
A REVIEW ON OCUSERTS

Pilli kusumanjana¹, Enagantivyshnavi², Keshamoni Bhanusandhya³, S. Rohini Reddy⁴,
CH, ShanthiPriya⁵

^{1,2,3}Student, Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Hyderabad, Telangana, India.

^{4,5}Associate professor, Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Hyderabad, Telangana, India.

DOI: <https://www.doi.org/10.58257/IJPREMS33964>

ABSTRACT

Ocuserts are sterile, solid or semisolid ocular formulations designed to utilize controlled release methods, prolonging the duration of medication within the eye and minimizing nasolacrimal drainage. Ocuserts represent a significant innovation in the treatment of eye diseases. The goal of ocuserts is to enhance the interaction between the medication and the conjunctival tissue, ensuring sustained drug release when placed in the lower cul-de-sac or conjunctival sac of the eye. Ocuserts are designed to optimize formulations to achieve a consistent release of medication, ensuring a sustained dosage over an extended duration. Three primary methods for preparing ocuserts include solvent casting, glass substrate, and melt extrusion techniques. The drug release characteristics primarily rely on the processes of bioerosion, osmosis, and diffusion, forming the basis of this review paper aimed at providing an overview of the innovative ocular drug delivery system.

Key words : Ocuserts, conjunctival tissue, cul-de-sac, bio erosion, osmosis, diffusion, extrusion

1. INTRODUCTION

Research by Dr. Amudha M *et.al* (2023). The human eye is truly a remarkable sensory organ that allows us to see and perceive the world around us. It is a complex structure that enables us to interpret and understand our surroundings through the reception of light and visual stimuli. The eye not only helps us to perceiving shapes, depth, colors and light. But it also plays a crucial role in our sense of balance. The eye functions through a series of intricate processes involving the cornea, iris, lens, retina and optic nerve among other components (Ocular drug delivery). Topical administration of drugs to the eye indeed a commonly used and accepted method for the treatment of various eye conditions. This route of administration involves applying medication directly on to the surface of the eye, usually in the form of eye drops or ointments. Topical administration offers several advantages for the treatment of various eye diseases and patient compliance. Research by Navneet Nagpal *et.al* (2021) Ophthalmic preparations are specifically designed for local therapy in the eye rather than for systemic treatment. The primary reason for this is to avoid high concentrations of medications in the bloodstream, which can lead to systemic side effects and potential harm to the rest of the body. When medications are administered directly to the eye through ophthalmic preparations such as eye drops or ointments, that are intended to act locally on the tissues of the eye itself. By keeping the concentration of the drug localized to the eye, the risk of systemic absorption and associated side-effects are minimized. Research by Dr. Amudha M *et.al* (2022) Ocuserts systems was firstly developed in 1975 by 'Alza corporation' in the United States of America. Research by Kaushal Kumar *et.al* (2014) Ocuserts are drug delivery designed as thin, flexible and usually disc-shaped inserts placed in the eye. They gradually release medication over an extended period, providing sustained drug delivery directly to the eye, reducing the frequency of administration. They are used for conditions like glaucoma, ocular infection and inflammation. Ocuserts offers continuous controlled drug delivery of ophthalmic ally active drugs to the eye. They provide sustained release of medication maintaining therapeutic levels over time, which can improve patient compliance and treatment outcomes of various ocular conditions and increased bioavailability by increased drug eye contact time is served. Generally, all types of ocusert consist of three components namely, "a central drug reservoir" in which the drug is incorporated in a polymer; "rate controlling membrane", which ensures the controlled release of medicament from the drug reservoir; and "an outer annular ring", meant for easy handling and proper insertion.

