Career Point International Journal of Research(CPIJR)
©2022 CPIJR | Volume 1 | Issue 2 | ISSN : 2583-1895

Ophthalmic Inserts

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Abstract-*Ophthalmic inserts are tiny, sterile medical devices that can be inserted into the eye for treatment or diagnosis. Polymers, hydrogels, and silicone are just a few of the materials that may be used to create these implants. They can be made to release the drug over hours, days, or weeks. They are used to release medications or offer sustained administration of therapeutic substances to the eye. Ophthalmic inserts provide a number of benefits over conventional eye drops, such as better medication distribution, less frequent dosage, and more patient compliance. Additionally, they can enhance treatment results and lower the danger of systemic adverse effects.*

Keywords: *-Chronic ocular diseases Drug loading capacity Sustained release profiles.*

I. INTRODUCTION

Specialised devices called ophthalmic inserts are made to administer medications to the eye over a prolonged period of time. They may be produced in a variety of forms and sizes, including rods, discs, and films, and are constructed of biocompatible polymers that release the medicine gradually. Ophthalmic inserts have become more popular as a result of the benefits they provide over conventional eye drops, such as improved patient compliance, decreased systemic adverse effects, and greater drug bioavailability. They are particularly helpful in the treatment of long-term ocular conditions including glaucoma and uveitis when continuous medication administration is necessary for the best possible therapeutic results. Despite these benefits, ophthalmic inserts still face several challenges, including difficulty in achieving sustained drug release and limited drug loading capacity. In order to improve the functionality of ophthalmic inserts and give patients with eye disorders with more effective treatment choices, research in the field strives to get beyond these constraints and create new materials and technologies. The eye's architecture, physiology, and biochemistry make it extraordinarily resistant to external chemicals. The task at hand for the formulator is to get past the eye's defences without enduring long-term tissue damage. The need for highly effective and sophisticated ocular drug delivery systems is driven by the development of newer, more sensitive diagnostic procedures and treatment agents. The creation of an effective drug is the aim of pharmacotherapeutics.

concentration for the required amount of time at the specified location of action. In order to reduce the potential of eye injury from high blood concentrations of drugs that are not designed for ocular usage, local treatment rather than systemic therapy is typically chosen as a gateway for drug delivery.

II. RECENT TRENDS INOCCULARDELIVERY SYSTEM:

The improvement of therapeutic effectiveness, patient compliance, and the mitigation of adverse effects have been recent advancements in ocular drug delivery systems. The following are a few examples of recent developments in ocular medication delivery systems:

1.Drug delivery using nanotechnology: Drugs may be tailored to release over an extended period of time into targeted eye tissues using nanoparticles. Treatment of ailments such age-related macular degeneration (AMD), glaucoma, and uveitis has showed potential using this strategy..

2.Hydrogels and mucoadhesive polymers: These substances may lengthen the period that a medicine remains on the ocular surface, improving effectiveness and decreasing the need for repeated administration.

3.Contact lenses for drug delivery: Drugs may be released slowly into the eye using contact lenses if they are so constructed. Treatment of ailments including glaucoma and dry eye syndrome has been researched using this strategy.

4.Micro and nanoscale drug delivery devices: Micro- and nanoscale devices can be implanted into the eye to release drugs over a prolonged period of time. These devices can also be designed to respond to changes in the ocular environment, such as changes in intraocular pressure.

The most current trends include: -

- To improve ocular bioavailability and prolong the effects of ocular medications, the below-mentioned novel approaches—sensitive, effective prolonged duration and controlled release ocular delivery methods such ocular inserts—are being developed. Therefore, using the principle of controlled release as shown by ocular inserts offers an alluring alternate strategy to the challenging issue of extending precorneal drug residence duration**.**
- Gene therapy: By replacing or fixing damaged genes, gene therapy offers the potential to cure hereditary eye illnesses. Treatment for disorders like retinitis pigmentosa and Leber congenital amaurosis has showed potential with this strategy.
- In conclusion, current developments in ocular drug delivery systems provide hopeful avenues for enhancing the treatment of ocular illnesses and disorders. These methods can boost patient compliance, decrease dose frequency, and increase medication efficacy, leading to better patient outcomes and a higher quality of life.

