Review

Nanotechnology Systems in Drug Delivery to the Anterior Segment of the Eye—A Narrative Review of the Latest Preclinical Research Results

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Nanotechnology Systems in Drug Delivery to the Anterior Segment of the Eye—A Narrative Review of the Latest Preclinical Research Results

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Abstract

Background: Eye diseases represent a significant public health problem. The effectiveness of ophthalmic pharmacotherapy largely depends on efficient drug delivery to the eye tissues. Conventional eye drops exhibit low bioavailability due to anatomical and physiological barriers. Nanotechnology offers novel strategies to enhance drug penetration, retention, and controlled release within the anterior segment of the eye. This study aimed to systematically analyze preclinical research on the use of nanocarriers in drug delivery to the anterior segment. **Methods**: A literature review was conducted using PubMed, Scopus, and Google Scholar databases, covering English-language publications from 2019 to 2025. Preclinical studies evaluating nanocarriers for the treatment of anterior segment eye diseases and available in full text were included. **Results**: The analyzed studies indicate that nanocarriers, including solid lipid nanoparticles, nanostructured lipid carriers, nanomicelles, and polymeric nanoparticles, enhance drug bioavailability by improving mucoadhesion, facilitating penetration through the corneal epithelium, and prolonging ocular surface retention time. Key physicochemical parameters include small particle size, low polydispersity index, appropriate zeta potential, and high encapsulation efficiency. Preclinical models demonstrated improved therapeutic outcomes, including greater intraocular pressure reduction in glaucoma, increased tear production in dry eye syndrome, and enhanced anti-inflammatory and antifungal effects compared with conventional preparations. **Conclusions**: Nanotechnology-based drug delivery systems represent a promising strategy for improving therapy of the anterior segment eye diseases. However, further preclinical and clinical studies are required to confirm their clinical applicability.

Keywords: nanocarriers; ocular drug delivery; nanoparticles; targeted therapy; ophthalmology

1. Introduction

According to the World Health Organization (WHO) World Report on Vision published in 2019, eye diseases represent a widespread public health problem. It is estimated that more than two billion people worldwide live with visual impairment or eye disease, of whom at least one million cases could have been prevented [1]. Studies indicate that patients suffering from chronic eye diseases have significantly reduced quality of life, additionally experiencing difficulties in daily and social functioning as well as impaired mental health [2]. This highlights the urgent need for effective ophthalmic interventions aimed at improving the quality of life of many patients [3].

Pharmacotherapy represents the fundamental approach in the management of most ocular pathologies [4]. The success of therapy largely depends on the drug delivery system to ocular tissues.

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Several routes of administration have been listed by researchers, including topical (eye drops), subconjunctival, sub-Tenon's, suprachoroidal, and intravitreal delivery. Topical eye drops represent the most common delivery method, particularly for treating disorders affecting the anterior segment of the eye. However, the bioavailability of this method is estimated to be less than 5%. This is due to the rapid drug elimination from ocular surface by blinking and the lacrimal drainage system, as well as the presence of physical barriers, primarily the corneal epithelium [5–7].

Advances in nanotechnology have led to the development of novel therapeutic options because of rapid progress in the field of ocular drug-delivery systems [8]. Various nanocarriers, including nanoparticles (NPs), nanomicelles, nanoemulsions (NEs), microemulsions, nanofibers, liposomes, dendrimers, nanowafers, and microneedles (MNs), have been investigated as potential therapies for both anterior and posterior segment eye diseases [9]. Researchers have noted that compared with conventional ocular drug-delivery methods, these novel carriers possess physicochemical properties that confer distinct advantages. Nanocarriers facilitate more efficient penetration of ocular barriers and enhance corneal permeability. By employing these nanotechnological approaches, drug residence time is significantly extended, while drug degradation is reduced. Furthermore, these systems enable controlled and targeted drug release [10,11]. As a result, they can notably improve drug bioavailability and therapeutic efficacy. However, each type of nanocarrier exhibits distinct physicochemical and pharmacokinetic characteristics [12].

