• Review Article •

Micro/nanoplastics and eye health: a review

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Abstract

● Micro/nanoplastics (M/NPs) have become pervasive environmental pollutants, posing significant risks to human health through various exposure routes, including ingestion, inhalation, and direct contact. This review systematically examined the potential impacts of M/NPs on ocular health, focusing on exposure pathways, toxicological mechanisms, and resultant damage to the eye. Ocular exposure to M/NPs can occur *via* direct contact and oral ingestion, with the latter potentially leading to the penetration of particles through ocular biological barriers into ocular tissues. The review highlighted that M/NPs can induce adverse effects on the ocular surface, elevate intraocular pressure, and cause abnormalities in the vitreous and retina. Mechanistically, oxidative stress and inflammation are central to M/NP-induced ocular damage, with smaller particles often exhibiting greater toxicity. Overall, this review underscored the potential risks of M/NPs to ocular health and emphasized the need for further research to elucidate exposure mechanisms, toxicological pathways, and mitigation strategies.

● **KEYWORDS:** micro/nanoplastics; exposure; ocular; toxicity

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INTRODUCTION

Plastic products have become ubiquitous globally due to their convenience, durability, and low cost. Since the commercialization of plastics in the 1950s, global plastic production has surged, exceeding 390 million tons in 2022[1]. While 49.6% of plastic waste is converted to energy and 27% is collected for recycling[2], substantial amounts continue to enter ecosystems. This untreated waste accumulates in the environment and degrades into microplastics (MPs; <5 mm) and nanoplastics (NPs; 1–1000 nm) through photochemical degradation, physical wear, and biological processes[3-4].

These particles pose significant health risks through three primary exposure routes: oral ingestion, respiratory inhalation, and dermal contact, with ingestion being the most prevalent[5-6]. Current estimates suggest humans ingest 0.1–5 g of MPs weekly, amounting to 39 000–52 000 particles annually[6-7]. This pervasive exposure has been detected in multiple human systems, including the digestive, respiratory, nervous system, cardiovascular, and reproductive systems[8-13]. These particles induce various health threats, such as elevated inflammatory markers [*e.g.*, interleukin (IL)-6] in lung tissue and decreased lung function[14-15]. Furthermore, plastic particles entering the brain can interact with neuronal protein fibers (*e.g.*, α-synuclein), inducing oxidative stress and inflammatory responses, possibly increasing the risk of neurodegenerative diseases[10].

As plastic pollution becomes a global environmental concern, its health impacts, including links to ocular health, have gained increasing attention. This review focuses on mammalian and human models to systematically explore the effects of micro/nanoplastics (M/NPs) on ocular health. By examining exposure pathways, impacts, and damage mechanisms, it aims to provide a scientific foundation for understanding the ocular risks of M/NPs and guide future research directions.

OCULAR EXPOSURE PATHWAYS

Ocular exposure to M/NPs primarily occurs through direct contact (ocular surface exposure) and oral ingestion. It is noteworthy that inhaled M/NPs can translocate from the lung tissue into the bloodstream and subsequently migrate to other tissues[16]. Thus, it is plausible that M/NPs entering the bloodstream *via* inhalation could also translocate to the eye.

However, no animal studies have utilized inhalation as an intervention method, and its impact on ocular health remains unexplored. Therefore, inhalation exposure will not be the focus of this review.

Direct Contact Choi *et al*[17] first detected MPs in pterygium tissue, primarily composed of polyethylene (PE) and polystyrene (PS). Subsequently, MPs (notably PE) were identified in the tear fluid and meibum of patients with dry eye disease (DED)[18]. These findings suggest that MPs in the environment may directly come into contact with the ocular surface.

Allen *et al*[19] confirmed the atmospheric transport of MPs by detecting them in remote mountainous regions. Dris *et al*[20] and Zheng *et al*[21] further reported high concentrations of MPs in both indoor and outdoor air, highlighting airborne exposure as a significant pathway. The ocular surface, comprising the corneal and conjunctival epithelia, is in direct contact with the external environment. Given the direct interface of the corneal and conjunctival epithelia with the external environment, the ocular surface is highly susceptible to airborne MPs, particularly in polluted or poorly ventilated settings.

