Bristol Publishers

Journal of Pharmaceutical and Pharmacology Research

Mini Review | Open Access | Volume: 01 Issue: 01 (October-December 2026) Pages: 01-13

The CC By License (https://creativecommons.org/licenses/by-nc-nd/4.0/)

Micellar Drug Delivery Systems in Ocular Therapeutics: Overcoming Challenges and Enhancing Treatment Outcomes for Ocular Diseases

Akash Vikal✉ and Rashmi Maurya

Department of Pharmaceutics, ISF College Pharmacy, GT Road, Moga, Punjab, India

Corresponding author: Akash Vikal, Department of Pharmaceutics, ISF College Pharmacy, GT Road, Moga-142001, Punjab, India. E-mail: akashvikal2112@gmail.com.

Received: 11 November 2024; **Revised:** 12 December 2024; **Accepted:** 24 January 2025; **Published:** 05 July 2026

Academic Editor: Prof Dr. Hanieh Safari

Abstract

Epidemiology of ocular diseases leading to vision impairment. Over 2.2 billion people worldwide have a distance near or uncorrected vision [1,2]. Nevertheless, a significant proportion of these cases either go untreated or are poorly treatable since existing therapies have limited bioavailability, suffer from fast clearance and ocular tissue barriers. Traditional treatments, like eye drops and oral medications, suffer from poor patient compliance and frequent dosing requirements. Micelle-based DDS have recently appeared as a promising solution for these challenges in ocular therapeutics. Micelles are nanosized colloidal carriers formed by amphiphilic molecules, capable of encapsulating hydrophobic drugs to enhance their penetration, retention, and sustained release in ocular tissues. Studies demonstrate that micellar formulations improve corneal permeability and extend therapeutic effects in preclinical models, offering significant potential for diseases requiring sustained drug levels. This review emphasizes the potential of micellar DDS to address critical limitations in current ocular treatments and to support the development of targeted, non-invasive therapies that could transform ocular care and enhance patient outcomes.

Keywords: Ocular drug delivery; Micelle-based delivery systems; Nanotechnology; Glaucoma; Age-related macular degeneration

Introduction

Ocular conditions like age-related macular degeneration (AMD), glaucoma, along with diabetic retinopathy., and infectious keratitis continue to be major factors that lead to blindness and visual impairment globally [1,2]. According to WHO, more than 2.2 billion people worldwide currently endure visual impairment, with a minimum of one billion cases that could have been prevented or remain untreated. With an estimated 285 million people affected by visual impairment as of 2020, the burden of ocular diseases continues to grow, particularly as the global population ages and the prevalence of systemic conditions like diabetes rises. Untreated or inadequately managed, these diseases lead to progressive vision loss, severely impacting quality of life and posing a significant public health challenge [1,3,4]. Despite advancements in understanding and managing ocular diseases, current treatment options remain limited by issues of low therapeutic efficacy, rapid drug clearance, and barriers within ocular tissues that hinder drug penetration and retention [5-7]. These limitations highlight the urgent need for innovative drug delivery systems capable of overcoming these challenges and improving patient outcomes.

Citation: Vikal A, Maurya R. Micellar Drug Delivery Systems in Ocular Therapeutics: Overcoming Challenges and Enhancing Treatment Outcomes for Ocular Diseases. J. Pharm. Pharmacol. Res. October-December 2026; 01(01): 01-13.

In recent years, micelle-based drug delivery system has appeared as a promising innovation for ocular therapeutics. Micelles, nanosized colloidal particles formed from amphiphilic molecules, offer several advantages for ophthalmic drug delivery, particularly for hydrophobic drugs [8,9]. Traditional treatments, such as eye drops and oral medications, suffer from poor patient compliance due to the need for frequent administration and limited efficacy due to rapid drug clearance and barriers like the corneal epithelium [10]. In contrast, micelle-based systems can encapsulate drugs, providing sustained and targeted release, reducing drug degradation, and enhancing bioavailability. Studies have shown that micellar formulations, such as those loaded with hydrophobic drugs like Brinzolamide (for glaucoma) and Diclofenac (for ocular inflammation), achieve better corneal permeability, prolonged release, and superior therapeutic outcomes in experimental models [11,12]. By enhancing drug retention in the ocular environment and improving penetration through corneal and scleral tissues, micelle-based formulations can significantly benefit a range of ocular diseases [13,14]. Micelles have a unique property that enables them to deliver drugs over prolonged periods of time (i.e.65, 118), reducing drug doses and the need for high-elimination rate systemic circulation thus improving patient compliance while decreasing the risk of side effects due to continuous drug administration. Furthermore, micelle-based systems can also be developed as biocompatible systems to provide a safe and effective method for ocular delivery. These advantages of micellar drug delivery technology have enabled it to potentially transform the management of ocular disease, by allowing a paradigm shift from conventional therapy to more smart and site specific approaches based on personalized nature of different types of eye conditions. Micelle-based treatments may prove to be a real innovation in the future, providing long-term non-invasive preventive treatments that could alter ocular care while preserving vision and improving quality of life for millions as research progresses.[7,14]. This highlight of the review, The possibility of micellar DDS in addressing the limitations of current ocular treatments and emphasizes the significant impact these innovations could have on the future of ophthalmology.

Micelles:

Micelles (Figure1) are nano-scaled amphiphilic molecule-based systems with hydrophilic and hydrophobic parts. In aqueous, these molecules have a leading to spherical structures (hydrophobic core) surrounded by hydrophilic shell which helps in containing the hydrophobic drugs. Conventional micelles are composed of the amphiphilic, surfactants such as phospholipids in which hydrophobic tails aggregate to form a core and hydrophilic heads orient towards water. They are an excellent solution for enhancing the solubility of nonsoluble drugs. In contrast, reverse micelles is formed from surfactants or block copolymers in low-water conditions. Hydrophilic heads are oriented internally to form the core while the hydrophobic tails project outward. They are useful for the encapsulation of hydrophilic drugs in organic solvents. Polymeric micelles are composed of block copolymers (ex: PEG and PLA), which provide better stability from covalent bonds in co-polymers. The hydrophilic part contributes the outer shell, and the hydrophobic segment is in the internal core, thus being useful for extended drug delivery and targeting therapies [15]. Micelles are selected according to the respective drug properties and the ocular release profile [8]. Micelles have a superb structure and properties which play an influential role in over passing ocular obstacles, thus micelles are particularly for ocular drug delivery. The various barriers in the eye like corneal epithelium, conjunctiva and blood-retina barrier can restrict therapeutic agent delivery [13].

