

# Occular Drug Delivery System: A Novel Review with Applications

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## Abstract

Among the many drug delivery systems, ocular drug delivery system, maintaining a therapeutic drug level at the site of action, is one of the most difficult issues pharmaceutical researchers and associates face for a long time. Programmable medication delivery mechanisms provide a lot of benefits, positive aspects in standard amount methods within regards for reduce dosing frequency, nontoxic and biocompatible, either water-friendly as well as a lipophilic substances had been enclosed, targeted drug delivery can be achieved, improves dissolution, therefore improving an accessibility of substances, large scale production is possible, intended medication delivery in simple exterior alterations, stops deterioration of a lipophilic substances and provides over time equilibrium, prevents medication explosion upon storage, prepared employing a combine of a solid and a liquid lipids as an essential matrices, clear, thermodynamically secure formulations with a droplet size of 100 nm, prevents general distribution, enhances beneficial effectiveness, protects drug form deterioration, elevates intercellular penetration, thus enhancing absorption by using niosomes, disomes, cubosomes, nanowafters, dendrimers, polymer-drug conjugates, nanosuspensions, nanoemulsions, polymeric nanomicelles, surfactant nanomicelles, polyion complex nanomicelles, nanostructure lipid carriers, solid lipid carriers, liposomes, polymeric nanoparticles, viscosity enhancers, produrg, ocular iontophoresis, hydrogels, nanoparticles, contact lens, microneedles, *in situ* gelling system, microemulsion, sonophoresis, phototherapy, and various medications through implants. These numerous designs have been made for some of the special routes of drug delivery such as Intravitreal administration, intracameral, periorbital, suprachoroidal, subconjunctiva, topical, and systemic with various mechanisms. The marketed preparations, such as natamycin solid lip nanoparticles, ciprocin, dex in isotonic acetate buffer, ophthalmic emulsion, napafenacc ophthalmic suspension, etc., are available in various modes of drug delivery.

**Key words:** Cubosomes, disomes, hydrophilic and lipophilic drugs, nanowafters, niosomes, nontoxic and biocompatible

## INTRODUCTION

The pharmaceutical scientist's most intriguing and difficult delivery mechanism is ophthalmic medication delivery. By virtue of its anatomy, physiology, and biochemistry, the eye is exceedingly resistant to extraneous substances. Avoiding irreversible tissue damage while avoiding the eye's protective barriers is a major difficulty

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for the formulator. The bioavailability of medications is impacted by these obstacles. The primary issue with ocular medicine delivery systems is the quick and thorough removal of traditional eye drops from the eye. This issue leads to significant medication loss. Merely, a small quantity of medication can reach the internal tissue of the eye through the corneal layer. Lachrymal drainage and medication dilution by tears are the primary areas of drug loss. This indulgence decreases the ocular bioavailability and leads to negative side effect and toxicity.<sup>[1-3]</sup>

One of the body's best-protected organs is the eye. It has a wide range of defense systems and is composed of numerous intricate layers and structures. The passage of active components into the eye is significantly impeded by these barriers, which are intended to shield the eye from foreign particles, chemicals, and infectious organisms. This poses a problem for the efficient delivery of medications to treat eye disorders. Numerous formulations on the market today have low bioavailability and quick clearance from the site of administration, necessitating frequent dosage schedules. Depending on the delivery method, the dosage frequency varies. For instance, intravitreal injections can be given every 4–6 weeks, while liquid eye drop formulations are typically provided daily, if not 2–3 times a day. It is critical that eye problems be effectively treated. Many of these disorders have a detrimental effect on the patient's vision, including age-related macular degeneration, which affects the posterior segment, and glaucoma, for which the majority of treatments target the anterior segment. The damage or loss of eyesight is irreversible if these disorders are not adequately treated, and the vision impairment is not avoided. A patient's quality of life might be severely impacted by a visual impairment. They are limited in their physical activities because they are incapable or restricted in their ability to complete daily duties. Given the difficulties in delivering medications to the eye, numerous advancements are being attempted to optimize this drug delivery pathway using both polymers and nanosystems. There are several advantages to using polymers, particularly biodegradable polymers, to improve therapeutic ophthalmic formulations. Their mucoadhesive quality is their main advantage, particularly in the cornea and conjunctiva area. This makes it possible for a formulation to have a longer residence period on the surface of the corneal epithelium, which enhances drug penetration. To improve ocular therapeutic preparations, nanoscaled drug delivery methods have been extensively studied. They offer several advantages, such as better penetration through ocular barriers and prolonged drug release profiles. They can enhance drug delivery to the posterior part of the eye, which is renowned for being a challenging area to treat, in addition to improving formulations used to treat the anterior segment of the eye. This review seeks to give a summary of current improvements in ocular drug administration and limitations of the traditional delivery devices on the market. By

demonstrating the prevailing difficulties in ocular drug administration and how they might be drastically altered for increased ocular bioavailability, the significance of disintegrating materials and nanotechnology in this area of biopharmaceutical development will be emphasized.

