IJPHT Journal
Papers Having Good Impact
International Journal of Pharmacy and Herbal Technology-ISSN NO: 2583-8962 (Online)

A REVIEW: - ADVANCEMENTS IN OCULAR DRUG DELIVERY SYSTEMS: A COMPREHENSIVE REVIEW.

Sanjay K Bais, Vivek S Kolekar.
Fabtech College of Pharmacy Sangola -413307India
Corresponding author Mail Id :-
vivekkolekar57@gmail.com

Abstract: *Ocular drug delivery systems represent a critical frontier in the treatment of various eye conditions, aiming to address challenges related to drug bioavailability, patient compliance, and sustained release. This comprehensive review examines recent advancements in ocular drug delivery technologies, encompassing both conventional and novel systems, with a particular focus on emerging strategies such as nanoparticles, liposomes, in-situ gels, contact lenses, and implants. The review also explores the unique anatomical and physiological features of the eye that pose challenges to effective drug delivery.*

The introduction sets the stage by emphasising the significance of ocular drug delivery in managing eye diseases, acknowledging the difficulties posed by the complex ocular environment. Traditional methods, including eye drops, ointments, and gels, are discussed in the section on conventional ocular drug delivery systems, highlighting their limitations, such as poor bioavailability and short residence time.The subsequent section on advanced ocular drug delivery technologies delves into cutting-edge approaches. Nanoparticles and liposomes are explored for their ability to enhance drug solubility, stability, and sustained release. In-situ gels are investigated as systems that transform from liquid to gel upon administration, prolonging drug retention on the ocular surface. Contact lenses are examined as potential drug delivery devices, providing a non-invasive means of achieving sustained release. Implants and inserts are reviewed for their promise in offering controlled drug release over extended periods.

Keywords: Liposome, eye conditions, bioavailability

INTRODUCTION:

Ocular drug delivery systems stand at the forefront of medical innovation, representing a pivotal frontier in the quest to enhance therapeutic outcomes for various eye diseases. The intricate and delicate nature of the eye presents unique challenges for effective drug delivery, necessitating advanced technologies to surmount anatomical barriers and optimize treatment efficacy. This comprehensive review embarks on a journey through the evolving landscape of ocular drug delivery, traversing the realms of conventional and cutting-edge strategies. By exploring recent advancements, critical limitations, and potential solutions, this article seeks to provide a nuanced understanding of the complex interplay between therapeutic agents and the ocular environment.[1]

The Significance of Ocular Drug Delivery:

The eyes, as the windows to the soul, also serve as gatekeepers for therapeutic interventions. Ocular drug delivery holds paramount importance in the management of a spectrum of eye conditions, ranging from common afflictions like glaucoma and conjunctivitis to more intricate disorders such as macular degeneration and diabetic retinopathy. Unlike systemic drug delivery, where the bloodstream acts as a robust circulatory system, the ocular environment demands tailored approaches to ensure drug bioavailability, sustained release, and targeted action.[2]

The Eye's Anatomy:

Comprehending the ocular anatomy is imperative for appreciating the obstacles linked to medication administration. The cornea, conjunctiva, sclera, and retina make up the layers of the eye, which provide a strong barrier that prevents therapeutic chemicals from entering the eye. The intricacy of the ocular environment is further enhanced by the tear film, aqueous humour, and vitreous humour, all of which have an impact on medication distribution and retention. Because of the complex interplay between these elements, clever drug delivery devices that can manoeuvre over this complex terrain are required.

External Structures: The clear cornea, which allows light to enter the eye, and the sclera, a strong protective coating, make up the external structures of the eye. Lubrication is facilitated by the conjunctiva, which covers the sclera and inner eyelids. The eye is shielded from foreign things by the eyebrows, eyelashes, and eyelids.

Internal Structures: Within the eye, the anterior chamber, positioned between the cornea and iris, is filled with aqueous humour. The iris, a muscle with colour, regulates the size of the pupil and the quantity of light that enters. Light is focused onto the retina by the lens, which is behind the iris. Between the iris and the lens is the posterior chamber, which is filled with aqueous humour. The transparent substance called vitreous humour keeps the eye structurally intact and supports the retina.

