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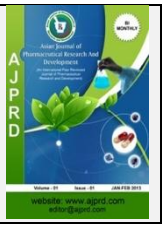

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Review Article

A Review on "Ocuserts (An Ophthalmic Insert)"

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A B S T R A C T

The eye is God's most wonderful creation of all the sense organs in the human body since it allows us to see numerous objects both near and far away. An ocular implant is a cutting-edge device for treating eye diseases. The design and development of an ocular insert has always been a difficulty for pharmaceutical researchers and manufacturers. Ocuserts, also known as ophthalmic inserts, are "sterile preparations in the form of solid or semisolid, whose size and shape are specially designed to be applied to the eyes". Solvent casting, the Glass Substrate technique, and hot melt extrusion were used to create ocuserts. The inserts can be classed as insoluble, soluble, or biodegradable based on their solubility. The drug's release from the insert is determined by its diffusion, osmosis, and bioerosion. The ocuserts' objective is to enhance pharmaceutical contact with conjunctiva tissue, resulting in constant dose release. Uniform ocular drug levels reduce systemic side effects, minimise doses, and improve patient compliance. Preparing ocular inserts aims to enhance medication bioavailability. Ocular inserts keep medication concentrations within the appropriate range. Using fewer administrations leads to better patient compliance. The page covers the eye's many parts and anatomy, along with an explanatory image.This study aims to offer an update on current understanding in ocular medication delivery. Also, this review focuses on the current usage of ocuserts to treat eye disorders.

Keywords: Ocuserts, Eye, Ocular inserts, Sterile, bioerosion, osmosis, Diffusion

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INTRODUCTION

The eye is a one-of-a-kind organ, both physically and physiologically, having a vast range of components that serve independent physiological roles. The intricacy of the eye poses distinct obstacles for medication delivery techniques. In recent years, ocular drug delivery systems (ODDS) for treating eye illnesses have grown in popularity and feasibility. Improving ocular contact time, enhancing corneal permeability and site specificity are the key points for the optimization of ocular drug delivery.[1]

The ocular organ impervious to foreign substances due to unique anatomy, physiology and biochemistry of the eye, thus presenting a constant challenge to the pharmaceutical formulator to circumvent the protective barriers of the eye without causing permanent tissue damage. Therefore, the target tissue absorbs a very less fraction of drug. As a result, concentrated solutions and frequent dosage are necessary for the instillation to have an appropriate therapeutic impact. [2]

Ocular inserts have been designed to administer drugs using a diffusional method. This solid dose form provides an ophthalmic medication at a very constant pace, reducing adverse effects by eliminating absorption peaks.[3] Ocular inserts are innovative drug delivery methods designed to release drugs at predefined and predictable rates, eliminating the need for frequent medication administration. Ocular inserts are sterile preparations with a thin, multilayered, drug-impregnated, solid or semisolid consistency.They are put into the cul-de-sac or conjuctival sac and are specifically designed for ocular use. Ophthalmic inserts provide several benefits over traditional dosage forms, including extended ocular residency, prolonged release, precise dosing, and lower dose frequency.[4]

In ocular inserts, the films are put directly to the cul-de-sac, boosting ocular bioavailability by extending the duration of contact with the corneal tissue and minimising the frequency of administration.[5]

Ocuserts are flexible, flat, insoluble devices made up of two layers that enclose a reservoir and are used commercially to administer a specific amount of medication. All ocuserts are made up of three parts: a central drug reservoir incorporated into the polymer, a rate regulating membrane that provides the regulated release of the medication from the reservoir, and an outside annular ring designed for simple handling and accurate insertion.[6]

The primary goal of ocusert development is to provide continuous, regulated administration of an ophthalmologically active medication to the eye. [1]

Anatomy and physiology of Eye:

The eye is a globe suspended in the ocular orbit, specialised for seeing with numerous tissues that concentrate, transmit, and detect light. It is a spherical construction with a wall made up of three layers.