Therefore, a rigorous comparison of available scientific evidence is necessary to accurately evaluate the effectiveness of these approaches. In this context, preclinical studies play a pivotal role. Conducted using in vitro, in vivo, and ex vivo models, these studies aim to generate critical information on the safety and biological efficacy of potential therapeutics before they are tested in humans. Preclinical research provides insights into adverse effects, as well as the pharmacokinetics and pharmacodynamics of candidate compounds [13]. The analysis of data derived from in vitro and in vivo models enables the characterization of different nanocarriers and allows conclusions to be drawn regarding their suitability for ocular drug delivery [14].

The aim of this systematic review is to analyze preclinical studies investigating the application of nanotechnology in ocular drug delivery to the anterior segment of the eye. By synthesizing the available literature, this review seeks to assess the utility and therapeutic effectiveness of current nanotechnology-based approaches.

2. Materials and Methods

A comprehensive search of literature was conducted in English using PubMed, Scopus and Google Scholar databases, covering publications from 2019 to 2025. The following keywords were used in the search strategy: *nanocarriers; ocular drug delivery; nanoparticles; targeted therapy; ophthalmology.*

The results section exclusively incorporated original research articles detailing preclinical investigations. The inclusion criteria comprised publications written in English and available in free full-text format. Case reports, letters to editor, and conference abstracts were excluded from analysis. Review articles were used solely as supporting sources in the Introduction and Discussion sections to provide the theoretical background and to compare the obtained findings with the current state of knowledge.

The selected publications were subjected to narrative analysis, focusing on parameters such as the type of nanocarrier used, the mechanism of drug release, bioavailability within the tissues of the anterior segment of the eye, and the safety profile.

Ultimately, 59 articles were included in the review after the removal of duplicates.

3. Results

Nanocarriers currently represent a cornerstone strategy in the development of modern ophthalmic therapies, enabling enhanced drug bioavailability and more effective overcoming

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numerous anatomical and physiological ophthalmic barriers. Among them, lipid nanocarriers (LNCs) are prominent due to their excellent biocompatibility and are being intensively investigated for the treatment of diseases affecting both the anterior and posterior segments of the eye. Lipid nanoparticles are colloidal systems categorized into two generations: the first generation comprising solid lipid nanoparticles (SLNs) and the second generation consisting of nanostructured lipid carriers (NLCs). SLNs are composed of lipids that remain solid at body temperature, such as fatty acids, fatty alcohols, glycerol esters, and waxes. NLCs, which are classified into imperfect, amorphous, and multiple types, contain a blend of solid and liquid lipids. A characteristic feature of these nanocarriers is their adhesive and lipophilic properties, which are primarily utilized to prolong corneal residence time. This effect is further enhanced by modifying their composition with phospholipids, chitosan, or stearylamines. Cationic compounds are also incorporated into the lipid matrix, which strengthens mucoadhesion through electrostatic attraction to the anionic ocular tissues. These systems enable the encapsulation of both hydrophilic and hydrophobic compounds. Furthermore, due to their formulation comprising biocompatible GRAS (Generally Recognized as Safe) lipids and the utilization of solvent-free manufacturing methods, LNPs exhibit a favourable safety profile. Lipid nanoparticles are applicable in the treatment of various ophthalmic conditions, most notably ocular inflammation, facilitating the delivery of anti-inflammatory agents such as diclofenac, ibuprofen, flurbiprofen, or cyclosporine A. Other potential indications for LNP-based therapy include glaucoma, corneal neovascularization, and microbial keratitis [15–17]. In 2023, Satyanarayana et al. evaluated the delivery of bimatoprost via SLNs for glaucoma management. In vitro drug release kinetics, assessed using a modified Franz diffusion cell, demonstrated a sustained-release profile. Concurrently, the irritancy potential was evaluated using the Hen's Egg Test on the Chorioallantoic Membrane (HET-CAM) assay, confirming that the formulation was non-irritating and showed no signs of ocular toxicity [18]. In clinical terms, the main advantages of this technology are its biocompatibility and high efficacy, while its main limitations remain its tendency to aggregate and its low stability.

