

A Review on Pilocarpine Ousert: A Controlled Ocular Drug Delivery Approach for Glaucoma

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Abstract:

Pilocarpine Ocusert is a controlled-release ocular implant used to treat glaucoma by directly delivering the muscarinic agonist pilocarpine to the eye. By delivering pilocarpine in a continuous release, this novel delivery method lowers intraocular pressure (IOP) and enhances therapeutic results. The benefits of the Ocusert include increased efficacy, decreased systemic adverse effects, and better patient compliance. The Ocusert slows the growth of glaucoma and preserves eyesight by ensuring a steady delivery of medication. The need for patient education and encouragement, retention issues (some patients were unaware when the device was lost), sporadic side effects like a cutting sensation (the Ocusert occasionally doubles over), eye movement, temporary blurring of vision, and miosis, and high cost were some of the drawbacks. All things considered, the Ocusert pilocarpine system has several clear benefits over pilocarpine eyedrops and is a very popular therapeutic approach for some glaucoma cases.

Keyword – Glaucoma, Ocusert ,Pilocarpine, Controlled Release, Ocular insert, Intraocular pressure.

Introduction

With its many diverse structures and distinct physiological roles, the eye is a distinctive organ in both anatomy and physiology. Drug delivery methods face particular difficulties because of the eye's complexity (1). Because of the prolonged medication activity during the night, an equivalent ocular drug dosage prevents systemic adverse effects and provides undisturbed sleep. Because the medication releases from the eyelids over time, it is also risky to give the medication to an irritated eye. Additionally, ocuserts help other healthcare workers save time. Any ophthalmic medication's ability to have the desired therapeutic effect depends on the tissues.

The controlled release type of delivery system known as zero order kinetics involves holding the medicine in a reservoir and releasing it into the tear film at a steady rate to maintain a constant concentration in the corner, which improves compliance (2). It is known that ocular implants can distribute drugs by a diffusion process. A solid dosage form such as this one reduces side effects by minimizing absorption peaks and providing an ophthalmic medication at a fairly consistent rate (3). Ocular inserts are cutting-edge drug delivery systems made to release medications at precise and regulated rates, doing away with the necessity for regular drug administration. Ocular inserts are sterile preparations that are solid or semisolid, thin, multilayered, and drug-impregnated. They are placed in the conjunctival sac or cul-de-sac and are made especially for use in the eyes. Ophthalmic inserts offer a number of advantages over conventional dosage forms, such as reduced dose frequency, precision dosing, delayed release, and

extended ocular residence [4]. The ocuserts are a major breakthrough in eye disease treatment (5)

Anatomy of Eye

The exquisitely detailed and designed human eye serves as a portal to the process known as vision. The eyeball is roughly one inch wide and spherical in shape. It contains numerous structures that cooperate to improve visibility. The human eye is made up of internal structures and layers. which each carry out specific tasks (6).

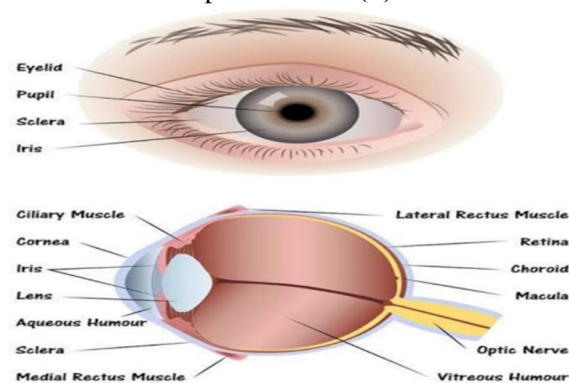


Figure No. 1: Anatomy of the eye

• Sclera

The white, visible portion of the eye is called the sclera. a hard layer that the cornea uses to provide the eye's outermost layer of defense. The sclera is where the muscles that move the eyeball are connected [6].

• Conjunctiva

The sclera and the interior of the eyelids are both parts of the conjunctiva, a thin, transparent layer of tissues that covers the front of the eye. Bacteria and strange

objects cannot get behind the eye due to the conjunctiva [7].

• Cornea

The clear, round portion of the eyeball's front. The light that enters the eye is refracted by it and focused onto the retina by the lens. The cornea is particularly sensitive to discomfort and lacks blood vessels [6].