The most popular non-invasive method of administering medication for conditions impacting the front part of the body is topical instillation. Ninety percent of the approved medications for the eyes are in standard dose forms, such as eye drops. Patient compliance and the convenience of administration could be the cause. However, topical drop delivery results in very limited ocular absorption. Deeper ocular medication penetration is hampered by a number of physiological and anatomical limitations, including retinal dynamic and static barriers, reflex blinking, nasolachrymal drainage, and tear turnover. As a result, <5% of the dose administered topically reaches the deeper tissues of the eyes.<sup>[4-9]</sup>

The most common and well-acknowledged method of administering medications for the treatment of different eye conditions is topical application to the eye.<sup>[10,11]</sup>

Newer treatment strategies for chronic ocular illnesses have been made possible by the rapid advancements in the field of ocular drug-delivery technologies over the last 20 years. Maintaining therapeutic drug concentrations at the target site, lowering dosing frequency, and getting past different dynamic and static ocular obstacles are the fundamental goals of any ocular drug-delivery system.

An organ that responds to pressure and light is the human eye. The mammalian eye is a sensory organ that enables vision. A three-dimensional, moving image that is typically colored during the day is provided by human eyes. The retina's rod and cone cells enable conscious light perception, vision, color distinction, and depth perception. The human eye may be able to detect a single photon and can distinguish between around 10 million colors. Because of its properties related to drug disposal, the eye is the most intriguing organ. In most situations, topical medication delivery is the preferred approach due to its safety and ease for ocular chemotherapy. One of the formulator's biggest challenges is to get beyond the eye's protective layers without permanently harming the tissue.

The advancement in this field is being driven by a number of scientific and technological developments. New smart technologies to improve ocular drug delivery may be made possible, particularly by developments in nanotechnology and biomaterials science. The main component could consist of a substance that is polymeric, mixed with an active compound effective in treating a disease of the eye, e.g. the pilocarpine inserts used in glaucoma therapy PILOCAR-20®, PILOCAR-40®.<sup>[12]</sup>

## IDEAL REQUIREMENTS

- A non-toxic preparation
- Free from foreign particles, fibers, and filaments
- It could be isotonic with lacrimal secretions
- Good has compatible pH with the eye and its composed fluids.
  - Easy to handle
  - An significant corneal piercing
  - A prolonged duration of drug interaction with corneal tissue
  - Installation and removal are simple
  - A non-irritative form
  - High rheological characteristics.<sup>[1]</sup>

## ADVANTAGES

- Increased precision in dosage. To get beyond the negative consequences that traditional systems' pulsed dosage causes
- To give an enduring or regulated drug delivery
- To improve the eyepiece accessibility of the drug by expanding the a corneal interaction time. This can be accomplished by efficient compliance to corneal surface
- To offer focusing on inside the optical globe so as to prohibit the loss to another ocular cells
- To overcome the security obstacles such as irrigation, lacrimation, and conjunctival absorption
- To offer convenience, better adherence to the patient, and to improve the therapeutic effectiveness of medication
- To provide comfort, better compliance to the patient and to improve the therapeutic performance of drug
- In order provide greater housing of delivery system
- These might simply managed by the patient himself
- They possess the rapid intake and fewer apparent and broad against one another impacts
- Ophthalmic drug delivery system has better individuals compliance
- To offer a more accurate housing of the delivery system.<sup>[1,13-16]</sup>

## DISADVANTAGES

- The medication solution remains on the surface of the eye for a relatively brief amount of time
- They may cause vision problems
- In general, the quick drug removal through eye blinking and tear production results in a brief therapeutic effect, necessitating a frequent dosage schedule
- The lacrimal duct absorbs the majority of the dose given, resulting in undesirable systemic side effects
- The cornea's restricted permeability, which results in poor absorption of ocular medication formulation, is the physiological limitation.<sup>[1,13-16]</sup>

## LIMITATIONS

- The dosage form cannot be terminated during emergency
- Interference with vision
- Placement and removal challenges
- Periodic loss while sleeping or scratching your eyes.<sup>[17]</sup>

## ANATOMY OF EYE

There are three major components to the eye:

- i. Eyeball
- ii. Orbit (eye socket)
- iii. Accessory (adnexal) structures.

### The eyeball

The eyeball, commonly known as the globe, is the primary component of the eye. Each sphere-shaped eye has a diameter of roughly 2.5 cm (1 inch) 6. There are many blood arteries in the eyeball. An outer, middle, and inner layer (from the outside to the inside of the eye) are its three layers, or tunics.

### Outer layer

The outermost barrier or coating of the wall of the eye is made up of the sclera and cornea and is called the fibrous tunic.

### Sclera

The strong, white fibrous tissue covering the majority of the eyeball's exterior is called the sclera. The sclera in the rear of the eye is where the optic nerve and blood vessels travel.

### Cornea

The cornea is the transparent material that forms a dome and covers both the pupil and the iris.

### Middle layer

Vascular tunic is the name given to the layer that is located in the middle of the wall of the eye. The uvea is composed of three primary components:

### Iris

It is the thin, muscular, and colored component of the eye that is known as the iris. Between the cornea and the lens, it can be found near the front of the eye, also known as the anterior region.

## Choroid

An extremely thin layer of tissue, the choroid is home to a multitude of minute blood veins that are responsible for delivering oxygen and nutrients to the retina.

## Ciliary body

The ciliary body is located just behind the iris and extends toward the front of the eye from the choroid. It alters the shape of the lens so that it can concentrate on objects that are either close or far away.

## Inner layer

The neural tunic, often known as the retina, is the layer of the eye's wall that is located at the very center of the eye. The retina, which is the thin layer of the eyeball, functions similarly to the film that is used in a camera. Nerve cells that are sensitive to light are the components that make up this molecule. The optic nerve is the nerve that connects these cells to the brain. It is responsible for transmitting information from the eye to the brain, which is what enables humans to see.