In addition to nanocarrier formulations, several studies have investigated strategies that enhance the penetration of nanoparticle-based drug delivery systems into ocular tissues. One such approach is iontophoresis, which uses a low-intensity electric current to facilitate drug transport across biological barriers [19]. Zhao et al. demonstrated that the application of a hydrogel ionic circuit (HIC) iontophoresis device enabled the delivery of nanoparticle-encapsulated dexamethasone and bevacizumab into ocular tissues within 10-20 minutes, whereas conventional low-current iontophoresis required several hours to achieve comparable concentrations. Importantly, the HIC system did not cause structural damage to ocular tissues, suggesting that this approach may represent a safe and efficient strategy for enhancing nanoparticle-based ocular drug delivery [20].

Several studies directly compared the therapeutic efficacy of nanoparticle-encapsulated drugs with that of conventional formulations. In experimental models of dry eye disease, gelatin-based nanoparticles increased tear production by approximately 80% compared with conventional formulations, whereas PLGA-coated (PLGA—Poly (Lactic-co-Glycolic Acid) nanoparticles increased tear production by about 50%. Similarly, in models of ocular and uveal inflammation, nanoparticle-encapsulated drugs significantly reduced polymorphonuclear cell counts in the aqueous humor, indicating a substantial decrease in intraocular inflammation. These findings suggest that nanoparticle encapsulation enhances the pharmacological potency of ophthalmic drugs compared with free drug formulations [21].

In the context of modern ocular drug delivery systems, nanomicelles deserve particular attention. Micelles are amphiphilic colloidal structures with particle diameters typically ranging from 5 to 100 nm. They consist of hydrophilic (polar) and hydrophobic (nonpolar) moieties [22]. Depending on the solvent environment, the spatial orientation of these molecules varies, resulting in the formation of either regular or reverse nanomicelles. In aqueous media, regular nanomicelles are formed, characterized by the localization of hydrophilic segments at the external surface and a hydrophobic core. Conversely, in nonpolar solvents, reverse nanomicelles are formed, in which

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hydrophobic moieties are exposed at the surface while hydrophilic groups are sequestered within the core [23,24]. Owing to this unique structural organization, nanomicelles have been widely investigated as carriers for various biologically active compounds. Regular nanomicelles are particularly suitable for the delivery of lipophilic drugs, which are incorporated into the hydrophobic core, whereas the surface of the micelles binds polar molecules. In contrast, reverse nanomicelles facilitate the transport of hydrophilic compounds, as their hydrophobic coating limits direct contact between the encapsulated drug and the surrounding medium [22–24]. Furthermore, nanomicelles exhibit high biocompatibility and high therapeutic efficacy of loaded agents. An additional advantage of these systems is their relatively simple and cost-effective synthesis process [24]. A study reviewed by Wang et al. (2021) demonstrates that topical administration of eye drops containing cyclosporine-loaded nanomicelles represents an effective strategy for drug delivery to the fundus of albino rabbit eyes. The resulting intraocular concentrations in the retina and choroid surpassed the predicted therapeutic threshold [25]. Despite numerous advantages, a critical limitation of nanomicelles is their insufficient systemic stability. Following intravenous administration, nanomicelles undergo dilution, which may induce micellar dissociation. Consequently, the encapsulated therapeutic substances may be prematurely released from the polymeric matrix. Therefore, further investigation is required to enhance structural stability through the optimization of their physicochemical properties [23].