• Humour in Aqueous

The anterior chamber of the eye, which is situated directly behind the cornea and in front of the lens, is filled with this transparent, watery substance. The ciliary process secretes it at the between 2 and 2.5 $\mu\text{L}/\text{min}$. It provides the lens and cornea, two circulatory tissues, with the majority of their nourishment and oxygen [8].

• Pupil

The round aperture in the middle of the iris that allows light to enter the eye's lens. [5] The light reflex controls pupil size regulation.

• Iris

The colored portion of the eye, the IRIS, regulates how much light enters the eye. The pupil's expansion and contraction are regulated by the iris [7].

• Ciliary Muscles

The ciliary muscles, a ring of striated smooth muscle in the central layer of the eye, regulate the flow of aqueous humor into Schlemm's canal and provide accommodation for viewing things at different distances. The eye can focus on far-off objects when the ciliary muscle is relaxed, and on close-by objects when the ciliary muscle is tight [8].

• Lens

A clear layer that is surrounded by ciliary muscles and located behind the pupil. It aids in refracting incoming light and focusing it onto the retina and is housed in a thin, transparent capsule [8].

• Humorous Vitreous

Another name for it is the vitreous body. Between the retina and lens is a transparent, jelly-like material [8].

• Retina

It is the layer lining the inside of the eye that is sensitive to light. It is made up of rod- and cone-shaped cells that are sensitive to light. Cones are vital for obtaining a clear, precise image and for differentiating colors, whereas rods are required for seeing in low light. When the retina detects light, it generates impulses that travel to the brain via the optic nerve [7].

• Macula

The macula is the center of the retina. Photoreceptor cells, which transform light into nerve signals, are highly concentrated in the macula [8].

• Fovea

Our best eyesight is found in the fovea, a central region of the macula. The area of the image that is focused on the fovea is the one that the brain registers the most precisely when the eye is focused on an item [8].

• Choroid

The primary role of the thin, blood-rich membrane that separates the retina from the sclera is to nourish the retina's photoreceptor cells. It has a dark brown hue

• Optical disc

A pigment that avoids impaired vision by absorbing excess light [7].

part of the optic nerve that is visible and is located on the retina. The optic disc marks the beginning of the optic nerve, which is where signals from rod and cone cells travel to the brain's optic center via nerve fibers. Another name for it is blind spot [8].

• Optic nerve

It is in charge of sending nerve impulses from the eye to the brain [8].

Controlled Release of Pilocarpine through Ocusert Technology

• Ocusert is a polymer-membrane ocular insert (device) used to treat glaucoma or ocular hypertension. It delivers pilocarpine gradually over a period of time, usually seven days (9).

• A 1975 study found that when 29 patients with open-angle glaucoma were put in the cul-de-sac once a week, Ocusert (both release rates) effectively reduced their intraocular pressure (IOP). There were little adverse effects (10).

• In long-term trials with 22 patients over up to one year, the insert was generally well tolerated, with acceptable retention (device staying in place), and no major side effects. It compared favorably with eye-drops (11).

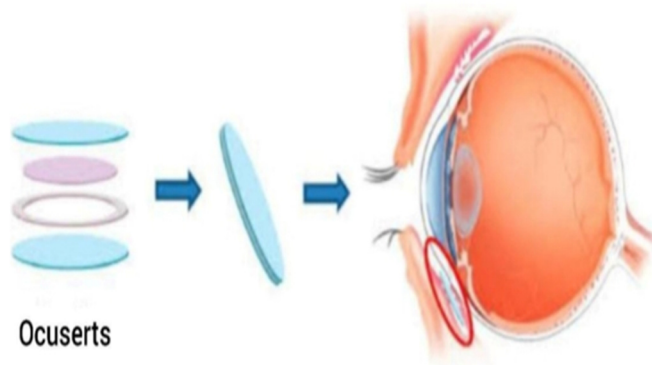


Figure No. 2: Ocuserts
Mechanism of Ocusert

• The rate of release was correlated with the degree of IOP reduction; a higher release (40 $\mu\text{g}/\text{hr}$) resulted in a greater lowering of pressure (12). A drug reservoir and a rate-controlling membrane made of different polymers make up the flat, flexible, solid, and semisolid Ocuserts device. The ocuserts, which release the medication at a preset rate

constant, are placed in the eye's upper or lower cul-de-sac (5).