## Len

The cornea and the iris are the two structures that are right behind the lens, which is a transparent structure that is located in the inner section of the eye. In order to enable the eye to focus on things, the lens undergoes a transformation.

## Orbit

The orbit, also known as the eye socket, is a bowl-shaped hollow that is produced from the skull and contains the eyeball as well as the connective tissues that surround the eyeball.

## Accessory structures

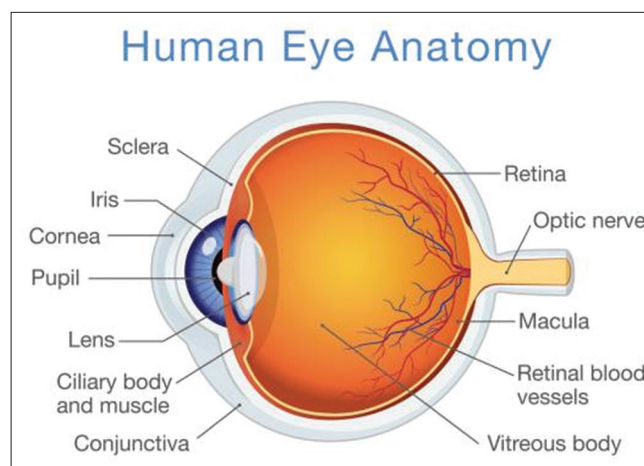
Eyelids, conjunctiva, caruncle, and lachrymal (tear) glands are examples of accessory structures of the eye, which are referred to as adnexal structures. Figure 1 illustrates these specific elements of the eye.

## Eyelids

Eyelids, also known as palpebrae, are folds of skin that lie above the eye and provide protection for it.

## Accessory structures

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**Figure 1:** Structure of eye

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## Conjunctiva

The conjunctiva is a mucous membrane that is transparent in appearance. It is a thin layer of tissue that is wet and lines some organs and cavities in the body, such as the nose, mouth, lungs, airways, vagina, and gastrointestinal tract. The inner surface of the eyelids and the outer surface of the eye are both lined with this substance. The mucus that is secreted by the conjunctiva helps to lubricate the eyeball and maintain its moisture.<sup>[16]</sup>

## Caruncle

The caruncle is a small, pinkish portion of the innermost corner of the eye, also known as the inner canthus. It is comprised of sebaceous glands, which are responsible for producing oil and sweat, as well as conjunctival tissue. The structure and visual parts of the eye were shown in Figures 1 and 2.<sup>[18-30]</sup>

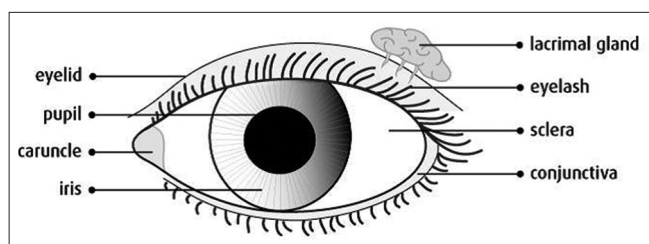
## Lacrimal gland

Lacrimal gland, also known as the tear gland, is the gland that has the shape of an almond and is situated in the upper, outer corner of each eye. Because tears are secreted by the lacrimal gland, they contribute to the maintenance of a moist and lubricated surface of the eye as well as the lining of the eyelids.

## BARRIERS OF DRUG PERMEATION

There are various barriers present within the eye, which is the reason why it is difficult to get therapeutic doses that are





**Figure 2:** Visual parts of eye

relevant to the eye. When the dosage form is administered topically or systemically, it encounters a number of obstacles before arriving to the specified location where it is supposed to exert its effects. Because of this, the bioavailability of the drug through the topical route is often just 1–7% of the dose that is administered. Anatomical barriers and physiological barriers are the two primary categories that are used to classify this type of barrier generally.

### Anatomical barrier

It is possible to administer the medicine topically by either the corneal or non-corneal route, depending on the situation. The cornea is a multilayered structure that is formed of five sections: The epithelium, Bowman's membrane, the stroma, Descemet's membrane, and the endothelium (principal barrier), which serves as a significant barrier to the transfer of hydrophilic drugs.

While the Stroma makes it possible for hydrophilic medications to flow through with ease, it makes it difficult for lipophilic drugs to do so. Therefore, the medicine ought to have the highest possible bioavailability, together with the appropriate equilibrium between its lipophilicity and hydrophilicity. Movement between the sclera and conjunctiva, which is more permeable to hydrophilic drugs, is required for the non-corneal route, which allows patients to avoid the cornea.

### Cornea

Due to the fact that it is the biggest static barrier, it prevents the medication molecule from entering the eye. A selective control over ocular medication penetration is provided by the corneal epithelium. As a result of the lipophilic nature of the epithelium, it acts as a barrier for ninety percent of the hydrophilic drug and for ten percent of the lipophilic medication. The oil–water partition coefficients of the drug molecules are what determine whether or not non-polar chemicals are able to pass through the cornea. This is because the cornea is composed of three layers: the epithelium, the stroma, and the endothelium, which is equal to a fat-water. The cornea functions as a reservoir for the medicine, which is then gradually released into the aqueous compartment of the eye. The medications are dispersed from the aqueous humor to the intraocular tissues, which include the iris ciliary body, lens, vitreous and choroids, retina, and then eliminated by the turnover of the aqueous humor and the

flow of venous blood in the anterior uvea. This occurs after the corneal permeation has occurred. When it comes to a hydrophilic medication, the ocular penetration from the sclera conjunctival channel is significantly faster than the ocular penetration through the transcorneal way.

