

## Ocular Drug Delivery System

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### **ABSTRACT:**

Ocular drug delivery remains a significant challenge for pharmacologists and drug delivery scientists due to the complex anatomy and physiology of the eye. Various barriers, including static barriers (corneal, scleral, and retinal layers, along with the blood-aqueous and blood-retinal barriers) and dynamic barriers (tear dilution, lymphatic clearance, and conjunctival and choroidal blood flow), hinder effective drug penetration, particularly into the posterior segment. Additionally, the presence of efflux pumps further complicates drug delivery. In recent years, researchers have focused on targeting influx transporters in different ocular tissues to enhance drug uptake. At the same time, advanced colloidal drug delivery systems, including nanoparticles, nanomicelles, liposomes, and microemulsions, have been extensively studied to overcome these physiological barriers. Moreover, novel formulations such as bioadhesive gels and fibrin sealant-based drug delivery approaches have been developed to prolong drug retention at the intended site. Efforts are being made to design noninvasive sustained-release drug delivery systems, as well as explore the potential of topical formulations for reaching the posterior segment. These advancements hold promise for significantly improving ocular drug delivery and addressing challenges associated with treating both anterior and posterior segment eye diseases.

**KEY WORDS:** Ocular, Barriers, Anatomy, Physiology, Dynamic, Corneal, Scleral, Retinal, Blood-Aqueous, Tear, Lymphatic, Penetration, Nanoparticles, Nanomicelles, Liposomes, Microemulsion.

### **I. INTRODUCTION:**

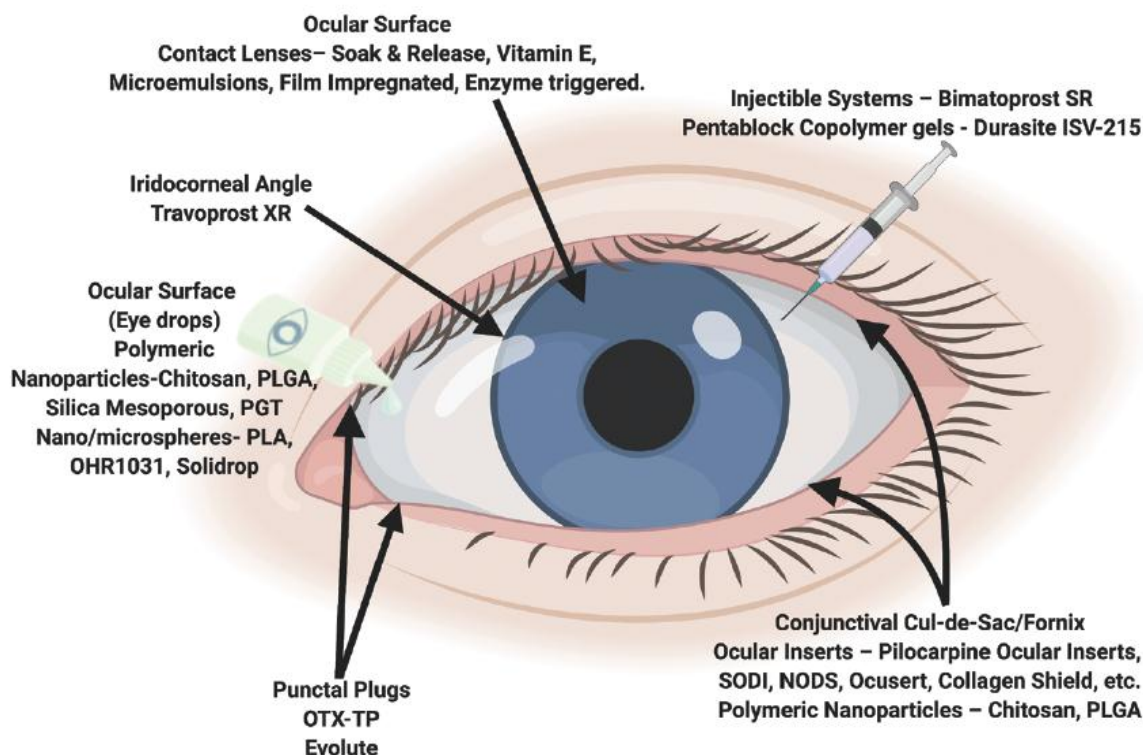
Developing a drug delivery system that specifically targets ocular tissues remains a significant challenge for researchers. The eye is anatomically divided into two main segments: the anterior and posterior regions. Each layer of ocular tissue exhibits unique structural characteristics that can hinder drug absorption, regardless of the chosen administration route—topical, systemic, or periocular. This study highlights the key barriers affecting drug absorption through these routes and explores how the structural properties of ocular tissues contribute to their role as barriers. The impact of efflux pumps in limiting drug bioavailability and the potential of transporter-targeted prodrug strategies to overcome these challenges are also discussed. Recent advancements in ocular drug delivery, particularly in the development of colloidal dosage forms, have shown promise in enhancing drug penetration and efficacy. Various static and dynamic barriers associated with ocular drug delivery have been addressed using innovative formulations. Additionally, progress in noninvasive drug delivery techniques has been examined, offering new possibilities for improved therapeutic outcomes in ophthalmic treatments.[11]