Mucoadhesive dosage forms.

a) Ocular inserts.

b) Collagen shields or corneal shields.

c) Artificial tear inserts.

d) Drug-presoaked hydrogel type contact

e) Lens.

f) Ocular iontophoresis.

g) Phase transition systems

Classification of Ocular Insert (Based upon their solubility)

1. Insoluble ocular inserts

2. Soluble ocular inserts

3. Bio erodible ocular insert

Three groups have been created from the insoluble inserts.: -

i. Diffusion systems

ii. Osmotic systems

iii. Hydrophilic contact lenses

i) Diffusion systems:

- quickly and helping to keep the eyes moist and lubricated.
- There are different types of diffusion system ophthalmic inserts available, made from various materials, including silicone, collagen, and hydrogel. These inserts are typically inserted by an eye care professional and can be removed or replaced as needed. The duration of their placement can vary depending on the type of insert and the individual patient.
- Chronic dry eye syndrome, a condition in which the eyes do not produce enough tears or the tears evaporate too rapidly, causes pain, irritability, and occasionally severe corneal damage, is most frequently treated using diffusion system ophthalmic inserts. These inserts can be particularly beneficial for people who have difficulty tolerating traditional eye drops or other medications.
- While diffusion system ophthalmic inserts are generally safe, there are some potential risks and side effects, including infection, discomfort, and blockage of the tear ducts. It is important to discuss Thaurissan benefits of this treatment option with an eye care professional before undergoing the procedure

ii) Osmotic systems:

Ophthalmology uses osmotic ophthalmic inserts as a form of medical device. They are tiny, biocompatible devices made with the purpose of delivering medications right to the eye. These inserts use osmotic principles to deliver the drug steadily and gradually over a long period of

time.

Here's how osmotic ophthalmic inserts generally work:

1.Design: Osmotic inserts typically consist of a drug reservoir, a semipermeable membrane, and a small laser-drilled hole in the membrane. The drug reservoir contains the medication in solid or liquid form.

2.Insertion: The insert is placed inside the eye, usually in the lower eyelid's conjunctival fornix, by an ophthalmologist or eye care professional. The exact location may vary depending on the specific design of the insert.

3.Osmotic Pressure: Once inserted, the osmotic insert utilizes the difference in osmotic pressure between the interior of the device and the surrounding ocular fluids. This creates a gradient that drives fluid into the device.

4.Drug Release: As fluid enters the insert through the laser-drilled hole, it dissolves or solubilizes the drug in the reservoir, forming a solution. The solution is then gradually released through the semipermeable membrane at a controlled rate.

5.Continuous Delivery: The osmotic inserts provide sustained drug delivery over an extended period, typically ranging from several days to several months. The release rate is predetermined during the manufacturing process and remains relatively constant throughout the device's lifespan.

6.Patient Monitoring: During treatment, the patient's ophthalmologist may monitor their progress and adjust the dosage or replace the insert as needed.

Osmotic ophthalmic inserts offer several advantages in ocular drug delivery:

7.Improved Compliance: They make it unnecessary to often administer eye drops, which is more convenient for patients and lowers the possibility of missing doses.

8.Consistent Drug Levels: Osmotic inserts provide a steady release of medication, ensuring a constant therapeutic concentration in the eye over time.

9.Reduced Side Effects: Osmotic inserts minimise systemic absorption by delivering medications directly to the eye, lowering the risk of systemic adverse effects..

10.Extended Duration: These inserts can administer drugs over an extended period of time, lowering treatment frequency and improving patient comfort.

It's important to note that specific details about osmotic ophthalmic inserts, such as their design, drug compatibility, and indications, may vary depending on the product and manufacturer. Therefore, it's always essential to consult with a qualified healthcareprofessional for accurate and up-to-date information.

iii. Hydrophilic contact lenses:

Hydrophilic contact lenses, also known as soft contact lenses, are a popular type of vision correction device that is made from hydrophilic (water-loving) materials. These lenses are designed to be comfortable, flexible, and allow oxygen to pass through to the cornea, providing a healthier option for vision correction compared to rigid gas permeable (RGP) lenses.