Ophthalmic products may represent another significant source of exposure M/NPs for the eyes. Patients with chronic ocular conditions require long-term use of eye drops for treatment, with eye drop bottles predominantly manufactured from plastic. The increasing prevalence of myopia has also led to greater use of contact lenses, thereby amplifying the dependence on plastic products such as contact lens solution bottles and storage cases. Samandra *et al*[22] have identified significant risks associated with MP release from pharmaceutical containers. During usage and transportation, these plastic products may undergo structural degradation due to surface cracking and mechanical stress[23-24]. Furthermore, interactions with drugs and their additives can induce polymer oxidation and chain cleavage, releasing M/NPs and associated byproducts[24]. Notably, MPs have been detected in artificial tears available in Republic of Korea[25]. This study estimated that patients using artificial tears four times daily could be exposed to 730 particles annually, though discarding the first two drops reduced exposure to 204 particles.

Contact lenses themselves may directly release M/NPs. Liu *et al*[26] investigated the effects of varying durations of sunlight exposure on silicone hydrogel contact lenses, calculating that a single contact lens could release approximately 90 698 particles during one year of wear. This study introduces a novel pathway for ocular M/NP exposure through contact lens usage. Given the widespread prevalence of myopia and extensive use of contact lenses globally, this exposure pathway warrants particular attention.

M/NPs in Cosmetics and Personal Care Products Plastic particles are widely utilized in cosmetic products for various functional purposes, including filling, emulsification, and enhancing aesthetic properties[27]. These particles also serve as physical abrasives that facilitate exfoliation, scrubbing, and cleansing[28]. The prolonged use of eye cosmetics and skin care products containing M/NPs, such as mascara, eyeshadow, and eye creams, may significantly elevate the risk of ocular exposure to M/NPs. Furthermore, spray-based cosmetics and personal care products can generate aerosols during application, thus increasing the likelihood of direct M/NP contact with the ocular surface.

Oral Ingestion The human eye is protected by several biological barriers, including the inner blood-retina barrier (iBRB) and outer blood-retina barrier (oBRB), which are critical for maintaining retinal homeostasis[29]. Previous studies have confirmed that ingested PS-NPs can disrupt and penetrate the blood-brain barrier (BBB) in mice, leading to accumulation in brain tissue[30-31]. The iBRB shares significant structural homology with the BBB, as both barriers are principally constituted by tight junctions between vascular endothelial cells[32-33]. Given this, PS-NPs may also potentially penetrate the iBRB and access retinal tissue.

Xiong *et al*[34] demonstrated that maternal mice exposed to 100 nm diameter PS-NPs at a concentration of 10 mg/L during pregnancy and lactation led to PS-NP accumulation in the offspring's retinas. This suggests that NPs may enter the bloodstream *via* the digestive tract, subsequently traverse the blood-retina barrier (BRB), and accumulate in ocular tissues. Notably, the retinal barrier in mice is not fully developed until postnatal day 18[35], which may facilitate the entry of plastic particles into the retina. Another study using 8-week-old C57 mice showed that exposure to 100 nm PS-NPs at 10 mg/L in drinking water for three months also resulted in retinal accumulation of PS-NPs[36].

Previous research has identified MPs in the vitreous humor of patients with macular holes, epiretinal membranes, retinopathies, and rhegmatogenous retinal detachment, with particle sizes predominantly below 50 μm[37]. A potential pathway for MP entry into the vitreous may involve gastrointestinal absorption into systemic circulation followed by penetration through the iBRB. Since this study involved individuals with retinal diseases, compromised barrier function might enable the entry of relatively larger particles, potentially accounting for the detection of micrometer-sized plastic particles in the vitreous.

Considering that oral ingestion is the primary exposure route for M/NPs, the pathway involving gastrointestinal absorption into systemic circulation followed by trans-barrier penetration into ocular tissues is likely a common exposure mechanism. The routes of ocular exposure to M/NPs are summarized in Figure 1.

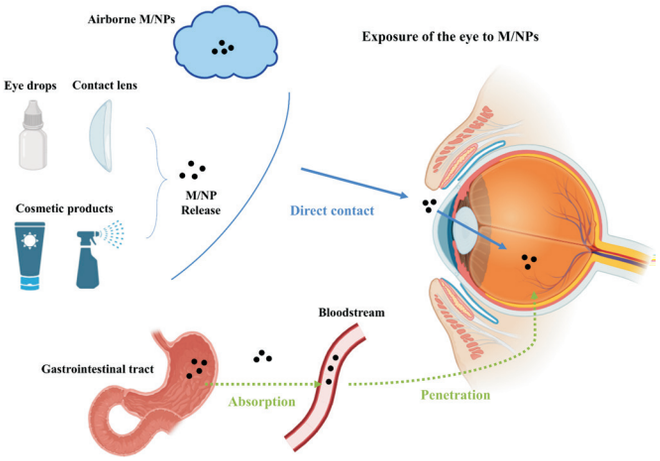

Figure 1 The pathways of ocular exposure to micro/nanoplastics (M/NPs).

