and their applications. Colloids Surf B Biointerfaces. 2020; 195:111252. doi: 10.1016/j.colsurfb.2020.111252
32. Jangi ARH, Jangi MRH, Jangi SRH. Detection mechanism and classification of peroxidase mimic based colorimetric sensors: A brief overview. Chin J Chem Eng. 2020;28(6):1585–1597. doi: 10.1016/j.cjche.2020.01.020
33. Su L, Qin S, Xie Z, Wang L, Khan K, Tareen AK, et al. multi-enzyme activity nanozymes for biosensing and disease treatment. Coord Chem Rev. 2022; 463:214784. doi: 10.1016/j.ccr.2022.214784
34. Ge F, Gao Y, Jiang Y, Yu Y, Bai Q, Liu Y, et al. Design and performance analysis of multi-

enzyme activity-doped nanozymes assisted by machine learning. Colloids Surf B Biointerfaces. 2024; 235:114468. doi: 10.1016/j.colsurfb.2024.114468
35. Zhang Y, Khalique A, Du X, Gao Z, Wu J, Zhang X, et al. Biomimetic design of mitochondria-targeted hybrid nanozymes as superoxide scavengers. Nat Commun. 2023.
36. Lin Z, Yuan J, Niu L, Zhang Y, Zhang X, Wang M, et al. Oxidase mimicking nanozyme: Classification, catalytic mechanisms and sensing applications. Nano Today. 2021; 36:101076. doi: 10.1016/j.nantod.2021.101076
37. Zhang D, Chen Q, Ren Q, Zhong W, Zhang H, Wang G, et al. Transition metal-based nanozymes: Classification, catalytic mechanisms and emerging biomedical applications. Coord Chem Rev. 2024;215771. doi: 10.1016/j.ccr.2024.215771
38. Xue, B.; Lu, Y.; Wang, S.; Xiao, Q.; Luo, X.; Wang, Y.; Yan, X.; Yang, Z.; Jiang, B. The Emerging Role of Nanozymes in Ocular Antioxidant Therapy. Nano Today 2024, 58, 102448. https://doi.org/10.1016/j.nantod.2024.102448
39. Zou H, Hong Y, Xu B, Wang M, Xie H, Lin Q. Multifunctional cerium oxide nanozymes with high ocular surface retention for dry eye disease treatment achieved by restoring redox balance. *Acta Biomater.* 2024. doi: 10.1016/j.actbio.2024.07.003
40. Unnikrishnan, B.; Lien, C.-W.; Chu, H.-W.; Huang, C.-C. A Review on Metal Nanozyme-Based Sensing of Heavy Metal Ions: Challenges and Future Perspectives. J. Hazard. Mater. 2021, 401, 123397.
https://doi.org/10.1016/j.jhazmat.2020.123397
41. Zou, Z.; Bi, X.; Ma, H.; Chen, L.; Jin, H.; Gong, S.; Li, X.; Liu, X. Recent Advances in Nanozymes for the Treatment of Atherosclerosis. Int. J. Nanomed. 2025, 9447–9472. https://doi.org/10.2147/IJN.S540010
42. Wang, Q.; Wei, H.; Zhang, Z.; Wang, E.; Dong, S. Nanozyme: An Emerging Alternative to Natural Enzyme for Biosensing and Immunoassay. TrAC Trends Anal. Chem. 2018, 105, 218–224. https://doi.org/10.1016/j.trac.2018.05.012
43. Cai, X.; Jiao, L.; Yan, H.; Wu, Y.; Gu, W.; Du, D.; Lin, Y.; Zhu, C. Nanozyme-Involved Biomimetic Cascade Catalysis for Biomedical Applications. Mater. Today 2021, 44, 211–228. https://doi.org/10.1016/j.mattod.2020.12.005
44. Meng, F.; Zhu, P.; Yang, L.; Xia, L.; Liu, H. Nanozymes with Atomically Dispersed Metal Centers: Structure–Activity Relationships and Biomedical Applications. Chem. Eng. J. 2023, 452, 139411. https://doi.org/10.1016/j.cej.2022.139411