### Conjunctiva

In addition to covering the anterior sclera, it is a thin tissue that is vascularized and lines the inside of the eyelids. There are two layers that make up this structure: The stroma layer and the outer epithelium, which serves as the primary barrier to penetration. Through the formation of tight connections, the outer apical epithelial cells of the conjunctiva make it possible for paracellular drugs to permeate through the layers of the surrounding cells. There is a barrier between hydrophobic medicines and the conjunctival sclera stroma, which also includes blood vessels and lymph vessels. Considering that the intercellular spacing in the conjunctival epithelium is bigger than that of the corneal epithelium, the permeability of medications across the conjunctiva is higher than the permeability of drugs over the cornea. In addition, the presence of conjunctival blood capillaries and lymphatics, which can cause considerable drug loss into the systemic circulation by lowering the overall ocular bioavailability, contributes to the fact that drug absorption through the conjunctiva is still relatively low.

23 esterase activity is present in the conjunctiva, which expresses efflux proteins as glycoproteins on the cell membrane. These glycoproteins are involved in the process of drug efflux from the cytoplasm of the cell.

### Physiological barrier

The eye's tear film is the principal defensive mechanism that it possesses. Lacrimal fluid is an isotonic solution that contains a mixture of proteins (lysozyme) and lipids. It is responsible for the production of tears. If there is an increase in lacrimation, which results in a dilution of the dose that is delivered. A decrease in drug concentration occurs as a consequence of this, which results in a reduction in medication absorption. This results in quick discharge from the precorneal area through lacrimation and through nasolacrimal drainage, which minimizes the contact time between tissue and drug molecules, thus lowering the period for absorption, which ultimately leads to a reduction in bioavailability. In order to avoid the loss of precorneal tissue, it is necessary for the medications that are provided in the form of eye drops to be non-irritating and isotonic.

### Lacrimal secretion

Lacrimal glands are responsible for the secretion of this fluid, which helps to keep the conjunctiva and cornea wet and

healthy. This fluid is drained to the nose and is maintained by the blinking movement of the eye. Thenasolacrimal drainage that occurs while blinking goes towards the nasolacrimal duct, which causes the removal of the dosage form that was administered. This causes more than 75% of the ophthalmic solution to be lost through the nasolacrimal drainage and absorbed systemically through the conjunctiva.

### Tear film

It is a structure that is formed of three layers: An outer lipid layer, a middle aqueous layer, and an interior mucin layer. It is responsible for covering the conjunctiva and the cornea. The pH level is 7.4, and it contains proteins, lipids, and electrolytes.

A decrease in ocular bioavailability may occur as a result of the drug being administered, which may bind to proteins or be partially hydrolyzed by enzymes. Due to the generation of tears (ranging from 0.5 to 2.2 mL/min) and the turnover of tears, the contact time with ocular tissue is reduced by 1–2 min. As a consequence of this, only a minute fraction of the free medication that is administered to the corneal epithelium is able to successfully pass through the cornea.

### Blood aqueous barrier (BAB)

The BAB serves to safeguard the aqueous humor from any potential harm. Iris and ciliary muscle vasculature endothelium, as well as the posterior iris and non-pigmented ciliary epithelium, are the components that come together to produce this structure.

Due to the presence of tight intracellular connections, this barrier has a low degree of permeability, which restricts the entry of molecules that have a high coefficient of hydrophilicity or a high molecular weight. The gap between cells is a medium through which ions and other tiny solutes move. However, depending on the selectivity of the active transporter, it can also have an effect on the passive diffusion of the drug.

### Blood retinal barrier

The choroid is the layer of the eye that is adhered to by the retina, which is a thin, transparent tissue that constitutes the innermost layer of the eye. The BRB prevents other substances from entering the retina.

Protecting the retina from foreign particles is the inner BRB, which is made up of retinal capillary endothelial cells. These cells have intercellular tight connections and are responsible for this protection. Retinal pigment epithelium (RPE), which is situated between photoreceptors and choriocapillaries, is the component that makes up the outer layer of the basal retinal layer (BRB). Through the limitation of drug delivery

in both the inward (blood to vitreous) and outward (vitreous to blood) directions, lipophilic molecules are able to transfer between the choroid and the retina in an effective manner. While lipophilic drugs are able to pass through the RPE via the transcellular route, hydrophilic substances are able to pass through the RPE through tight junctions (paracellular routes).

### Bruch's-choroid complex (BC complex)

An extremely vascularized and innervated tissue, the choroid is responsible for supplying blood to the retina. It is made up of a network of capillaries that have been fenestrated and is maintained by Bruch's membrane. It is very thin, measuring between 2 and 4 micrometers. Although the sclera is a significant barrier to drug administration via the transscleral pathway, the BC complex is a more significant obstacle. The permeability of the BC complex is influenced by the molecule size. The barriers of drug permeation were shown through Figure 3.<sup>[30-32]</sup>

## ROUTES OF OCULAR DRUG DELIVERY

### Intravitreal

It is a method of administering a medicine or other material that involves injecting it into the vitreous humor of the eye. This method allows the substance to be delivered into the eye. There are a variety of eye disorders that can be treated with intravitreal delivery of medications. There are also several routes of administration. Delivery of drugs through the eyes, as depicted in Figure 4.