1. Outer sclera.
2. Middle choroid layer
3. Inner retina.

1. **Sclera:** The sclera is usually referred to as "the white of the eye." The stiff, opaque tissue acts as the eye's protective outer layer. Six small muscles link to it surrounding the eye, controlling its motions. The optic nerve connects to the sclera at the very rear of the eye. Children's sclera is thinner and more transparent, allowing the underlying tissue to shine through and giving it a blue tint. The sclera yellows with ageing.[5]
2. **Choroid layer:** The choroid is located between the retina and the sclera. It is made up of layers of blood vessels that supply the rear of the eye. The choroid joins the ciliary body in the front of the eye with the margins of the optic nerve in the rear. It is located inside the sclera, includes many blood vessels, and is transformed at the front of the eye into the coloured iris. The biconvex lens is located directly behind the pupil.The chamber behind the lens is filled with vitreous humour, a viscous fluid that occupies 80% of the eyeball. The anterior and posterior chambers are located between the cornea and iris, and the iris and lens, respectively, and are filled with aqueous humour. The retina detects light and is located in the rear of the eye.[5]
3. **Retina:** The retina is the third and inner coat of the eye, consisting of a light-sensitive tissue layer. The retina includes photosensitive components (rods and cones) that convert light into nerve impulses, which are then sent to the brain via the optic nerve. [6]

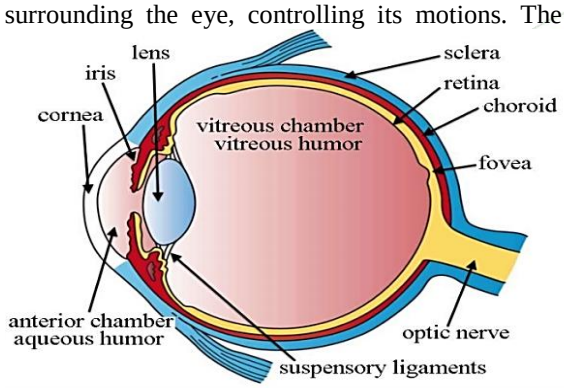

Figure 1: Anatomy and physiology of Eye [7]

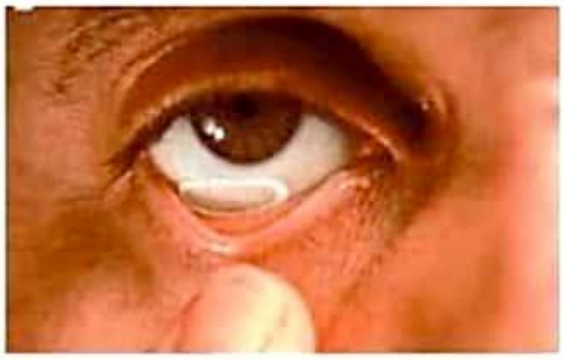

Figure 2: Delivery of Drug via Ocular Insert [8]

History:-

The first solid drug was created in the nineteenth century by impregnating squares of dry filter paper with dry solutions (such as atropine sulphate and pilocarpine hydrochloride). Small pieces were cut and inserted beneath the eyelids. Lamellae, the forerunners of modern soluble inserts, were later developed. They were produced from glycerinated gelatin and contained many ophthalmic medicines. Until the early twentieth century, official compendia included glycerinated gelatin 'lamellae'. Lamellae were utilised, however they were phased out when tougher sterility criteria for ophthalmic medicines were introduced. Ophthalmic inserts are currently receiving more attention.[7]

Benefits of Ocular Inserts: [8, 9, 10].

- Increased ocular contact time, which improves medication absorption.
- Higher ocular permeability compared to normal formulation, resulting in prolonged drug action and higher ocular bioavailability of the medication.
- Administering an appropriate amount in the eye provides better treatment
- Fewer systemic side effects.
- Compared to standard dose forms, less frequent administration is necessary.
- It is feasible to overcome the consequences of repeatedly administering a traditional dose form.
- Enhanced comfort and patient compliance
- Handling is easy.
- Vision and oxygen permeability are not impaired.
- Replicable release kinetics
- Sterile preparation
- Better patient compliance, resulting from a decreased frequency of administration and a lower incidence of ocular and systemic adverse effects.
- Possible to target interior ocular tissues using non-corneal (conjunctival scleral) pathways.
- Increased shelf life compared to aqueous solutions

Disadvantages of Ocular Inserts: [11,12]

- The "solidity" of ocular inserts, or the patient's perception that an unknown substance is in his or her eye, is a serious problem

- The unintentional loss that happens occasionally when sleeping or rubbing one's eyes
- The ocular inserts are difficult to apply (and remove, particularly insoluble types)
- Their movement about the eye, in rare cases, makes easy removal more difficult due to unintended migration of the insert to the upper fornix

Generally, all types of ocuserts have three layers.