Dry Eye Syndrome (DES) is a multifactorial condition characterized by impaired tear film homeostasis, hyperosmolarity, and inflammation of the ocular surface. The etiopathogenesis of DES involves dysfunction of the nasolacrimal unit (comprising the lacrimal glands, corneal surface, and eyelids) resulting in insufficient tear film production or tear film instability due to abnormal composition [26–28]. It is estimated that approximately 10-20% of the population over the age of 40 reports symptoms of DES of varying severity [28]. One of the pharmacological agents currently being evaluated for the treatment of DES is Cyclosporine A (CyA, CsA). It has been officially approved by the U.S. Food and Drug Administration (FDA) for use in clinical trials, although research is still being conducted on optimizing concentrations and delivery methods [29]. Cyclosporine A is a calcineurin inhibitor with immunosuppressive, anti-apoptotic, and protective effects on the human conjunctival epithelium. Its mechanism of action involves inhibiting the infiltration and activation of T lymphocytes, thereby suppressing the release of pro-inflammatory cytokines. The pivotal advantage of CyA over glucocorticoids in the management of DES stems from its favorable safety profile with fewer adverse effects. CyA enables chronic pharmacotherapy without the risk of inducing steroid-induced cataracts, elevated intraocular pressure (IOP), or secondary opportunistic infections, representing a significant alternative to corticosteroid-based anti-inflammatory therapy [30]. However, Cyclosporine A is characterized by poor aqueous solubility and a high molecular weight. These properties significantly hinder their solubility in aqueous solutions at therapeutic concentrations, thereby limiting the effectiveness of conventional topical ophthalmic formulations, such as eye drops [30,31].

Weiss et al. (2019) evaluated the ocular biodistribution, tolerability, and systemic exposure of Cyclosporine A in an in vivo model. The study utilized 112 New Zealand white rabbits, which were administered either a nanomicellar formulation—OTX-101 0.05% (containing 0.05% CyA) or a 0.05% CyA ophthalmic emulsion (Restasis®; Allergan, Irvine, California) as a comparator in two distinct phases. In the single-dose phase, a single drop of OTX-101 0.05% or the comparator was administered, with subsequent tissue and fluid sampling up to 72 hours post-administration. In the repeated-dose phase, OTX-101 (0.01%, 0.05%, or 0.1% CyA) or the comparator was administered four times daily for seven days. Following the treatment period, samples were collected up to 18 hours after the final dose on day 7. A total of 2,799 whole blood samples and 2,663 ocular tissue/fluid samples were analyzed. The results indicate that OTX-101 yielded approximately a twofold increase in CsA concentration in the conjunctiva and cornea after both single (0.05%) and repeated dosing (0.05% and 0.1%) relative to the comparator. In contrast, CyA concentrations in other evaluated tissues and fluids remained comparable between both formulations across both phases. Minimal systemic absorption

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was observed, with negligible CyA concentrations found in peripheral blood for both formulations. Elevated therapeutic concentrations of Cyclosporine A on the ocular surface, achieved through the application of the OTX-101 nanomicellar formulation, may result in superior clinical outcomes in patients with DES compared to conventional 0.05% CsA ophthalmic emulsions [32]. This enhanced efficacy is attributed to the nanomicellar structure, which encapsulates CyA within its core, facilitating penetration into the corneal and conjunctival tissues and significantly increasing the bioavailability of the active agent.

Terreni et al. (2020) conducted a study in which the ASMP-Nano (Assembling Surfactants-Mucoadhesive Polymer Nanomicelles) system was designed and underwent the biopharmaceutical evaluation. The ASMP-Nano platform is based on a binary surfactant system combined with hyaluronic acid (HA), which serves as a mucoadhesive polymer. The study utilized a stable Nano1HAB-CyA formulation containing 0.105% CyA (w/w) encapsulated in 14.41 nm nanomicelles. The in vitro release profile indicated that the Nano1HAB-CyA formulation exhibited rapid diffusion of CyA, releasing twice as much active substance as the EtOH-CyA reference solution within 6 hours (52.96 ± 16.05 μg and 25.89 ± 4.51 μg, respectively). These findings suggest a positive effect of nanomicelles on drug release, regardless of the physical state (molecular or colloidal dispersion). In addition, in vitro permeation assays and in vivo pharmacokinetic studies demonstrated that the nanomicellar carrier promotes prolonged drug release in the precorneal area, which may be attributed to the presence of HA and the sustained drug release from the unstructured system. Furthermore, the tested formulations did not cause discomfort or affect tear production, unlike the commercial product, which contains a lyophilized carrier that is poorly tolerated by the ocular surface. The bioavailability of CyA in Nano1HAB-CyA was at the same level as in the reference product Ikervis®, with approximately four times lower elimination rate constant [31].