### Intra cameral

The process of administering a medicine through a chamber, such as the anterior or posterior chamber of the eye, is referred to as the route of administration. The injection of an anesthetic drug into the anterior chamber of the eye, which is typically performed during surgical procedures, is an example of anesthesia.

### Peril ocular

The term "peril ocular" refers to the method of administering a medicine which involves the eye. When treating intraocular inflammation or swelling of the eye, for instance, a percutaneous ocular steroid injection entails placing a steroid material around the eye.

### Suprachoroidal

The medication is administered in the eye's suprachoroid area. There is a space between the choroid and the sclera called the suprachoroidal space.

## Subconjunctiva

The way that the medication is administered to the mucous membrane lining the inner surface of the eyelids and the exposed part of the eyeball.

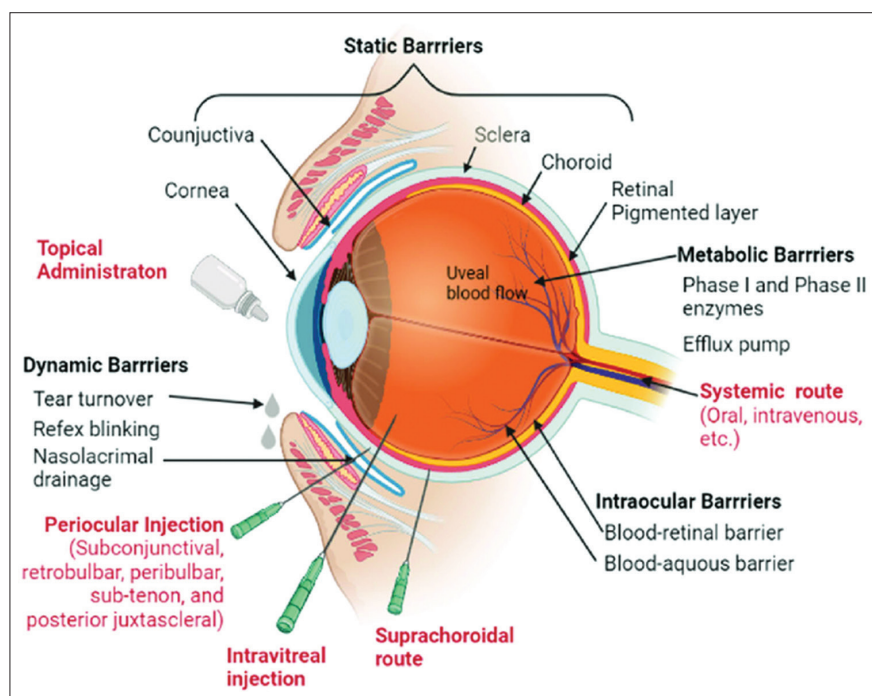
## Topical

The most common forms of topical administration used to treat anterior segment illnesses are eye drops, ointments,

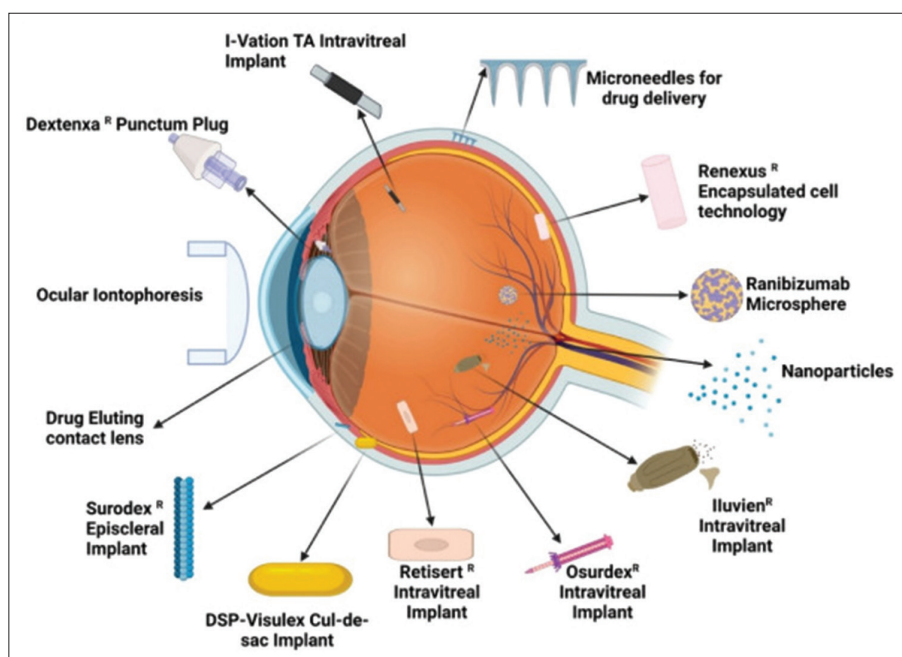
gels, or emulsions. It is the most popular approach because it is inexpensive and easy to administer.