The particle size of DDSs is crucial in ocular applications as it significantly influences the ability to overcome the physical and biological barriers of the eye, and the pore diameter of ocular tissues plays a key role in this process [16]. Ocular tissues, such as the cornea, sclera, and conjunctiva, have tight junctions and extracellular matrices with pore diameters typically ranging from 20 to 50 nm, depending on the tissue [17]. Nanoparticles or micelles in this size range have the advantage of being able to penetrate these barriers and therefore may improve penetration and delivery of drugs to deeper ocular tissues. In addition, an ideal size of the particles prevents loss by rapid clearance from the surface due to tear turnover and blinking.

Citation: Vikal A, Maurya R. Micellar Drug Delivery Systems in Ocular Therapeutics: Overcoming Challenges and Enhancing Treatment Outcomes for Ocular Diseases. J. Pharm. Pharmacol. Res. October-December 2026; 01(01): 01-13.

For instance, particles too large (>200 nm) cannot penetrate into the eye and may be washed away quickly from the surface [18], while very small particles (<10 nm) could serve poorly since they drain rapidly through the nasolacrimal duct [18]. In addition, target targeting to specific tissues depends on particle size; for example, small micelles can penetrate into tight junctions of corneal epithelium and facilitate drug transport into the anterior chamber.

The size also affects drug release kinetics, as smaller particles provide a larger surface area, enabling a more controlled and sustained release [19]. Importantly, smaller particles are less likely to irritate sensitive ocular tissues, improving patient comfort and compliance. Since the pore diameter of ocular tissues acts as a physical sieve, it is essential to design DDSs that align with these dimensions to ensure effective penetration and drug delivery. Ultimately, particle size is a critical parameter in ocular DDSs, influencing penetration, retention, release kinetics, and tissue compatibility for effective therapeutic outcomes [20]. The hydrophilic outer shell enables interaction with the aqueous environment of the eye, while the hydrophobic core of micelles encapsulates drugs, improving the solubility of hydrophobic compounds that are otherwise difficult to deliver. This makes micelles particularly suitable for delivering hydrophobic drugs to ocular tissues. Furthermore, their ability to modify release rates and sustain drug release over time is highly beneficial for ocular therapies, reducing the need for frequent dosing. Micelles also help increase drug retention in the eye by reducing drug clearance and enhancing muco-adhesion, which is important for prolonged therapeutic effects. By improving drug stability, solubility, and targeting, micelles offer a promising approach for effective ocular drug delivery, overcoming the challenges posed by the eye's protective barriers [21-25].

The effectiveness of ocular micellar delivery system can be considerably influenced by their size and charge since these factors impact the penetration of micelles across ocular barriers and subsequent delivery of drug molecules. Micelles should ideally have a size of about 10–100nm [26]. Particles smaller than 10 nm are rapidly cleared, while those greater than 100 nm encounter obstacles with the penetrability of corneal and conjunctival barriers [27]. Likewise, a small and positive membrane charge of about +10 to 30 mV is ideal. It allows favourable interactions with the negatively charged eyeball surface for either adhesion and/or cellular uptake so that it reduces toxicity and irritation. Micellar systems can provide the required prolonged retention, efficient penetration and even better therapeutic outcome if these parameters are well optimized [28].

Micelles indeed have a hydrophilic character due to their hydrated shell, which enhances their affinity for hydrophilic ocular tissues such as the corneal stroma. However, as noted, the most significant barrier in the cornea is the lipophilic epithelium, not the hydrophilic stroma or its tight junctions. This aspect deserves closer attention when discussing the advantages of micelles for ocular drug delivery [29]. Micelles provide a unique advantage in overcoming the lipophilic epithelium due to their amphiphilic structure. While their outer shell is hydrophilic, their core is lipophilic, enabling them to encapsulate hydrophobic drugs. This dual character allows micelles to interact with both lipophilic and hydrophilic environments, facilitating drug transport across the corneal epithelium [30]. Upon contact with the lipophilic epithelial layer, micelles can potentially disrupt the barrier or enhance permeability through mechanisms like paracellular transport or interaction with cellular membranes, depending on their size and surface properties [31]. In addition, micelles can act as carriers that shield hydrophilic drugs from the lipophilic epithelium, effectively enhancing their transport. By altering the surface chemistry or incorporating penetration enhancers, micelles can further improve their ability to navigate through tight junctions and epithelial cells. Therefore, micelles not only provide an advantage in the stroma but also offer solutions to the challenges posed by the lipophilic corneal epithelium [32,33].

Citation: Vikal A, Maurya R. Micellar Drug Delivery Systems in Ocular Therapeutics: Overcoming Challenges and Enhancing Treatment Outcomes for Ocular Diseases. J. Pharm. Pharmacol. Res. October-December 2026; 01(01): 01-13.

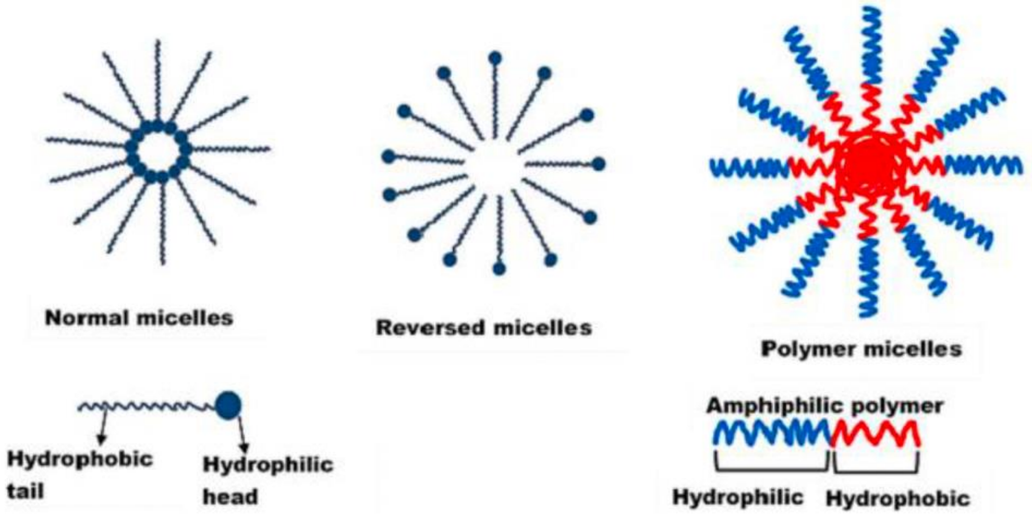

Figure 1: The structure of normal, reverse, and polymeric micelles. Ref [7].