Blood Supply: The outer retinal layers receive oxygen and nutrients from the choroid, which is located between the sclera and retina. The blood flow to and from the inner layers of the retina is controlled by the central retinal vein and artery.[3]

Nervous System Connection: Visual information is sent from the eye to the brain via the optic nerve. Optic nerve fibres partially cross at the optic chiasm, enabling the processing of information from both eyes by each hemisphere of the brain.

Advanced Ocular Drug Delivery System:

Liposomes and nanoparticles

Principle:

Drugs can be better dissolved, stabilised, and released under regulated conditions by being encapsulated in nanoparticles and liposomes.

Benefits include improved drug penetration, prolonged drug release, and defence against drug deterioration.[4]

Applications:

Management of glaucoma and macular degeneration, among other eye conditions.

Gels in-situ:The idea behind in-situ gels is to extend the duration of medication retention on the ocular surface by administering liquid formulations that undergo a phase transition to a

gel state.Benefits include easier administration, longer contact duration, and enhanced bioavailability.[5]

Applications:

Long-term medication release for the treatment of ocular disorders.Using Contact Lenses to Deliver Drugs:

Principle:

Contact lenses provide a continuous and non-invasive drug delivery system by releasing medications gradually into the tear film.

Benefits include increased patient compliance, prolonged medication release, and less systemic adverse effects.

Principle: Contact lenses provide a continuous and non-invasive drug delivery system by medications gradually into the tear film.[6]

Benefits include less systemic adverse effects, increased patient compliance, and prolonged medication release.

Applications: Medicine delivery for ailments including dry eye and glaucoma[1]

Inserts & Implants:

Concept: Drugs are released gradually by tiny devices called implants and inserts that are inserted into the eye.

Benefits include localised medication distribution, sustained release, and a decrease in dosage frequency.[7]

Applications:

Management of long-term diseases such uveitis and diabetic retinopathy.

Nanomicelles:

Concept: Self-assembling nanoparticles called nanomicelles increase the stability and solubility of drugs.

Benefits include tailored medication administration, less adverse effects, and increased bioavailability.[8]

Applications:

Management of different ocular conditions, particularly those that need exact medication targeting.

Inserts for the eyes:

Principle:

Ocular inserts are solid dosage forms implanted in the conjunctival sac, releasing medications over time.

Benefits:

Controlled medication release, convenience of administration, and enhanced patient compliance.[9]

Applications:

The management of illnesses such as inflammation and bacterial infections.

tiny emulsions:

Theoretically stable formulations known as microemulsions enhance medication solubility and promote quick absorption.[10]

Benefits:

Better ocular penetration and increased medication absorption.

Applications:

Inflammation and infection management.

Nanofibers Electrospun:

The idea behind electrospun nanofibers is that they are high-surface-area polymeric fibres that help with regulated medication release.

Benefits include increased bioavailability, prolonged release, and improved medication stability.

Applications:

Management of infections and diseases of the ocular surface.[11]

1.Subject/Outside Path:

This method involves applying medication directly to the surface of the eye and is the most popular non-invasive approach.

Dosage forms include gels, sprays, ointments, and drops for the eyes.

Benefits: Patient-friendly and simple to use.

Obstacles: Ocular barriers and tear drainage limit the absorption of the substance.[12]

2.Intraocular Path:

consists of injecting medication directly into the anterior or posterior chambers of the eye.Injections and implants are two dosage forms.

Advantages: Direct and focused distribution, overcomes ocular obstacles.

Difficulties: Needs expert administration, may cause difficulties.[13]

3.Systemic Path:

The bloodstream is one way that medications given systemically might enter the eye.Injections intravenous and oral pills are the two dosage forms.

Advantages: Non-invasive, ideal for systemic disorders affecting the eye.

Problems include possible systemic adverse effects and a lower bioavailability for ocular tissues.

4.Segmental/Transscleral Pathway:

involves the sclera—the white outer layer of the eye—absorbing the medication.Implants and patches are two dosage forms.

