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Original Article

A Review: Ocular Drug Delivery System

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ABSTRACT

Delivering drugs to the eye has long been a major challenge for pharmacologists and drug delivery scientists because of the eye's complex anatomy and physiology. Static barriers such as the corneal, scleral, and retinal layers, along with the blood–aqueous and blood–retinal barriers, combined with dynamic barriers like choroidal and conjunctival blood flow, lymphatic clearance, and tear dilution, as well as efflux pumps, make effective drug delivery—particularly to the posterior segment—very difficult. Recently, increasing attention has been given to identifying influx transporters in different ocular tissues and developing transporter-targeted strategies for delivering parent drugs.The page discusses the various structures and anatomy of the eye, supported by an illustrative figure. This work seeks to provide an overview of the present knowledge in ocular drug delivery. In addition, it emphasizes the present application of ocuserts in managing eye diseases.Keeping up with recent progress in ocular drug delivery is essential, as it guides drug delivery scientists in refining their approach and in creating innovative and safe drug delivery strategies.Applying the concepts of controlled release through ocular inserts provides a promising method to address the challenge of extending drug residence time on the precorneal surface.Tools like punctal plugs are employed to extend the retention period and enhance the absorption of eye drops by preventing drainage through the nasolacrimal system. The eye, being one of the most delicate and precious sensory organs, presents significant challenges for the topical delivery of drugs.

Keywords: Ocular Drug Delivery System, Eye Drops, Controlled Drug Release ,Corneal permeability

INTRODUCTION

Developing a drug delivery system that specifically targets a particular tissue of the eye remains a significant challenge for researchers. The eye is generally divided into two main segments: anterior and posterior. The structural differences within each ocular tissue layer act as major barriers to drug absorption, regardless of the route of administration—topical, systemic, or periocular. In this study, our focus is on the various absorption barriers associated with all three delivery routes. The eye is resistant to foreign substances because of its distinct anatomy, physiology, and biochemistry, thereby posing an ongoing challenge for pharmaceutical scientists to overcome its protective barriers without inducing permanent tissue damage. In order to bypass ocular drug delivery barriers and enhance ocular bioavailability, several traditional and advanced drug delivery systems have been formulated, including emulsions, ointments, suspensions, aqueous gels, nanomicelles, nanoparticles, liposomes, dendrimers, implants, contact lenses, nanosuspensions, microneedles, and in situ thermosensitive gels for the previously mentioned ocular disorders. Traditional ophthalmic formulations such as solutions, suspensions, and ointments are no longer adequate to effectively treat these conditions. Moreover, such drugs typically fail to reach deeper ocular tissues like the retina, vitreous, or choroid, making alternative routes of administration more suitable as new technologies continue to emerge. From a drug delivery perspective, the eye remains highly challenging to study, as its anatomy, physiology, and biochemistry make it resistant to external substances. It provided a detailed overview of ocular drug delivery, covering aspects such as the eye's anatomical structures, various ocular diseases, barriers to drug delivery, different administration routes, classification of dosage forms, a range of nanostructured platforms, methods of characterization, strategies to enhance ocular delivery, and emerging future technologies.

Conventional Ophthalmic Formulations:

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Conventional ophthalmic formulations refer to the traditional dosage forms used for delivering drugs to the eye. These mainly include:

Eye drops/solutions –

The most common form, but limited by rapid precorneal elimination and low bioavailability. Topical liquid or solution-based eye drops are the most common, safe, noninvasive, and patient-friendly method of ocular drug delivery, providing rapid therapeutic action. After instillation, they produce a burst of drug permeation, followed by a rapid decline in concentration, typically following near first-order kinetics. To enhance drug retention, penetration, and overall ocular bioavailability, various excipients can be incorporated into eye drop formulations, such as viscosity enhancers, permeation enhancers, and cyclodextrins. Viscosity enhancers help extend precorneal residence time and improve bioavailability by increasing the formulation's thickness; common examples include hydroxy methyl cellulose, hydroxy ethyl cellulose, sodium carboxymethyl cellulose, hydroxypropyl methyl cellulose, and polyalcohols. On the other hand, permeation enhancers facilitate corneal absorption by temporarily altering corneal integrity.