Ocular Drug Delivery Routes:

The simplest way of treating anterior segment disorders such as dry eye, and infections such conjunctivitis or keratitis is by topical delivery via eye drops but they have their limitations related to significant pre-corneal drug loss. This is why intraocular injections have emerged as a standard modality since the drug can be kept in close proximity to intended lysosomes. Aqueous humor flow and other barriers inhibit the therapeutic levels to be achieved in the posterior segment, therefore intracameral injections were designed primarily for application after cataract surgery or treating anterior segment infections. For posterior segment diseases, intravitreal injections are preferred, although they carry risks of complications such as infection or retinal toxicity. Periocular injections (e.g., subconjunctival, sub-tenon) pose fewer risks and allow larger volumes, providing prolonged drug action via transscleral, systemic, or anterior pathways. Yet, frequent periocular injections may still be necessary. Developing non-invasive systems that offer sustained drug release with minimal discomfort remains crucial for safe, effective ocular treatment [9,19,25,34-36].

Micelle-Mediated Pathways for Ocular Drug Delivery:

When administered topically as an eye drop, a drug may penetrate the posterior segment of the eye through two distinct pathways: corneal and conjunctival-scleral. About 85-90% of the cornea consists of a highly hydrophilic stroma (the layer that comprises the major structure of the cornea), and at the same time it is one of main hindrance for topological hydrophobic drugs. Polymeric micelles composed of highly water-soluble polymers can therefore encapsulate these hydrophobic drugs in the lipophilic core, which addresses this challenge. The polymeric micelles are nano-sized and have been known to crossover the corneal barrier or take the conjunctival-scleral route from the front of eye (anterior segment) to its back part (posterior segment). Utilizing the conjunctival-scleral route with a larger surface area permits lateral diffusion of micelles, thus enhancing drug delivery to posterior ocular tissues. The hydrophilic corona of these micelles helps to transport the micellar-drug complex via scleral pores or channels. Moreover, drug washout into systemic circulation is minimized by utilizing the scleral distribution route compared with conjunctival drainage through blood vessels and lymphatics. After arriving in the posterior segment, polymeric micelles may be internalized by retinal pigment epithelial (RPE) through endocytosis allowing for therapeutic drug dosages to enter these tissues. Furthermore, as previously mentioned, the surface charge and size of micelles influences their absorbance by nearby tissues and cellular uptake efficiency [9,19,36-38]. Schematic illustration of a polymeric micellar formulation (topical eye drop) penetrating towards posterior ocular tissues (adapted from Figure 2).

Citation: Vikal A, Maurya R. Micellar Drug Delivery Systems in Ocular Therapeutics: Overcoming Challenges and Enhancing Treatment Outcomes for Ocular Diseases. J. Pharm. Pharmacol. Res. October-December 2026; 01(01): 01-13.

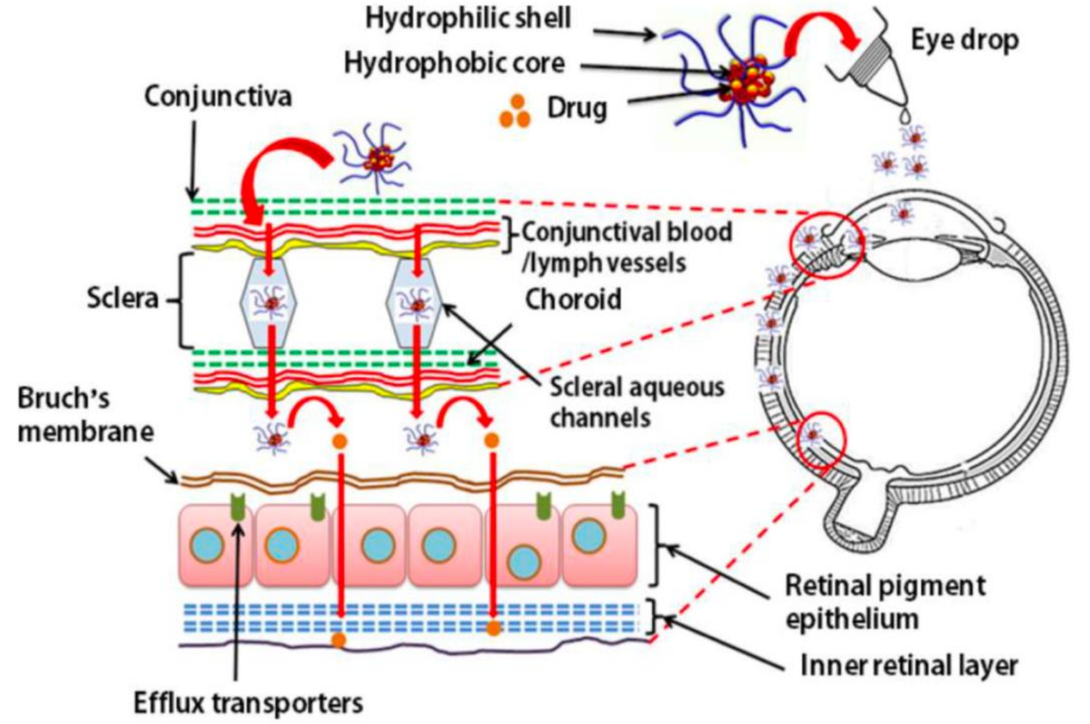

Figure 2: Illustrates a schematic representation of polymeric micelles traveling through the transscleral pathway to reach posterior ocular tissues after topical application. Reproduced from ref. [9].

Enhanced Therapeutic Efficacy:

Micelles have significantly improved therapeutic efficacy compared to conventional treatments by addressing several key limitations in drug delivery. Many therapeutic agents, particularly hydrophobic drugs, have poor solubility in aqueous environments, limiting their bioavailability in traditional formulations [39]. Micelles, formed by amphiphilic molecules, overcome this challenge by creating a hydrophobic core that encapsulates poorly soluble drugs, enhancing their solubility and enabling more effective delivery [40]. Additionally, micelles protect drugs from enzymatic or chemical degradation, improving stability and prolonging therapeutic activity in vivo. Unlike conventional treatments that often result in systemic drug release and off-target effects, micelles allow for controlled and sustained release. When functionalized with ligands, they can actively target specific tissues or cells, such as tumors, further enhancing efficacy while minimizing side effects [21].