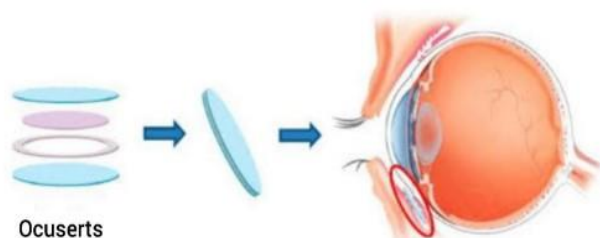


Figure 1: Ocuserts

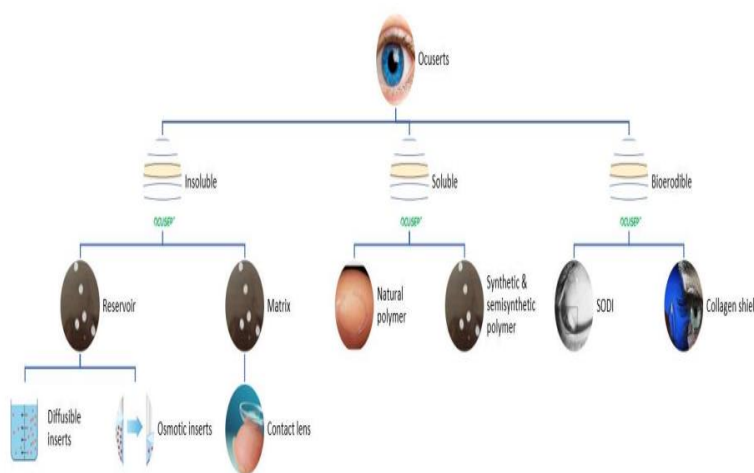


Figure 2: Classification of ocuserts

Classification of ocuserts

1. Insoluble ocuserts: Reservoir system. Matrix systems.
2. Soluble ocuserts: Natural polymers. Synthetic and semi-synthetic polymers.
3. Bio-erodible ocuserts: Soluble ophthalmic drug insert (SODI). Collagen shields.

Insoluble ocuserts: Research by Navneet Nagpal *et.al* (2023). This delivery system offers controlled and varied drug administration, yet necessitates removal once depleted.

1. Insoluble ocuserts are divided into 2 categories:
2. Reservoir system: In this system, drugs are released through diffusion or osmosis, utilizing various mediums such as colloids, gels, semisolids, liquids, solid matrices, or carriers.
3. Diffusional inserts - In this configuration, drug release occurs through diffusion. The ocular insert functions as a permeable membrane for delivering medication.
4. Osmotic inserts - These include a central component encircled by another section and can be categorized into two groups:
5. Type 1 - The central compartment comprises a drug reservoir encased in polymer, potentially containing an osmotic solute. Encircling this is a semi-permeable, insoluble polymeric membrane. As a result of osmotic pressure, drug molecules are released through apertures in the matrix.
6. Type 2 - This type features a dual-compartment core: one section holds the medication while the other contains an osmotic solute. Encircling the solute compartment is a semipermeable membrane, while the medication compartment remains impermeable.
7. Matrix systems: This setup incorporates ocular devices and non-soluble ophthalmic equipment. Within a three-dimensional matrix, water, aqueous solutions, or solids are housed. It comprises cross-linked polymers, either hydrophilic or hydrophobic, such as contact lenses for vision correction. This system serves to both correct vision and dispense medications.
8. Soluble ocuserts: Research by Navneet Nagpal *et.al* (2023). The soluble inserts, known as homogenous polymeric ocuserts, gradually dissolve within the eye and release medication. Dissolution and erosion occur through enzymatic or chemical hydrolysis. Tear fluid penetration prompts swelling and chain relaxation, facilitating drug diffusion and subsequent release. Removal after administration is unnecessary.

9. The classification of these inserts into two groups can be based on the type of polymer source they utilize:
10. Natural polymers: Soluble ophthalmic inserts are crafted using collagen, a process involving soaking, drying, and subsequent rehydration of the ocusert prior to application. The quantity of medication contained within the ocusert is contingent upon factors such as concentration during preparation, soaking duration, and the concentration of binding agents utilized. The release of medication occurs concomitantly with the dissolution of the collagen.
11. Synthetic and semi-synthetic polymers: Ophthalmic inserts can be manufactured from synthetic and semisynthetic materials, including cellulose derivatives and synthetic polymers such as polyvinyl alcohol. Coating the ocusert with eudragit has the potential to decelerate the release process.
1. Bio-erodible ocusert: Bio-erodible ocuserts utilize cross-linked gelatin and polyester derivatives, offering the advantage of modifiable final structures through manufacturing alterations or the incorporation of anionic or cationic surfactants to control erosion.
12. Soluble ophthalmic drug insert (SODI) :SODI, a small oval wafer, is designed for use in weightless environments where traditional eye drops are impractical.
13. Collagen shields: Research by Navneet Nagpal *et.al* (2023) Collagen, which constitutes approximately 25% of mammalian body proteins, is present in various tissues such as bones, tendons, ligaments, and skin. This intestinal collagen protein serves multiple biological purposes, one of which is catgut suturing. Application of this insertion necessitates an anesthetized cornea and the use of blunt forceps.

