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A Review: Ocular Drug Delivery System

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ABSTRACT:

Topical administration is the best option for ocular therapies due to its quick beginning of action, lack of systemic toxicity, and fewer doses needed than systemic use. Transcorneal penetration is thought to be the main pathway for drug absorption, and topically applied ocular medications must reach the interior regions of the eye. Elimination happens much more quickly than corneal absorption. Achieving the ideal medication concentration at the active site for the right amount of time is the specific goal of therapeutic system design. The best ophthalmic medication delivery system must be able to maintain the drug's release and stay close to the front of the eye for an extended amount of time.

Keywords: ocular delivery, corneal absorption, Controlled and sustained drug delivery, Anatomy and physiology, corneal barriers .

Introduction:

Because of its properties related to drug disposal, the eye is the most intriguing organ. When it comes to ocular chemotherapy, topical administration is typically the preferred approach due to its simplicity and safety. Avoiding irreversible tissue damage while avoiding the eye's protective barriers is a major difficulty for the formulator. Ocular delivery systems with excellent treatment efficacy are still being made possible by the development of new, more sensitive diagnostic methods and innovative therapeutic substances. Traditional ophthalmic formulations, such as ointment, suspension, and solution, have numerous drawbacks that contribute to the drug's low bioavailability in the ocular cavity. Achieving the ideal medication concentration at the active site for the right amount of time is the specific goal of therapeutic system design. The state of the eyes and Many ocular barriers, including tear film, corneal, conjunctival, and blood-ocular barriers, limit the effectiveness of powerful medications that are available to treat the majority of ocular ailments. Blinking and tear production waste traditional eye drops. As a result, their bioavailability is reduced to under 5%. The stroma, endothelium, and epithelium make up the cornea. Only tiny, lipophilic drugs can get through the epithelium. However, hydrophilic medications can flow through the stroma. The endothelium allows hydrophilic medications and macromolecules to enter the aqueous humor selectively while maintaining the cornea's transparency.

Anatomy of eye:

The exquisitely detailed and designed human eye serves as a portal to the process known as vision. The eyeball is roughly one inch wide and spherical in shape. It contains numerous structures that cooperate to make seeing easier. Each of the internal components and layers that make up the human eye has a specific function. Below is a thorough explanation of each eye component.

Sclera:

The tough white sheath that makes up the ball's outer covering is called the sclera, or white part of the eye. The eye's roughly globe-shaped form is preserved by this tough, fibrous membrane. Compared to the front or anterior of the eye, it is somewhat thicker toward the back or posterior side of the eye.

Conjunctiva:

The anterior portion of the eyeball is covered by the conjunctiva, a thin, transparent mucous epithelial barrier that borders the inside of the eyelids. The palpebral and bulbar conjunctiva are the names given to the corresponding parts of the conjunctiva. An outer layer of epithelium and its underlying stroma (substantia propria) make up the conjunctiva. The tear film covers the conjunctiva and cornea, which are the parts of the eye that are exposed. By secreting significant amounts of fluid, electrolytes, and mucins, the conjunctiva aids in the development of the tear film.

Cornea:

The cornea is a prominent, transparent protrusion in the front of the eye. The adult cornea's surface has a radius of around 8 mm. It performs a crucial optical function by refracting light entering the eye, which is subsequently focused onto the retina by the lens after passing through the pupil. The