### **II. MODES OF ADMINISTRATION:**

Ocular drug delivery presents significant challenges compared to drug delivery in other parts of the body due to the presence of multiple protective barriers. These barriers, which are intrinsic to the eye's unique anatomy and physiology, make it difficult for drugs to reach their intended target effectively. The nature of these barriers varies depending on the route of administration, including topical, systemic, and injectable methods. Most ocular barriers serve a protective function, shielding the eye from harmful substances. However, these same mechanisms can also limit drug absorption and bioavailability. In addition to anatomical and physiological barriers, several preformulation and formulation factors must be carefully evaluated when developing ophthalmic drug formulations. A summary of different administration routes, along with their advantages and challenges, is presented in Table I. Figure 1 provides a visual representation of key ocular structures and highlights the various drug administration pathways in italics.[1]

**TABLE:1: BENEFITS, AND CHALLENGES IN OCULAR DELIVERY:**

S.N	ROUTE	BENEFITS	CHALLENGES
1.	Topical	High patient compliance, self-administrable and noninvasive.	Higher tear dilution and turnover rate, cornea acts as barrier, efflux pumps, BA <5%.
2.	Oral/Systemic	Patient compliant and noninvasive.	BAB, BRB, high dosing causes.
3.	Intravitreal	Direct delivery to vitreous and retina, sustains drug levels, evades BRB.	Retinal detachment, hemorrhage, cataract, endophthalmitis, patient incomppliance.
4.	Intracameral	Provides higher drug levels in the anterior chamber, eliminates usage of topical drops, reduces corneal and systemic side effects seen with topical steroid therapy	TASS, TECDS
5.	Subconjunctival	Delivery to anterior and posterior segment, site for depot formulations.	Conjunctival and choroidal circulation.
6.	Subtenon	High vitreal drug levels, relatively noninvasive, fewer complications unlike intravitreal delivery.	RPE, chemosis, subconjunctival hemorrhage.
7.	Retrobulbar	Administer high local doses of anesthetics, more effective than peribulbar, minimal influence on IOP.	Retrobulbar hemorrhage, globe perforation, respiratory arrest.
8.	Posterior juxtasceral	Safe for delivery of depot formulations, sustain drug levels up to 6 months to the macula, avoids risk of endophthalmitis and intraocular damage.	Requires surgery and RPE AMD acts as barrier.



**FIGURE 1: MODES OF ADMINISTRATION**

**2.1.BA (Bioavailability):** Bioavailability refers to the proportion of a drug or substance that enters the systemic circulation and is available for therapeutic action. It plays a crucial role in determining drug efficacy.[21]

**2.2.BAB (Blood–Aqueous Barrier):** The blood–aqueous barrier is a physiological barrier that regulates the exchange of substances between the blood and aqueous humor, maintaining ocular homeostasis and preventing harmful agents from entering the eye.[9]

**2.3.BRB (Blood–Retinal Barrier):** The blood–retinal barrier is a selective barrier that prevents the entry of toxins, pathogens, and large molecules into the retina, thereby protecting visual function. It consists of inner and outer layers, primarily formed by endothelial cells and retinal pigment epithelium.[2]

**2.4.AMD (Age-Related Macular Degeneration):** AMD is a progressive eye condition affecting the macula, leading to vision loss, particularly in older adults. It is classified into dry (atrophic) and wet (neovascular) forms.[24]