All types of ocuserts typically have three layers -

- A thin disk of drug complex serves as a core drug reservoir. Here, the medication diffuses from the reservoir thanks to its incorporation into a polymer.
- A outer yearly ring facilitates simple handling and correct insertion;
- A rate-controlling membrane consists of two transparent discs of microporous membrane, usually made of ethylene vinyl acetate, a copolymer that permits the controlled release of medication from drug reservoirs (13).

•By allowing pharmaceuticals to diffuse from a reservoir through a rate-controlling membrane over a predetermined lifespan until the drug reservoir is empty, the Ocuserts system achieves zero order release. The technology used in this is an insoluble delicate sandwich technology. Tear fluid can enter the drug reservoir compartment and dissolve the drug from the complex because the reservoir is surrounded by microporous membranes that contain the drug complex. Patients can easily visualize the insert since it is surrounded by a retention ring made of the same material that has been treated with titanium dioxide (13).

The following mechanisms underpin ocuserts' controlled drug

Release -

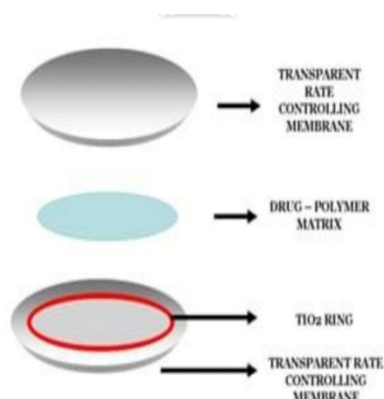


Figure No. 3: Schematic diagram of ocuserts

1. Diffusion
2. Osmosis
3. The process of bio-erosion

1. Diffusion

The medicine is continuously delivered into the tear fluid through the membrane at a regulated pace in the diffusion mechanism. The medicine is released through the pores by diffusion if the insert is made of a solid, non-erodible body with pores and a distributed drug (14).

2. Osmosis

A transverse impermeable elastic membrane in the osmosis mechanism separates the insert's interior into a first compartment and a second compartment. The first compartment is surrounded by an impermeable elastic membrane and a semi-permeable membrane, while the second compartment is surrounded by an impermeable and elastic membrane.

The insert's impermeable wall has a medication release hole (14).

3. Bio – Erosion

The medicine is distributed within a matrix of biodegradable material that makes up the insert in the bio-erosion mechanism. When the insert comes into touch with tear fluid, the matrix bio-erodes, causing a controlled, prolonged release of the medication. Although the drug may be evenly distributed throughout the matrix, it is thought that a more controlled release occurs when the drug is only slightly concentrated in the matrix (14).

Advantages of Ocusert (9)

1. Constant release, consistent medication levels, and fewer IOP swings
2. Convenience is increased by administering less frequently (monthly as opposed to many times daily).
3. less miosis and less impact on accommodation than frequent high concentration dips (rate dependent).
4. Better compliance, perhaps.

Disadvantages of ocusert

1. Problems with device retention: occasionally, patients misplaced the device or were not informed when it stopped working.(9).
2. Potential discomfort could be movement, insert sensation, momentary blurring, or soreness (9).
3. Cost and complexity are increased; patients must be trained (9).
4. Rarely, there is a chance of abrupt leakage that could cause toxicity and systemic absorption (10).

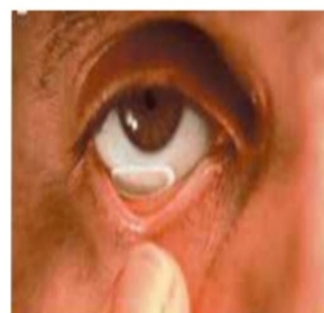


Figure No. 4: Placement of ocuserts into eye

2. Fabrication & Formulation Components

The original Ocusert was a polymer-membrane device that was inserted once a week into the lower conjunctival sac. It consisted of a pilocarpine reservoir encircled by a rate-controlling polymer membrane (16).