Micelles also improve pharmacokinetics and biodistribution by evading recognition by the immune and reticuloendothelial systems, increasing circulation time and enabling better accumulation at target sites via the EPR effect [41]. This targeted delivery not only boosts therapeutic outcomes but also reduces systemic toxicity by minimizing drug exposure to non-target tissues, thereby allowing lower doses to achieve the desired effect. Studies have demonstrated that micelle-based drug delivery systems can increase therapeutic efficacy by 2-10 times compared to conventional treatments, depending on the disease model and drug formulation. For instance, micelle-formulated paclitaxel has shown superior tumor reduction rates and significantly lower systemic toxicity compared to traditional formulations like Taxol. Overall, micelles represent a transformative approach to drug delivery, offering enhanced solubility, stability, targeting capabilities, and reduced toxicity, ultimately resulting in improved therapeutic outcomes across a range of applications [42,43].

Citation: Vikal A, Maurya R. Micellar Drug Delivery Systems in Ocular Therapeutics: Overcoming Challenges and Enhancing Treatment Outcomes for Ocular Diseases. J. Pharm. Pharmacol. Res. October-December 2026; 01(01): 01-13.

The Application in Ocular delivery:

The application of micelles in ocular drug delivery has been in-depth explored in recent years as a solution to overcome the inherent challenges of conventional ocular treatments. Micelles, with their unique ability to solubilize poorly water-soluble drugs and improve their ocular bioavailability, are being increasingly investigated for a variety of eye conditions. Their small size, biocompatibility, and potential to deliver both hydrophilic and lipophilic drugs make them ideal candidates for enhancing the therapeutic efficacy of ophthalmic formulations [30,44,45].

Ozturk et al. Here we present a study on the preparation of an intelligent drug DDS based on thermo-sensitive amphiphilic poly(ε-caprolactone)-poly(N-vinylcaprolactam-co-N-vinylpyrrolidone) [PCL-g-P(NVCL-co-NVP)] graft copolymers. These copolymers assembled into micelles for the co-delivery of Indomethacin (IMC) and Dorzolamide to treat open-angle glaucoma. DLS characterization demonstrated that Dorzolamide enhances, and IMC reduces micelle size. Mediated micelles loaded with drugs had excellent stability within 30 days. FTIR analysis confirmed the successful encapsulation of both drugs, with notable interactions between the polymer matrix and IMC. In vitro studies demonstrated the biocompatibility of the micelles, showing high cellular viability (>80%) and low haemolysis (<3%). The micelles provided sustained drug release, confirmed by in vivo tests on rabbit eyes, where a long-lasting reduction in intraocular pressure was observed. This delivery system addresses the challenge of frequent dosing and poor patient compliance in glaucoma treatment, offering a sustained-release platform that could minimize the need for invasive procedures. The findings suggest these micelles hold promise for further in vivo testing and potential clinical use [46].

Lin et al. developed cationic block copolymer micelles surface modified with hexapeptides to improve their interaction ability with the ocular surface. The positively charged modification also had higher retention on and permeation through the eye for a hydrophobic immunosuppressant, tacrolimus ecc in ameliorating keratoconjunctivitis sicca. Among the listed formulations, maximum corneal permeation with doses of NC-1 (PEP-PEG-PBG) was visualized as well as significant decrease in proinflammatory cytokines IL-17 and IL-1β observed indicating a great therapeutic avenue for treating inflammatory eye disease. Zhang et al. studies based on a PEG-PCL block copolymer with α-cyclodextrin as an amphiphilic co-block, which will be used to prepare the supramolecular thixotropic hydrogel. The hydrogel is aimed at extended and sustainable release of diclofenac (a hydrophobic nonsteroidal anti-inflammatory drug) to the eye with a long retention time along the ocular surface. Another benefit of incorporating this sol–gel transition feature into the gel is response to blinking, allowing controlled and sustained drug release in excess of 216 hours in an eye model [19].

Safwat et al. formulated block copolymer micelles with PEG-b-PLA and PEG-b-PCL to enhance the delivery of triamcinolone acetonide for anterior segment inflammation. In a rabbit model of inflammation, these micelles demonstrated sustained drug release and substantial anti-inflammatory effects. The PLA micelles in particular showed reduced inflammatory markers and preservation of corneal structure, positioning them as promising candidates for treating anterior eye inflammation [47].

Zhang et al. designed amphiphilic glycopolymer based micelles encapsulated with ciprofloxacin for the treatment of bacterial keratitis. Micelles functionalized with boronic acid showed enhanced penetration ability of bacterial cells, selectively targeting the bacterial infection. This strategy provided greater resolution of bacterial keratitis compared with standard formulations by reducing proinflammatory cytokines in a rat model [48].

Zhao et al. developed a triple crosslinked micelle-hydrogel lacrimal implant for prolonged glaucoma treatment. Latanoprost and Timolol were encapsulated in PEG-PLA micelles and incorporated into the hydrogel, providing sustained drug release. Using a unique fixation technology, the implant was securely placed in the lacrimal duct.

Citation: Vikal A, Maurya R. Micellar Drug Delivery Systems in Ocular Therapeutics: Overcoming Challenges and Enhancing Treatment Outcomes for Ocular Diseases. J. Pharm. Pharmacol. Res. October-December 2026; 01(01): 01-13.

In vitro studies showed that drug release lasted up to 28 days, and in vivo tests on rabbits with elevated intraocular pressure (IOP) demonstrated effective IOP reduction for over 28 days. The implant's pharmacological availability was 5.7 times higher than eye drops. Ocular irritation tests confirmed its safety. Zhao et al. concluded that this implant offers a promising non-invasive approach for long-term glaucoma management with excellent safety and efficacy [49].

Stack et al. designed a specific nano functionalized therapy to modulate the mechanical properties of outflow tissue, specifically SC and lower IOP in glaucoma. Peg-b-PPS micelles loaded with Latrunculin A (tLatA-MC, where t stands for targeting) were modified to bind a peptide that targets the VEGFR3/FLT4 receptor which is overexpressed on SC cells. In vitro, this led to increased uptake of micelles by SC cells and reduced uptake of micelles in other endothelial cells. Atomic force microscopy also confirmed the SC cell stiffness reduction by tLatA-MC. In vivo, tLatA-MC reduced IOP by 30–50% in a mouse model. Stack et al. reported that this kind of targeted therapy could be a new way to sensitively ↓ IOP by softening SC cells for glaucoma treatment[50].