OCULAR TOXICITY AND POTENTIAL MECHANISMS OF M/NPS

The potential toxicity of M/NPs has garnered significant attention in recent years. M/NPs may induce adverse biological effects through diverse mechanisms, including physical injury, chemical toxicity, immunological responses, endocrine disruption, and genotoxicity[38], which lead to significant health risks. These particles often contain chemical additives, such as plasticizers and flame retardants, and can adsorb environmental contaminants, possibly exacerbating their toxic potential through secondary exposure[39-40]. *In vitro* studies have consistently demonstrated the cytotoxic effects of M/NPs on human cells. Chronic exposure to M/NPs increases the risk of chronic inflammation and immune dysregulation[41], and may induce DNA damage, mutations, and cellular transformation, potentially leading to carcinogenesis[42]. We have summarized the relevant studies on the impact of M/NPs on human or mammalian eyes in Table 1[17-18,34,36,38,43-46]. Herein, we comprehensively review the ocular toxicity and underlying mechanisms associated with M/NPs based on ocular structure and function.

Ocular Surface The ocular surface comprises the mucosal epithelium extending from the gray lines of the upper and lower eyelids, along with accessory glands such as the lacrimal gland, accessory lacrimal glands, and meibomian glands. This anatomical region serves as the primary interface between the eye and the external environment, fulfilling essential functions in ocular protection, lubrication, and sensory perception. Its integrity is critical for maintaining visual acuity[47]. Its vulnerability to environmental insults can lead to conditions such as dry eye syndrome and keratitis, severely impairing ocular health.

Wang *et al*[18] investigated the presence of MPs in human tear fluid and meibum and explored their potential impact on DED. MPs such as polyvinyl chloride (PVC) were identified in the tear fluid and meibum of 45 patients with DED. The study found that PE levels significantly correlated with key DED parameters, such as tear secretion volume and tear film break-up time (FBUT). *In vitro* experiments showed that PE exposure reduced the viability and induced apoptosis in human corneal and conjunctival epithelial cells in a dose-dependent manner. *In vivo* mouse models demonstrated that topical PE exposure led to typical dry eye signs, reduced goblet cell numbers, and triggered conjunctival inflammation. The study concludes that airborne MPs, especially PE, can accumulate on the ocular surface and induce inflammatory responses that may contribute to DED pathogenesis.

Zhou *et al*[43] also observed similar plastic particle-induced ocular surface damage. They found a significant accumulation of M/NPs in the conjunctival sac of mice following topical ocular administration of PS-M/NPs. A 2-4-week intervention period induced corneal epithelial defects, reduced goblet cell density, and decreased tear secretion, accompanied by upregulation of pro-inflammatory cytokines (*e.g.*, IL-1β, IL-6, TNF-α). These changes in the ocular surface caused by PS-M/NPs are analogous to clinical manifestations of DED. Notably, NPs induced more severe ocular surface damage compared to MPs. This size-dependent toxicity, where smaller plastic particles exhibit greater detrimental effects, has been corroborated in other organ systems[48-49]. *In vitro* toxicity studies further revealed that M/NPs can alter corneal and conjunctival epithelial cell morphology while reducing cell viability and proliferative capacity. Mechanistically, oxidative stress and inflammation are central to these pathological changes.

After a 14-day ocular instillation of 2 mg/mL PE-MPs in mice, MPs were found to penetrate the cornea and enter the intraocular space, resulting in corneal structural alterations and a decrease in endothelial cell density[44]. Exposure to MPs also induced lacrimal hyposecretion, corneal inflammation, and apoptosis. Importantly, surface-modified MPs exhibited enhanced toxicity, with oxidation increasing the number of carboxyl and hydroxyl functional groups on their surfaces. These modifications increase surface properties such as specific surface area, charge density, roughness, and hydrophilicity, promoting tissue adhesion and expanding contact interfaces[50-52]. Furthermore, some researchers have suggested that positively charged PS-NPs display stronger membrane affinity, facilitating cellular interactions[53]. Given the complexity of M/NP surface modifications, further in-depth investigation is needed to elucidate the mechanisms underlying these enhanced toxic effects.