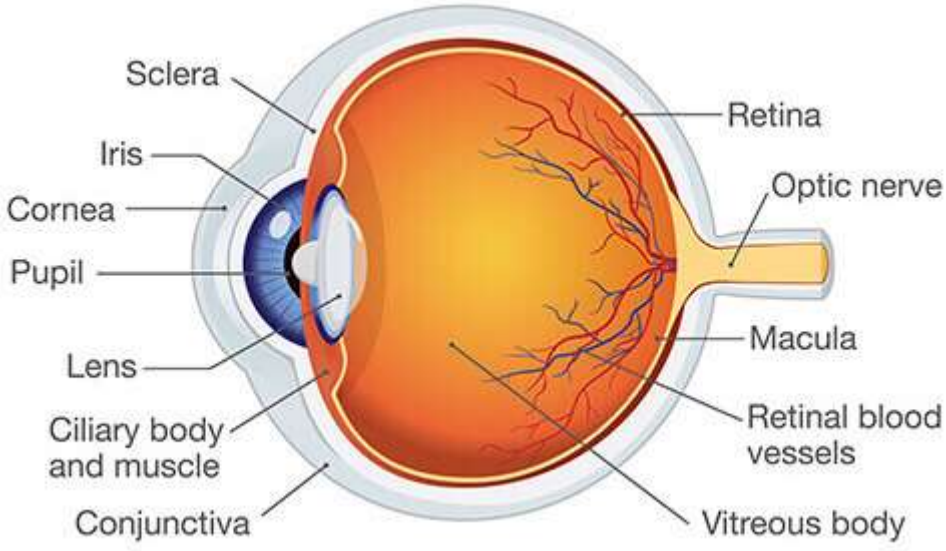
capillaries that end in loops around the cornea, a non-vascular structure (one devoid of blood vessels), provide the necessary nutrition. Numerous nerves that are descended from the ciliary nerves supply it. These penetrate the cornea's layered tissue. Because of this, it is very sensitive.

Aqueous humor:

The outer/front chamber of the eye contains a jelly-like material called aqueous humor. Immediately beneath the cornea and in front of the lens, the "anterior chamber of the eye" is filled with this watery substance. Tiny amounts of sodium and chloride ions are present in the aqueous humor, which is a very mildly alkaline salt solution.

Pupil:

The pupil, which is more precisely defined as the circular aperture in the center of the iris through which light enters the eye, usually seems to be the dark "centre" of the eye. The pupillary reflex (sometimes called the "light reflex") controls the pupil's size and, consequently, the amount of light that enters the eye.



Iris:

The iris is a thin, round, contractile veil that sits behind the cornea but in front of the lens. The purpose of the iris, a variable-sized diaphragm, is to control the pupil's size and the amount of light that enters the eye. It is the colored portion of the eye (several colors, such as blue, green, brown, hazel, or grey, might exist).

Ciliary Muscle:

The central layer of the eye has a ring of striated smooth muscles called the ciliary muscle, which controls the flow of aqueous humor into Schlemm's canal and accommodates for viewing things at different distances. Both sympathetic and parasympathetic nerves innervate the muscle. The ciliary muscle's contraction and relaxation change the lens's curvature. This process can be summed up as the constant balancing between two states: constricted ciliary muscles, which allow the eye to focus on close things, and relaxed ciliary muscles, which allow the eye to focus on faraway objects.

Lens:

Encased in a narrow, transparent capsule, the lens is a transparent structure. It is surrounded by ciliary muscles and situated behind the pupil of the eye. It aids in the refraction of light entering the eye, which the cornea first refracted. Light is focused by the lens onto the retina to create a picture. It can do this because the lens's shape changes based on how far away the thing or objects the person is looking at are from their eye. By contracting and relaxing the ciliary muscles, the lens's shape can be adjusted, a process known as accommodation.

Retina:

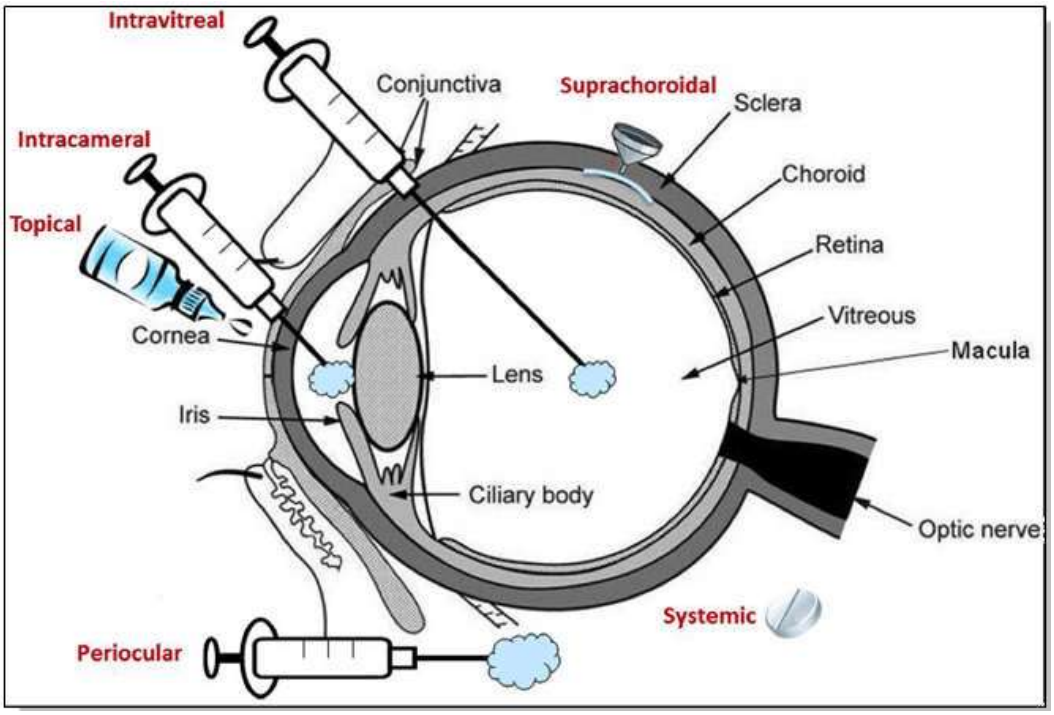
The rear of the human eye contains the retina. It is possible to think of the retina as the "screen" on which light that has entered the eye through the cornea, aqueous humor, pupil, lens, and lastly the vitreous humor before arriving at the retina forms a picture.

ROUTES OF OCULAR DRUG DELIVERY:

Drug transport into the ocular tissues can occur via a number of different pathways. The target tissue is the primary determinant in the choice of delivery route.

Topical route:

Eye drops are typically used to administer topical ocular drugs, however their duration of contact with the eye surface is brief. Formulation design (e.g., gels, gelifying formulations, ointments, and inserts) can extend the duration of pharmacological activity by extending the contact.



Sub-conjunctival administration:

Sub-conjunctival injections have historically been used to administer medications to the urea in higher concentrations. For a number of reasons, this drug delivery method is currently gaining new traction. The development of controlled release formulations to distribute medications to the posterior segment and direct the healing process following surgery has become possible because to advancements in pharmaceutical formulation and materials sciences.

Intravitreal administration:

One clear benefit of administering drugs directly into the vitreous is that it provides easier access to the retina and vitreous. It should be mentioned, too, that the RPE (Retinal Pigment Epithelium) barrier makes distribution from the vitreous to the choroid more difficult. Large molecules, especially those that are positively charged, have limited mobility in the vitreous, whereas small molecules can diffuse quickly.

Barriers of eye:

Drug loss from the ocular surface:

Following instillation, the lacrimal fluid flow eliminates the implanted substances from the eye's surface. The surplus amount of the injected fluid is quickly transported to the nasolacrimal duct in a matter of minutes, despite the lacrimal turnover rate being just around 1 µl/min. Systemic absorption of the medicine rather than ocular absorption is another cause of ineffective drug clearance. Either after the solution flows to the nasal cavity or straight from the conjunctival sac via nearby blood capillaries, systemic absorption can occur.

Lacrimal fluid-eye barriers:

Drug absorption from the lacrimal fluid into the eye is restricted by the corneal epithelium. Tight connections formed by the ocular epithelial cells restrict the paracellular drug penetration. Therefore, compared to hydrophilic medicines, lipophilic medications usually have permeability in the cornea that is at least an order of magnitude higher. The conjunctiva's surface area is almost 20 times larger than the cornea's, and it generally has a leakier epithelium.