Advantages of ocusert :

1. Research by Navneet Nagpal *et.al* (2023). Enhanced pre-corneal residence time leading to increased ocular bioavailability (When the medication has prolonged contact with the eye, it enhances the bioavailability of the drug, leading to improved therapeutic outcomes.)
2. Research by Nida Parveen *et.al* (2020). This formulation allows for greater penetration into the eye compared to the standard version. This translates to a longer-lasting effect of the drug and a higher amount reaching its target site within the eye.
3. Research by Nida Parveen *et.al* (2020). Administering the right amount of dose in the eye leads to better therapy.
4. Research by Navneet Nagpal *et.al* (2023). By reduction of the number of administered dose. We can improve better patient compliance.
5. Research by Nida Parveen *et.al* (2020). By ensuring a constant release of drug, we can achieve better efficacy.
6. Research by Nida Parveen *et.al* (2020). It has a better chance of reaching internal ocular tissue targeting through non-corneal, (conjunctival and sclera) penetration routes.
7. Research by Nida Parveen *et.al* (2020). Due to the absence of water in the formulation it enhanced stability and increased shelf life with respect to standard formulation.
8. Research by Nida Parveen *et.al* (2020). It signifies that the medication exhibits diminished systemic absorption, thereby resulting in a decreased incidence of adverse effects.
9. Research by Navneet Nagpal *et.al* (2023). Easy in handling.
10. Research by Navneet Nagpal *et.al* (2021). Vision and oxygen permeability are not effected.
11. Research by Navneet Nagpal *et.al* (2023). Reproducible release kinetics.
12. Research by Navneet Nagpal *et.al* (2023). Barriers can be avoided like drainage, lacrimation, conjunctival absorption, etc.
13. Research by Navneet Nagpal *et.al* (2023). Sterile preparation.

Disadvantages of ocusert

1. Research by Nida Parveen *et.al* (2020). Ocular discomfort upon circumocular movement.
2. Research by Navneet Nagpal *et.al* (2023). The occasional loss of an eyelash, either while sleeping or due to rubbing the eye.
3. Research by Nida Parveen *et.al* (2020). Visual limitations hinder precise placement and intervention.
4. Research by Nida Parveen *et.al* (2020). The patient reports a sensation of a foreign object lodged within the ocular cavity.
5. Research by Navneet Nagpal *et.al* (2023). The retrieval of an ocusert can be impeded by its inadvertent migration to the superior fornix of the ocular globe.
6. Research by Nida Parveen *et.al* (2020). It is not easy to administer the ocuserts and also difficult for removal in case of insoluble ocuserts.

7. Research by Navneet Nagpal *et.al* (2023) An implantable medication disc called Ocusert can move out of position in the eye, blocking the pupil and potentially slowing down the release of medication.
8. Research by Navneet Nagpal *et.al* (2023) There is a chance of leakage.

Formulation methods of ocuserts

There are three methods for formulation of ocuserts

1. Solvent casting method: Research by Navneet Nagpal *et.al* (2023). Solvent casting is commonly employed for manufacturing ocuserts due to its cost-effectiveness and simplicity. During this process, the rheological characteristics of the polymer are carefully assessed as they influence factors such as ocusert thickness, drying rate, and homogeneity. De-aeration is essential to eliminate air bubbles that may form during polymer mixing. Once adequately mixed, the polymers are cast onto the appropriate substrate. As the mixture dries, the solvent evaporates, resulting in the formation of the ocusert film. Finally, the ocusert films are trimmed to the required size.
2. Glass substrate technique: Research by Navneet Nagpal *et.al* (2021). Glass substrate technology is employed in the production of thin films. A transparent polymer solution is utilized to create a film for drug reservoirs. The polymer solution is agitated using vortexing to incorporate the medication. Following drug dissolution, plasticizer is added. The solution is then poured into a glass mold to form films, which are dried. Drying typically requires 24 hours at room temperature. Once dried, the films are trimmed to the desired size and stored.
3. Melt extrusion technique: Research by Navneet Nagpal *et.al* (2023). Melt extrusion serves as an alternative to solvent casting, particularly suitable for non-organic solvents. This method involves melting polymers and other constituents, which are subsequently passed through a die to form films. The resulting films are then trimmed. However, it is not suitable for thermolabile substances.