Material: Hydrophilic lenses are made from soft, gel-like materials that contain a high percentage of water. The most common material used is hydrogel, which is a water-absorbing polymer. More recent advancements have introduced silicone hydrogel materials, which offer improved oxygen permeability.

Flexibility and Comfort: The soft and pliable nature of hydrophilic lenses allows them to conform to the shape of the eye, providing a comfortable fit. They tend to be more comfortable upon initial wear and require less adaptation time compared to RGP lenses.

Water Retention: The hydrophilic nature of the lens material enables it to retain moisture, which helps keep the lenses lubricated and hydrated. This feature contributes to improved comfort throughout the day.

Oxygen Permeability: Hydrophilic lenses are designed to allow oxygen to pass through the lens material and reach the cornea, ensuring adequate oxygen supply to the eye. This helps maintain eye health and reduces the risk of complications associated with low oxygen levels.

Disposable Options: Hydrophilic contact lenses are available in various wearing schedules, including daily disposables, biweekly or monthly disposables, and extended wear options. Daily disposable lenses are popular for their convenience and hygiene, as they are discarded after each use.

Wide Range of Corrective Powers: To treat a variety of refractive problems, including nearsightedness (myopia), farsightedness (hyperopia), astigmatism, and presbyopia, hydrophilic lenses are offered in a wide range of correction powers.

Colored and Cosmetic Options: Hydrophilic contact lenses also come in colored and cosmetic variants, allowing individuals to change or enhance their eye color for cosmetic purposes.

Care and Maintenance: Proper lens care and cleaning routines are crucial to maintaining eye health and preventing infections. Following the prescribed cleaning and disinfection regimen recommended by your eye care professional is essential.

Sensitivity: Some individuals may experience sensitivity or allergies to certain lens materials or contact lens solutions. If you experience discomfort or irritation, it's important to consult with your eye care professional.

Replacement Schedule: It's essential to follow the recommended replacement schedule for your specific type of hydrophilic lenses to ensure optimal vision and eye health.

Before using hydrophilic contact lenses, it's important to undergo a comprehensive eye examination and consultation with an eye care professional. They will assess your eye health, prescribe the appropriate lenses, and provide guidance on proper usage, care, and maintenance to ensure a safe and comfortable wearing experience.

Further, it is classified into two types

- **Pilo-20**
- **Pilo-40**

Pilo-20 releases pilocarpine at a rate of twenty micrograms per hour for the first week and then at a rate of forty micrograms per hour for the second week. On the other hand, Pilo-40 releases pilocarpine at a constant rate of forty micrograms per hour for two weeks.

Pilocarpine is a medication used to lower intraocular pressure in the eye, especially in conditions such as glaucoma. The pilocarpine alginate is the form of pilocarpine used in the inserts and is enclosed in a thin EVA (ethylene-vinyl acetate) membrane to regulate the release of the drug and protect it from degradation.

It's important to note that specific details about the drug, dosage, and the ophthalmic inserts may vary depending on the specific product and manufacturer. Therefore, it is always best to consult with a healthcare professional or refer to the product labeling for accurate and detailed information.