Redesigned Gum-Based Inserts (Examples of Pilocarpine Nitrate)

- Using modified karaya gum (MKG) as a release-retarding polymer, either by itself or in conjunction with sodium alginate (SA) by solvent-casting and cross-linking techniques, researchers have created ocular inserts (17).
- MKG (400–600 mg), glycerol plasticizer (~0.066–1 mL), and SA (0.5 mg) were different in six formulations (F1–F6). Formulation F4 (600 mg MKG + 0.5 mg SA) had the most sustained release (~69% in 12 hours), fitting a non-Fickian (anomalous) diffusion model with 0.672 and $R^2 \approx 0.9975$. Drug release over 12 hours varied from ~69.2% to ~90.5% (17).

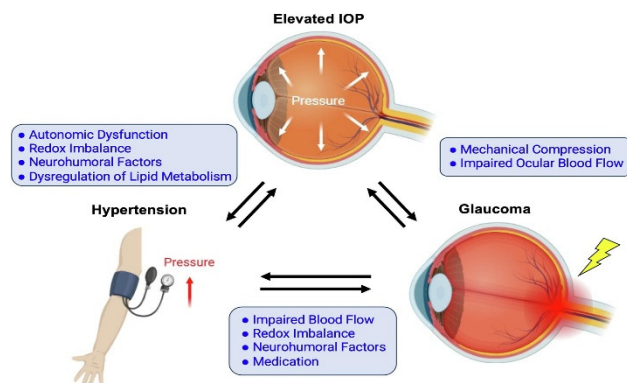
3. Limitations

- Some patients had temporary impaired vision, device loss, discomfort (such as double-over folding), and retention risk (9).
- Infrequent reports of systemic toxicity, such as in a pediatric case where nausea and dizziness resulted from a pilocarpine reservoir leaking during swimming (15)

4. Formulation

Section	Details
Drug Form	Pilocarpine hydrochloride (or nitrate in atoms gum inserted) is the drug form.
Release rate for about seven days	~20 µg/h (Pilo-20) or ~40 µg/h (Pilo-40).
Polymer system Traditional	Polymer – membrane device ; substitute: solvent – cast MKG and SA cross -linked film.
Physical parameters	Some designs have occuserts that are ~0.2–0.3 mm thick, pH ~6.6–6.8, and ~5 mm in diameter. (17).
Release mechanism	Diffusion – controlled (Korsmeyer – Pappas): membrane system zero – order.
Clinical performance	Mechanism of release Diffusion –controlled (Korsmeyer – Peppas):
Safety considerations	Rare systemic toxicity in the event of a reservoir rupture ; minimal eye irritation ; retention training necessary.

Intraocular Pressure in Glaucoma



- One of the main risk factors for glaucoma development and progression is intraocular pressure (IOP) (18). Furthermore, despite all treatments aiming at lowering IOP, IOP remains the single modifiable factor in the prevention and treatment of glaucomatous optic neuropathy (19). Even if there are more surgical treatments available, topical medicines are still the most often prescribed first line of treatment by doctors (20). Due of its benefits, prostaglandin analogs (PGAs), which primarily reduce IOP by increasing uveoscleral outflow, are now the most commonly used medication class for first-line therapy (21).
- They consist of once-daily dosage, strong efficacy, and outstanding tolerability. Treatments for glaucoma that lower intraocular pressure (IOP) not just during the day or office hours but also at night are becoming more and more important in order to provide a 24-hour period (22). Even with managed IOP during the day, glaucoma patients with progressing illness may experience a substantial increase in IOP at night (23). Even with managed IOP during the day, glaucoma patients with progressing illness may experience a substantial increase in IOP at night (24).
- Alpha agonists and beta-blockers have little effect at night, however PGAs and carbonic anhydrase inhibitors (CAIs) are medications that lower IOP during the day and at night (25). Pilocarpine has been used as a topical glaucoma treatment for a long time; it was first used in the late 1800s and received FDA approval in 1974. The cholinergic agent works as a direct muscarinic agonist of the ciliary muscles, resulting in contraction and tension on the scleral spur that increases trabecular outflow facility with a 15%–25% reduction intraocular region (26).