Evaluation tests of ocuserts



Figure 3: Evaluation tests of ocuserts

- Uniformity of weight : Research by Hindustan Abdul Ahad *et.al* (2023). The ocuserts were evaluated for physical characterization such as color, shape, texture and appearance.
- Content uniformity: Research by Navneet Nagpal *et.al* (2023) The ocuserts are placed in 5 mL of pH 7.4 STF (phosphate buffer saline[6]) and are shaken in orbital shaker incubator at 50 rpm to extract the drug from ocuserts. After incubation for 24 h, the solution is filtered through a 0.45µm filter and the filtrate is suitably diluted with STF solution. The absorbance of the resulting solution is measured using a UV-spectrophotometer.
- Surface pH: Research by Dr. Amudha M *et.al* (2022). The inserts were permitted to expand within a sealed petri dish at room temperature for 30 minutes, submerged in 0.1 ml of distilled water. Subsequently, the enlarged device was extracted and positioned beneath a digital pH meter to assess the surface pH [1]. The surface pH of the ocuserts was assessed by immersing them in a petri dish containing 10 mL of distilled water at room temperature for 30 minutes, allowing them to swell. Subsequently, the swollen devices were taken out and positioned on the sensing electrode of a pH meter to determine the average surface pH.
- Swelling index: Research by Dr. Amudha M *et.al* (2023). Initially, a portion of the film is cut and measured before being immersed in tear fluid with a pH level of 7.4 for an hour. Following this immersion period, the film's weight is measured once more.

The swelling index is determined by the formula

$$\text{Swelling index} = \frac{\text{Initial weight} - \text{weight of swollen insert}}{\text{Initial weight}} \times 100$$

- Uniformity of thickness: Research by Dr. Amudha M et.al(2022).The thickness of ocuserts was assessed using digital vernier calipers with a least count of 0.01 mm. Measurements were taken at various points on the ocuserts, and the average thickness of 20 ocuserts was determined. Statistical analysis using ANOVA was performed to examine variations in thickness. Research by Navneet Nagpal et.al (2021) Uniformity of thickness can also be determined by using a Micrometre screw gauge
- % Moisture absorption: Research by Navneet Nagpal et.al (2023)The moisture absorption test evaluates the physical stability of ocuserts in moist conditions. Each batch is weighed, and then three ocuserts are placed in aluminum chloride desiccators. After three days, the ocuserts are reweighed.

The % moisture absorption is determined by the formula

$$\% \text{ Moisture absorption} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

- % Moisture loss: .Research by Navneet Nagpal et.al (2021)This procedure is conducted to assess the integrity of the ocuserts under dry conditions. The ocuserts were initially weighed and then placed in desiccators filled with anhydrous calcium chloride. After a period of three days, the ocuserts were removed from the desiccators and weighed once more. The % moisture absorption is determined by the formula by,

$$\% \text{ Moisture loss} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

- Folding Endurance: Research by Devu.Satya Sireesha et.al (2022) A small strip of ocusert was uniformly cut and then folded repeatedly at the same location until it fractured. The folding endurance was determined by counting the number of times the ocusert could be folded at the same spot without breaking.
- Sterility Test: Research by Navneet Nagpal et.al (2021). The sterility test, as per the Indian Pharmacopoeia, involves aseptically transferring 2 mL of the prepared ocusert solution into separate fluid thioglycollate and soybean-casein digest media. These media are then incubated for a minimum of 14 days at 30°C to 35°C for fluid thioglycollate and at 20°C to 25°C for soybean-casein digest medium. The sterility test, as per the Indian Pharmacopoeia, involves aseptically transferring 2 mL of the prepared ocusert solution into separate fluid thioglycollate and soybean-casein digest media. These media are then incubated for a minimum of 14 days at 30°C to 35°C for fluid thioglycollate and at 20°C to 25°C for soybean-casein digest medium. In each test, three sterility test tubes were used in the study and labeled as “positive control”, “negative control”, and “test”.
- Percentage Elongation: Research by Jayesh K et.al (2014.)When stress is exerted, a strip sample undergoes stretching, which is termed as strain. Strain essentially represents the deformation of the strip divided by its original dimensions.As the amount of plasticizer increases, the elongation of the strip generally tends to rise. The % Elongation is determined by the formula by

$$\% \text{ Elongation} = \frac{\text{increase in length of strip at breakpoint}}{\text{initial length of strip}} \times 100$$