45. Cheng, C.; Wang, H.; Zhao, J.; Wang, Y.; Zhao, G.; Zhang, Y.; Liu, X.; Wang, Y. Advances in the Application of Metal Oxide Nanozymes in Tumor Detection and Treatment. Colloids Surf. B Biointerfaces 2024, 235, 113767. https://doi.org/10.1016/j.colsurfb.2024.113767
46. Xue, B.; Ge, M.; Fan, K.; Huang, X.; Yan, X.; Jiang, W.; Jiang, B.; Yang, Z. Mitochondria-Targeted Nanozymes Eliminate Oxidative Damage in Retinal Neovascularization Disease. J. Control. Release 2022, 350, 271–283. https://doi.org/10.1016/j.jconrel.2022.08.026
47. Xia M, Ge L, Rogachev A, Wang Z, Wang H. Recent advances in antioxidant cerium-based nanozymes: Catalytic mechanisms and biomedical applications. Chin J Anal Chem. 2025;100640. doi: 10.1016/j.cjac.2025.100640
48. Wang Z, Hou Y, Tang G, Li Y, Zhao Y, Yu Y, et al. Intelligent nanozymes: Biomimetic design, mechanisms and biomedical applications. Fundam Med Res Express. 2024. doi: 10.1016/j.fmre.2024.11.013
49. Lopez-Cantu DO, González-González RB, Melchor-Martínez EM, Hernández Martinez SA, Araújo RG, Parra-Arroyo L, et al. Enzyme-mimicking capacities of carbon-dots nanozymes: Properties, catalytic mechanism, and applications. Int J Biol Macromol. 2021. doi: 10.1016/j.ijbiomac.2021.11.112
50. Xu Y, Zhou Z, Deng N, Fu K, Zhu C, Hong Q, Shen Y, Liu S, Zhang Y. Molecular insights of nanozymes from design to catalytic mechanism. Sci China Chem. 2023;66(5):1318–1335. doi:10.1007/s11426-022-1529-y
51. Sen A, Oswalia J, Yadav S, Vachher M, Nigam A. Recent trends in nanozyme research and their potential therapeutic applications. Curr Res Biotechnol. 2024;100205. doi: 10.1016/j.crbiot.2024.100205
52. Li T, Huo Y, Ji H, Yan W, Jia M, Xiong C, et al. Multifunctional L-arginine-linked melanin nanozyme for theranostic applications in liver fibrosis. J Colloid Interface Sci. 2025;138872. doi: 10.1016/j.jcis.2025.138872
53. Mohsin M, Shams F, Li H, Alam A, Xia C, Fan L, et al. Nanozymes in neuropathic pain: Strategies bridging oxidative stress, mitochondrial repair, and neuroimmune modulation. J Neuroinflammation. 2025. doi:10.1186/s12974-025-03456-w
54. Tai QD, Tang Y, Xie ST, Ye YY, Tang X, Lyu Q, et al. Glucose-responsive nanozyme hydrogel for glycemic control and diabetic wound healing. *Mater Today Bio.* 2025;102405. doi: 10.1016/j.mtbio.2025.102405
55. Hu C, Wang Y, Liao S, Zhang L, Li C, Zhou D, et al. Neutrophil–macrophage hybrid membrane-coated nanozyme for ulcerative colitis treatment. *J Nanobiotechnol.* 2025; 23:43. doi:10.1186/s12951-025-03123-5
56. Yu H, Yu X, Huang Y, Yu T, Lan H, Zhang Q, et al. Engineering biocompatible carbon dots nano-enzyme hydrogel for antioxidative and anti-inflammatory treatment of dry eye disease. *J Control Release.* 2025. doi:10.1016/j.jconrel.2025.01.081