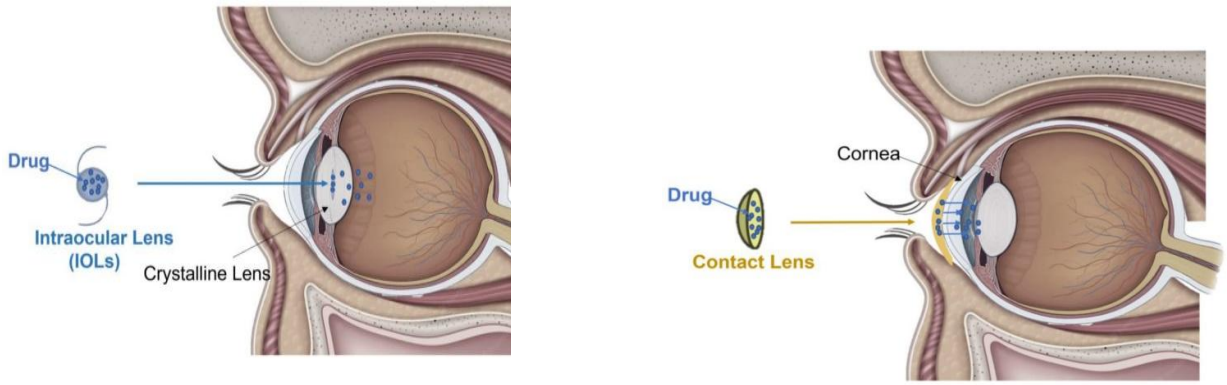

Fig. **Figure- Novel Treatment of Eye**

III. AKNOWLEDGEMENT

The mechanical properties of ocular inserts can vary depending on their specific design and composition. However, here are some general mechanical properties associated with ocular inserts:

1. Size and Shape: Ocular inserts are typically small, ranging in size from a few millimeters to a centimeter in diameter. They can have various shapes, such as discs, cylinders, or rings, depending on the intended application and desired drug release profile.
2. Flexibility: Ocular inserts often possess a certain degree of flexibility to allow for comfortable insertion and conform to the shape of the eye. This flexibility enables them to fit the curvature of the ocular surface and reduces discomfort during wear.
3. Mechanical Strength: Ocular inserts need to have sufficient mechanical strength to withstand the forces exerted during insertion and while in the eye. They should be able to retain their shape and integrity without deformation or breakage.
4. Swelling or Expanding Ability: Some ocular inserts are designed to swell or expand upon contact with tear fluid. This property allows them to adhere to the ocular surface, ensuring prolonged drug release and preventing their expulsion from the eye.
5. Biodegradability: Depending on the intended duration of therapy, ocular inserts can be designed to biodegrade over time. Biodegradable inserts gradually degrade within the eye, eliminating the need for removal, and reducing the risk of complications.
6. Lubricity: Ocular inserts may incorporate lubricious coatings or materials to reduce friction and improve comfort during insertion and wear. This property helps minimize irritation or damage to the ocular tissues.

The physicochemical properties of ocular inserts include:

1. Drug Compatibility: Ocular inserts should be compatible with the specific drug or active ingredient they are intended to deliver, ensuring stability and effectiveness of the medication.
2. Solubility: The solubility of the ocular insert material in tear fluid is important to ensure proper dissolution and drug release.
3. Permeability: To allow for the diffusion of medications or therapeutic agents from the insert to the ocular tissues, ocular inserts need to have the right level of permeability.
4. Biocompatibility: The materials used in ocular inserts should be biocompatible, meaning they do not cause irritation, inflammation, or damage to the ocular tissues.
5. Optical Transparency: Ocular inserts should be optically transparent to minimize visual disturbances or interference with vision when placed in the eye.
6. Stability: Ocular inserts should maintain their structural integrity and drug release properties over the intended duration of therapy, without degradation or loss of effectiveness.
7. Water Content: Some ocular inserts, such as hydrogels, may have a specific water content to provide hydration to the ocular surface and enhance comfort.

8. pH Sensitivity: Certain ocular inserts can be designed to respond to changes in pH within the eye, triggering specific drug release patterns or actions.

The safety, effectiveness, and use of ocular inserts as drug delivery devices in ophthalmic applications depend on these physicochemical characteristics.

- For the first week, the dosage was micrograms per hour, and for the second week it was raised to micrograms per hour. Contrarily, Pilo-40 continuously releases pilocarpine at a rate of 40 micrograms per hour for the whole two-week period.
- Both Pilo-20 and Pilo-40 inserts include a thin EVA (ethylene-vinyl acetate) membrane enclosing the pilocarpine alginate to guarantee regulated medication release and protection..
- It's vital to remember that depending on the manufacturer and intended use, certain ophthalmic inserts may differ in terms of medication kind, release rates, and other features. As a result, it is advised to seek advice from medical specialists or study the product documentation for accurate and comprehensive information on a specific ophthalmic insert..