- Bio adhesive strength: Research by Jayesh K et.al .The bioadhesive strength of the insert was assessed using a modified physical balance. A membrane was secured to the open mouth of a glass vial containing isotonic phosphate buffer. This vial was positioned centrally within a glass beaker filled with simulated tear fluid (pH 7.2, maintained at 37 ± 1°C). Meanwhile, the insert was affixed to the underside of a rubber stopper, which was connected to the lever of the physical balance. The mass applied to the opposite limb of the balance, necessary to detach the patch from the conjunctival surface, served as a measure of bioadhesive strength.
- Tensile strength: Research by Jayesh K et.al. The tensile strength represents the maximum stress reached at the point of rupture in the strip specimen. It is determined by dividing the applied load at rupture by the cross-sectional area of the strip, as equation given below.

$$\text{Tensile Strength} = \frac{\text{Load at failure (Kg)}}{\text{Strip thickness} \times \text{strip width}} \times 100$$

- Stability study: Research by Navneet Nagpal et.al (2021).Stability studies, conducted in accordance with ICH guidelines, utilize accelerated decomposition methods, often involving increased temperature, to project the shelf-life of a product. Various characteristics such as alterations in drug concentration, color, folding endurance, etc., are monitored throughout these studies. Ocuserts, enveloped in aluminum foil and housed within a glass bottle, were subjected to storage at 40 °C and 75% relative humidity (RH) within a stability chamber. Subsequently,

physical appearance, % weight variation, folding endurance, and drug release of the Ocuserts were analyzed at intervals of 0, 1, 2, 3, and 6 months.

- Ocular Irritation: Research by Hindustan Abdul Ahad et.al (2023) . The ocular irritation and potential damage caused by the tested ocusert were assessed by monitoring for signs such as redness, inflammation, or increased tear production in the eyes of five rabbits. The inserts were placed in the cul-de-sac of the left eye, and both eyes were examined for signs of irritation before treatment and observed for up to 12 hours thereafter.
- Kinetics of drug release: Research by Navneet Nagpal et.al (2021). The mechanism and kinetics of drug release were investigated by utilizing the outcomes of both in-vitro drug release and ex-vivo permeation studies, applying kinetic equations including zero order, first order, Higuchi, and Korsmeyer-Peppas models.
- In Vitro Drug release studies: Research by Hindustan Abdul Ahad et.al (2023). The ocuserts from each batch were placed in 15 mL vials containing 10 mL of pH 7.4 phosphate buffered saline and then subjected to an oscillating water bath at $32 \pm 1^\circ\text{C}$ with 25 oscillations per minute. At various time intervals (1, 2, 4, 8, 12, 16, and 20 hours), 1 mL of the drug releasing media was withdrawn and replaced with an equal volume of phosphate buffer saline pH 7.4. These samples underwent filtration through a $0.45 \mu\text{m}$ membrane filter and were suitably diluted with buffer [23, 24]. The drug content in each batch was determined using a double beam UV-Vis spectrophotometer (Elico SL 210, Mumbai, India) at 254 nm, and the obtained data was analyzed using mathematical kinetic modeling.
- In Vivo Drug Release Study: Research by Dr. Amudha M et.al (2023). The ocuserts were sterilized using UV radiation prior to the in vivo study. Post-sterilization, they were transferred into a polyethylene bag using forceps within the sterilization chamber itself. Albino rabbits of both genders, weighing between 2.5 and 3.0 kg, were utilized for the experiment. Each ocusert intended for in vivo study was carefully placed into the lower conjunctival cul-de-sac of six rabbits, while the other eye of each set of six rabbits was designated as the control. At designated intervals of 30, 60, 90, 120, and 150 minutes, the ocuserts were cautiously removed and subjected to drug content analysis. The remaining drug content was then subtracted from the initial drug content of the ocuserts, revealing the amount of drug released into the rabbit's eye.