## Systemic

The primary obstacles for the anterior and posterior segments of ocular medication transport are the blood-aqueous and blood-retinal barriers, respectively. The routes of administration are shown in Figure 4.<sup>[33-37]</sup>



**Figure 3:** Barriers of drug permeation



**Figure 4:** Routes of drug administration to eye

**Table 1:** The various ocular drug delivery systems with its benefits

S. No.	Drug delivery systems	Benefits
1	Liposomes (Marketed product: Ciprocin)	Decrease dosing frequency Non-toxic and biocompatible Liposomes range in size from 0.08 to 10. The medications were encapsulated in both hydrophilic and lipophilic forms.
2	Polymeric nanomicelles	Dissolves hydrophobic medications that are smaller than 200 nm. Targeted drug delivery can be achieved Biologically compatible with less adverse effects and toxicity Increased capacity of ocular medications to pass through ocular barriers
3	Polyion complex nanomicelles	Efficient in delivering drugs through ionic macromolecules Target-specific
4	Nanosuspensions (Marketed product: Rimoflo T eye drops, ILEVRO (Napafenac ophthalmic suspension)	Improves the solubility of medications, increasing their bioavailability.
5	Solid lipid nanoparticles (Marketed product: Natamycin solid lipid nanoparticles)	A nanotoxic carrier that is between 10 and 500 nm in size Large-scale production is possible drug delivery that is targeted and surface modification that is simple provides long-term stability and stops lipophilic medications from degrading
6	Nanostructured lipid carriers	Stable and biocompatible Stops medication explosions while being stored Increases the ocular tissue's bioavailability created as a core matrix by combining liquid and solid lipids.
7	Surfactant nanomicelles (Marketed product: DEX in isotonic acetate buffer, pH 4.5).	Improves penetration Increasing the supplied drug's bioavailability
8	Nanoemulsion (marketed as Durezol (difluprednate ophthalmic suspension) and Cationorm ophthalmic emulsion)	Formulations that are clear and thermodynamically stable with a 100 nm droplet size
9	Polymeric nanoparticles (Marketed products: Iluvein® Ozurdex® Retisert®)	Typically less than 400 nm, nanoparticles are appropriate for use in ophthalmology. Drug delivery to ocular tissues that is targeted Prevents indiscriminate spreading Increases the effectiveness of treatment prevents drug degradation Increases absorption by increasing intercellular penetration.
10	Dendrimers (Marketed products: PAMAM (G1.5–4.0) PANAM Core micelle	It is feasible to provide hydrophilic and lipophilic medications. Star-shaped, highly branching polymeric macromolecule with a size range of 5–20 nm Improves the solubility of drugs Shows prolonged drug release and high drug loading.
11	Nanowafers	Drug-loaded circular discs that are nanosized and applied to the surface of the eye Reduces the toxicity of the encapsulated medication and enhances drug stability. Extended action improves patient compliance and therapeutic efficacy. Beneficial in treating corneal neovascularisation
12	Niosomes	Niosomes range in size from 10 to 1000 nm. Because nonionic surfactants make up their composition, they are less toxic, biocompatible, biodegradable, and mucoadhesive. Drug leaching from encapsulation Delivery to ocular tissues with specificity Increased drug bioavailability
13	Cubosomes	Liquid crystalline nanoparticles that self-assemble and are <500 nm With a large loading capacity, it is possible to incorporate hydrophilic, lipophilic, and amphiphilic medicines.

(Contd...)



**Table 1: (Continued)**

S. No.	Drug delivery systems	Benefits
14	Polymer-drug conjugates	Promotes a drug's stability and solubility in bodily fluids
15	Discomes	These are huge niosomes prevents systemic drainage
16	Conventional ophthalmic dosage forms	Widely used for its available cost and rapid action
17	Viscosity enhancers	Slower elimination Improve precorneal residence time
18	Eye ointments	Stays in a cul-de-sac as a drug depot for a long time.
19	Penetration enhancers	Improve ophthalmic drug bioavailability Enhances absorption
20	Prodrug	Enhance corneal drug permeability through modification
21	Ocular iontophoresis	Mild electric charges are used in active medicine delivery to effectively pass through ocular barriers.
22	Hydrogels	Biocompatible Continuous drug release and maintenance of drug concentration
23	Nanoparticle	Colloidal carries Delivers drugs both to posterior and anterior segment
24	Contact lens	Drug loading on contact lens for numerous drugs Greater medication delivery efficiency than traditional eye drops
25	Microneedles	Treating glaucoma using the device Delivery of hydrophilic and hydrophobic drugs
26	<i>In situ</i> gelling system	Residence time is more Improves bioavailability
27	Microemulsion	Improved solubility Improved corneal permeation
28	Sonophoresis	Improved transcleral permeation
29	Phototherapy	Involves tumor removal and site-specific vascular blockage with little harm to nearby structures.
30	Implants (Marketed products: Vitrasert Retisert Medidur Posurdex Surodex).	Prolong the activity of the drug Removal is easy

## OCCULAR DRUG DELIVERY SYSTEMS

The names of the various drug delivery methods, their commercial preparations, and the advantages they provide are listed below. The illustration is given in Table 1.<sup>[38-54]</sup>

## CONCLUSION

Since centuries, controlled drug delivery system was made by several physicians or by formulators by available natural materials, i.e., polymers from natural and other sources. However, at present, synthetic polymers have been used through various methodologies and equipment and wave mechanisms for effective drug delivery. The major challenge is the barrier that could be overcome. The alternative for the overcoming methods is intraroutes of drug delivery for immediate and targeted action of drugs during surgeries and emergency medical administration. Both the conventional

and controlled forms were available, but the selection depends on its use and disease.