FIGURE: RELEASE OF BRIMONIDINE TARTRATE FROM HEMA INSERTS

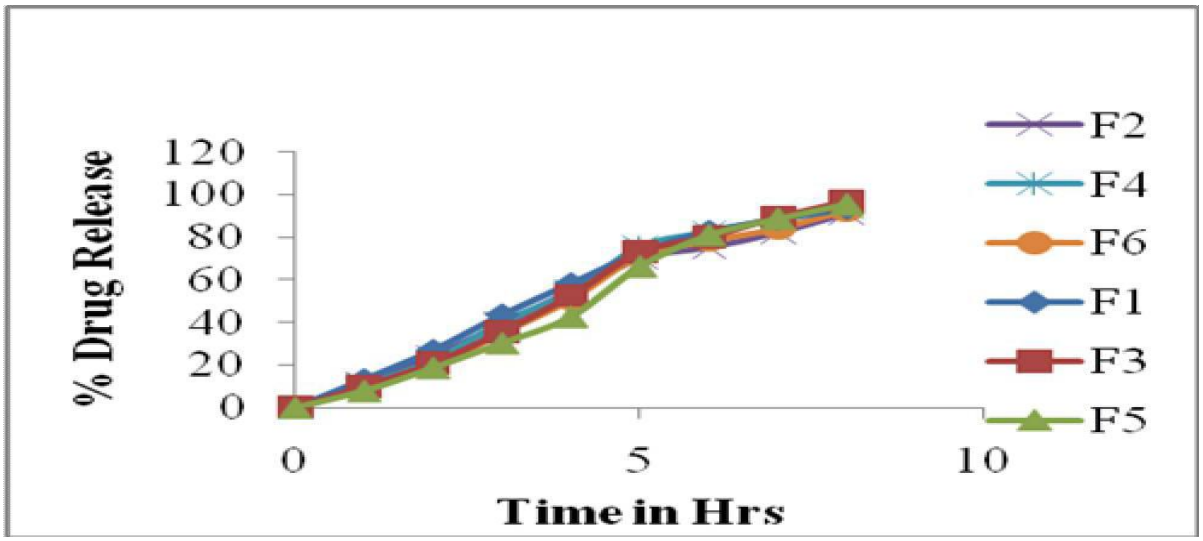

Figure: Brimonidine tartrate Dissolution from Eudragit RL-100 & RS-100 Inserts

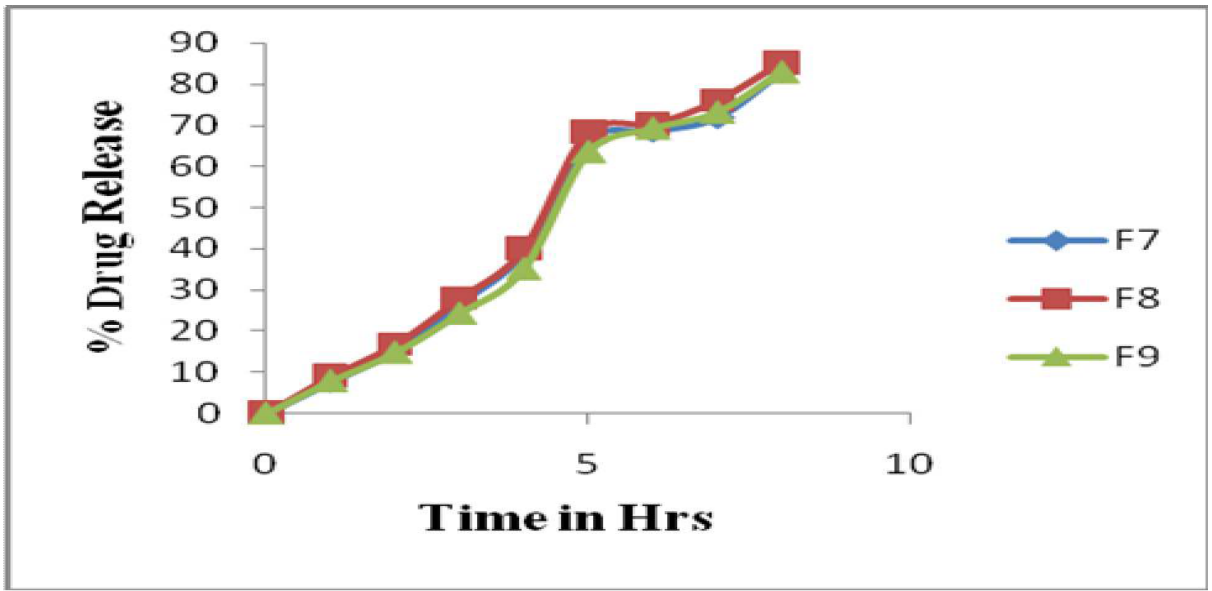

Figure: Brimonidine Tartrate Extraction from HEMA Inserts

IV. CONCLUSION:

- In conclusion, ophthalmic inserts are specialized devices used in ophthalmology for targeted drug delivery or therapeutic purposes within the eye. They can be categorized into different types based on the specific drug they contain and their release mechanisms.
- One example of ophthalmic inserts is the Pilo-20 and Pilo-40 inserts. These inserts contain pilocarpine alginate, and they release the drug at different rates over a two-week period. Pilo-20 releases pilocarpine at a rate of twenty.

V. REFERENCES:

1. 1.Gupta H, Aqil M, Khar RK, et al. Ophthalmic inserts: A promising ocular drug delivery system. J Control Release. 2013;171(3):280-297. doi: 10.1016/j.jconrel.2013.07.011
2. 2.Fariselli C, Barros LF, Gaspar L, et al. Ophthalmic drug delivery systems: Recent advances, challenges, and opportunities. Pharmaceutics. 2020;12(5):465. doi:10.3390/pharmaceutics12050465.