Blood-ocular barriers:

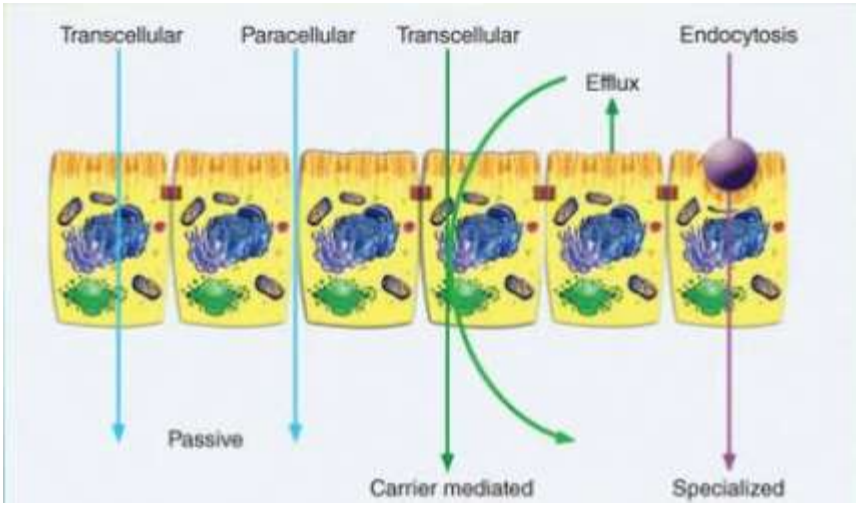
MECHANISM OF OCULAR DRUG ABSORPTION:

Blood-ocular barriers shield the eye from the xenobiotics in the blood. The blood-retina barrier and the blood-aqueous barrier are the two components of these barriers.

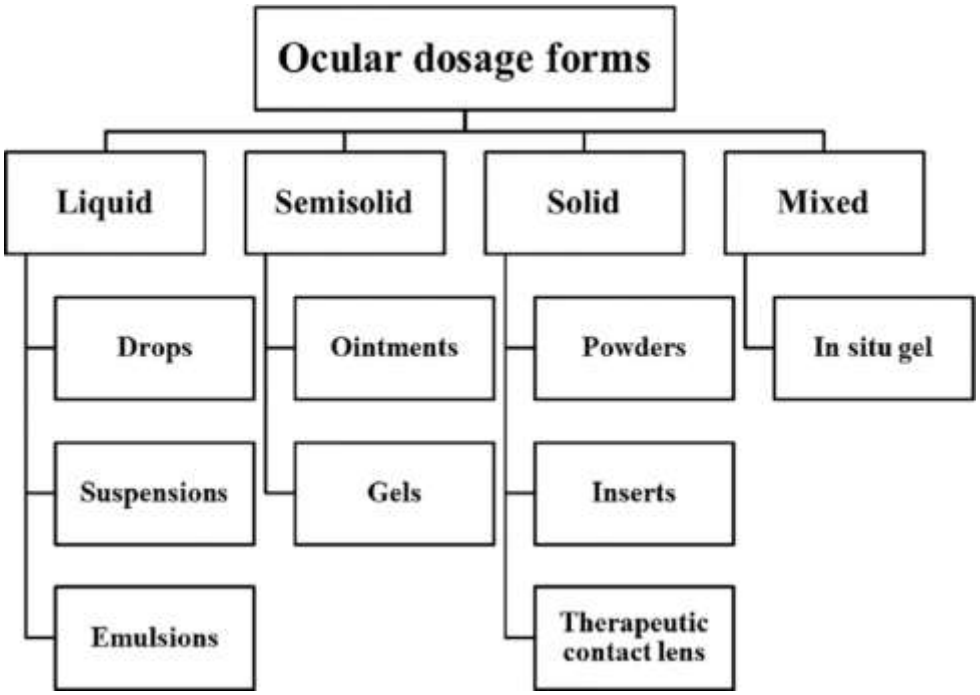
The endothelial cells in the uveam, the middle layer of the eye underneath the sclera, make up the anterior blood-eye barrier. It is made up of the choroid, ciliary body, and iris. This barrier restricts the entry of hydrophilic medications from plasma into the aqueous humor and stops plasma albumin from

entering the aqueous humor. The retinal pigment epithelium (RPE) and the taut walls of retinal capillaries make up the posterior barrier that separates the bloodstream from the eye. The choroid's vasculature has permeable walls and high blood flow, in contrast to retinal capillaries. Drugs can readily enter the choroidal Instilling drugs requires them to enter the eye, mainly through the cornea and then through non-corneal pathways. Drugs that are poorly absorbed by the cornea seem to benefit greatly from these non-corneal pathways, which entail drug diffusion over the conjunctiva and sclera.

Corneal permeation: Drugs enter the eye through the precorneal space and pass through the corneal membrane.