## FINANCIAL ASSISTANCE

Nil.

## AUTHORS CONTRIBUTIONS

All authors contributed equally.

## AVAILABILITY OF SUPPORTING DATA

On reasonable request, the corresponding author will make the datasets used in this study available.

## REFERENCES

1. Zaki I, Fitzgerald P, Hardy JG, Wilson CG. A comparison of the effect of viscosity on the precorneal residence of solutions in rabbit and man. *J Pharm Pharmacol* 1999;38:463-66.
2. Lee VH, Robinson JF. Topical ocular drug delivery: Recent developments and future challenges. *J Ocular Pharmacol* 2009;2:67-108.
3. Sikandar MK, Sharma PK, Visht Sikandar S. Ocular drug delivery system: An overview. *Int J Pharm Sci Res* 2011;2:1168-75.
4. Vu HT, Keefe JE, McCarty CA, Taylor HR. Impact of unilateral and bilateral vision loss on quality of life. *Br J Ophthalmol* 2005;89:360-3.
5. Ludwig, A. The use of mucoadhesive polymers in ocular drug delivery. *Adv Drug Deliv Rev* 2005;57:1595-639.
6. Xu Q, Kambhampati SP, Kanna RM. Nanotechnology approaches for ocular drug delivery. *Middle East Afr J Ophthalmol* 2013;20:26-37.
7. Sack RA, Nune I, Beaton A, Morris C. Host-defense mechanism of the ocular surfaces. *Biosci Rep* 2001;21:463-80.
8. Barar J, Aghanejad A, Fathi M, Omid Y. Advanced drug delivery and targeting technologies for the ocular diseases. *Bioimpacts* 2016;6:49-67.
9. Gupta H, Velpandian T, Jain S. Ion and pH-activated novel *in-situ* system for sustained ocular drug delivery. *J Drug Target* 2010;18:499-505.
10. Bourlais CL, Acar L, Zia H, Sado PA, Needham T, Leverage R. Ophthalmic drug delivery systems--recent advances. *Prog Retin Eye Res* 1998;17:33-58.
11. Gulsen D, Chauhan A. Ophthalmic drug delivery through contact lenses. *Invest Ophthalmol Vis Sci* 2004;45:2342-7.
12. Sampath Kumar KP, Bhowmik D, Harish G, Duraivel S, Pragathi Kumar B. Ocular inserts: A novel controlled drug delivery system. *Pharma Innov J* 2013;1:1-16.
13. Arul Kumaran KS, Karthika K, Padmapreetha J. Comparative review on conventional and advanced ocular drug delivery formulation. *Int J Pharm Pharm Sci* 2010;2:668-674.
14. Ravindra Reddy K, Ravi Shankar Yadav M, Sabitha Reddy P. Preparation and evaluation of aceclofenac ophthalmic *in situ* gels. *J Chem Biol Phys Sci* 2011;1:289-98.
15. Reddy KR, Yadav MR, Reddy PS. Preparation and evaluation of aceclofenac ophthalmic *in-situ* gels. *J Chem Biol Phys Sci* 2011;1:289-98.
16. Gaudana R, Ananthula HK, Parenky A, Mitra AK. Ocular drug delivery. *AAPS J* 2010;12:348-360.
17. Champalal KD, Sushilkumar SP. Current status of ophthalmic *in-situ* forming hydrogel. *Int J Pharm Bio Sci* 2012;3:372-88.
18. Schoenwald RD. Ocular drug delivery. Pharmacokinetic considerations. *Clin Pharmacokinet* 1990;18:255-69.
19. Ei-Kamel A. *In vitro* and *in vivo* evaluation of Pluronic F127-based ocular delivery system for timolol maleate. *Int J Pharm* 2002;24:47-55.
20. Saini R. *In situ* gels: A new trends in ophthalmic drug delivery systems. *Int J Recent Adv Pharm Res* 2015;5:285-9.
21. Swapnil S, Patil Ravindra Y, Meenal L. A review on polymers used in novel *in situ* gel formulation for ocular drug delivery and their evaluation. *J Biol Sci Opin* 2003;1:132-7.
22. Pandya TP, Modasiya MK, Patel VM. Ophthalmic *in-situ* gelling system. *Int J Pharm Life Sci* 2011;2:730-8.
23. Jitendra PK, Sharma A, Banik A, Dixit S. A new trend ocular drug delivery system. *Int J Pharm Sci* 2011;2:720-44.
24. Nagyova B, Tiffany JM. Components responsible for the surface tension of human tears. *Curr Eye Res* 1999;19:4-11.
25. Jain R, Shastri P. Study of ocular drug delivery system using drug-loaded liposomes. *Int J Pharm Sci Investig* 2011;1:35-41.
26. Vandamme TF, Brobeck L. Poly(amidoamine) dendrimers as ophthalmic vehicles for ocular delivery of pilocarpine nitrate and tropicamide. *J Control Release* 2005;102:23-38.
27. Vandamme TF. Micro emulsions as ocular drug delivery systems recent development. *Sch Acad J Pharm* 2015;4:340-6.
28. Pignatello R. Flurbiprofen-loaded acrylate polymer nanosuspensions for ophthalmic application. *Biomaterials* 2002;23:3247-55.
29. Gariepy ER, Leroux GC. *In situ*-forming hydrogels--review of temperature-sensitive systems. *Eur J Pharm Bio Pharm* 2004;58:409-26.
30. Masteikova R, Chalupova Z, Sklupalova Z. Stimuli-sensitive hydrogels in controlled and sustained drug delivery. *Medicina (Kaunas)* 2003;39:19-24.
31. Huang AJ, Tseng SC, Kenyon KR. Paracellular permeability of corneal and conjunctival epithelia. *Investig Ophthalmol Vis Sci* 1989;30:684-9.
32. Hughes PM, Mitra AK. Overview of ocular drug delivery and iatrogenic ocular cytopathologies. In: Mitra AK, editor. *Ophthalmic Drug Delivery Systems*. New York: Marcel Dekker, Inc.; 1993. p. 1-27.
33. Sasaki H, Igarashi Y, Nagano T, Yamamura K, Nishida K, Nakamura J. Improvement of the ocular bioavailability of timolol by sorbic acid. *J Pharm Pharmacol* 2013;47:17-21.
34. Burgalassi S, Chetoni P, Monti D, Saettone MF. Cytotoxicity of potential ocular permeation enhancers evaluated on rabbit and human corneal epithelial cell lines. *Toxicol Lett* 2001;122:1-8.
35. Keister JC, Cooper ER, Missel PJ, Lang JC, Hager DF. Limits on optimizing ocular drug delivery. *J Pharm Sci* 1991;80:50-3.
36. Shen J, Gan L, Zhu C, Zhang X, Dong Y, Jiang M, *et al.* Novel NSAIDs ophthalmic formulation: Flurbiprofen axetil emulsion with low irritancy and improved