In a mechanistic study, PS-NPs injected into the lacrimal glands of mice induced lacrimal gland cell damage and significant tear secretion reduction[45]. Topical ocular

Table 1 Effects of M/NPs on the ocular

Characteristics of M/NPs	Model	Exposure method/dose/duration	Main findings	Ref.
Human study				
MPs	Pterygium tissue (43-year-old female patient)	N/A	MPs were detected in pterygium tissue, with PE being the most common type	[17]
MPs; predominantly <50 μm	Human vitreous humor samples (patients with ocular diseases)	N/A	MPs were detected in vitreous humor samples, with PA66 being the most prevalent type, followed by PS and PVC; The majority of MPs were smaller than 50 μm; Significant correlations were observed between MP levels and both IOP and vitreous opacities; Higher MP levels were observed in female patients	[37]
MPs	Human tear fluid and meibum samples (patients with DED)	N/A	MPs were identified in human tear fluid and meibum, with PE being predominant; Age-related accumulation of MPs was observed; Tear and meibum MP levels significantly correlated with DED severity	[18]
In vivo animal study				
PS; 50 nm, 2 μm	Male C57BL/6 mice (6-week old)	Topical ocular administration; 1 mg/mL suspension (2.5 μL per eye, 3 times/d); 2 or 4wk	M/NPs accumulated in the conjunctival sac of mice, leading to a decrease in goblet cell density; M/NPs induced dry eye-like symptoms, characterized by reduced tear secretion and corneal epithelial defects; M/NPs upregulated the expression of IL-1β, IL-6, and TNF-α in the conjunctiva and lacrimal gland, causing inflammation; M/NPs induced oxidative stress by increasing ROS levels and reducing NQO1 expression, leading to cell apoptosis	[43]
PE	Male BALB/c mice (6-week old)	Topical ocular administration; 1 and 5 mg/mL suspension (10 μL per eye, 3 times/d); 0, 1, 2, or 4wk	PE exposure induced typical dry eye signs, including reduced tear secretion and increased corneal damage; PE decreased conjunctival goblet cell density, and increased corneal epithelial cell apoptosis and stromal edema; PE induced inflammation in conjunctival tissue, with elevated levels of IL-10, IL-17, IFN-γ, IL-6, IL-4, and IL-2	[18]
Virgin-LDPE and modified-LDPE; 2.67-12.61 μm	Female C57BL/6 mice (6-week old)	Topical ocular administration; 2 mg/mL suspension (3.7 μL per eye, 3 times/d); 14d	MPs reduced tear secretion and increased IOP; MPs were detected in the cornea and retina, where they reduced cell density and tissue thickness; MPs induced inflammation by upregulating TNF-α, IL-1β, and IL-6 *via* NF-κB activation; MPs induced oxidative stress by downregulating SOD and increasing MDA levels Modified-MPs (oxidized with carboxyl and hydroxyl groups) exhibited greater toxicity than virgin-MPs	[44]
PS; 118 nm	Female C57BL/6J mice (7–8 weeks old)	Intralacrimal injection; 10 mg/mL suspension (10 μL, 4 times); 0, 2, 4, 6, and 8d	Significant reductions in tear gland weight and tear secretion were observed after PS-NP treatment; NPs increased the destruction of lacrimal gland cells and goblet cells in the conjunctiva; NPs induced ocular surface damage, including corneal epithelial defects; NPs increased the expression of inflammatory markers and reduced the number of Ki67-positive cells in the cornea and conjunctiva	[45]
PS; 50 nm, 2 μm	Male Sprague-Dawley rats (6–8 weeks old)	Intravitreal injection; 5 μL of MPs or NPs suspension; 24h	NPs significantly increased inflammatory cell infiltration in the retina and vitreous humor, with elevated levels of TNF-α and IL-1β expression in the retina; NPs potentially induced retinal thinning, particularly in the rod and cone cells, as well as in the inner nuclear layer	[46]
PS; 100 nm	Pregnant C57BL/6 mice (ICR)	Drinking water; 10 mg/L; Gestation to lactation (21d post-birth)	NPs delayed retinal vessel development and reduced the number of retinal ganglion cells and bipolar cells in neonatal mice. NPs induced abnormal ERG responses with significant decreases in a-wave and b-wave amplitudes; NPs increased ROS levels in the retinas of mice progeny; NPs induced dysregulation of amino acids (*e.g.*, glutamate, aspartate, alanine) and metabolites related to neurotransmission; NPs downregulated the Fos gene and pathways related to angiogenesis and retinal development	[34]