57. Gao X, Li K, Huang Y, Long Z, Xiang Y, Zheng W, et al. Fe-curcumin nanozymes-mediated reactive oxygen species scavenging and anti-apoptotic effects on age-related cataracts. *Mater Today Bio.* 2025;101850. doi: 10.1016/j.mtbio.2025.101850
58. Kong H, Li W, Tian X, Wu J, Wang Y, Zhang P. NIR-activated FeCoOx nanozymes with tri-modal synergy for drug-resistant bacterial keratitis. *Chem Eng J.* 2025;166724. doi: 10.1016/j.cej.2025.166724
59. Geng X, Zhang H, Zhang N, Li J, Zhao M. Iron-doped nanozymes with spontaneous peroxidase mimic activity as antibacterial therapy for bacterial keratitis. *[Journal details not available]*
60. Lyu S, Yin M, Wang H, Cao D, Ma L, Zhang T, et al. Multifunctional ceria nanozyme with dual anti-fungal/anti-MMP activity for severe fungal keratitis. *Chem Eng J.* 2025;169421. doi: 10.1016/j.cej.2025.169421
61. Sun, Q.; Ni, Y.; Wang, K.; Zhang, H.; Liu, J.; Xu, L.; Zhao, Y. Rhodium Nanozyme Mitigates RPE Degeneration in Age-Related Macular Degeneration. Mater. Today Bio 2024, 101230. https://doi.org/10.1016/j.mtbio.2024.101230
62. Zhang, Y.; Chen, M.; Tian, Y.; Qin, B.; Chen, X.; Zhou, Y.; Huang, J.; Yang, M.; Sun, X.; Lei, Y.; Chen, Y. CeMOF Nanozyme Regulates Intraocular Pressure for Glaucoma Treatment. 2025. https://doi.org/10.1002/VIW.20250039
63. Shi, D.; Qi, X.; Ma, L.; Zhao, L.; Dou, S.; Wang, Y.; Zhou, Q.; Zhang, Y.; Yang, C.; Wang, H.; Xie, L. Fabrication of nanozyme-thixotropic anionic hydrogel coating with multi-enzyme-mimicking activity for the treatment of fungal keratitis. Chemical Engineering Journal 2024, 486, 150264. https://doi.org/10.1016/j.cej
64. Ghorbani, M.; Derakhshankhah, H.; Jafari, S.; Salatin, S.; Dehghanian, M.; Falahati, M.; Ansari, A. Nanozyme Antioxidants as Emerging Alternatives for Natural Antioxidants: Achievements and Challenges in Perspective. Nano Today 2019, 29, 100775. https://doi.org/10.1016/j.nantod.2019.100775
65. Yu, H.; Yu, X.; Huang, Y.; Yu, T.; Lan, H.; Zhang, Q.; Huang, Y.; Peng, X.; Jiang, Z. Engineering biocompatible carbon dots nano-enzymes hydrogel for efficient antioxidative and anti-inflammatory treatment of dry eye disease. Journal of Controlled Release 2025, 381, 113490. https://doi.org/10.1016/j.jconrel.2025.01.081
66. Urtti, A. (2006). Challenges and obstacles of ocular pharmacokinetics and drug delivery. Adv. Drug Deliv. Rev. https://doi.org/10.1016/j.addr.2006.07.027
67. del Amo, E. M.; Urtti, A. (2008). Current and future ophthalmic drug delivery systems. Adv. Drug Deliv. Rev. https://doi.org/10.1016/j.addr.2008.02.001
68. Gaudana, R.; Jwala, J.; Boddu, S. H. S.; Mitra, A. K. (2009). Recent perspectives in ocular drug delivery. Pharm. Res. https://doi.org/10.1007/s11095-008-9694-0
69. Bourlais, C. L.; Acar, L.; Zia, H.; Sado, P. A.; Needham, T.; Leverge, R. (1998). Ophthalmic drug delivery systems—Recent advances. Prog. Retin. Eye Res.