Mechanism of Control Drug Release Into The Eye

Drug from the ocuserts can be released by one of the following methods depending upon the type of ocusert:

- Diffusion
- Osmosis
- Bioerosion

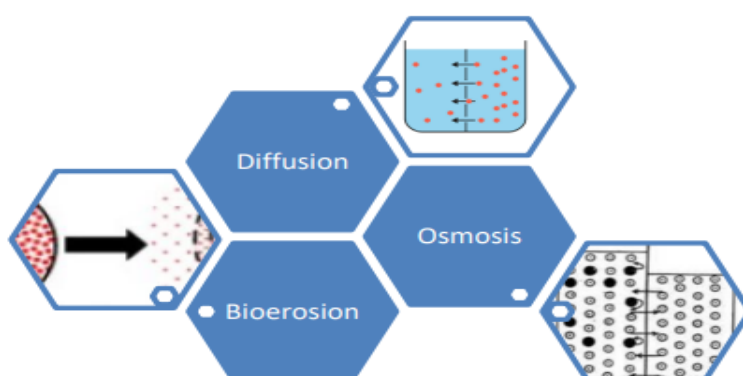


Figure 4: Mechanism Of Control Drug Release Into The Eye

- Diffusion: Research by Nida Parveen *et.al* (2020). In the diffusion mechanism, the drug is continuously released at a controlled rate through the membrane into the tear fluid. If the insert consists of a solid, non-erodible body with pores containing dispersed drug, drug release happens through these pores via diffusion. The controlled release of the drug can be further modulated by the gradual dissolution of the solid dispersed drug and the matrix itself due to directed diffusion of aqueous solutions. In a soluble device, true dissolution primarily occurs through polymer swelling. In devices controlled by swelling, the active ingredient is uniformly dispersed in a glassy polymer. These glassy polymers are essentially impermeable to the drug, and no diffusion occurs through the dry matrix. When the ocular insert is placed in the eye, water from the tear fluids starts to penetrate the matrix, initiating swelling, polymer chain relaxation, and subsequent drug diffusion. The dissolution of the matrix follows the swelling process, which is dependent on polymer structure.

- Osmosis: Research by Devu.Satya Sireesha *et.al* (2022) The osmosis mechanism involves an insert with a transverse impermeable elastic membrane, dividing its interior into two compartments: one bounded by a semipermeable membrane and the impermeable elastic membrane (the first compartment), and the other bounded by an impermeable membrane and the elastic membrane (the second compartment). The impermeable wall of the insert has a drug release aperture. The first compartment contains a solute unable to pass through the semipermeable membrane, while the second compartment serves as a reservoir for the drug, typically in liquid or gel form. Upon placement of the insert in the aqueous environment of the eye, water diffuses into the first compartment, stretching the elastic membrane to expand it while contracting the second compartment, thereby facilitating the release of the drug through the drug release aperture.
- Bioerosion: Research by Dr. Amudha M *et.al* (2023). In the bio-erosion mechanism, the insert comprises a matrix of bio-erodible material wherein the drug is dispersed. Upon contact with tear fluid, controlled and sustained drug release occurs through the erosion of the matrix. While the drug may be evenly dispersed within the matrix, it is thought that a more regulated release is attained when the drug is concentrated at the surface of the matrix.

2. CONCLUSION

In this review, our focus has been on innovative approaches to administering ocular medication. Ocuserts offer several advantages: accurate and consistent dosing, delayed drug release enhancing efficacy, prolonged contact time, and improved bioavailability. They may also lead to reduced systemic absorption, potentially lowering systemic side effects. Additionally, less frequent administration promotes better patient compliance and decreases the occurrence of visual side effects. Ocuserts represent sterile ophthalmic formulations designed to employ a controlled release strategy, thereby prolonging drug retention and minimizing nasolacrimal drainage. This is achieved by carefully regulating the release of medication into the eye. Available in various forms, each tailored to specific applications, ocuserts prolong the duration of drug contact with the conjunctiva, ensuring consistent dosing. By maintaining a stable drug level in the eye, they mitigate adverse systemic effects. Additionally, they reduce dosing frequency, enhancing patient adherence. Ocuserts are manufactured using methods such as solvent casting, the glass substrate technique, or melt extrusion.