3. Reddy IK, Economou JS. Ophthalmic drug delivery systems: An overview. In: Rathbone MJ, ed. Controlled Drug Delivery: Fundamentals and Applications. 2nd ed. Springer; 2017:555-586. doi:10.1007/978-3-319-42485-1_15
4. Dohlman CH, et al. Ophthalmic inserts for drug delivery. In: Dohlman CH, et al., eds. A Manual for Eye Care Professionals. Springer; 2018:1055-1061. doi:10.1007/978-3-319-17220-6_139.
5. Lallemand F, Felt-Baeyens O, Besseghir K, et al. Ophthalmic drug delivery systems: Recent advances, challenges, and opportunities. J Control Release.2017;247:154-172. doi: 10.1016/j.jconrel.2016.12.033.
6. Song X, Zhao Y, Wu W, et al. Advances of drug delivery systems for protection of ocular surface and treatment of ocular diseases. Adv Colloid Interface Sci. 2018;256:117-132. doi:10.1016/j.cis.2018.01.011.
7. Balguri SP, Adelli GR, Majumdar S. Topical ophthalmic delivery of NSAIDs. AAPS J. 2015;17(2):327-343. doi:10.1208/s12248-014-9695-9
8. Badugu R, Pawar P, Jhansi Rani M, et al. In situ gelling systems for ocular drug delivery. J Control Release.2018;286:217-231. doi:10.1016/j.jconrel.2018.07.033
9. Lam H, Li P, Li K, et al. Recent advances in ophthalmic drug delivery systems. Drug Des Devel Ther. 2014;8: 1941-1951. doi:10.2147/DDDT.S66779