70. Patel, A.; Cholkar, K.; Agrahari, V.; Mitra, A. K. (2013). Ocular drug delivery systems: An overview. World J. Pharmacol. https://doi.org/10.5497/wjp.v2.i2.47
71. Huang, D.; Chen, Y.-S.; Rupenthal, I. D. (2018). Overcoming ocular drug delivery barriers through the use of physical forces. Adv. Drug Deliv. Rev. https://doi.org/10.1016/j.addr.2017.09.008
72. Vandamme, T. F. (2001). Microemulsions as ocular drug delivery systems. Adv. Drug Deliv. Rev. https://doi.org/10.1016/S1350-9462(01)00017-9
73. Ammar, H. O.; Salama, H. A.; Ghorab, M.; Mahmoud, A. A. (2009). Nanoemulsions as ophthalmic drug delivery systems. AAPS PharmSciTech https://doi.org/10.1208/s12249-009-9226-3
74. Sahoo, S. K.; Dilnawaz, F.; Krishnakumar, S. (2008). Nanotechnology in ocular drug delivery. Drug Discov. Today https://doi.org/10.1016/j.drudis.2008.04.018
75. Diebold, Y.; Calonge, M. (2010). Applications of nanoparticles in ophthalmology. Prog. Retin. Eye Res. https://doi.org/10.1016/j.preteyeres.2010.01.002
76. Fathi-Karkan, S. et al. (2024). Nanosuspensions in ophthalmology. Int. J. Pharm. https://doi.org/10.1016/j.ijpharm.2024.124226
77. Al Yabhouni, S. A. et al. (2024). Nanocarrier-based ocular drug delivery. Int. J. Pharm. https://doi.org/10.1016/j.ijpharm.2024.124899
78. Chen, Y.; Ye, Z.; Chen, H.; Li, Z. (2024). Nanomedicine-based drug delivery for cataract treatment. Int. J. Nanomedicine https://doi.org/10.2147/IJN.S463679
79. Jiang, B.; Zhang, L.; Hong, N.; Wen, Y.; Li, A.; Shi, Y.; Dong, F. Recent Progress in Selenium Nanomedicines for Ocular Diseases. Int. J. Nanomed. 2026. https://doi.org/10.2147/IJN.S583175
80. Wang, H.; Liu, Y.; Ma, L.; Sun, X.; Li, N.; Sui, X.; Qi, X.; Dou, S.; Li, T.; Shi, W.; Wang, T. Antibiotic Nanozyme Hydrogel Depot for MDR Bacterial Keratitis Therapy. Mater. Today Bio 2026, 36, 102602. https://doi.org/10.1016/j.mtbio.2025.102602
81. Jin, Y.; Cai, D.; Mo, L.; Jing, G.; Zeng, L.; Cheng, H.; Guo, Q.; Dai, M.; Wang, Y.; Chen, J.; Chen, G.; Li, X.; Shi, S. Multifunctional Nanogel Loaded with Cerium Oxide Nanozyme and CX3CL1 Protein for Retinal Protection in Uveitis.

Biomaterials 2024, 309, 122617. https://doi.org/10.1016/j.biomaterials.2024.122617
82. Falahati, M.; Sharifi, M.; Ten Hagen, T. L. M. Explaining Chemical Clues of Metal Organic Framework-Nanozyme Nano-/Micro-Motors in Targeted Treatment of Cancers: Benchmarks and Challenges. J. Nanobiotechnol. 2022. https://doi.org/10.1186/s12951-022-01375-z
83. Phan-Xuan, T.; Breitung, B.; Dailey, L. A. Nanozymes for Biomedical Applications: Multi-Metallic Systems May Improve Activity but at the Cost of Higher Toxicity? WIREs Nanomed. Nanobiotechnol. 2024, 16, e1981. https://doi.org/10.1002/wnan.1981
84. Haider, S. N.-U.-Z.; Qaiser, M. A.; Qureshi, W. A.; Ali, A.; Khan, S.; Moradian, J. M.; Naveed, A.; Liu, Q.; Yang, J. Recent Advances in Single-Atom Nanozymes for Improved Food Safety and Nutritional Analysis. Int. J. Food Sci. 2026. https://doi.org/10.1155/ijfo/5087992
85. Elkomy, H. A.; El-Naggar, S. A.; Elantary, M. A.; Gamea, S. M.; Ragab, M. A.; Basyouni, O. M.; Mouhamed, M. S.; Elnajjar, F. F. Nanozyme as Detector and Remediator to Environmental Pollutants: Current Situation and Future Prospective. Environ. Sci. Pollut. Res. 2024, 31, 3435–3465. https://doi.org/10.1007/s11356-023-31429-0