Mohan et al. developed Brinzolamide (BRZ)-loaded TPGS-Chitosan conjugate micelles (BTCM) using the solvent evaporation approach for glaucoma treatment. The micelles, with a size of 74.32±1.46 nm, showed sustained BRZ release for up to 8 hours, enhanced corneal permeability, and better mucoadhesion compared to the marketed formulation (MF). In vivo tests on a rabbit glaucoma model demonstrated improved anti-glaucoma efficacy and corneal compatibility. Mohan et al. concluded that BTCM is a promising option for enhancing BRZ's therapeutic potential in glaucoma management [51]. Table: summarizes studies on the application of copolymeric micelles designed to overcome barriers in the eye for effective drug delivery.

Table: Overview of copolymeric micelle systems developed for ocular targeted drug delivery.

Nanoparticle Platform	Encapsulated Agent	Particle Size (nm)	Surface Charge (mV)	Therapeutic Focus	Target Cell Group	Key Study Findings	Ref.
MPEG-hexPLA copolymeric micelles	Cyclosporine-A (CsA)	N/A	N/A	Preventing cornea graft rejection	Corneal epithelial and stromal cells	Micelles containing CsA bypass corneal barriers, sustaining therapeutic levels to support graft survival.	[52]
F68 copolymeric micelles	Plasmids (pCMV-Lac Z, pK12-Lac Z, pKera3.2-Lac Z)	187	–12	Corneal gene expression	Corneal epithelial and stromal cells	Enabled specific gene expression in the stroma and corneal epithelium using cornea-specific promoters, achieving non-invasive gene delivery in mice and rabbits through eye drops.	[53]
Polyoxyl 40 stearate copolymeric micelles	Cyclosporine A (CsA)	200	N/A	Immune-mediated ocular diseases	Corneal and lacrimal gland cells	Increased corneal permeation and wider CsA distribution across eye tissues, consisting of cornea and lacrimal glands, showing promise for treating immune-mediated ocular conditions.	[54]
Copolymeric micelles (NIPAAM-VP-AA)	Ketorolac tromethamine (KT)	35	N/A	Anti-inflammatory effects	Corneal epithelial cells	Achieved superior corneal absorption and prolonged anti-inflammatory effects, showing significantly improved therapeutic outcomes compared to traditional drug suspensions.	[54]
PEG-polyglutamic acid benzyl ester micelles	Tacrolimus (FK506)	270	+14	Dry eye syndrome (DES)	Corneal epithelial and conjunctival cells	Positive charge enhanced ocular retention and corneal permeability of FK506, improving outcomes compared to commercially available FK506 formulations.	[55]

Citation: Vikal A, Maurya R. Micellar Drug Delivery Systems in Ocular Therapeutics: Overcoming Challenges and Enhancing Treatment Outcomes for Ocular Diseases. J. Pharm. Pharmacol. Res. October-December 2026; 01(01): 01-13.

Triblock copolymer PEG-PCL-g-PEI	Cyclosporine A (CsA)	27.74	+12	Dry eye syndrome (DES)	Corneal epithelial cells	Micelle-encapsulated CsA showed extended retention and enhanced corneal penetration, demonstrating improved outcomes over non-encapsulated versions in dry eye management.	[56]
PVCL-PVA-PEG micelles	Myricetin (Myr)	-	-2.58	Ocular anti-inflammatory	Corneal epithelial and stromal cells	Myricetin-loaded micelles improved solubility, stability, and ocular tolerance. These micelles facilitated higher cellular uptake and corneal permeation, indicating potential as anti-inflammatory eye drops with enhanced bioavailability.	[12]

Commercial Formulations of Micelles for ODDS:

Several commercial products in the form of micelles have been developed for ODDS, aimed at improving the bioavailability and therapeutic efficacy of drugs while overcoming the challenges of ocular barriers. Some examples include:

1. **Restasis® (Cyclosporine A) by Allergan:** Although not a micellar preparation in the strictest terms, Restasis utilizes a nanoparticulate delivery system to increase the solubility and bioavailability of cyclosporine A, an immunosuppressant therapy for dry eye disease. Much like micelles improve the delivery of drugs, this technology provides stability and prolonged release from the ocular surface [57].
2. **Miebo® (Perfluorohexyloctane) by Novaliq:** This product is an ocular lipid-based formulation used for the treatment of dry eye disease. While not a typical micellar system, its innovative approach in using nanostructured lipid carriers shares similarities with micelle-based systems in enhancing ocular drug retention and minimizing tear drainage [58].
3. **Ocular Nanoemulsions:** Nano emulsion and micelle-based delivery system often are used for poorly water-soluble drugs Cyclosporine A (as part of other formulations) etc. These systems are capable of prolonging the drug residence time and increasing absorption in the eye, providing an innovative way to deliver hydrophobic and hydrophilic drugs [59].
4. **Nanodrops for Glaucoma:** Various formulations for glaucoma therapy use micelles or nanoparticle-based systems for controlled and sustained release of drugs like timolol or latanoprost. The micellar systems help improve ocular bioavailability, reduce side effects, and increase drug retention on the ocular surface, which is critical for the management of glaucoma [60].
5. **Dextenza® (Dexamethasone Intracanalicular Insert):** While not a typical micellar formulation, Dextenza offers sustained drug release using a hydrogel insert, and some similar drug delivery approaches in ocular systems involve micellar systems to extend the drug's action and release profile, particularly for inflammatory conditions like post-surgical inflammation [61].

Micelles are still a novel method for ocular delivery, but a new interest is in creating micellar formulations of old drugs to enhance their ability to treat dry eye, glaucoma and post-surgical inflammation. The micelle-systems presented here represent considerable potential for solubility and bioavailability enhancement along with enteric release, sustained release or range-controlled delivery, all of which should encourage the development of new commercial applications in ocular therapies [44,62].

Conclusion

Micelle-based drug delivery systems, due to their ability to overcome one or more of the major drawbacks concerning conventional ocular therapeutic approaches including low bioavailability, rapid clearance and poor patient compliance can be proven extremely beneficial in changing future paradigm of ophthalmic therapeutics. Micelles represent a flexible strategy to load hydrophobic drugs and provide sustained release from these designed micelles at both anterior and posterior eye segments. This feature is essential for chronic conditions such as glaucoma, AMD, and ocular inflammation when sustained drug levels are required for efficient treatment.