3. REFERENCES

- [1] Devu.Satya Sireesha¹, B.Lakshmi Prasanna², M.Harini³, V.Shirisha⁴, T.Rama Rao⁵.
- [2] Formulation and evaluation of ocular inserts of diclofenac sodium for controlled release drug delivery.2022 sept 9;Vol(7), Iss 9 ISSN: 2456-4184.
- [3] Kaushal Kumar¹, Lakshyaveersingh.Review Article on Ocusert: A Novel Ophthalmic Drug Delivery System.Aug 2014 vol (1);(ISSN-2349-5162).
- [4] Dr. Amudha M, Dr. Ganesan V. Dr. Ethiraj T, Jeevalakshmi R, Deepika R, Supriya M, and Manivannan P.Preparation and Evaluation of Ocuserts for increasing the Bioavailability of an Anti- fungal Drugs.2022 May 16; vol(6)17-23.
- [5] Navneet Nagpal ¹, Sukhmanpreet Singh ², Prince Ahad Mir ³, Mandeep Singh Chhina ², Manisha Arora ³, Deepinder Jeet Kaur ², Rahul Kumar ⁴, Abhay Sharma ³, Priyanka ³ and Nishant Kumar ³.Ocuserts: A novel ocular-drug delivery method: An update.2023, 13(01), 470–477.
- [6] Deepak Nautiyal*, Vikram Singh, Sahadat Ali. Formulation and Evaluation of Sustained Release of Ofloxacin Ocular Inserts.vol-5,iss-12 -2012
- [7] Hindustan Abdul Ahad,¹J. Sreeramulu,²B. Suma Padmaja,¹M. Narasimha Reddy,¹and P. Guru Prakash¹.Preparation of Fluconazole β -Cyclodextrin Complex Ocuserts: In Vitro and In Vivo Evaluation.25 Aug 2011;vol 2011.
- [8] Jayesh K. jethava and Gaurang K. jethava.Design, formulation, and evaluation of novel sustain release bioadhesive in-situ gelling ocular inserts of ketorolac tromethamine.2014 Oct-Dec; 4(4): 226–232.
- [9] Navneet Nagpal¹, Sukhmanpreet Singh¹, Guraasdeep Kaur¹, Parminderjit Kaur¹, Ravi Kumar Dhawan², Mandeep Singh Chhina³, Manisha Arora³.Formulation and evaluation of controlled release ocusert of gatifloxacin and prednisolone.15 Oct 2021;67(4):227-237.
- [10] Dr. Amudha M, Dr. Ganesan V. Dr. Ethiraj T, Jeevalakshmi R, Deepika R, Supriya M, and Manivannan P.Ocular drug delivery system-An overview entrenched on ocuserts.2023 Apr 15;79(2).
- [11] Nida Parveen,, Himanshu Joshi.Ocuserts :A Novel Formulation Approach in Drug Delivery System.vol.06,iss:05,pp 420-425(2020).
- [12] Kumar, B. P., Harish, G., & Bhowmik, D. (2013). Ocular inserts: A novel controlled drug delivery system. The Pharma Innovation, 1(12):1-14.15.

-
- [13] Cheien Y.W., “Drugs and the pharmaceutical sciences novel drug delivery systems”, Second edition, revised and expanded, volume 50.
- [14] 8. Thakur Richa and Swami Gaurav, “Promising implication of ocuserts in ocular disease”, JDDT 2012; Volume 2(2): 18&19.
- [15] G. Levy, “Effect of certain tablet formulation factors on dissolution rate of the active ingredients,” Journal of Pharmaceutical Sciences, vol. 52, pp. 1039–1051, 1963.
- [16] S. El-Samaligy, S. A. Yahia, and E. B. Basalious, “Formulation and evaluation of diclofenac sodium buccoadhesive discs,” International Journal of Pharmaceutics, vol. 286, no. 1-2, pp. 27–39, 2004.
- [17] Karki, S., et al., Thin films as an emerging platform for drug delivery. Asian Journal of Pharmaceutical Sciences, 2016. 11(5): p. 559-74.
- [18] Shankar V., et al. “A text book of novel drug delivery system”. 2012, Pharmamed press 4-4-316.