**2.5.DME (Diabetic Macular Edema):** DME is a complication of diabetes where fluid accumulates in the macula due to damaged blood vessels, causing vision impairment. It is a leading cause of blindness in diabetic patients.[4]

**2.6.BRVO (Branched Retinal Vein Occlusion):** BRVO occurs when a branch of the retinal vein becomes blocked, leading to blood leakage, swelling, and reduced vision in the affected area of the retina.[3]

**2.7.CRVO (Central Retinal Vein Occlusion):** CRVO is a condition where the central retinal vein becomes obstructed, resulting in retinal hemorrhage, macular edema, and vision loss. It is often associated with hypertension and diabetes.

**2.8.RVO (Retinal Vein Occlusion):** RVO is a general term for blockages in the retinal veins, leading to impaired blood flow, retinal damage, and potential vision loss. It includes both BRVO and CRVO.[16]

**2.9.CME (Cystoid Macular Edema):** CME is a condition characterized by fluid accumulation in the macula, forming cyst-like spaces that distort vision. It can result from various ocular diseases or surgical complications.

**2.10.UME (Uveitic Macular Edema):** UME refers to macular swelling associated with uveitis, an inflammatory condition affecting different parts of the eye, potentially leading to vision loss.[29]

**2.11.CMV (Cytomegalovirus):** CMV is a herpesvirus that can cause severe eye infections, particularly in immunocompromised individuals. CMV retinitis can lead to retinal necrosis and vision loss.[11]

**2.12.IOP (Intraocular Pressure):** IOP is the fluid pressure inside the eye, which is essential for maintaining eye structure. Abnormal IOP levels can contribute to conditions like glaucoma.

**2.13.TASS (Toxic Anterior Segment Syndrome):** TASS is a severe inflammatory reaction in the anterior segment of the eye, typically occurring after cataract surgery due to toxic substances. It requires immediate medical intervention.

**2.14.TECDS (Toxic Endothelial Cell Destruction Syndrome):** TECDS is a rare condition that results in permanent damage to the corneal endothelial cells, often due to exposure to toxic agents during ocular procedures.

**2.15.RPE (Retinal Pigmented Epithelium):** The retinal pigmented epithelium is a layer of pigmented cells in the retina responsible for supporting photoreceptor function, nutrient transport, and light absorption. Dysfunction of the RPE is linked to retinal diseases like AMD.

**2.16.PU (Posterior Uveitis):** PU is inflammation affecting the posterior segment of the eye, including the retina and choroid. It can be caused by infections, autoimmune diseases, or systemic conditions, potentially leading to vision impairment.

### III. TOPICAL DRUG ADMINISTRATION IN OCULAR DELIVERY:

Topical administration, primarily in the form of eye drops, is the most commonly used method for treating anterior segment disorders. Upon instillation, drugs target various ocular structures, including the cornea, conjunctiva, sclera, and anterior uvea (iris and ciliary body). However, drug bioavailability is significantly affected by both precorneal and anatomical barriers, limiting the effectiveness of topical formulations.[27]

#### 3.1.PRECORNEAL BARRIERS:

*Several factors contribute to drug loss from the ocular surface before absorption:*

- Tear film dynamics: Rapid tear turnover reduces drug contact time.
- Blinking and lacrimation: Induced tear production washes away the drug.
- Solution drainage: Limited tear volume leads to drug loss into the nasolacrimal duct.

The tear film, which maintains ocular surface health, plays a major role in drug clearance. It forms a hydrophilic layer due to mucin content, which binds debris and microorganisms. With an estimated volume of 7  $\mu\text{L}$  and a transient holding capacity of 30  $\mu\text{L}$  in the conjunctival sac, most topical drug solutions are eliminated within 15–30 seconds of administration. Consequently, less than 5% of the applied dose reaches intraocular tissues.[1][5]

#### 3.2.ANATOMICAL BARRIERS:

*In addition to precorneal factors, structural features of the eye regulate drug permeation:*

##### 3.2.1.CORNEAL BARRIER:

*As the outermost layer of the eye, the cornea acts as a selective barrier preventing the entry of foreign substances.*

*It consists of three primary layers:*

- Epithelium: Lipophilic in nature and accounts for 90% of corneal cells, restricting hydrophilic drug permeation. Tight junctions (zonula occludens) further limit drug passage between cells.
- Stroma: Comprising 90% of corneal thickness, it consists of collagen fibrils and an extracellular matrix. Its hydrophilic nature hinders lipophilic drug molecules.[2][8]
- Endothelium: A monolayer of hexagonal cells that maintains corneal transparency and facilitates selective transport between the stroma and aqueous humor.