Ocular dosage forms:



Liquid Dosage Forms:

Eye Drops:

The most practical, secure, instantly effective, patient-compliant, and non-invasive method of administering medications to the eyes is by topical drops. Following topical drop instillation, an eye drop solution offers a pulse medication penetration, following which its concentration quickly drops. Drug concentration drop kinetics could roughly follow a first order pattern.

Emulsion:

One benefit of using an emulsion-based formulation strategy is that it can increase the solubility and bioavailability of medications. Oil in water (o/w) and water in oil (w/o) emulsion systems are the two forms of emulsions that are used commercially as carriers of active medicinal ingredients. O/w emulsions are popular and generally preferred over w/o systems for ocular medication delivery. Less discomfort and improved ocular tolerance of the

o/w emulsion are among the causes. Examples of ocular emulsions that are currently on the market in the US are RestasiseTM, Refresh Endura® (a non-medicated emulsion for eye lubrication), and AzaSite®. Numerous studies have shown that emulsions can be used to improve medication corneal penetration, precorneal residence duration, sustained drug release, and ultimately ocular bioavailability.

Suspension:

Another type of non-invasive ocular topical drop drug carrier method is a suspension. The dispersion of finely divided insoluble API in an aqueous solvent that contains an appropriate dispersing and suspending agent is known as suspension. Stated otherwise, the carrier solvent system is an API-saturated solution. In comparison to pharmacological solution, suspension particles prolong the duration of action and improve drug contact time by remaining in the precorneal pocket. The duration of pharmacological activity in suspension depends on the size of the particles. The medication that is taken into the ocular tissues from the precorneal pocket is replenished by smaller particles.

Semi-solid:

Ointment:

Another type of carrier system created for topical use is ophthalmic ointments. A blend of semisolid and solid hydrocarbon (paraffin) makes up ocular ointment, according to Patel et al. Page 6. World Journal of Pharmacol. Available in PMC 2015 January 12 is the author's manuscript. The NIH-PA NIH-PA Author Manuscript NIH-PA Author Manuscript The melting point of the author's manuscript is 34 °C, which is normal eye temperature. Hydrocarbon selection is based on biocompatibility. Ointments aid in maintaining the drug's release and enhancing ocular bioavailability.

Eye gels:

Eye gels are a type of semisolid medication that contains a lot of water. Because of their viscosity, they have improved bioavailability and retention time. Despite the high water content of gels, hazy vision may still occur. Ocular gels could be made from a variety of polymers, including carboxymethyl cellulose, hydroxypropyl methylcellulose, acrylic acids, and polyacrylic acid [105]. A proniosomal gel containing curcumin with improved anti-inflammatory action and a significant reduction in particle size was created using the coacervation process.

Solid:

Eye Powders:

They are sterile solid dose forms for medications that are sensitive to water. Cefuroxime, moxifoxacin, and voriconazole are administered intracamerally as injectable formulations. Voriconazole is reconstituted in water, whereas cefuroxime and moxifoxacin are reconstituted in saline. After reconstitution, cefuroxime and voriconazole solutions remain stable for seven days. Moxifoxacin solution, however, remains steady for a full 24 weeks.

Ocular Inserts:

Ocular inserts are biodegradable polymers in a solid dose form. They display a drug release model of zero order. High residence time, sustained medication delivery, continuous release, and less adverse effects are some benefits of inserts. Triamcinolone acetonide-loaded nanofibers were created using the electrospinning process. They displayed decreased side effects, systemic absorption, and particle size. Additionally, it was demonstrated that the insert maintained the bimatoprost's action for several months.

Conclusion:

The intricate process of ocular drug distribution necessitates thorough consideration of the eye's structure and physiology in addition to the obstacles that prevent drugs from being absorbed. For the treatment of many eye conditions, the creation of efficient ocular medication delivery systems is essential. Numerous delivery routes and dosage forms have been investigated; each has pros and cons. In order to overcome the current obstacles and enhance therapeutic results, future research should concentrate on creating innovative and focused ocular drug delivery systems. Researchers and clinicians can collaborate to create novel and efficient treatments for eye disorders by comprehending the intricacies of ocular drug transport, which will eventually enhance patients' quality of life.

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