- A central drug reservoir is a narrow disc containing a drug combination. The medicine is integrated into a polymer, allowing it to spread from the reservoir.
- A rate-controlling membrane consists of two transparent discs made of ethylene vinyl acetate, a copolymer. This membrane allows for regulated release of medication from the drug reservoir.
- An outer yearly ring for easier handling and accurate insertion.[1]

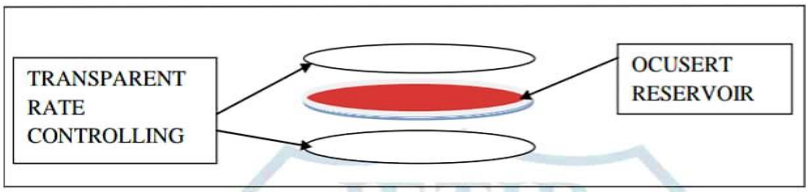

Figure 3: Schematic diagram of Ocusert [3]

Mechanism of Ocusert:

Ocuserts are a flexible, solid, and semisolid device with a drug reservoir and rate-controlling membrane made of different polymers. The ocuserts are put into the upper or lower cul-de-sac of the eye and deliver the medication at a specified rate.[1]

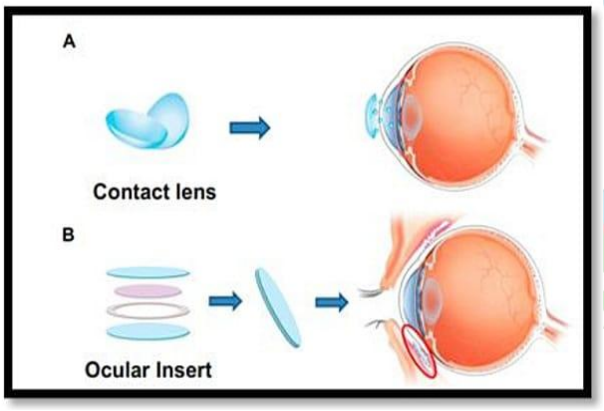

Figure 4: Mechanism of Ocusert [10]

Composition of Tear:

Tear fluid consists of salts, carbohydrates, chemical compounds, 0.7% protein, and lysozyme.

Water: 98.2 percent, Solids: 1.8 percent

Organic elements: Protein (0.67%), Sugar (0.65%), NaCl (0.66%), and NPN (0.05%).

Urea - 0.03%.

Other mineral elements: sodium, potassium, and ammonia - 0.79% [13]

Classification of Ophthalmic Insert:

Ophthalmic inserts are classed according on their solubility behaviour.

1. Insoluble ophthalmic inserts or ocuserts
2. Soluble ophthalmic inserts or ocuserts
3. Bio-erodible ophthalmic inserts or ocuserts

1. Insoluble ophthalmic inserts/ocuserts are divided into three kinds.

a) Diffusional inserts/ocuserts.
b) Osmotic Insert
c) Contact lenses.

a) Diffusional inserts/ocuserts:

The Ocuserts system is a revolutionary drug delivery technology that is based on a porous membrane. Diffusional inserts/ocuserts release drugs using a diffusional release mechanism. The diffusional inserts/ocuserts are made up of a core drug reservoir surrounded in a specifically constructed semipermeable/microporous membrane that allows the medication to diffuse from the reservoir at a precise pace. The lachrymal fluid penetrates the membrane until adequate internal pressure is achieved, which regulates medication release from such a system. The Fick diffusion equation can be used to explain its action.

$$J=DA\ dc/dx.$$

Where J represents the solute flux.

D represents the differential co-efficient for the medication within the polymer membrane.

A equals membrane area.

dc/dx is the drug concentration gradient within the membrane along the direction of drug flow [3]

b) Osmotic Insert: Osmotic inserts are normally composed of a centre section surrounded by a peripheral part and are classified into two types:

Type 1: The centre component is made up of a single reservoir of a drug, with or without an extra osmotic solution, that is spread in a polymer matrix and surrounded by discrete tiny deposits. The second peripheral component of these inserts is a cover film composed of an insoluble semi-permeable polymer. The osmotic pressure on the polymer matrix leads it to rupture, resulting in holes. These

perforations allow the medicine to be released from deposits near the device's surface.