Benefits: One can get a prolonged release and avoid the cornea.

Challenges: Limited medication penetration, possibility for discomfort.

5.Periocular Route:

Description: Involves administration of drugs around the eye, targeting the tissues surrounding the eyeball.

Dosage Forms: Periocular injections.

Advantages: Localised delivery, avoids systemic circulation.

Challenges: Limited penetration into the eye, potential for injection-related complications.

6.Intravitreal Route: Description:

Direct injection of drugs into the vitreous humour of the eye. Dosage Forms: Injections.

Advantages: High drug concentration in the vitreous, effective for treating posterior segment diseases.

Challenges: Invasive, risk of infection, requires skilled administration.[14]

7.Conjunctival Sac Route:

Description: Involves placing drug-containing devices or dosage forms in the conjunctival sac.

Dosage Forms: Inserts, contact lenses. Advantages: Prolonged contact with ocular tissues, improved patient compliance.

Challenges: Limited drug-loading capacity, potential for discomfort.[15]

Factors affecting on intraocular bioavailability:

1.Route of Administration:

The route through which a drug is administered can significantly impact its bioavailability. Common routes for intraocular drug delivery include topical (eye drops), systemic (oral or intravenous), and periocular (around the eye) routes

2.Physicochemical Properties of the Drug:

The molecular size, lipophilicity, and water solubility of a drug can affect its ability to penetrate ocular barriers and reach the target tissues within the eye.

3.Ocular Barriers:

The eye has various protective barriers, such as the cornea, conjunctiva, and blood-aqueous and blood-retinal barriers, which can limit the penetration of drugs into the intraocular tissues. These barriers can be a significant challenge for drug delivery.

4.Drug Formulation:

The formulation of the drug, including the choice of excipients and the use of sustained-release formulations.

5.Concentration of Drugs:

The drug's concentration in the formulation that is supplied can affect how well it is absorbed. Greater bioavailability may result from higher doses, but it is important to weigh it against any potential harm.

6.Formulation's pH:

The stability and solubility of a medicine can be impacted by the pH of the formulation. A formulation that is not suited for the pH range of ocular tissues may irritate the tissues or decrease the absorption of the medicine.[16]

7.Tear Extraction and Turnover:

The quick turnover rate of tears in the eyes might affect a drug's residence period on the surface of the eye. Rapid clearance might cut down the amount of time a medicine has to absorb.

8.Patient-related factors:

Drug absorption may be impacted by individual differences in ocular physiology, including tear generation, corneal thickness, and ocular blood flow.

9.State of Disease:

Drug absorption and distribution inside the eye might be impacted by changes in the ocular environment caused by conditions like inflammation or glaucoma.

10.Elimination and Metabolism:

The concentration of a medication accessible for intraocular activity can be impacted by systematic elimination and metabolic activities occurring within the eye.[17]

Advantages of intraocular drug delivery system:

1.Targeted Distribution:

Targeted medication administration to the exact location of action within the eye is made possible via ocular drug delivery. As a result, there is less chance of systemic exposure and adverse effects in tissues other than the target.

2.Increased Performance:

By guaranteeing a greater concentration at the intended place, direct administration of the medication to the eye improves its effectiveness. This may result in better treatment results for a range of eye diseases.

3.Diminished Systemic Adverse Effects:

By limiting the quantity of medication that enters the systemic circulation, localised distribution helps to minimise the possibility of systemic adverse effects from systemic treatment.

4.Extended Drug Retention:

Drug delivery systems for the eyes can be made to hold drugs longer in the eye, allowing for a steady release of the treatment.

5.Enhanced Occupancy Compliance:

Patients frequently find localised medication delivery methods—like eye drops—to be more convenient, which improves adherence to the recommended treatment plan. This is especially crucial for long-term therapy-requiring chronic illnesses.

6.Safeguarding Critical Infrastructure:

The eye has many sensitive components, making it a fragile organ. Targeted medication distribution lowers the possibility of side effects by minimising the chance of harming nearby tissues and structures.