Table 1 Effects of M/NPs on the ocular (continued)

Characteristics of M/NPs	Model	Exposure method/dose/duration	Main findings	Ref.
PS; 100 nm	C57BL/6 and BALB/c mice (8 weeks old)	Drinking water; 10 mg/L; 3mo	NPs significantly reduced scotopic ERG responses in C57BL/6 mice, indicating impaired photoreceptor cell function; NPs increased ROS levels and reduced activities of SOD and CAT in the retinas of C57BL/6 mice; NPs exacerbated light-induced photoreceptor cell degeneration and retinal inflammation in BALB/c mice, with increased microglial activation; Transcriptomic analysis revealed the upregulation of genes related to complement activation and inflammation, similar to those observed in AMD patients	[36]
In vitro cell study				
PS; 50 nm, 2 μm	HCECs and HConjECs	0, 5, 25, 75, and 100 μg/mL; 48h	M/NPs were internalized by HCECs and HConjECs and accumulated around the cell nuclei; M/NPs significantly reduced cell viability and inhibited cell proliferation in a concentration-dependent manner; M/NPs induced oxidative stress, increased ROS levels, and subsequently led to cell apoptosis	[43]
PE	HCECs and HConjECs	0, 100, 300, 1000, 3000, 5000 μg/mL; 48h	PE was internalized by HCECs and HConjECs, causing significant morphological changes and reduced cell density; PE exposure led to vacuolization and pyknotic nuclei in HCECs and smaller, rounder shapes in HConjECs; PE significantly reduced cell viability and induced apoptosis in a concentration-dependent manner	[18]
Virgin-LDPE and modified-LDPE; 2.67-12.61 μm	Primary MCECs	50 and 100 μg/mL; 48h	MPs were endocytosed by MCECs and reduced cell viability in a dose-dependent manner; MPs compromised membrane integrity due to increased LDH release; MPs induced ROS production and the depolarized MMP in MCECs; Modified-MPs (oxidized with carboxyl and hydroxyl groups) exhibited greater toxicity than virgin-MPs	[44]
PS; 118 nm	HCECs	1, 2.5, 5, and 10 mg/mL; 24h	NPs were internalized by HCECs and accumulated in the perinuclear region; NPs might induce cytotoxicity by disrupting cellular functions and inhibiting cell viability, proliferation, and migration; NPs induced oxidative stress and mitochondrial dysfunction	[45]
PS; 50 nm, 2 μm	Human RPE cells (ARPE-19)	0, 50, 100, 200, and 400 μg/mL; 48h	NPs were observed to penetrate into RPE cells and reduce cell viability; NPs induced oxidative stress through increased ROS levels and SOD2 expression; NPs caused mitochondrial fission and autophagy, as shown by increased expression of FIS1, Drp1, and LC3B proteins; NPs significantly increased the expression of inflammatory cytokines, including TNF-α and IL-1β in RPE cells	[46]
PS; 100 nm	Murine photoreceptor cell line (661 W cells) and ARPE-19	10, 100, and 500 μg/mL (661 W cells); 100 μg/mL (ARPE-19 cells); 24h	NPs were taken up by 661 W cells with perinuclear localization and reduced cell viability; NPs induced ROS accumulation in both 661 W and ARPE-19 cells, reducing SOD and CAT activities, leading to oxidative stress-mediated cytotoxicity; In ARPE-19 cells, NPs downregulated LAMP1 expression and decreased lysosomal activity, indicating impaired phagocytic function; NPs disrupted tight junctions in ARPE-19 cells, as shown by decreased ZO-1 expression and altered cell morphology	[36]