Suspensions –

Useful for poorly water-soluble drugs, providing longer contact time than solutions. Suspensions represent another type of noninvasive ocular topical drug delivery system. They are defined as dispersions of finely divided, insoluble active pharmaceutical ingredients (API) in an aqueous medium containing appropriate suspending and dispersing agents. Essentially, the solvent system serves as a saturated solution of the API. The suspended drug particles remain in the precorneal area, which helps extend drug contact time and prolong the duration of action compared to drug solutions. The length of drug activity in suspensions is influenced by the particle size.

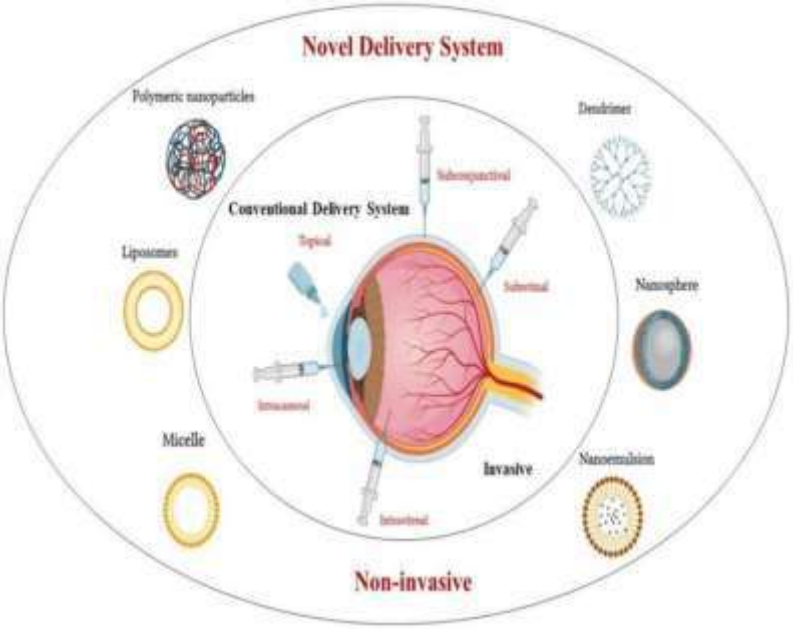
Ointments –

Increase drug retention due to their viscosity, but may cause blurred vision and discomfort.

Ophthalmic ointments are another category of carriers designed for topical drug delivery. These formulations consist of a blend of semisolid and solid hydrocarbons (such as paraffin) with melting points close to the physiological temperature of the eye (around 34 °C). The selection of hydrocarbons is based on their biocompatibility. Ointments enhance ocular bioavailability and provide sustained drug release.

Emulsion –

Emulsion-based formulations provide a useful strategy to enhance both the solubility and bioavailability of drugs. Two primary types of emulsions are employed as carriers for active pharmaceutical ingredients: oil-in-water (o/w) and water-in-oil (w/o) systems. For ophthalmic applications, o/w emulsions are more commonly used and are preferred over w/o emulsions because they cause less irritation and offer better ocular tolerance. Examples of marketed ocular emulsions in the United States include Restasis™, Refresh Endura® (a non-medicated emulsion for eye lubrication), and AzaSite®. Research has shown that emulsions can extend precorneal retention, improve corneal drug permeation, enable sustained drug release, and consequently enhance ocular bioavailability.



Anatomy of the Eye in Ocular Drug Delivery Systems:

Understanding the anatomy of the eye is essential for designing effective ocular drug delivery systems, as its unique structural and physiological features create barriers to drug absorption. The eye can broadly be divided into two main segments:

1. Anterior Segment:

This portion includes the structures at the front of the eye, which are the primary targets for many topical formulations.

Cornea – A transparent, multi-layered structure that acts as the major barrier to drug penetration.

Conjunctiva – A thin vascularized membrane covering the sclera and inner eyelids; contributes to drug absorption and systemic loss.

Aqueous humor – A clear fluid filling the anterior chamber that maintains intraocular pressure and nourishes ocular tissues.

Iris and ciliary body – Regulate light entry and aqueous humor dynamics, also influencing drug transport.

Lens – Focuses light on the retina but serves as a barrier to drug penetration into the posterior segment.

2. Posterior Segment:

This region includes structures critical for vision but difficult to target with conventional drug delivery methods.

Vitreous humor – A gel-like substance filling the space between the lens and retina, limiting drug diffusion.

Retina – The light-sensitive tissue responsible for vision; highly protected by blood-retinal barriers.

Choroid – A vascular layer that supplies oxygen and nutrients to the retina, with high blood flow leading to rapid drug clearance.