1. Core composition (reservoir ocusert, in the style of Ocusert)

- Pilocarpine HCl is the drug (reservoir); the drug load is formed into a hydrophilic polymer reservoir, which is often an alginate or gel based on alginate (26).
- Sodium alginate or another hydrophilic polymer is used as a reservoir polymer (matrix) to retain the

pilocarpine; occasionally, pilocarpine alginate is specifically specified (27).

- Rate-controlling membranes (both faces): To regulate diffusion, thin, semi-permeable sheets of ethylene-vinyl acetate (EVA) are positioned above and below the drug reservoir (26).

- The EVA ring that encloses and seals the sandwich is the peripheral holding ring. It is frequently treated with TiO₂ for opacity/visibility and mechanical strength (28)

- When a larger release rate is required, additional plasticizers or flux enhancers can be added, such as di(2-ethylhexyl)phthalate (DEHP), which is utilized in Pilo-40 designs (28).

2. Normal specifications and quantities (published/commercial Pilo devices)

- Pilo-20: the traditional Ocusert Pilo-20, which is intended to deliver 20 µg each hour for seven days. The typical dimensions of the gadget, as mentioned in the literature, are around 13.4 mm by 5.7 mm and 0.3 mm in thickness. Some regulatory/product listings have a pilocarpine content of around 5 mg per insert (29).

- The reservoir formulation is similar to Pilo-40, which is intended to release 40 µg/hour for seven days. However, it incorporates a thinner rate-control membrane and a flux enhancer, such as the

approximately 90 mg DEHP mentioned in previous descriptions, to boost flux (29).

3. Overview of the high-level preparatory procedure (non-actionable)

1. Create a homogeneous drug-loaded gel or film or compressed reservoir by combining pilocarpine HCl with a hydrophilic matrix polymer, such as sodium alginate (formulation variables: polymer type/amount, plasticizer) (30).

2. Create EVA membranes: To create rate-controlling membranes, create thin EVA films with a predetermined thickness using solvent casting or hot-melt extrusion/film forming (30).

3. Put the sandwich together by sandwiching the drug reservoir between two EVA membranes, enclosing it, and sealing it with an EVA retaining ring (you can add TiO₂ to the ring to make it visible).

Solvent-casting on glass substrates, molds, and hot-melted extrusion variants for continuous manufacturing are among the assembly techniques mentioned (30).

4. Sterilization & QC: To ensure the intended zero-order/steady release profile, final devices must undergo suitable sterilization and comprehensive in-vitro release testing. Release testing demonstrating consistent delivery (e.g., 20 µg/h) is documented in regulatory and product documentation (29).

4. Example

Component	Typical role	Typical example/ notes
Pilocarpine HCL	Reservoir matrix to Hold drug	~5 mg per insert (product listings), With a 20 or 40 µg/h targeted Release.
Sodium alginate	Reservoir matrix	creates a reservoir of pilocarpine-alginate (30).
EVA Film rate of release	Rate controlling Membrane	Thickness adjusted to the desired rate of release Membrane (26).
EVA Retaining rate of release (TiO ₂)	Mechanical support	Thickness adjusted to the desired rate (28)
Plasticizer / flux Enhancer	Adjusted permeability	Keeps the encircling device in the c conductive sac (28).

Method of Preparation of Pilocarpine Ocular Insert (Ocusert)

A controlled-release ocular medication delivery system called Pilocarpine Ocusert is used to treat glaucoma. It is intended to distribute pilocarpine steadily over a long period of time, often seven days.

1. Ocusert System Components (31)

- Medication: hydrochloride or nitrate of pilocarpine.
- Ethylene-vinyl acetate copolymer (EVA) is the rate-controlling membrane.

Pilocarpine distributed in a polymeric matrix, such as hydroxypropyl cellulose or PVA, serves as the drug reservoir.

- To stop drug loss from the rear surface, the backing membrane (supporting layer) should be made of poly(ethylene terephthalate) (PET) or EVA without any medication.

2. Preparation Method

a) The widely used solvent casting technique

Several batches are made using varying proportions in this procedure. A appropriate solvent is used to dissolve the polymer. A precisely weighed quantity of medication is added to the aforesaid solution, plasticizer is added, and after constant stirring, a uniform dispersion is achieved. To enable gradual and consistent evaporation at room temperature until the film dries, the solution is poured into the petridish using an inverted funnel once the right blend has been created. A cork borer is used to cut the dried films into the appropriate size and shape. After preparation, the ocuserts are kept in an airtight container (32).