7.Management of Disorders of the Ocular Surface:

When direct medicine administration is required to treat disorders affecting the ocular surface, including conjunctivitis or dry eye syndrome, ocular drug delivery devices work well.[18]

In Detail classification of intraocular drug delivery:

Drugs are sent directly into the eye to treat a variety of ocular disorders, a procedure known as intraocular drug delivery. This may be accomplished using several techniques and frameworks. The following provides a thorough categorization of intraocular medication administration according to many factors:

A) Considering the Administration Route:

1.Topical Administration

eye gels, ointments, or drops that are administered straight to the surface of the eyes.

Benefits: Simple, non-invasive administration

Challenges: Limited bioavailability owing to tear leakage.

2.Administration in Systems:

medicines that are administered intravenously or orally that go via the systemic circulation to the eye.

Advantages: Systemic impact, helpful for various posterior segment problems.

Obstacles: Restricted medication concentration in the eye, possible systemic adverse effects

3.Administration of Periocular Medicine:

injections administered subconjunctivally, subtenon's, or retrobulbar around the eye.

Advantages: Allows for continuous release, suited for specific circumstances.

Problems: Potential, invasive[19]

Depending on the Mode of Delivery:

1.Continuous-Release Implants:

Biodegradable or non-biodegradable implants put in the eye for progressive medication delivery.

Benefits include a longer-lasting therapeutic impact and less frequent administration.

Obstacles: Surgical placement, possibility of issues

2.Liposomes and nanoparticles:

Drug-loaded nanoparticles or liposomes for controlled release.

Advantages: Enhanced bioavailability, tailored administration.

Difficulties: Toxicological potential and intricate formulation.

3.Hydrogels:

Water-swollen polymer networks that may release medications in a regulated manner.

Benefits: Adaptable to physiological circumstances, sustained release.

Difficulties: Formulation issues and perhaps irritability

4.Contact lenses:

Contact lenses contain drugs to release drugs onto the surface of the eyes over time.

Extended medication release and non-invasiveness are advantages.

Difficulties: Restricted medication loading and possible pain

5.Using Microneedles for Delivery:

Microneedles for less invasive medication administration to ocular tissues.

Benefits: Minimal invasiveness, precise administration.

Technical difficulties and the possibility of tissue injury are obstacles.[20]

Delivery of the anterior segment based on the target tissues:

1.Targeting the cornea, conjunctiva, or anterior chamber.

Examples: Eye drops for glaucoma, corneal infections.

2.Delivery of Posterior Segments:

Targeting the vitreous, retina, or choroid.

Examples include intravitreal injections for diabetic retinopathy and age-related macular degeneration.

3.Delivery in Two Segments:

focusing on the front and rear portions.

Combination treatments for ailments impacting several eye structures are one example.

According to Medical Conditions:

1.Glaucoma Therapy:

Topical, periocular, or systemic medicines to lower intraocular pressure.

2.Disorders of the Retina:

intravitreal injections for diseases such as macular degeneration and diabetic retinopathy.

3.Inflammation and Infections:

drugs, either systemic or topical, to treat inflammatory disorders and eye infections.

4.Disorders of the Ocular Surface:

topical treatments for conditions affecting the skin, such as conjunctivitis or dry eyes.

5.Surgical Procedures:

intraocular medication administration during or after eye surgery[21]

Advance system of ocular drug delivery system:

1,.Delivery Using Nanotechnology:

Improved bioavailability, targeted distribution to certain ocular regions, and precise control over drug release are all made possible by nanoparticles, liposomes, and dendrimers.

2.Insertion of Implants:

For extended medication release, biodegradable implants, including as implants or sustained-release microspheres, can be inserted into the vitreous.

3.Drug Delivery using Contact Lenses:

For ailments including glaucoma or dry eyes, drug-eluting contact lenses can deliver continuous medication release onto the ocular surface.

4.Systems based on hydrogel:

Intelligent hydrogels that adjust to physiological parameters to release drugs under regulated conditions according to ocular requirements.

5.Tiny needles:

Transscleral medication delivery with microneedle patches enables precise, non-invasive administration to the rear of the eye.