Optic nerve – Transmits visual signals to the brain, generally inaccessible for drug delivery.

3. Barriers to Drug Delivery:

Static barriers: Corneal epithelium, sclera, retina, blood-aqueous and blood-retinal barriers.

Dynamic barriers: Tear turnover, blinking, conjunctival and choroidal blood flow, lymphatic clearance.

Biochemical barriers: Efflux pumps and metabolic enzymes.

Key Approaches:

1. Formulation-Based Approaches:

Viscosity enhancers – Polymers like HPMC, CMC, or polyvinyl alcohol increase formulation thickness, prolonging precorneal residence.

Mucoadhesive polymers – Interact with ocular mucin to enhance adhesion and drug retention.

In situ gels – Liquid upon instillation but transform into a gel in response to temperature, pH, or ions, increasing residence time.

Emulsions & suspensions – Improve solubility and sustain drug release. Ointments – Extend drug contact but may blur vision.

2. Novel Drug Delivery Systems:

Nanoparticles & nanomicelles – Improve penetration, protect drugs from degradation, and provide controlled release.

Liposomes & niosomes – Vesicular systems that enhance corneal permeation and drug bioavailability.

Dendrimers – Highly branched carriers that increase solubility and targeting. Nanosuspensions – Enhance solubility of poorly soluble drugs with prolonged action.

Implants & inserts (e.g. Ocuserts) – Provide sustained, controlled drug release directly in the eye. Contact lenses (drug-eluting) – Act as reservoirs for prolonged drug release.

3. Permeation Enhancement Strategies:

Permeation enhancers – Modify corneal or conjunctival membranes temporarily to increase drug uptake.

Prodrug approach – Structural modification of drugs to improve lipophilicity/permeability, later converted back to the active form.

Cyclodextrins – Form inclusion complexes with drugs to improve solubility and corneal penetration.

Iontophoresis – Uses a mild electric current to enhance penetration of charged drug molecules. Microneedles – Create tiny channels for direct drug delivery into ocular tissues.

4. Alternative Routes of Administration:

Periocular delivery (subconjunctival, peribulbar, retrobulbar injections) – Targets tissues bypassing precorneal losses.

Intraocular delivery (intravitreal injections/implants) – Direct drug delivery to the posterior segment.

Systemic delivery (oral or IV) – Limited use due to systemic side effects and barriers, but useful for some conditions.

Factors Limiting ocular Bioavailability Of Drug:-

Here are the main factors that limit ocular bioavailability of drug -

1. Anatomical Barriers:

Corneal epithelium – Tight junctions restrict hydrophilic drug penetration. Sclera and retina – Act as barriers for drug diffusion.

Blood-aqueous barrier – Limits drug entry into the anterior chamber.

Blood-retinal barrier – Prevents most drugs from reaching the posterior segment.

2. Physiological Barriers:

Tear turnover and dilution – Tears wash away drugs within minutes of instillation Blinking and reflex tearing – Cause mechanical loss of drugs from the precorneal area.

Nasolacrimal drainage – Rapidly clears drugs into systemic circulation, reducing local availability.

Conjunctival and choroidal blood flow – Promotes systemic absorption instead of local ocular retention.

Lymphatic clearance – Contributes to rapid drug elimination.

3. Biochemical Barriers:

Efflux pumps (e.g., P-glycoprotein) – Actively remove drug molecules from ocular tissues.

Enzymatic degradation – Metabolic enzymes in tears and ocular tissues can break down drugs before absorption.

Formulation-Related Factors:

Low solubility of drugs – Poor aqueous solubility reduces effective concentration. pH and tonicity mismatch – May cause irritation and rapid drug loss. Short residence time of conventional formulations – Solutions and suspensions are eliminated quickly.

CONCLUSION: -

Effective treatment of ocular diseases remains a challenging task due to the complex nature of these disorders and the presence of various ocular barriers. Some of these challenges have been addressed by identifying specific transporters and modifying drug molecules to target them. Utilizing transporter specificity enables precise drug delivery to ocular tissues, reducing side effects and enhancing bioavailability. Furthermore, the advancement of noninvasive delivery methods is expected to transform the field of ocular drug delivery. Controlled ocular drug delivery systems enhance therapeutic effectiveness by minimizing drug loss and promoting better absorption through prolonged contact with the ocular surface. These systems reduce the frequency of administration, leading to improved patient compliance, while also decreasing the required dosage and minimizing drug-related side effect.

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