1. Supplies and justification (what to use and why)

- Polymer: Ethylene-vinyl acetate copolymer (EVA) is frequently utilized in pilocarpine Ocusert designs as the translucent, lipophilic rate-controlling membrane. Permeability is controlled by the vinyl-acetate content and film thickness of EVA (33).
- Solvent(s): EVA is frequently dissolved in dichloromethane (DCM) or chloroform for solution casting. (Take the proper safety measures when handling solvents) (34)
- Optional plasticizer/modifiers: PEG-400, triethyl citrate, or tiny amounts of plasticizer can change permeability and flexibility if necessary (plastic substance)

2. The solvent-casting method: a detailed (useful recipe)

Materials (for instance, quantities)

- 5 g of commercial-grade EVA copolymer
- 100 mL of anhydrous dichloromethane (DCM) → yields a 5% w/v solution (alter concentration to change film thickness)
- A vacuum oven or desiccator, a magnetic stirrer, a spatula, a thickness gauge or micrometer, and a glass petri dish (diameter of around 90 mm) or flat glass plate

Procedure –

1. Dissolve EVA: Put 100 mL DCM in a dry beaker in a fume hood, then add 5 g EVA (5% w/v). Depending on the grade of the polymer, agitate with a magnetic stirrer at room temperature (or slightly warm, about 30 to 35 °C) until a clear, uniform solution forms; this may take several hours. To get rid of bubbles, temporarily degas (35).

2. (Optional) Add plasticizer: Add PEG-400 at 10–30% w/w of the polymer (i.e., 0.5–1.5 g for 5 g EVA) and mix until uniform if a softer film or greater permeability is needed (36).

3. Cast the film: Fill the middle of a flat glass plate or Teflon-coated petri dish with a predetermined volume of polymer solution. For instance, a thin film is usually produced by pouring 20–30 mL into a 90 mm dish; adjust the thickness by varying the volume and polymer percentage. If necessary, spread lightly to create a consistent coating (37).

4. Slowly evaporate the solvent: Let the solvent evaporate in a fume hood at room temperature or a little higher until the film is tack-free, which could take up to 24 hours, depending on the circumstances. Steer clear of quick evaporation to avoid holes or flaws (38).

5. Post-drying: To get rid of any remaining solvent, place the film to a vacuum oven or desiccator and dry it under low pressure (for example, for two to twenty-four hours). Ensure complete solvent removal (important for ocular safety) (38).

6. Cut / punch membranes: Peel film off substrate and cut/punch discs or elliptical pieces to match ocusert geometry. One of the main factors influencing release rate is thickness, so measure and record it in micrometers (39).

7. Optional annealing/conditioning: Film handling can be enhanced by mild annealing (for example, a brief period at 40 to 50 °C). Verify that annealing doesn't unintentionally alter permeability (39).

8. Assemble the ocusert by sandwiching the drug reservoir (a hydrogel disc or pilocarpine-alginate pellet) between two EVA membranes and sealing or encircling it with an EVA retention ring in accordance with the reservoir ocusert design. (Classic designs use an annular ring and two EVA disks.) (39).

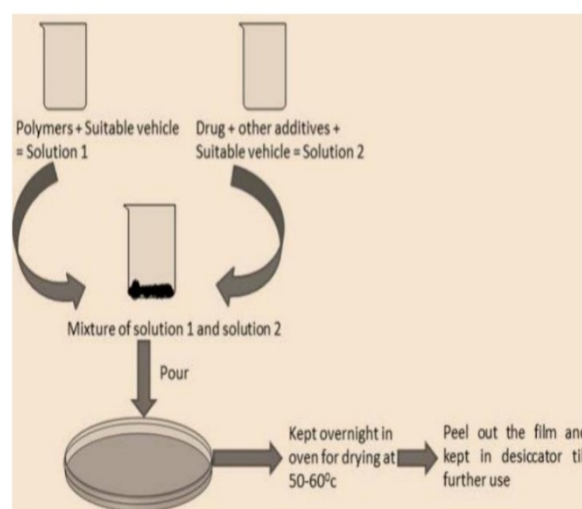


Figure No. 5: Solvent casting method

Adjusting the rate of release (39)

- Reduced flux (slower release) results from thicker membranes.
- To alter permeability, use EVA with varying vinyl acetate (VA) contents or blend polymers.
- Controlled microporosity or plasticizer → accelerates release.
- Observed flow is also significantly impacted by reservoir drug loading and formulation (such as pilocarpine alginate hydrogel).