Micellar formulations not only enhance drug penetration through corneal and scleral barriers but also reduce dosing frequency, which may significantly improve patient adherence to treatment regimens. The demonstrated biocompatibility and ability to bypass traditional barriers further underscore micelles' promise as a safe and efficient alternative to invasive procedures like intravitreal injections. Continued research into optimizing micelle composition, stability, and targeting can lead to tailored therapies for a range of ocular diseases, ultimately enhancing patient outcomes and quality of life. In conclusion, micelle-based delivery systems represent a promising frontier in ophthalmology, with the potential to reshape future ocular disease management through more effective, non-invasive treatment options.

Future perspective:

Building on the promising advancements in micelle-based drug delivery systems, future research is poised to further refine and expand their potential in ocular therapeutics. Further exploration of micelle composition to enhance the stability, controlled liberation, and accurate targeting of drugs can render personalized treatment for countless eye pathologies. “Smart” (i.e., stimuli responsive) micelles that anchor drug in a carrier until specific environmental signals are given cannot only provide more controlled and effective treatments but can address long-term treatment of chronic diseases like age-related macular degeneration and glaucoma. Additionally, as understanding deepens around corneal and scleral penetration pathways, micellar formulations can be customized to overcome individual patient barriers, advancing personalized ocular therapies. By integrating micelles with gene therapy or peptide-based drugs, there is potential for a new class of treatments capable of addressing genetic and degenerative ocular disorders. Enhanced biocompatibility and non-invasive administration methods may also allow these therapies to reduce dependence on intravitreal injections and improve patient adherence significantly. Looking ahead, collaborations across ophthalmology, nanotechnology, and pharmacology will be crucial. The fusion of artificial intelligence and machine learning may lead to a new era of rational design of optimized micellar systems resulting in more accurate predictions of stability and action profiles for developers. It offers the potential for less invasive, non-invasive applications and approaches that are efficacious, safe, simplified and more affordable to patients — potentially transforming how we manage better control of ocular diseases challenging our patients' quality of life..

List of Abbreviations:

- **AMD:** Age-related Macular Degeneration.
- **IOP:** Intraocular Pressure.
- **IMC:** Indomethacin.
- **PEG:** Polyethylene Glycol.
- **PCL:** Poly(ε-caprolactone).
- **PLA:** Polylactic Acid.
- **RPE:** Retinal Pigment Epithelium.
- **WHO:** World Health Organization.
- **DDS:** Drug Delivery System.

Consent for Publication: NA.

Availability of Data and Materials: NA.

Citation: Vikal A, Maurya R. Micellar Drug Delivery Systems in Ocular Therapeutics: Overcoming Challenges and Enhancing Treatment Outcomes for Ocular Diseases. J. Pharm. Pharmacol. Res. October-December 2026; 01(01): 01-13.

REFERENCES

1. Welp A, Woodbury RB, McCoy MA, et al. National Academies of Sciences E, Medicine. Understanding the Epidemiology of Vision loss and Impairment in the United States. Making eye Health a Population Health Imperative: Vision for tomorrow. National Academies Press (US). 2016.
2. Zhou C, Li S, Ye L, et al. Visual Impairment and Blindness Caused by Retinal Diseases: A Nationwide Register-based Study. J Glob Health. 2023; 13: 04126. doi: 10.7189/jogh.13.04126.
3. Kamińska A, Pinkas J, Wrześniewska-Wal I, et al. Awareness of Common Eye Diseases and Their Risk Factors-A Nationwide Cross-Sectional Survey among Adults in Poland. Int J Environ Res Public Health. 2023; 20. doi: 10.3390/ijerph20043594.
4. Assi L, Chamseddine F, Ibrahim P, et al. A Global Assessment of eye Health and Quality of Life: A Systematic Review of Systematic Reviews. JAMA Ophthalmology. 2021; 139: 526-541.
5. Liu LC, Chen YH, Lu DW. Overview of Recent Advances in Nano-Based Ocular Drug Delivery. Int J Mol Sci. 2023; 24. doi: 10.3390/ijms242015352.
6. Wu KY, Tan K, Akbar D, et al. A New Era in Ocular Therapeutics: Advanced Drug Delivery Systems for Uveitis and Neuro-Ophthalmologic Conditions. Pharmaceutics. 2023; 15. doi: 10.3390/pharmaceutics15071952.
7. Onugwu AL, Nwagwu CS, Onugwu OS, et al. Nanotechnology Based Drug Delivery Systems for the Treatment of Anterior Segment eye Diseases. Journal of Controlled Release. 2023; 354: 465-488.
8. Mandal A, Bisht R, Rupenthal ID, et al. Polymeric Micelles for Ocular Drug Delivery: From Structural Frameworks to Recent Preclinical Studies. Journal of Controlled Release: Official Journal of the Controlled Release Society. 2017; 248: 96-116. doi: 10.1016/j.jconrel.2017.01.012.
9. Mandal A, Bisht R, Rupenthal ID, et al. Polymeric Micelles for Ocular Drug Delivery: From Structural Frameworks to Recent Preclinical Studies. Journal of Controlled Release. 2017; 248: 96-116.
10. Li S, Chen L, Fu Y. Nanotechnology-based Ocular Drug Delivery Systems: Recent Advances and Future Prospects. J Nanobiotechnology. 2023; 21: 232. doi: 10.1186/s12951-023-01992-2.
11. Li X, Zhang Z, Li J, et al. Diclofenac/biodegradable polymer micelles for ocular applications. Nanoscale. 2012; 4: 4667-4673.
12. Sun F, Zheng Z, Lan J, et al. New Micelle Myricetin Formulation for Ocular Delivery: Improved Stability, Solubility, and Ocular Anti-inflammatory Treatment. Drug Delivery. 2019; 26: 575-585.
13. Assiri AA, Glover K, Mishra D, et al. Block Copolymer Micelles as Ocular Drug Delivery Systems. Drug Discovery Today. 2024; 29: 104098. doi: https://doi.org/10.1016/j.drudis.2024.104098.
14. Cholkar K, Patel A, Vadlapudi AD, et al. Novel Nanomicellar Formulation Approaches for Anterior and Posterior Segment Ocular Drug Delivery. Recent Pat Nanomed. 2012; 2: 82-95. doi: 10.2174/1877912311202020082.
15. Cabral H, Miyata K, Osada K, et al. Block Copolymer Micelles in Nanomedicine Applications. Chemical Reviews. 2018; 118: 6844-6892. doi: 10.1021/acs.chemrev.8b00199.
16. Gabai A, Zeppieri M, Finocchio L, et al. Innovative Strategies for Drug Delivery to the Ocular Posterior Segment. Pharmaceutics. 2023; 15. doi: 10.3390/pharmaceutics15071862.
17. Bachu RD, Chowdhury P, Al-Saedi ZHF, et al. Ocular Drug Delivery Barriers-Role of Nanocarriers in the Treatment of Anterior Segment Ocular Diseases. Pharmaceutics. 2018. doi: 10.3390/pharmaceutics10010028.
18. Lee H, Noh H. Advancements in Nanogels for Enhanced Ocular Drug Delivery: Cutting-Edge Strategies to Overcome Eye Barriers. Gels (Basel, Switzerland). 2023. doi: 10.3390/gels9090718.