Type 2: The middle section comprises of two distinct themes. The drug and osmotic solutes are separated into two compartments, with the drug reservoir enclosed by an elastic impermeable membrane and the osmotic dissolved reservoir by a semipermeable barrier. The second peripheral component is comparable to that of Type 1. The crack diffuses into the osmotic compartment, causing an osmotic pressure to stretch the elastic membrane and compress the compartment, containing the drug, forcing the active component through the single drug release orifice.[14]

c) Contact Lenses:

Contact lenses are made of covalently bonded hydrophilic or hydrophobic polymers that form a three-dimensional network capable of storing aqueous medication solutions or solid components. Contact lenses are structures designed to correct eyesight. Contact lenses are commonly employed as a possible medication delivery mechanism after being presoaked in drug solutions. The fundamental advantage of this technique is that it increases the probability of accurate eyesight while also releasing drugs.[3] Refojo proposed separating the contact lenses into five classes. There are five types of materials: stiff, semi-rigid, elastomer, softly hydrophilic, and biopolymer. [14]

2. Soluble Ophthalmic Inserts/Ocuserts:

Because these soluble inserts are totally soluble, they do not need to be removed from their intended location, limiting the intervention to insertion alone. They may be loosely classified into two types: natural polymers and synthetic or semi-synthetic polymers.

A. Natural polymers:

The first form of soluble insert is made from natural polymers. The preferred natural polymer for soluble ophthalmic implants is collagen. The therapeutic substance is best absorbed by soaking the insert in a drug-containing solution, then drying and rehydrating before applying to the eye.The amount of drug loaded is determined by the amount of binder used, the concentration of drug solution in which the composite is soaked, and the period of soaking. As the collagen degrades, the medication gradually emerges from the gaps between the collagen molecules.

B. Synthetic and Semi-synthetic Polymers:

The second type of soluble application often relies on semi-synthetic polymers (e.g.,cellulose derivatives) or synthetic polymers such as polyvinyl alcohol. The release rate can be reduced by coating the insert with Eudragit, a polymer typically used for enteric coating.[14]

3. Bio-erodible ophthalmic inserts or ocuserts:

These inserts are made of bio-erodible polymers (for example, cross-linked gelatin derivatives and polyester derivatives), which dissolve due to chemical bond hydrolysis. The ability to modulate the erosion rate of these bio-erodible polymers by synthesis modifications and the addition of anionic or cationic surfactants is a significant benefit. A cross-linked gelatin insert was employed to improve dexamethasone's bioavailability in the rabbit eye. The amounts of dexamethasone in the aqueous humour were found to be four times higher than in a dexamethasone solution. However, erodible systems can have drastically different erosion rates depending on individual patient physiology and lachrimation patterns, and breakdown products and residual solvents employed in polymer manufacture might elicit inflammatory reactions.The solid inserts absorb aqueous tear fluid and eventually dissolve or disintegrate. The medication is progressively leached from the hydrophilic matrix. After medication administration, bio-erodible ocular implants do not need to be removed. Erodible medication inserts are sold as Lacriserts, SODI, and Minidisc. [4]

a) SODI: A soluble ocular drug insert (SODI) is a little oval wafer created by Soviet scientists for cosmonauts who were unable to utilise eye drops in weightless conditions.[6]ABE is a sterile thin oval film composed of acrylamide, N-vinyl pyrrolidone, and ethylacrylate. It is used to treat glaucoma and trachoma. It is put into the inferior cul-de-sac and wets and softens within 10-15 Seconds. After 10-15 minutes, the film becomes a viscous polymer mass, and after 30-60 minutes, it transforms into polymer solutions that supply the medicine for about 24 hours.[15]

b) Lacrisert: Lacriserts are rod-shaped, preservative-free instruments made of hydroxypropyl cellulose that are beneficial for dry eye syndrome. Its dimensions are 3.5 mm long, 12.7 mm wide, and weighs 5 mg. When artificial tears fail to relieve keratitis symptoms, a sacrist can assist. It is delivered into the cul-de-sac cavity, where it pulls moisture from the conjunctiva and cornea to form a hydrophilic coating that balances the tear film, moisturising and lubricating the cornea. It fades after one day. [11]

c) Minidisc: The minidisc is a curved disc with a concave rear and an eyeball-contact-pointed convex front. It has a diameter of 4 to 5 mm and resembles a little contact lens. The minidisc is made of the silicone-based pre-polymer bis 4-methacryl oxyethyl polydimethylsiloxane. Minidiscs can be hydrophilic or hydrophobic to enable for more rapid release of both water-soluble and insoluble medicines. [11]

Mechanism for Drug Release from Ocular Inserts:

The mechanism of controlled drug delivery into the eye is described below:

A. Diffusion.

B. Osmosis

C. Bio-Erosion

A. Diffusion: In this process, the medication is delivered at a constant rate via the membrane. If the insert is made of a solid, non-erodible body with pores and the medicine is disseminated, it is released by diffusion via the pores. Controlled drug release can be maintained by gradually dissolving the solidly distributed drug in the matrix due to inward diffusion of aqueous solutions. True dissolving in a soluble device happens mostly via polymer swelling. In swelling-controlled devices, the active ingredient is disseminated uniformly in a glassy polymer. Glassy

polymers are virtually drug-impermeable, hence no diffusion occurs through the dry matrix. When the insert is inserted in the eye, water from the tear fluid penetrates the matrix, causing swelling, polymer chain relaxation, and drug diffusion. The polymer structure determines the breakdown of the matrix and subsequent swelling. Linear amorphous polymers disintegrate quicker than cross-linked or partly crystalline polymers.[4]

B. Osmosis: Osmosis is determined by the degree to which one solvent's free energy is reduced relative to another. In the osmosis process, the inserts have a transverse impermeable elastic membrane that separates the inside of the insert into compartments I and II. The first compartment is constrained by a semi-permeable membrane and an impermeable elastic membrane, while the second compartment is bounded by an impermeable membrane and serves as a repository for the medicine, which is in liquid or gel form. When the insert is put in the aqueous environment of the eye, water diffuses into compartment I, stretching the elastic membrane to expand the first compartment and contracting the second compartment to force the drug through the drug release aperture. When the insert is put in the aqueous environment of the eye, water diffuses into compartment I, stretching the elastic membrane to expand the first compartment and contracting the second compartment to force the drug through the drug release aperture.[6]

C. Bio-erosion: The functional unit of an insert's body is made up of a matrix of bio-erodible material that disperses the medication. When the insert comes into touch with tear fluid, the medication is released in a regulated and sustained manner by bio-erosion of the matrix. The drug may be disseminated equally throughout the matrix, however it is hypothesised that a more controlled release occurs when the drug is superficially concentrated in the matrix.[6]

Formulation methods for ocular inserts:

Here are several popular approaches for creating ocular implants.

1. **Solvent Casting Method:** This approach involves preparing many batches in varied quantities. The polymer is dissolved in an appropriate solvent. Plasticizer is added to this solution while stirring continuously; a properly weighed amount of medication is added to the aforesaid solution, resulting in a uniform dispersion. When the right mix has been established, the solution is cast into the petri dish using an inverted funnel, allowing for gradual and uniform evaporation at room temperature until the film has dried. The dry films are sliced into the desired sizes and shapes using a cork borer. The prepared ocuserts are kept in airtight containers.[16]

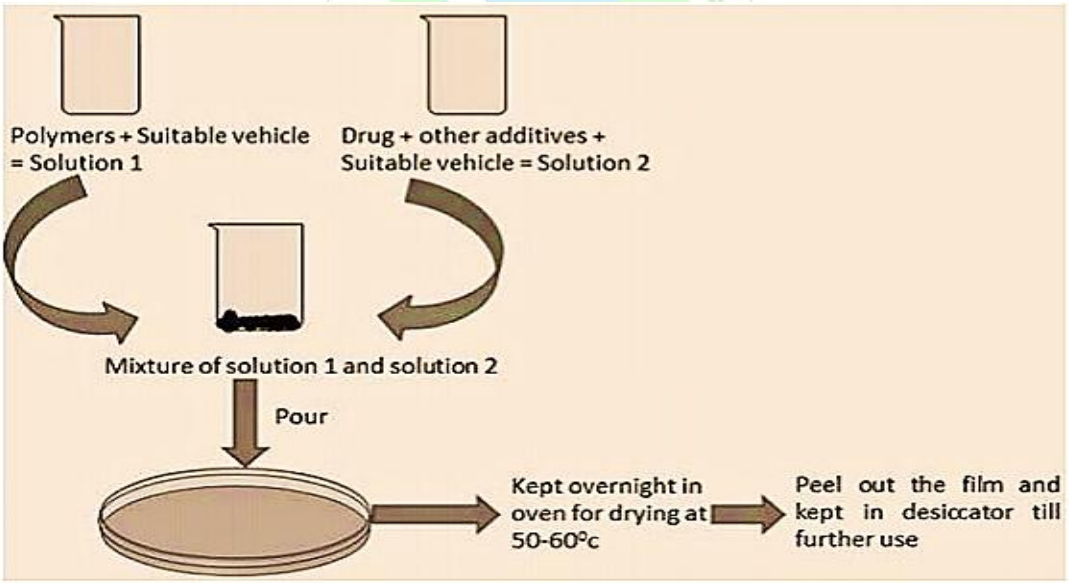

Figure 5: Solvent Casting Method [1]