Glaucoma represents the second leading cause of irreversible blindness worldwide [33]. It comprises a group of ocular disorders characterized by progressive degeneration of the optic nerve head and thinning of the retinal nerve fiber layer. If left untreated, the condition leads to irreversible vision loss [34,35]. There are three main categories of glaucoma: primary, secondary, and the less common juvenile and congenital glaucoma. Primary glaucoma presents in two clinical phenotypes: primary open-angle glaucoma (POAG) and angle-closure glaucoma [34]. The primary risk factor for glaucoma, regardless of its type, is elevated intraocular pressure, typically above 21 mmHg [33,34]. According to Schuster et al. (2020), reducing elevated IOP (21-32 mm Hg) by 22.5% can decrease the 5-year risk of developing POAG from 9.5% to 4.4% [33]. Consequently, lowering IOP remains a fundamental element in the management of glaucoma. Pharmacotherapy is one of the methods used to treat glaucoma, utilizing standard eye drops, ointments, or oral medications to reduce IOP. However, these drug delivery methods exhibit significant limitations, such as insufficient bioavailability due to tear secretion, nasolacrimal drainage, and reflex blinking [36,37]. To improve the bioavailability of these drugs, new advanced drug delivery systems are being investigated, including liposomes, dendrimers, nanoparticles and injectable hydrogels [36].

Luo et al. (2020) developed a bifunctional anti-glaucoma nanocarrier system aimed at the targeted and sustained delivery of pilocarpine to the ocular tissues. The system comprised chitosan and ZM241385 functionalized onto the surface of hollow cerium oxide nanoparticles (hCe NPs). This configuration enabled the nanocarriers to open the tight junctions of the corneal epithelium, thereby enhancing drug delivery efficiency to the ciliary body. In vitro assays on rabbit corneal cells and in vivo histopathological analysis (hematoxylin and eosin staining; H&E) demonstrated the antioxidant and anti-inflammatory properties of the nanocarriers, which alleviate pathological changes associated with the disease. Moreover, it was proven that a single topical installation of pilocarpine-loaded nanomicelles effectively suppressed disease progression for 7 days in an experimental glaucoma model. In contrast, conventional commercial eye drops exhibited therapeutic efficacy for a maximum of 4 hours. These results are likely attributed to optimized pharmacokinetics and enhanced intraocular penetration, as evidenced by an approximately 250-fold increase in bioavailability within the ciliary body [37].

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Table 1. Physicochemical parameters and therapeutic efficacy of ocular nanocarriers in selected research models.

Author	Disease	Type of nanoparticle	Drug	Nanoparticle Size	Experimental Model	EE% (Encapsulation Efficiency)	Main Results
Satyanarayana et al. (2023) [18]	Glaucoma	SLNs	Bimatoprost	183,3 ± 13,3 nm	In vitro, HET-CAM test	71,8 ± 1,1%	Extended release of the drug; no irritation or toxicity
Weiss et al. (2019) [32]	DES	Nanomicelles (OTX-101)	CyA	No data available	In vivo (New Zealand White rabbits)	No data available	2-fold increase in drug concentration in the cornea; minimal systemic absorption
Terreni et al. (2020) [31]	DES	Nanomicelles (ASMP-Nano)	CyA	14,41 ± 0,41 nm	In vitro, ex vivo, in vivo (albino rabbits)	77,66 ± 1,77%	Extended drug release, 4 times lower steady-state elimination rate than in the reference product while maintaining the same bioavailability of the drug, no discomfort
Luo et al. (2020) [37]	Glaucoma	hCe NPs	Pilocarpine	No data available	In vitro, in vivo (Statens Serum institut rabbit cornea (SIRC) cells, from New Zealand white rabbits)	5,3-22,7%	Effective for 7 days compared to 4 hours for eye drops; 250-fold increase in bioavailability in the ciliary body