Due to its dual lipophilic and hydrophilic nature, corneal permeability requires drugs to exhibit amphipathic properties for effective penetration.

### 3.2.2. CONJUNCTIVAL BARRIER:

*Drug absorption through the conjunctiva is considered inefficient due to:*

- Presence of blood capillaries and lymphatic drainage, leading to systemic drug loss.
- Tight junctions in the conjunctival epithelium, which limit hydrophilic drug movement.

### 3.2.3. SCLERAL BARRIER:

The sclera, which extends from the limbus to the posterior eye, is primarily composed of collagen and proteoglycans. Drug permeability through the sclera is influenced by:

- Molecular size: Smaller molecules exhibit higher permeability.
- Molecular charge: Positively charged drugs bind to the negatively charged proteoglycan matrix, reducing permeability.

Studies indicate that permeability decreases with increasing molecular radius, with linear molecules such as dextrans being less permeable compared to globular proteins.[22]

## IV. SYSTEMIC (PARENTERAL) ADMINISTRATION IN OCULAR DRUG DELIVERY:

Administering drugs systemically, either orally or through intravenous injection, presents challenges in ocular drug delivery due to the presence of protective barriers. The blood-aqueous barrier and blood-retinal barrier play critical roles in restricting drug penetration into the anterior and posterior segments of the eye.[1][7]

### • BLOOD-AQUEOUS BARRIER:

- Composed of the endothelium of the iris/ciliary blood vessels and the non-pigmented ciliary epithelium.
- Tight junctions in these layers prevent solutes from passing into the aqueous humor, limiting drug penetration.

### • BLOOD-RETINAL BARRIER (BRB):

- Divided into the inner BRB (formed by retinal capillary endothelial cells) and the outer BRB (retinal pigment epithelium or RPE).
- The RPE, positioned between the retina and choroid, regulates molecular transport and maintains retinal function.
- While the choroid has a high vascular supply, the outer BRB (RPE) limits drug penetration into the retina, necessitating specialized drug delivery techniques.

## V. STRATEGIES TO OVERCOME THE BLOOD-RETINAL BARRIER:

### 5.1. NANOPARTICLE-BASED DRUG DELIVERY:

*Advances in nanotechnology have enabled better drug penetration across ocular barriers:*

- Gold Nanoparticles (20 nm): Successfully crossed the BRB in mice without cytotoxic effects, whereas larger (100 nm) particles failed to do so.
- PEG-Conjugated Immunoliposomes: Facilitated gene delivery to the RPE, inner retina, and conjunctiva.
- Functionalized PLGA Nanoparticles: Successfully transported antivascular endothelial growth factor (VEGF) therapy to choroidal neovascularization (CNV) lesions.[12]

### 5.2. GENE THERAPY APPROACHES:

- Intravenous administration of SV40/ $\beta$ -galactosidase gene resulted in expression in various ocular tissues.
- Targeted delivery using transferrin and peptide-functionalized nanoparticles has shown promise in enhancing retinal drug delivery.[13]

### 5.3. SYSTEMIC DRUG ADMINISTRATION STUDIE:

- Drugs like micafungin, marbofloxacin, and amphotericin B have been studied for ocular tissue distribution after intravenous administration.[4]
- Visudyne, an FDA-approved intravenous drug, is used in photodynamic therapy for age-related macular degeneration (AMD).

## VI. CHALLENGES OF SYSTEMIC OCULAR DRUG DELIVERY:

- Limited Drug Penetration: Blood-ocular barriers restrict most systemically administered drugs.
- Toxicity Risks: Systemic drug exposure may lead to unintended effects on other organs.
- Low Bioavailability: Only a small fraction of the drug reaches the eye.
- Need for Targeted Delivery Systems: Functionalized nanoparticles and other advanced strategies are required for effective transport.