2. **Glass substrate process:** The polymer is submerged in a 1% (v/v) carboxylic acid solution for about 24 hours to produce a transparent solution. The necessary quantity of medication is then added to the aforementioned solution, and the conjugate is dissolved in the polymer solution with a vortex mixer for 15 minutes. The solution absorbs the plasticizer. A viscous solution was prepared and left to sit for 30 minutes to allow the film to control the rate of growth and remove air bubbles from the solution. The membranes were cast onto flat glass moulds and allowed to cool for two hours. The dry film is pushed to a predetermined shape and size with a water-soluble, non-toxic, non-irritating adhesive, and the matrix is placed between the flow control membranes. They are individually wrapped in aluminium foil and stored in a desiccator.[17]

3. **Hot Melt Extrusion:** This technique weighs and blends the medicine and polymer after passing through a 60# mesh. A plasticizer is then added to the mixture. The mixture is then dumped into the melter tank and drained. Materials were measured precisely, trimmed, wrapped in laminated aluminium foil, heat sealed, and gamma sterilised.

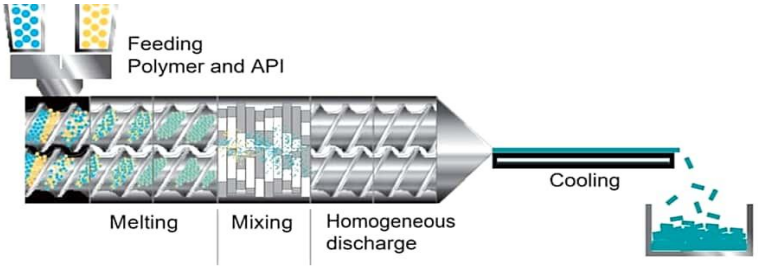

Figure 6: Hot Melt Extrusion process [1]

Evaluation of Ophthalmic Inserts:

1. **Weight variation test:**

   A random sample of inserts from each batch is weighed on an electronic balance.

   The mean insert weight for each formulation is tracked [18]

2. **Eye irritation test:**

   Check for redness, inflammation, or increased tear production to assess the test's potential for causing eye irritation or injury.

   Five rabbits were employed in the formulation test, with the inserts placed in the left eye's cul-de-sac [18]

3. **Sterility study:**

   The inserts were sterilised with gamma radiation prior to the ocular irritation and in vivo drug release tests. No microbiological or fungal development was detected in any of the formulations, indicating that the films had been thoroughly sterilised [19]

4. **Weight Uniformity:**

   Three patches of the same formulation were weighed and sliced at three distinct spots, and the individual weight of each piece was calculated using a digital scale[16]

5. **Thickness Uniformity:**

   Thickness was measured using a Vernier-calliper and a micrometre. Thickness was measured at five distinct places on each implant. A mean value was determined[16]

6. **Surface pH:**

   In this experiment, ocular implants were removed and placed in a petri dish to swell freely at 270°C for 30 minutes in zero point one millilitre of double-distilled water. The enlarged inserts were isolated, and the surface pH was determined [16]

7. **Percentage moisture absorption:**

   The percentage moisture absorption test is used to assess the physical stability and integrity of ocular implants. Ocular implants are weighed and placed in desiccators containing 100 ml of saturated aluminium chloride solution, with 79.5% humidity maintained. After three days, the ocular implants are removed and reweighed. The formula is used to compute the percentage of moisture absorption.

   Percentage moisture absorption = final weight - initial weight/initial weight × 100 [13]

8. **Percentage Moisture Loss:**

   The percentage moisture loss test is performed to ensure the film's integrity under dry conditions. Ocular inserts are weighed and stored in desiccators that contain anhydrous calcium chloride. After three days, the ocular inserts are removed and reweighed; the % moisture loss is calculated using the method.

9. Percentage moisture loss = Initial weight - Final weight\Initial Weight × 100 [13]

10. **In-vivo Drug Release:**

    Gamma radiation was used to sterilise the ocuserts before the drug release trial, which involved two groups of healthy rabbits. Each rabbit had ocular inserts injected in its cul-de-sac. The inserts are removed at regular intervals of 2, 4, 6, 8, 12, and up to 24 hours. The remaining drug content was computed and deducted from the beginning number, yielding the precise amount of medication discharged into the eyes[16]

11. **Accelerated Stability Studies:**

    Accelerated stability studies are used to anticipate the breakdown that may occur over an extended storage term under typical shelf conditions. The formulation films are placed in a separate Petri dish and stored at three different temperatures: 400°C, 500°C, and 600°C, while the duration of breakdown or degradation of the ocular inserts is monitored. When ocuserts demonstrate degeneration, the time in days is recorded [16]