SLNs—solid lipid nanoparticles. DES—Dry Eye Syndrome. CyA—cyclosporine A. hCe NPs—hollow cerium oxide nanoparticles. HET-CAM—Hen's Egg Test on the Chorioallantoic Membrane. ASMP-Nano—Assembling Surfactants-Mucoadhesive Polymer Nanomicelles.

4. Discussion

The effectiveness of nanocarrier-based ocular drug delivery systems depends largely on their biocompatibility and physicochemical properties. In the context of ophthalmic therapy, biocompatibility refers to the absence of toxic effects on ocular tissues while maintaining stable and controlled drug release. These properties are influenced by parameters such as particle size, surface charge, chemical composition, and degradation pathways [10].

Drug delivery to the eye is significantly limited by the presence of multiple anatomical and physiological barriers [10]. Dynamic barriers include tear film turnover, blinking, and nasolacrimal drainage, all of which rapidly eliminate topically administered drugs [19,41,42]. Static barriers consist primarily of the corneal epithelium with tight intercellular junctions, as well as the conjunctiva and

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sclera [38,43,44]. These structures restrict drug penetration and contribute to the extremely low bioavailability of conventional eye drops, which is typically estimated at below 5% [5–7,38,45,46]. Nanotechnology-based drug delivery systems have the potential to overcome these limitations by increasing drug residence time on the ocular surface, protecting active compounds from degradation, and improving penetration through ocular tissues. As a result, nanoparticle formulations often demonstrate improved pharmacokinetic profiles and reduced systemic exposure compared with conventional ophthalmic preparations [10,19,25,32,39–41].

The therapeutic performance of nanoparticle-based formulations is strongly influenced by their physicochemical characteristics. Among these, particle size represents one of the most critical parameters. Smaller nanoparticles are able to penetrate the mucin layer more efficiently and interact more effectively with corneal and conjunctival epithelial cells. Previous studies indicate that nanoparticle sizes between approximately 50 and 400 nm are generally considered optimal for ophthalmic applications. Particles within this range exhibit improved mucoadhesion, enhanced tissue penetration, and lower irritation potential compared with larger particles [47–49]. In contrast, extremely small nanoparticles may be cleared rapidly from the ocular surface, reducing their therapeutic effectiveness [50].

Another key parameter is the zeta potential, which reflects the surface charge of nanoparticles and influences both stability and interaction with ocular tissues. The ocular surface is negatively charged due to the presence of mucins in the tear film [10,38,41,47,51,52]. Consequently, positively charged nanoparticles tend to exhibit stronger electrostatic interactions with the ocular surface, resulting in improved mucoadhesion and prolonged retention time. These interactions contribute to increased drug bioavailability and sustain therapeutic effects. At the same time, an appropriate zeta potential is essential for maintaining colloidal stability, as electrostatic repulsion between particles helps prevent aggregation within the formulation [10,47,51].

In addition to particle size and surface charge, the polydispersity index (PDI) plays an important role in determining the stability and uniformity of nanoparticle systems. Low PDI values typically indicate a homogeneous particle population, which contributes to improved physicochemical stability and more predictable drug release profiles. Homogeneous nanoparticle systems are less prone to aggregation and therefore maintain their functional properties for longer periods [53].

Encapsulation efficiency represents another critical determinant of therapeutic performance. High encapsulation efficiency allows a larger amount of the active compound to be incorporated within the nanocarrier, which often translates into prolonged drug release and enhanced therapeutic efficacy [53]. Studies have demonstrated that nanoparticle systems with high encapsulation efficiency are capable of delivering sustained drug concentrations in ocular tissues, thereby improving the pharmacological effect compared with conventional formulations [21,41,50,54,55].