Citation: Vikal A, Maurya R. Micellar Drug Delivery Systems in Ocular Therapeutics: Overcoming Challenges and Enhancing Treatment Outcomes for Ocular Diseases. J. Pharm. Pharmacol. Res. October-December 2026; 01(01): 01-13.

19. Ahmed S, Amin MM, Sayed S. Ocular Drug Delivery: A Comprehensive Review. AAPS PharmSciTech. 2023; 24: 66. doi: 10.1208/s12249-023-02516-9.
20. Goyal S, Dwivedi P, Kaushik J, et al. Innovations in Ocular Drug Delivery. Southeast Asian Journal of Health Professional. 2024; 7: 59-64. doi: 10.18231/j.sajhp.2024.015.
21. Negut I, Bita B. Polymeric Micellar Systems-A Special Emphasis on "Smart" Drug Delivery. Pharmaceutics. 2023; 15. doi: 10.3390/pharmaceutics15030976.
22. Perumal S, Atchudan R, Lee W. A Review of Polymeric Micelles and Their Applications. Polymers. 2022. doi: 10.3390/polym14122510.
23. Jones M-C, Gao H, Leroux J-C. Reverse Polymeric Micelles for Pharmaceutical Applications. Journal of Controlled Release. 2008; 132: 208-215. doi: https://doi.org/10.1016/j.jconrel.2008.05.006.
24. Perumal S, Atchudan R, Lee W. A Review of Polymeric Micelles and Their Applications. Polymers (Basel). 2022; 14. doi: 10.3390/polym14122510.
25. Binkhathlan Z, Ali R, Alomrani AH, et al. Role of Polymeric Micelles in Ocular Drug Delivery: An Overview of Decades of Research. Molecular Pharmaceutics. 2023; 20: 5359-5382.
26. Li Z, Liu M, Ke L, et al. Flexible Polymeric Nanosized Micelles for Ophthalmic Drug Delivery: Research Progress in the Last three Years. 2021; 3: 5240-5254.
27. Bachu RD, Chowdhury P, Al-Saedi ZHF, et al. Ocular Drug Delivery Barriers-Role of Nanocarriers in the Treatment of Anterior Segment Ocular Diseases. Pharmaceutics. 2018; 10. doi: 10.3390/pharmaceutics10010028.
28. Van Setten G-B. Cellular Stress in Dry Eye Disease-Key Hub of the Vicious Circle. Biology. 2024. doi: 10.3390/biology13090669.
29. Cai R, Zhang L, Chi H. Recent Development of Polymer Nano micelles in the Treatment of eye Diseases. 2023; 11. doi: 10.3389/fbioe.2023.1246974.
30. Ghezzi M, Pescina S, Padula C, et al. Polymeric Micelles in Drug Delivery: An Insight of the Techniques for their Characterization and Assessment in Biorelevant Conditions. Journal of Controlled Release. 2021; 332: 312-336. doi: https://doi.org/10.1016/j.jconrel.2021.02.031.
31. Hansen ME, Ibrahim Y, Desai TA, et al. Nanostructure-Mediated Transport of Therapeutics through Epithelial Barriers. International journal of molecular sciences. 2024; 25. doi: 10.3390/ijms25137098.
32. Spleis H, Sandmeier M, Claus V, et al. Surface Design of Nanocarriers: Key to more efficient Oral Drug Delivery Systems. Advances in Colloid and Interface Science. 2023; 313: 102848. doi: https://doi.org/10.1016/j.cis.2023.102848.
33. Xu W, Ling P, Zhang T. Polymeric Micelles, a Promising Drug Delivery System to Enhance Bioavailability of Poorly Water-soluble Drugs. Journal of Drug Delivery. 2013; 2013: 340315. doi: 10.1155/2013/340315.
34. Patel A, Cholkar K, Agrahari V, et al. Ocular Drug Delivery Systems: An Overview. World J Pharmacol. 2013; 2: 47-64. doi: 10.5497/wjp.v2.i2.47.
35. Mofidfar M, Abdi B, Ahadian S, et al. Drug Delivery to the Anterior Segment of the Eye: A Review of Current and Future Treatment Strategies. Int J Pharm. 2021; 607: 120924. doi: 10.1016/j.ijpharm.2021.120924.
36. Del Amo EM. Topical Ophthalmic Administration: Can a Drug Instilled onto the Ocular Surface Exert an Effect at the back of the Eye? Frontiers in Drug Delivery. 2022; 2. doi: 10.3389/fddev.2022.954771.
37. Löscher M, Seiz C, Hurst J, et al. Topical Drug Delivery to the Posterior Segment of the Eye. Pharmaceutics. 2022; 14. doi: 10.3390/pharmaceutics14010134.
38. Vaneev A, Tikhomirova V, Chesnokova N, et al. Nanotechnology for Topical Drug Delivery to the Anterior Segment of the Eye. International Journal of Molecular Sciences. 2021. doi: 10.3390/ijms222212368.

Citation: Vikal A, Maurya R. Micellar Drug Delivery Systems in Ocular Therapeutics: Overcoming Challenges and Enhancing Treatment Outcomes for Ocular Diseases. J. Pharm. Pharmacol. Res. October-December 2026; 01(01): 01-13.