Novel approaches for ocular drug delivery:

1. **Nanoparticles:** Nanoparticles vary in size from 10 to 1000 nanometers. For the administration of opthalmic medications. Nanoparticles are composed of lipids, proteins, and natural or manufactured polymers such as albumin, sodium alginate, chitosan, poly (lactide-co-glycolide) (PLGA), polylactic acid (PLA), and polycaprolactone. Nanoparticles can take the shape of nanocapsules or nanospheres in pharmaceuticals. A nanocapsule's polymer covering protects the drug within. Nanospheres are used to evenly distribute the drug throughout the polymeric matrix. Nanoparticles have recently gained popularity for ocular medication administration, and a few researchers have loaded nanoparticles for distribution to both the anterior and posterior portions of ocular tissue. Chitosan coating is the most extensively investigated nanoparticle for

improving pre-corneal residence.Because chitosan is positively charged, it adheres to the cornea's negatively charged surface. As a result, precorneal residence improves, whereas clearance diminishes. Kanamycin-loaded chitosan nanoparticles demonstrated higher ocular absorption at lower dosage frequencies in rabbit eyes than commercial solutions. Nanoparticles have also been chosen as an alternate method of long-term medicine delivery to ocular tissue in the posterior region. Nanoparticle deposition for posterior segment delivery is governed by their size and surface characteristics. A commercialised sustained drug release in the aqueous humour was obtained by utilising PLA nanospheres colloidal solution containing acyclovir. The concentration of acyclovir is much greater than in the free medicine formulation. [20]

2. **Niosomes:** Niosomes are chemically stable, bilayered Nano vendors composed of nonionic surfactants. It functions as a vendor for both hydrophilic and hydrophobic medicines. Niosomes offer several advantages, including the fact that they are biocompatible, biodegradable, and nonimmunogenic, which increases the contact period between the medication and the cornea, increasing drug bioavailability. Niosomes developed to avoid the restrictions of liposomes by chemically entrapping both hydrophilic and hydrophobic drugs. Discosomes are a kind of niosome that has altered form. Discosomes also serve as suppliers for ophthalmic drugs. This has the advantage of no longer allowing it to enter inside the ideal motion, and its disc shape provides a better fit into the conjunctival cavity. The benefits of niosomes include improved patient compatibility as well as a greater healing impact than traditional methods. [21]

3. **liposomes:** Liposomes are biodegradable and harmless lipid vesicles that include one or more phospholipid bilayers and an aqueous core. The liposome's length ranges from 0.08 to 10.00 micrometres. Liposomes are classified into three types: tiny unilamellar vesicles (10-100 nm), large unilamellar vesicles (100-300 nm), and multilamellar vesicles (composed of several bilayers). Liposomes are ideal for ocular procedures due to their high biocompatibility, movable form, and ability to contain both hydrophilic and hydrophobic medicines. Several investigations have shown that liposomes are equally efficient in both the anterior and posterior phases of ocular shipping. Liposomes can be formed by sonicating phospholipid dispersion, evaporating the opposite part, injecting solvent, and fusing calcium.These formulations are made up of phosphatidylcholine and other ingredients such as ldl cholesterol and lipid linked hydrophilic polymer. Phospholipids consist of phosphatidylcholine, phosphatidic acid, and sphingomyelin. Liposomes can cautiously adhere to the attention floor, increasing house time and bioavailability. [21]

4. **Dendrimers:** A nanosized, highly branching, star-shaped polymeric structure. This system is available in a variety of molecular weights and includes terminal end amine, hydroxyl, or carboxyl functional groups. the terminal functional group used to conjugate the targeted moieties. Dendrimers serve as a carrier mechanism in medication delivery. To distribute a medicine, it is vital to choose the appropriate molecular weight, surface charge, molecule shape, and functional group. The highly branching structure of dendrimers allows for the inclusion of a wide spectrum of drugs, both hydrophilic and hydrophobic.[22]

5. **Use of Viscosity Enhancers:** Viscosity-increasing polymers are recommended additives in ophthalmic preparations because they increase viscosity, hence improving medication penetration into the anterior chamber of the eye. by lowering the clearance rate from the preocular region, resulting in an increase in precorneal residence duration and transcrenial penetration, but with very little effect on bioavailability in humans. Examples of polymers include polyvinyl alcohol (PVA), polyvinylpyrrolidone (PVP), hydroxymethylcellulose, hydroxypropylmethylcellulose (HPMC), and hydroxypropyl cellulose.[22]