10. Verhoeven RS, Tong YC, Mrukwa-Kominek E, et al. The current and future landscape of ophthalmic drug delivery systems. Pharm Res. 2020;37(5):87. doi:10.1007/s11095-020-02848-2
11. Eljarrat-Binstock E, Peer J, Domb AJ. New techniques for drug delivery to the posterior eye segment. Pharm Res. 2010;27(3):530-543. doi:10.1007/s11095-009-0036-3
12. Wadhwa S, Paliwal R, Paliwal SR, et al. Ocular inserts - Advancements in the treatment of eye diseases. Curr Eye Res. 2016;41(5):559-572. doi:10.3109/02713683.2015.1051010
13. Loftsson T, Stefánsson E. Cyclodextrins in ophthalmic drug delivery: An overview. Int J Pharm. 2017;531(1): 327-338. doi: 10.1016/j.ijpharm.2017.08.072
14. Thrimawithana TR, Young S, Bunt CR, et al. Drug delivery to the posterior segment of the eye. Drug Discov Today. 2011;16(5-6):270-277. doi: 10.1016/j.drudis.2010.12.010
15. Cholkar K, Patel SP, Vadlapudi AD, et al. Recent advances in protein and peptide drug delivery systems. Crit Rev Ther Drug Carrier Syst. 2015;32(4):307-361. doi:10.1615/CritRevTherDrugCarrierSyst.2015012748
16. Nagarsenker MS, Londhe VY. Ocular inserts for controlled delivery of drugs: A review. Drug Dev Ind Pharm. 2008;34(6): 539-560. doi:10.1080/03639040801932439
17. Bourlais CL, Acar L, Zia H, et al. Ophthalmic drug delivery systems—recent advances. Prog Retin Eye Res. 1998;17(1):33-58. doi:10.1016/S1350-9462(97)00007-0
18. Ali J, Fazil M, Qumbar M, et al. Ocular drug delivery systems: An overview. World J Pharmacol. 2013;2(2):47-64.
19. Ciolino JB, Hudson SP, Mobbs AN, et al. A prototype antifungal intraocular lens. Invest Ophthalmic Vis Sci. 2011;52(1): 193-202. doi:10.1167/iovs.10-5542
20. Zaki NM, Awad GA, Mortada ND, et al. Enhanced bioavailability of timolol maleate via ocular administration of mucoadhesive liquid crystalline in situ gelling system. J Control Release. 2007;124(3):154-162. doi: 10.1016/j.jconrel.2007.08.015
21. Kalam MA, Alshamsan A. Ocular drug delivery systems: An overview. In: Alshamsan A, ed. Ocular Drug Delivery: Advances, Challenges, and Applications. CRC Press; 2016:1-16.
22. Desai SD, Blanchard J. Bimatoprost ophthalmic solution 0.03% for the treatment of eyelash hypotrichosis: A review of clinical efficacy and safety. Clin Cosmet Investig Dermatol. 2011;4: 123-129. doi:10.2147/CCID.S17657
23. Ali HS, York P, Ali AM, et al. Ocular inserts for extended delivery of ciprofloxacin hydrochloride. Int J Pharm. 1993;91(1):11-22. doi:10.1016/0378-5173(93)90255-D
24. Purohit SS, Agharkar SK. Design and evaluation of ocular inserts for controlled release of betaxolol hydrochloride. J Pharm Res. 2009;2(3):419-423.