PS: Polystyrene; M/NPs: Micro/Nanoplastics; DED: Dry eye disease; PE: Polyethylene; LDPE: Low-density polyethylene; IOP: Intraocular pressure; SOD: Superoxide dismutase; MDA: Malondialdehyde; ROS: Reactive oxygen species; NQO1: NAD(P)H quinone oxidoreductase 1; PA66: Polyamide 66; PVC: Polyvinyl chloride; ERG: Electroretinogram; AMD: Age-related macular degeneration; HCECs: Human corneal epithelial cells; HConjECs: Human conjunctival epithelial cells; MMP: Mitochondrial membrane potential; FIS1: Fission 1; Drp1: Dynamin-related protein 1; LC3B: Microtubule-associated protein 1A/1B-light chain 3B; RPE: Retinal pigment epithelium; ARPE-19: Adult retinal pigment epithelial cell line-19; IL: Interleukin; NF-κB: Nuclear factor kappa-light-chain-enhancer of activated B cells; ICR: Institute of cancer research; MCECs: mouse corneal epithelial cells; LAMP1: Lysosome-associated membrane protein 1; ZO-1: Zonula occludens protein-1; CAT: Catalase. N/A: Not applicable.

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administration of PS-NPs also rapidly induced corneal epithelial defects and histopathological changes characteristic of dry eye syndrome. Notably, the negative surface charge of PS-NPs at environmental pH>1.6 may interact with the sclera's polyelectrolyte hydrogel-like composition, causing scleral matrix deformation[54]. This alteration can subsequently induce clinical symptoms including ocular hyperemia, nociceptive responses, and visual acuity impairment. These findings highlight the ocular surface hazards of M/NPs and provide novel insights into dry eye pathogenesis related to environmental pollutant exposure.

Elevated Intraocular Pressure Aqueous humor, secreted by the ciliary body, is drained through the aqueous humor outflow system, which includes the iridocorneal angle, trabecular meshwork, and Schlemm's canal. Intraocular pressure (IOP) is maintained through a dynamic balance between aqueous humor production and outflow. Disruptions to this balance can result in elevated IOP[55].

Accumulating evidence links MP exposure to IOP elevation. Murine studies demonstrate that topically administered MPs penetrate the corneal barrier into the anterior chamber, with subsequent IOP elevation observed after 14d[44]. Clinically, a positive correlation exists between vitreous MP levels and IOP in patients with retinal diseases[37]. Once intraocular, these particles may migrate to the trabecular meshwork, where they obstruct aqueous outflow *via* inflammation and reactive oxygen species (ROS)-mediated dysfunction[56]. Inflammatory mediators from this process may concurrently stimulate excessive aqueous production through ciliary body activation. This dual mechanism of impaired drainage and enhanced secretion may create synergistic pressure elevation. Moreover, MP-induced corneal stromal thickening[44], may elevate tonometry readings and physically compress the anterior chamber, contributing to true IOP elevation.

Vitreous and Retina The vitreous, a transparent gelatinous substance located posterior to the lens, fills the space between the lens and the retina. It maintains ocular refractive properties and stabilizes retinal position. The retina, an extension of the central nervous system (CNS), is a highly specialized, layered tissue that converts light signals into neural signals. These signals are transmitted *via* the optic nerve to the visual cortex, forming visual perception. Abnormalities in the vitreous or retina can severely impair visual function[57].

Zhong *et al*[37] identified MPs in human vitreous humor, demonstrating a positive correlation between the concentration of MPs in the human vitreous and the incidence of vitreous opacification. M/NPs induce vitreous inflammation by releasing pro-inflammatory cytokines (*e.g.*, TNF-α, ILs), causing local tissue edema and protein exudation, contributing to vitreous opacification.

M/NPs also exert significant impacts on retinal tissue. *In vivo* experiments in rats demonstrated that intravitreal injection of PS-NPs induces retinal inflammation, with NPs showing greater inflammatory cell infiltration and stronger induction of TNF-α and IL-1β expression compared to MPs[46]. *In vitro* validation using human retinal pigment epithelial cells (ARPE-19) also revealed that M/NPs induce oxidative stress by increased ROS levels and upregulated SOD2 expression[36].

Moreover, maternal exposure to PS-NPs through drinking water during gestation and lactation impairs retinal development and function in offspring mice[34]. Specifically, this exposure induces aberrations in retinal vascularization, depletes the number of retinal ganglion cells and bipolar cells, and elicits altered electroretinogram (ERG) responses. These effects are likely mediated by disruptions in the metabolic profiles of the offspring, exacerbating oxidative stress and contributing to developmental abnormalities. The Fos gene emerges as a potential key target underlying the impact of PS-NP exposure on retinal development and function. Furthermore, oral administration of PS-NPs in mice enables these particles to cross the BRB and accumulate in retinal tissues, increasing oxidative stress and reducing dark-adapted retinal ERG responses[36]. PS-NPs exacerbate light-induced photoreceptor degeneration and retinal inflammation, exhibiting gene expression profiles similar to those observed in patients with age-related macular degeneration (AMD), characterized by complement-mediated phagocytosis and pro-inflammatory responses. These findings suggest that long-term exposure to PS-NPs may represent an environmental risk factor for retinal degenerative diseases.