6. **Nanospheres/Microspheres-** Drug penetration is determined by the size, charge, architecture, and surface of the carrier nanoparticle systems. The nanospheres' design is made up of a diblock copolymer with a hydrophobic block [polycaprolactone (PCL)] and a hydrophilic component [polyethylene glycol (PEG). The unique shape of nanospheres allows for a longer residence period on the corneal surface, providing the medication with a carrier before fusing with the corneal epithelial membrane, lowering dosage frequency.[23]

7. **Microneedles** - Microneedles are medication delivery devices made of metals or polymers with diameters ranging from 10 to 200 µm. The ultradimensions of these devices enable medication delivery less intrusive and more tailored to the drug's action locations. Jiang and colleagues employed 500- to 750-µm-long coated stainless steel microneedles to administer pilocarpine into the anterior chamber through the intrascleral pathway. The authors showed a 45-fold increase in medication absorption compared to standard eye drops. [24]

8. **Nanosuspensions and nanodispersions** - Nanosuspensions are formed by suspending weakly water-soluble medicines at nanoscale in a suitable dispersion medium. This method is particularly useful for medicinal molecules that generate high-energy crystals that are insoluble in organic (lipophilic) or hydrophilic environments. Polymeric nanoparticle solutions are being developed employing inert polymeric resins, which can be employed as critical drug delivery vehicles, increasing drug release while also improving bioavailability. Carriers with these qualities can be employed as inert carriers for ophthalmic medications since they do not irritate the cornea, iris, or conjunctiva. A polymeric nanoparticle dispersion with flurbiprofen (FLU) as an active component, as well as eudragit RS 1001 and RL 1001 polymers, is one example of such carrier. Morsi et al. (2015) reported on nanodispersions of alginate chitosan generated for prolonged drug administration and better transcorneal permeability. [25]

9. **Penetration enhancers -** Increasing the permeability of the corneal epithelium can improve the cornea's overall commercial autonomy. The normal epithelial lining of the eye is a powerful molecule that moves tissue. One strategy for increasing ocular medication bioavailability is to rapidly improve corneal permeability with suitable chemicals known as invasive enhancers or admission enhancers. These conditions include vision impairment and toxicity. The rate-limiting process is transporting the medication from the cornea to the receptor location. Gait enhancers improve corneal absorption by changing the uniqueness of the corneal epithelium.Cetroid chloride, benzalkonium chloride, ionophore (for example, razaroside), tween 20, parabens, saponins, suspensions 35, 78, and 98 interact with ethylene diamine tetraacetic acid, bile salts, and bile acids (such as sodium). Under different settings, damaging agents such as fusidic acid, azone, saponins, hexamethylene tanamide, and decylmethyl sulfoxide significantly enhance corneal agent absorption (Gadbey RE, 1979). [26]

10. **Prodrug -** Prodrugs improve the permeability of drugs to the cornea by modifying their hydrophilic and lipophilic characteristics. Following intracorneal or corneal infiltration, prodrugs are administered artificially or enzymatically to boost the compounds' effect. As a result, the ideal prodrug would be more lipophilic and have a larger modulus of elasticity, while simultaneously having a significant disadvantage during mobility. Tissue protein structure is visually obvious, and it includes esterase, ketone reductase, and steroid-6-hydroxylase. The prodrug is an additional component of the drug. As a result, appropriate disposal necessitates detailed pharmacokinetic and pharmacological information.Several incidences of susceptible prodrugs have been linked to the antiviral drugs ganciclovir and acyclovir. Ganciclovir, an acyl ester-producing medication, has a very low packing ratio, which significantly boosts the amount of Drug in the Cornea. [26]

CONCLUSION:

Because eye problems present more obstacles than skin disorders, there is a greater need to focus on non-invasive continuous medication delivery for both segments. The primary goal of innovative ocular drug delivery methods developed during the last two decades has been to increase the ocular residence period of medications. Ocuserts should be able to deliver an effective medication concentration to the target location for an extended length of time while minimising systemic exposure.The use of inserts, which are solid items that may be put in the cul-de-sac or on the cornea, is one option for increasing residency duration. Controlled ocular drug delivery systems improve drug efficiency by reducing waste and improving absorption by increasing the medication's contact time with the absorbing surface. They minimise dose frequency, which improves patient compliance. They also lower dosage and drug-related side effects.Finally, the current review effort demonstrates that ocular diseases can be treated using ocuserts.

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