- anti-inflammation effect. *Int J Pharm* 2011;412:115-22.
37. Vandamme TF. Microemulsions as ocular drug delivery systems: Recent developments and future challenges. *Prog Retin Eye Res* 2002;21:15-34.
  38. Liang H, Brignole-Baudouin F, Rabinovich Guilatt L, Mao Z, Riancho L, Faure MO, *et al.* Reduction of quaternary ammonium-induced ocular surface toxicity by emulsions: An *in vivo* study in rabbits. *Mol Vis* 2008;14:204-16.
  39. Patravale VB, Date AA, Kulkarni RM. Nanosuspensions: A promising drug delivery strategy. *J Pharm Pharmacol* 2004;56:827-40.
  40. Gulsen D, Li CC, Chauhan A. Dispersion of DMPC liposomes in contact lenses for ophthalmic drug delivery. *Curr Eye Res* 2005;30:1071-80.
  41. Cholkar K, Patel A, Vadlapudi DA, Mitra AK. Novel Nanomicellar formulation approaches for anterior and posterior segment ocular drug delivery. *Recent Patents Nanomed* 2012;2:82-95.
  42. Li CC, Abrahamson M, Kapoor Y, Chauhan A. Timolol transport from microemulsions trapped in HEMA gels. *J Colloid Interface Sci* 2018;315:297-306.
  43. Bian F, Shin CS, Wang C, Pflugfelder SC, Acharya G, De Paiva CS. Dexamethasone drug eluting nanowafers control inflammation in alkali-burned corneas associated with dry eye. *Investig Ophthalmol Visual Sci* 2018;57:3222-30.
  44. Watrad K, Mitra AK. Drug delivery in ocular disease: Barriers and strategies. *World J Pharmacol* 2013;2:78-83.
  45. Jiang J, Gill HS, Ghate D, McCarey BE, Patel SR, Edelhauser HF, *et al.* Coated microneedles for drug delivery to the eye. *Invest Ophthalmol Vis Sci* 2007;48:4038-43.
  46. Patel A, Cholkar K, Agrahari V. Ocular drug delivery systems: An overview. *World J Pharmacol* 2013;2:47-64.
  47. Kaur IP, Garg A, Singla AK. Vesicular systems in ocular drug delivery: An overview. *Int J Pharmacol* 2004;269:1-14.
  48. Kirchhof S, Goepferich AM, Brandl FP. Hydrogels in ophthalmic applications. *Eur J Pharm Biopharm* 2015;95:227-38.
  49. Tiruchurai GS, Dias C, Mitra AK. Effect of hydroxypropyl beta cyclodextrin complexation on aqueous solubility, stability, and corneal permeation of acyl ester prodrugs of ganciclovir. *J Ocul Pharmacol Ther* 2012;18:535-48.
  50. Bhattacharjee A, Das JP, Adhikari P, Marbaniang D, Pal P, Ray S. Novel drug delivery systems for ocular therapy: With special reference to liposomal ocular delivery. *Eur J Ophthalmol* 2019;29:113-26.
  51. Buech G, Bertelmann E, Pleyer U, Siebenbrodt I, Borchert HH. Formulation of sirolimus eye drops and corneal permeation studies. *J Ocul Pharmacol Ther* 2017;23:292-303.
  52. Schmidt-Erfurth U, Hasan T, Gragoudas E, Michaud N, Flotte TJ, Birngruber R. Vascular targeting in photodynamic occlusion of subretinal vessels. *Ophthalmology* 1995;1:1953-61.
  53. Raj VK, Mazumder R, Madhra M. Ocular drug delivery system: Challenges and approaches. *Int J Appl Pharm* 2020;12:49-57.
  54. Amrutkar CS, Patil SB. Nanocarriers for ocular drug delivery: Recent advances and future opportunities. *Indian J Ophthalmol* 2023;71:2355-66.

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