## VII. PERIOcular AND INTRAVITREAL DRUG ADMINISTRATION IN OCULAR THERAPY:

Periocular and intravitreal routes of drug administration are often employed when topical and systemic approaches fail to deliver effective drug concentrations to the posterior segment of the eye. While these methods are not ideal in terms of patient compliance, they offer targeted drug delivery, reducing the risk of systemic side effects. This makes them particularly useful in treating ocular diseases, especially in geriatric patients who may be more sensitive to systemic drug effects.[24][29]

### VIII. PERIOcular DRUG ADMINISTRATION:

Periocular delivery involves subconjunctival, subtenon, retrobulbar, and peribulbar injections—methods that are less invasive than intravitreal administration. Drugs administered through periocular injections can reach the posterior segment through three primary pathways:

1. Transscleral Route – Direct diffusion through the sclera.
2. Systemic Circulation via Choroid – Entry through the vascularized choroid.
3. Anterior Pathway – Movement through the tear film, cornea, aqueous humor, and vitreous humor.

#### 8.1.SUBCONJUNCTIVAL INJECTION AND DRUG PERMEABILITY:

Subconjunctival injections bypass the conjunctival epithelial barrier, which typically limits the penetration of water-soluble drugs. However, several barriers still influence drug distribution, including:

- Scleral Permeability – The sclera allows easier drug penetration than the cornea and conjunctiva, and its permeability is independent of lipophilicity.[9]
- Choroidal Clearance – The high blood flow in the choroid can rapidly eliminate drugs before they reach the neural retina and photoreceptor cells.[2]
- Conjunctival Blood & Lymphatic Circulation – These dynamic barriers can accelerate drug clearance, reducing ocular bioavailability.

Since a significant amount of the drug is absorbed into systemic circulation, optimizing drug formulations to prolong retention and enhance permeability is crucial for improving therapeutic efficacy.

#### 8.2.INTRAVITREAL DRUG ADMINISTRATION:

Unlike periocular delivery, intravitreal injections provide a direct route for drug delivery into the vitreous humor, increasing drug concentrations in the retina. However, this approach presents challenges:

- Non-Uniform Drug Distribution – Small molecules diffuse easily, while larger molecules face restricted movement.
- Vitreous as a Barrier – The vitreous contains hyaluronan, a negatively charged glycosaminoglycan that interacts with cationic nanoparticles, potentially leading to aggregation and reduced drug mobility.
- Inner Limiting Membrane (ILM) Restriction – The ILM acts as a physical barrier to gene-based therapies, limiting the penetration of adeno-associated viruses (AAVs) used in retinal treatments.

To enhance drug penetration, researchers have explored strategies such as surface modification of nanoparticles (e.g., polyethylene glycol [PEG] coating) and mild enzymatic digestion of ILM to improve gene delivery.[7]

#### 8.3.DRUG ELIMINATION AND HALF-LIFE CONSIDERATIONS:

*Following intravitreal administration, drugs are eliminated through two primary routes:*

1. Anterior Route – Drug diffuses into the aqueous humor, followed by elimination via aqueous turnover and uveal blood flow.
2. Posterior Route – Drug permeates across the blood-retinal barrier, requiring optimal passive permeability or active transport mechanisms.

#### 8.4.KEY FACTORS AFFECTING DRUG HALF-LIFE:

- Hydrophilic drugs and large molecules generally have a longer retention time.
- Lipophilic molecules and small drugs are more prone to rapid clearance through the blood-retinal barrier.

#### 8.5.ORAL ADMINISTRATION IN OCULAR DRUG DELIVERY:

Oral administration has been explored as a potential approach for delivering drugs to the eye, particularly when topical delivery alone fails to achieve therapeutic concentrations in the posterior segment. It is also considered a patient-preferred and non-invasive alternative to injectable routes for chronic retinal diseases. However, this approach presents challenges due to limited accessibility to ocular tissues, requiring higher doses, which can lead to systemic side effects.[24]



### 8.6.ADVANTAGES OF ORAL ADMINISTRATION:

Non-Invasive and Patient-Friendly: Preferred over injections, improving patient compliance.

Potential for Treating Posterior Segment Diseases: Can deliver drugs to retinal tissues when topical routes are ineffective.

Combination Therapy: Can be used alongside topical administration to enhance treatment effectiveness.