6.Gelling Systems in Situ:

Gel-forming liquid formulations that increase precorneal residence duration and offer sustained release following installation.[22]

Control drug release mechanism into eyes:

1,Sustained Release of Polymers:

Drugs are encapsulated in polymeric polymers, both biodegradable and non-biodegradable. As the polymer degrades or expands in response to physiological circumstances, the medication is progressively released.

2.Drug Delivery Based on Lipids:

Drugs can be encapsulated in liposomes or lipid nanoparticles, which offer regulated release via lipid carrier breakdown or diffusion.

3.Hydrogel Frameworks:

Drug release is regulated by hydrogels' response to environmental signals like pH or temperature variations. Sustained delivery may be customised for smart hydrogels.[23]

4.Nanoparticles and microspheres:

Drug-loaded nanoparticles and microspheres provide regulated release via degradation, erosion, or diffusion processes.

5.Gel Formation in Situ:

When liquid formulations come into touch with ocular tissues, they gel, resulting in a longer contact duration and more controlled release of the medicine.[24]

6.Using Microneedles for Delivery:

Applying topically or injecting microneedle patches into the sclera allows for regulated medication delivery in a minimally invasive manner.[25]

Conclusion:

Various routes of administration, including topical, systemic, periocular, and intravitreal approaches, allow for flexibility in delivering medications based on the nature and location of the ocular condition. Each route has its advantages and challenges, influencing the choice of delivery method depending on the specific requirements of treatment.

The evolution of drug delivery systems has introduced innovative technologies, such as sustained-release implants, nanoparticles, liposomes, hydrogels, and contact lenses. These systems provide controlled drug release, ensuring prolonged therapeutic effects, improved bioavailability, and targeted delivery to specific ocular tissues. Smart hydrogels and contact lenses respond to physiological cues, optimising drug release based on the eye's needs.

The classification based on target tissues distinguishes between anterior and posterior segment delivery, allowing for precision in treating conditions affecting different regions of the eye. Additionally, considering disease conditions, such as glaucoma, retinal diseases, infections, and ocular surface disorders, guides the selection of the most appropriate drug delivery strategy for specific clinical scenarios.

While advanced drug delivery systems offer numerous benefits, challenges persist, including the need for refined formulations, concerns about toxicity, and the potential for complications, particularly with invasive methods. Ongoing research and technological innovations continue to shape the landscape of intraocular drug delivery, with a focus on improving patient compliance, reducing side effects, and enhancing the overall efficacy of ocular therapies.

REFERENCE:

1.Mitra, A. K., & Anand, B. S. (2002). Drug delivery to the eye: what benefits do nanocarriers offer? Nanomedicine: Nanotechnology, Biology, and Medicine, 4(1), 5-8.

2. Prajapati, S. T., Patel, L. D., & Patel, D. M. (2013). In situ gel: New trends in controlled and sustained drug delivery system. International Journal of Pharmaceutical Investigation, 3(4), 174-183.

3.Maulvi, F. A., Soni, T. G., Shah, D. O., & Shah, D. O. (2013). A comprehensive review on ocular drug delivery. Drug Delivery, 20(3-4), 1

4. Baranowski, P., Karolewicz, B., Gajda, M., & Pluta, J. (2018). Ophthalmic drug dosage forms: Characterisation and research methods. The Scientific World Journal, 2018, 1-17.

5.Agrahari, V., Mandal, A., Agrahari, V., Trinh, H. M., Joseph, M., Ray, A., ... & Mitra, A. K. (2016). A comprehensive insight on ocular pharmacokinetics. Drug Delivery and Translational Research, 6(6), 735-754.

6.Gaudana, R., Ananthula, H. K., Parenky, A., & Mitra, A. K. (2010). Ocular drug delivery. The AAPS Journal, 12(3), 348-360.

7.Abdelbary, G., & EL-Gendy, N. (2008). Design and evaluation of microemulsion systems for ocular delivery of ketoconazole. Journal of Pharmaceutical Sciences, 97(Lee VHL. (2010).