39. Hwang D, Ramsey JD, Kabanov AV. Polymeric Micelles for the Delivery of Poorly Soluble Drugs: From nano formulation to Clinical Approval. Advanced Drug Delivery Reviews. 2020; 156: 80-118. doi: 10.1016/j.addr.2020.09.009.
40. Vinchurkar RH, Kuchekar ABJBBRA. Polymeric Micelles: A Novel Approach Towards Nano-drug Delivery System. 2021; 18: 629-649.
41. Mitchell MJ, Billingsley MM, Haley RM, et al. Engineering Precision Nanoparticles for Drug Delivery. Nature Reviews Drug Discovery. 2021; 20: 101-124. doi: 10.1038/s41573-020-0090-8.
42. Zhao Z, Ukidve A, Kim J, et al. Targeting Strategies for Tissue-Specific Drug Delivery. Cell. 2020; 181: 151-167. doi: https://doi.org/10.1016/j.cell.2020.02.001.
43. Elumalai K, Srinivasan S, Shanmugam A. Review of the Efficacy of Nanoparticle-based Drug Delivery Systems for Cancer Treatment. Biomedical Technology. 2024; 5: 109-122. doi: https://doi.org/10.1016/j.bmt.2023.09.001.
44. Cai R, Zhang L, Chi H. Recent Development of Polymer Nano micelles in the Treatment of eye Diseases. Frontiers in Bioengineering and Biotechnology. 2023; 11: 1246974. doi: 10.3389/fbioe.2023.1246974.
45. Mandal A, Bisht R, Rupenthal I, et al. Polymeric Micelles for Ocular Drug Delivery: From Structural Frameworks to Recent Preclinical Studies. Journal of Controlled Release. 2017; 248: 96-116. doi: 10.1016/j.jconrel.2017.01.012.
46. Ozturk M-R, Popa M, Rata DM, et al. Drug-Loaded Polymeric Micelles Based on Smart Biocompatible Graft Copolymers with Potential Applications for the Treatment of Glaucoma. International Journal of Molecular Sciences. 2022. doi: 10.3390/ijms23169382.
47. Safwat MA, Mansour HF, Hussein AK, et al. Polymeric Micelles for the Ocular Delivery of Triamcinolone Acetonide: Preparation and in Vivo Evaluation in a Rabbit Ocular Inflammatory Model. Drug Delivery. 2020; 27: 1115-1124. doi: 10.1080/10717544.2020.1797241.
48. Zhang Y, Yunjian Y, Li G, et al. Epithelium-Penetrable Nanoplatform with Enhanced Antibiotic Internalization for Management of Bacterial Keratitis. Biomacromolecules. 2021; 22. doi: 10.1021/acs.biomac.1c00139.
49. Zhao J, Xiong J, Ning Y, et al. A Triple Crosslinked Micelle-hydrogel Lacrimal Implant for Localized and Prolonged Therapy of Glaucoma. European Journal of Pharmaceutics and Biopharmaceutics. 2023; 185: 44-54. doi: https://doi.org/10.1016/j.ejpb.2023.02.011.
50. Stack T, Vincent M, Vahabikashi A, et al. Targeted Delivery of Cell Softening Micelles to Schlemm's Canal Endothelial Cells for Treatment of Glaucoma. Small. 2020; 16: 2004205.
51. Mohan P, Rajeswari J, Kesavan K. TPGS-chitosan Conjugated Mucoadhesive Micelles of Brinzolamide for Glaucoma Therapy: In Vitro and in Vivo Evaluation. Materialia. 2023; 28: 101711. doi: https://doi.org/10.1016/j.mtla.2023.101711.
52. Di Tommaso C, Bourges J-L, Valamanesh F, et al. Novel Micelle Carriers for Cyclosporin A Topical Ocular Delivery: In Vivo Cornea Penetration, Ocular Distribution and Efficacy Studies. European Journal of Pharmaceutics and Biopharmaceutics. 2012; 81: 257-264. doi: https://doi.org/10.1016/j.ejpb.2012.02.014.
53. Tong Y-C, Chang S-F, Kao WWY, et al. Polymeric Micelle Gene Delivery of bcl-xL via Eye Drop Reduced Corneal Apoptosis Following Epithelial Debridement. Journal of Controlled Release. 2010; 147: 76-83. doi: https://doi.org/10.1016/j.jconrel.2010.06.006.
54. Kuwano M, Ibuki H, Morikawa N, et al. Cyclosporine A Formulation Affects its Ocular Distribution in Rabbits. Pharm Res. 2002; 19: 108-111. doi: 10.1023/a:1013671819604.
55. Lin S, Ge C, Wang D, et al. Overcoming the Anatomical and Physiological Barriers in Topical Eye Surface Medication Using a Peptide-Decorated Polymeric Micelle. ACS Applied Materials & Interfaces. 2019; 11: 39603-39612. doi: 10.1021/acsami.9b13851.

Citation: Vikal A, Maurya R. Micellar Drug Delivery Systems in Ocular Therapeutics: Overcoming Challenges and Enhancing Treatment Outcomes for Ocular Diseases. J. Pharm. Pharmacol. Res. October-December 2026; 01(01): 01-13.

56. Li J, Li Z, Zhou T, et al. Positively Charged Micelles Based on a Triblock Copolymer Demonstrate Enhanced Corneal Penetration. International Journal of Nanomedicine. 2015: 6027-6037.
57. Ames P, Galor A. Cyclosporine Ophthalmic Emulsions for the Treatment of Dry Eye: A Review of the Clinical Evidence. Clinical Investigation. 2015; 5: 267-285. doi: 10.4155/cli.14.135.
58. Bausch+Lomb and Novaliq Announce FDA Approval of MIEBOTM (Perfluorohexyloctane Ophthalmic Solution) for the Treatment of the Signs and Symptoms of Dry Eye Disease - Novaliq.
59. Gawin-MA, Nartowski KP, Dyba AJ, et al. Ophthalmic Nanoemulsions: From Composition to Technological Processes and Quality Control. Molecular pharmaceutics. 2021; 18: 3719-3740. doi: 10.1021/acs.molpharmaceut.1c00650.
60. Occhiutto ML, Maranhão RC, Costa VP, et al. Nanotechnology for Medical and Surgical Glaucoma Therapy-A Review. Advances in therapy. 2020; 37: 155-199. doi: 10.1007/s12325-019-01163-6.
61. Zheng Q, Ge C, Li K, et al. Remote-controlled Dexamethasone-duration on Eye-surface with a Micelle-magnetic Nanoparticulate Co-delivery System for Dry Eye Disease. Acta Pharmaceutica Sinica B. 2024; 14: 3730-3745. doi: https://doi.org/10.1016/j.apsb.2024.05.004.
62. Nagai N, Otake H. Novel Drug Delivery Systems for the Management of Dry Eye. Advanced Drug Delivery Reviews. 2022; 191: 114582. doi: https://doi.org/10.1016/j.addr.2022.114582.

Citation: Vikal A, Maurya R. Micellar Drug Delivery Systems in Ocular Therapeutics: Overcoming Challenges and Enhancing Treatment Outcomes for Ocular Diseases. J. Pharm. Pharmacol. Res. October-December 2026; 01(01): 01-13.