### 8.7.CHALLENGES AND LIMITATIONS:

- Low Ocular Bioavailability: Drugs must pass through the gastrointestinal tract, enter systemic circulation, and cross the blood-aqueous and blood-retinal barriers to reach the eye.
- High Systemic Dosage Required: Leads to an increased risk of toxicity and side effects.
- Limited Drug Candidates: Only a few drug classes have been explored for oral ocular delivery.

### 8.8.EXAMPLES OF DRUGS STUDIED FOR ORAL OCULAR DRUG DELIVERY:

Glaucoma Therapy: Oral carbonic anhydrase inhibitors (e.g., acetazolamide, ethoxzolamide) were once used but were largely discontinued due to systemic toxicity.

- Analgesics: Studied for ocular pain management.
- Antibiotics: Investigated for ocular infections.
- Antivirals & Antineoplastic Agents: Explored for viral and cancer-related eye conditions.
- Omega-6 Fatty Acids: Examined for potential neuroprotective effects on the retina.

### 8.9.KEY CONSIDERATIONS FOR ORAL OCULAR DRUG DELIVERY:

- ✓ High Oral Bioavailability: The drug must be efficiently absorbed in the gastrointestinal tract.
- ✓ Ability to Penetrate Ocular Barriers: Must cross blood-ocular barriers to reach therapeutic levels in the eye.
- ✓ Safety & Toxicity Profile: High doses required for ocular efficacy may lead to systemic side effects, necessitating careful dose optimization.

## IX. MELANIN BINDING:

### 9.1.INFLUENCE OF MELANIN ON OCULAR DRUG DISPOSITION:

Melanin, a naturally occurring pigment found in ocular tissues, plays a crucial role in drug binding and distribution. Its presence can significantly alter drug availability at the targeted site, potentially reducing pharmacological activity. This interaction must be carefully considered when designing ocular drug delivery systems.[4][7][12]

### 9.2.MELANIN AND DRUG BINDING MECHANISMS:

*Melanin is present in the uvea (iris, ciliary body, and choroid) and the retinal pigment epithelium (RPE). It interacts with drugs through:*

- ✓ Electrostatic forces.
- ✓ Van der Waals interactions.
- ✓ Charge transfer mechanisms.

Studies suggest that basic and lipophilic drugs have a high affinity for melanin. While this binding is not necessarily linked to ocular toxicity, it can significantly affect drug efficacy by limiting the free drug concentration available for receptor interaction.

### 9.3.IMPACT ON OCULAR DRUG DISTRIBUTION:

*The influence of melanin binding varies across different ocular tissues:*

#### 1. ANTERIOR SEGMENT (IRIS–CILIARY BODY):

- Melanin in the iris and ciliary body can sequester drugs, leading to reduced bioavailability in anterior tissues.

- This necessitates higher drug dosages to achieve therapeutic effects.

#### 2. POSTERIOR SEGMENT (CHOROID AND RPE):

- Melanin in the choroid and RPE impacts drug uptake following transscleral or systemic administration.
- Lipophilic beta-blockers exhibit longer permeation lag-times through the choroid-RPE barrier, delaying their therapeutic effects.
- Melanin-rich choroid-Bruch's membrane shows greater drug binding than the sclera, which lacks melanin. This results in higher resistance to drug permeation.

### 9.4.PHARMACOLOGICAL CONSEQUENCES OF MELANIN BINDING:

- **PROLONGED DRUG RETENTION** – Melanin can act as a drug reservoir, leading to sustained drug release over time.

- **DELAYED DRUG ACTION** – Strong melanin binding reduces the amount of free drug, requiring higher doses for effectiveness.
- **BARRIER TO DRUG PERMEATION** – The choroid-Bruch’s membrane, rich in melanin, presents greater resistance to drug movement compared to the sclera.