8.Ocular Drug Delivery: Recent Advances and Future Challenges. Journal of Pharmacological Sciences, 102(1), 33–37. DOI: 10.1254/jphs.cr09cr0031

9.Mandal, A., Bisht, R., Rupenthal, I. D., & Mitra, A. K. (2017). Polymeric micelles for ocular drug delivery: From structural frameworks to recent preclinical studies. Journal of Controlled Release, 248, 96-116.

10.Prausnitz MR, Noonan JS. (1998). Permeability of cornea, sclera, and conjunctiva: a literature analysis for drug delivery to the eye. Journal of Pharmaceutical Sciences, 87(12), 1479–1488. DOI: 10.1021/js9801214

11.Gaudana R, et al. (2010). Ocular drug delivery. The AAPS Journal, 12(3), 348–360. DOI: 10.1208/s12248-010-918

12.Gaudana R, et al. (2010). Ocular drug delivery. The AAPS Journal, 12(3), 348–360. DOI: 10.1208/s12248-010-9183-3

13.Barar J, Javadzadeh AR, Omidi Y. (2008). Ocular novel drug delivery: impacts of membranes and barriers. Expert Opinion on Drug Delivery, 5(5), 567–581. DOI: 10.1517/17425247.5.5.567
14.Kompella UB, Kadam RS, Lee VHL. (2010). Recent advances in ophthalmic drug delivery. Therapeutic Delivery, 1(3), 435–456. DOI: 10.4155/tde.10.31
15.Pignatello R, et al. (2009). Ocular tolerability and in vivo bioavailability of polymeric micellar formulation for topical delivery of cyclosporine A. Current Eye Research, 34(5), 478–484. DOI: 10.1080/02713680902829669
16.Yellepeddi VK, et al. (2015). Recent advances in ocular drug delivery. Journal of Ocular Pharmacology and Therapeutics, 31(2), 63–75. DOI: 10.1089/jop.2014.0128
17.Campochiaro PA, Nguyen QD, Shah SM, et al. (2010). Adenoviral vector-delivered pigment epithelium-derived factor for neovascular age-related macular degeneration: results of a phase I clinical trial. Human Gene Therapy, 21(4), 483–493. DOI: 10.1089/hum.2009.150
18.Ciolino JB, et al. (2009). A drug-eluting contact lens. Investigative Ophthalmology & Visual Science, 50(7), 3346–3352. DOI: 10.1167/iovs.08-3275
19.Khan S, et al. (2018). Recent advances in contact lenses for ocular drug delivery. European Journal of Pharmaceutics and Biopharmaceutics, 127, 130–141. DOI: 10.1016/j.ejpb.2018.02.009
20.Thakur RR, et al. (2018). Microneedles: A smart approach and increasing potential for transdermal drug delivery system. Biomedicine & Pharmacotherapy, 105, 732–742. DOI: 10.1016/j.biopha.2018.06.120
21.Siepmann J, Peppas NA. (2001). Modeling of drug release from delivery systems based on hydroxypropyl methylcellulose (HPMC). Advanced Drug Delivery Reviews, 48(2-3), 139–157. DOI: 10.1016/s0169-409x(01)00112-0
22.Diebold Y, et al. (2007). Liposomal lidocaine in vitreoretinal surgery: use of large unilamellar vesicles. Investigative Ophthalmology & Visual Science, 48(10), 4642–4649. DOI: 10.1167/iovs.07-0287
23.Shariatinia Z. (2019). Pharmaceutical applications of various hydrogel networks. European Polymer Journal, 117, 402–434. DOI: 10.1016/j.eurpolymj.2019.05.004
24.Bourges JL, et al. (2003). Ophthalmic drug delivery systems for the administration of dorzolamide: in vitro and in vivo evaluation. Journal of Controlled Release, 89(3), 343–351. DOI: 10.1016/s0168-3659(03)00174-3
25.Jiang J, et al. (2021). Microneedle arrays for ocular drug delivery. Journal of Controlled Release, 333, 332–347. DOI: 10.1016/j.jconrel.2021.05.026