In addition to these physicochemical parameters, mucoadhesion and mucopenetration play essential roles in determining the bioavailability of ocular nanocarriers. Mucoadhesion enables nanoparticles to adhere to the mucous layer covering the ocular surface, thereby prolonging the residence time of the drug at the site of administration [56]. Various polymers, including chitosan, alginate, hyaluronic acid, and hydroxypropyl methylcellulose, have been widely used to enhance mucoadhesive properties. These polymers interact with mucin through hydrogen bonding and electrostatic interactions, resulting in improved retention of the drug delivery system on the ocular surface [46,52,57].

Conversely, mucopenetration refers to the ability of nanoparticles to diffuse through the mucus layer and reach deeper ocular tissues. Nanoparticles designed for mucopenetration are typically smaller and may possess surface modifications that reduce strong interactions with mucin, allowing them to move more freely through the mucus barrier [17,46,56,57]. The balance between mucoadhesion and mucopenetration therefore represents an important design consideration for nanoparticle-based ocular drug delivery systems.

Despite the promising results observed in preclinical studies, several challenges remain in translating these technologies into clinical practice. One important limitation is the variability

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between animal models and human ocular physiology. Differences in corneal thickness, tear composition, and ocular anatomy may influence nanoparticle distribution and pharmacokinetics, making it difficult to directly extrapolate preclinical findings to human patients [25,32,58]. Additionally, large-scale manufacturing of nanoparticle-based formulations require strict control of particle size distribution, stability, and reproducibility. Ensuring consistent production standards and maintaining formulation stability remain important challenges that may increase production costs [40,58].

Overall, current evidence suggests that nanotechnology-based drug delivery systems represent a promising strategy for improving ocular pharmacotherapy in anterior segment diseases. By optimizing physicochemical parameters such as particle size, surface charge, and encapsulation efficiency, nanocarriers can significantly enhance drug bioavailability and therapeutic outcomes. Nevertheless, further studies, particularly well-designed clinical trials, are required to confirm the long-term safety and clinical effectiveness of these systems in human patients.

5. Conclusions

Current evidence indicates that nanotechnology-based drug delivery systems represent a promising therapeutic strategy for the treatment of anterior segment diseases. Compared to conventional methods of administration, nanocarriers enable a significant increase in the bioavailability of active substances by more effectively overcoming ophthalmic barriers and prolonging the retention time of the drug within the eye. Preclinical studies confirm their effectiveness in models of dry eye syndrome and glaucoma, indicating a potential improvement in therapeutic effects while reducing side effects. Although most of the formulations analyzed show low toxicity in preclinical studies, further evaluation of the long-term interactions of nanomaterials with eye tissues is necessary. Differences between the response of animal models and the human ocular tissues are a major limitation in the extrapolation of results. Nanotechnology-based drug delivery systems have significant potential in ophthalmology, but their clinical application requires further well-designed clinical trials.

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Abbreviations

The following abbreviations are used in this manuscript:

WHO	World Health Organization
NPs	nanoparticles
NEs	nanoemulsions
MNs	microneedles
LNCs	lipid nanocarriers
SLNs	solid lipid nanoparticles
NLCs	nanostructured lipid carriers
GRAS	Generally Recognized as Safe
HET-CAM	Hen's Egg Test on the Chorioallantoic Membrane
HIC	hydrogel ionic circuit
PLGA	Poly (Lactic-co-Glycolic Acid)

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DES	Dry Eye Syndrome
CyA	Cyclosporine A
FDA	U.S. Food and Drug Administration
IOP	intraocular pressure
ASMP-Nano	Assembling Surfactants-Mucoadhesive Polymer Nanomicelles
HA	hyaluronic acid
POAG	primary open-angle glaucoma
hCe NPs	hollow cerium oxide nanoparticles
H&E	hematoxylin and eosin staining
EE%	encapsulation efficiency
PDI	polydispersity index

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