### X. TRANSPORTERS IN EYE:

A conventional method to enhance ocular bioavailability involves chemical modification of the drug to optimize solubility and lipophilicity. However, a more strategic approach involves transporter-targeted drug modification. Transporters are membrane-bound proteins that facilitate the active transport of essential nutrients across biological membranes. Their presence has been identified in various ocular tissues, but this discussion specifically focuses on those found in the epithelial layers of the cornea, conjunctiva, and retina. These transporters have the potential to bind and transport ligand-modified drug molecules, offering a targeted drug delivery mechanism. Ocular drug delivery involves two primary transporter systems: efflux transporters and influx transporters. Efflux transporters, which belong to the ATP-binding cassette (ABC) superfamily, reduce drug bioavailability by actively expelling molecules from the cell membrane and cytoplasm. Notable efflux transporters found in ocular tissues include P-glycoprotein (P-gp), multidrug resistance protein (MRP), and breast cancer resistance protein (BCRP). P-gp is known for its role in expelling lipophilic compounds, which can contribute to drug resistance in both normal and cancerous cells.[4] The presence and functional activity of P-gp have been detected in the cornea, conjunctiva, and retinal pigment epithelium (RPE). However, some studies suggest that P-gp expression in human corneal epithelium may be minimal or absent. Similarly, MRP transporters, which primarily transport organic anions and conjugated compounds, have been identified in different ocular tissues, with MRP2 and MRP5 in the corneal epithelium and MRP1 in conjunctival and RPE cells.[7] BCRP expression has also been reported in the corneal epithelium. The variation in expression patterns of these transporters across different cell lines may depend on tissue origin and culture conditions. Some recent studies using cultured human ocular cells and human ocular tissues indicate that MRP1, MRP5, and BCRP are predominantly expressed in freshly excised human corneal epithelium, whereas cultured cell models may overexpress additional efflux transporters. In contrast, influx transporters, which belong to the solute carrier (SLC) superfamily, play a crucial role in facilitating the uptake of essential nutrients and xenobiotics. These transporters include carriers for amino acids, peptides, vitamins, glucose, lactate, and nucleosides/nucleobases.[5] Inspired by the success of valacyclovir, researchers have explored prodrug strategies that target influx transporters for enhanced ocular drug delivery. Transporter-targeted prodrugs provide several advantages: they can increase the absorption of poorly permeable drugs, evade efflux transporters, and improve the solubility and stability of the active compound compared to the parent drug.[24][30]

**TABLE:2 : TRANSPORTER-TARGETED PRODRUGS FOR OCULAR DRUG DELIVERY:**

TRANSPORTER TARGETED TISSUE	SYSTEM-	DRUG/PRODRUGS	RESULT
B(0,+)	on the cornea	l-aspartate ACV	Fourfold higher transcorneal permeability of l-aspartate ACV compared to ACV
B(0,+)	on the cornea	Gamma-glutamate-ACV (EACV)	Higher aqueous solubility of the prodrug along with the transporter recognition
B(0,+)	on the cornea	Phenylalanine-ACV and gamma-glutamate-ACV	The prodrugs inhibited the transport of l-arginine <sup>e</sup> across the cornea implied that they are substrates of B(0,+)
OPT system	on the cornea	l-valine ACV	Threefold higher transcorneal permeability of l-valine ACV compared to ACV
SMVT	on the retina	Biotin-GCV	Higher biotin-GCV permeability into the retina-choroid and slower elimination from vitreous
GLUT1	on the HRPE cells	Glu-dopamine	Transporter recognizes prodrug, not the parent drug

### XI. CONCLUSION:

Effectively treating ocular diseases remains a significant challenge due to the complexity of these conditions and the presence of multiple ocular barriers. Efforts to enhance drug delivery have led to the identification of specific transporters and the modification of drug molecules to improve targeting. These transporters play a crucial role in directing drugs to specific ocular tissues, thereby reducing side effects and enhancing bioavailability. The development of noninvasive drug delivery methods is expected to transform ocular therapy. Additionally, sustained-release drug delivery systems utilizing advanced polymers offer promising potential for controlled and prolonged drug release, particularly for vision-threatening disorders. Innovations in nanotechnology and noninvasive approaches continue to drive progress in ophthalmic drug delivery, paving the way for more effective treatment strategies.

**ABBREVIATION:****MAJOR FULL FORMS :**

CODE	FULL FORM
BA	Bioavailability
BAB	Blood–Aqueous Barrier
BRB	Blood–Retinal Barrier
AMD	Age-Related Macular Degeneration
DME	Diabetic Macular Edema
BRVO	Branched Retinal Vein Occlusion
CRVO	Central Retinal Vein Occlusion
RVO	Retinal Vein Occlusion
CME	Cystoid Macular Edema
UME	Uveitic Macular Edema
TASS	Toxic Anterior Segment Syndrome

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