Exposure of the mouse ocular surface to MPs can also lead to retinal abnormalities. Yang *et al*[44] found that PE-MPs can penetrate the cornea and accumulate in the photoreceptor layer of the mouse retina after topical administration. These particles induce thinning of the outer and inner nuclear layers, reduce the number of retinal ganglion cells, disrupt retinal tight junctions, and activate retinal microglia. Oxidation significantly enhances the toxicity of PE-MPs to the mouse eye, likely by increasing oxidative stress and inflammatory responses.

CONCLUSION AND FUTURE PERSPECTIVES

This review comprehensively summarizes the potential impacts of M/NPs on ocular health, revealing their adverse effects on the ocular surface, IOP, vitreous body, and retina following exposure through various routes. Oxidative stress and inflammation are considered key mechanisms underlying M/NP-induced ocular damage. However, significant knowledge gaps remain in our understanding of the full spectrum of M/NP ocular toxicity, requiring further exploration.

Standardization of Exposure Models Current research primarily relies on animal models, with limited human data. The diverse physicochemical properties, exposure routes, and dosages of M/NPs result in varying biological effects. Utilizing a single dose and fixed exposure duration makes it challenging to simulate the complex scenarios of long-term, low-dose, mixed exposures encountered in real-world environments. Although human exposure data could guide experimental dosage selection, the complex and variable nature of real-world exposure necessitates a broad dosage range. Additionally, establishing multi-route exposure models that integrate airborne deposition, gastrointestinal absorption, and medical device release will better simulate real-world exposure scenarios. Long-term, low-dose exposure studies are crucial for assessing the cumulative effects of M/NPs on ocular structure and function.

In-depth Mechanistic or Clinical Studies While oxidative stress and inflammation are recognized as important mechanisms of M/NP-induced ocular toxicity, the upstream regulatory mechanisms remain unclear. M/NP-induced cytotoxicity and tissue damage may also involve multiple associated mechanisms, such as endoplasmic reticulum stress, ferroptosis, and mitophagy[58-60]. Importantly, clinical causality remains unestablished between ocular microplastics and specific pathologies (*e.g.*, glaucoma or AMD). Additionally, surgical contribution is unquantified—whether phacoemulsification or vitrectomy amplifies microplastic release and subsequent ocular damage requires validation. Future research should clarify fundamental biological mechanisms of M/NP-induced ocular tissue damage to enable targeted interventions, while establishing high-risk cohorts to correlate exposure levels with clinical endpoints.

Comparative Toxicology Most current studies focus on PS and PE, neglecting the toxicological differences of other common plastic types, such as PVC and PA. Systematic assessments of these polymers are needed. Given that environmental plastic particles may undergo various surface modifications, studying the effects of modified M/NPs (*e.g.*, $-NH_2$ and -COOH) on ocular health may be meaningful.

Diagnostic Challenges and Translational Opportunities Current clinical diagnosis of M/NP-associated ocular diseases faces dual limitations: blood assays lack sensitivity for low-concentration particles, while highly specific tissue biopsies are clinically impractical due to invasiveness. Resolving this dilemma necessitates multidisciplinary collaboration among ophthalmology, analytical chemistry, and materials science. Notably, lens tissues routinely discarded during cataract surgery present a unique translational resource. This approach enables direct quantitative assessment of M/NP accumulation within the lens or eyes using analytical techniques such as micro-fourier transform infrared spectroscopy (μ-FTIR). Such a strategy could establish causal links between M/NP exposure and ocular pathology while accelerating diagnostic criteria development. Critically, developing therapeutic strategies to clear M/NPs from ocular surfaces and intraocular compartments represents an essential future priority.

In summary, this review highlights the potential risks of M/NPs to ocular health and underscores the urgency of conducting in-depth research in this emerging field. Future research should focus on developing standardized methods, exploring mechanisms in depth, and expanding translational applications to address the growing threat of plastic pollution to human health.

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