25. Akinlade B, Soleye J, Ajayi E, et al. Formulation, characterization, and in vitro evaluation of pilocarpine-loaded gellan gum mucoadhesive inserts for controlled ocular drug delivery. Sci Pharm. 2017;85(4):32. doi:10.3390/scipharm85040032
26. Zhou HY, Li JS, Li XR, et al. In vitro evaluation of a scleral cross-linked HA membrane as a drug reservoir. Acta Ophthalmic. 2011;89(8):e655-e660. doi:10.1111/j.1755-3768.2011.02213.x
27. Alhalafi AM, Chauhan A. Ophthalmic drug delivery: Impact of in vitro cell culture models. J Pharm Sci. 2017;106(9):2190-2208. doi: 10.1016/j.xphs.2017.05.010
28. Kalam MA, Alshamsan A. Ophthalmic drug delivery systems: An overview. In: Alshamsan A, ed. Ocular Drug Delivery: Advances, Challenges, and Applications. CRC Press; 2016:1-16.
29. Feng X, Wang J, Yu J, et al. Formulation and evaluation of dexamethasone-loaded microemulsion-based ocular inserts. Drug Dev Ind Pharm. 2016;42(8):1273-1282. doi:10.3109/03639045.2016.1147889
30. Das S, Suresh PK, Deshmukh R. In vitro and in vivo evaluation of an ocular insert for controlled release of moxifloxacin hydrochloride. AAPS PharmSciTech. 2009;10(2):464-471. doi:10.1208/s12249-009-9234-5
31. Khurana S, Jain NK, Bedi PM. Design and evaluation of gatifloxacin-loaded mucoadhesive vaginal inserts for controlled release. J Drug Target. 2008;16(4):296-304. doi:10.1080/10611860801895007
32. El-Gizawy SA, El-Alim SH, Ahmed OA, et al. Development and evaluation of gellan gum based ocular inserts for sustained delivery of ciprofloxacin hydrochloride. Int J Pharm Pharm Sci. 2013;5(3): 435-443.
33. Shetty A, Nayak UY, Udupa N. Preparation and evaluation of liposomal formulations of tropicamide for ocular delivery. Eur J Pharm Biopharm. 2003;56(1):65-71. doi:10.1016/S0939-6411(03)00005-3
34. Raghavan CV, Mundada AS, Sawant KK. Developments in ocular drug delivery systems: The specialized role of nanotechnology. J Drug Target. 2013;21(6): 519-535. doi:10.3109/1061186X.2012.757960
35. Rosenthal RA, Dassanayake N, Rees TD, et al. Effectiveness of punctal plugs in managing dry eyes. Ann Plast Surg. 2006;57(6):637-641. doi: 10.1097/01.sap.0000234419.97180.9c
36. Gurtler F and Gurny R. Patent literature review of ophthalmic inserts. Drug Dev Ind Pharm. 1995; 21:1-18.
37. Chien YW. Novel drug delivery systems. Marcel Dekker, New York. 1991;2nd Edn:269-300.

38. Khar RK and Vyas SP. Targeted and controlled drug delivery novel carrier systems. CBS Publishers and Distributors, New Delhi. 2002;384-389.
39. Patel JM, Shah KK and Patel MM. Formulation and evaluation of temperature dependant ophthalmic gel solution of Brimonidine tartrate. IJPCS. 2012; 1:1190-1199.
40. SultanaY,Aquil M andAli, A.Ocular inserts for controlled delivery of pefloxacin mesylate: preparation and evaluation. Acta Pharm. 2005; 55:305- 314.
41. Murthy SN and Hiremath SR. Biodegradable polymers matrix based Ocuserts. Int J Pharm Excip. 2002;34- 37.
42. Ahad HA, Sreeramulu J, Padmaja BS, Reddy MN and Guruprakash P. Preparation of fluconazole β- cyclodextrin complex ocuserts: invitro and invivo evaluation. ISRN Pharm. 2002;2011:1-8.
43. DaveV,YadavS,PaliwalS,SharmaSand Kumar D. Design and evaluation of accelofenac ocular insert with special reftocataracts andconjunctivitis. JCPS. 2013;22:449-455.
44. Attiashafie MA and Hassanrady MA. In vitro and in vivo evaluation of timolol maleate ocular inserts using different polymers. J Clin Exp Ophthalmic. 2013; 3:246.
45. Indian Pharmacopoeia. Ministry of HealthandFamilywelfare.Government of India. Controller of Publication, New Delhi.1996; 2:117-147.
46. Michael HA, Mostafa H, MehdiJ and Taravat G. Draize rabbit eye test compatibility with eye irritation threshold in humans: a quantitative structural-activityrelationshipanalysis. Toxicol Sci. 2003; 76:384-391.
47. GeethalakshmiA,KarkiR,SagiP,JhaSK and Venkatesh DP. Temperature triggered in situ gelling system for Betoxololinglaucoma.JApplPharmSci. 2013; 3:153-159.
48. New crosslinked hydrogels derivatives of 2-hydroxyethyl methacrylate: Synthesis, modifications and properties. express Polymer Letters. 2012;6:759-771.