In-vitro testing and characterization (minimum suggested)

1. Micrometer (report mean $\pm$ SD) for thickness and homogeneity. One of the main parameters for simulating diffusion is membrane thickness (39).
2. Mechanical characteristics: elongation and tensile strength if handling and flexibility are crucial (35).
3. Residual solvent assay: GC analysis to verify that DCM/chloroform is within permissible levels (essential for eye devices) (38).
4. Release testing in vitro: Make use of a USP apparatus or flow-through cell designed for ophthalmic inserts (simulated tear fluid, 34–35 °C). Calculate the cumulative amount of pilocarpine released over time and fit it to diffusion or zero-order models. Near zero-order was the goal of the classic Ocusert (Pilo-20: ~20 μ g/h, Pilo-40: ~40 μ g/h) (38).
5. Compatibility: If the medication is integrated into the membrane, FTIR or DSC can be used to verify the polymer-drug compatibility (38)

Safety, legal, and pragmatic warnings

- Because solvents like DCM and chloroform are hazardous and may cause cancer, complete all procedures in a fume hood, use personal protective equipment (PPE), and make sure that any leftover solvent is tested and removed (38).
- Sterility: The finished eye devices need to be sterile; select a sterilizing technique that works with the EVA or reservoir (check for drug stability) (38).
- Biocompatibility and stability: confirm pilocarpine stability, ocular irritation, and sterility under the conditions of planned use and storage. Before going on sale, the original Ocusert underwent a rigorous clinical testing process (38).

Ocuserts Evaluation Test

1. Surface pH
2. Uniformity of thickness
3. Uniformity Test
4. Swelling index
5. Folding endurance test
6. Drug content uniformity

7. In-vitro drug release study /In-vitro diffusion study
8. Percentage moisture absorption
9. Accelerated stability studies
10. Sterility Testing

1. Surface pH

To measure the surface pH, SURFACE pH ocuserts are placed in a closed petridish with 1 ml of distilled water for 30 minutes at room temperature. The swollen device is then taken out and put under a digital pH meter (41).

2. Uniformity of thickness

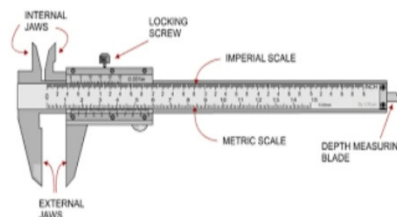


Figure No. 8: Vernier calliper apparatus

A Vernier caliper was used to measure the ocuserts' thickness at five different locations on each device. Five randomly chosen ocuserts are examined for thickness for each recipe.

3. Uniformity Test

Five ocuserts were removed from each batch and weighed separately on a digital scale. The ocuserts' average weight was recorded (43).

4. Swelling Index

After a little bit of film has been cut and weighed, it is soaked for an hour in tear fluid with a pH of 7.4. The film is reweighed an hour later. (44). The formula for calculating the swelling index is: swelling index = beginning weight / final weight 100.

5. Folding Endurance Test

The film was folded repeatedly in the same spot until it broke or showed the first indication of breaking in order to measure folding endurance. The number of folds in a film indicates how long it can fold before breaking. The film's overall folding endurance is measured (41).

6. Drug Content Uniformity

Each ocusert was put in a glass vial with 10 milliliters of artificial tear fluid to test the drug's homogeneity. A magnetic stirrer was subsequently used to dissolve the ocuserts, and the resulting solution was filtered. A UV-visible spectrophotometer was used to measure absorbance after 1 milliliter of the filtrate was removed and diluted with 10 milliliters of distilled water (41).

7. In – vitro drug release study / In vitro diffusion study

A Franz diffusion cell was used to conduct an in vitro diffusion or drug release investigation of ocuserts. It is the tool used to investigate a drug's permeability. It is divided into two sections: the donor section, where ocuserts or other dosage forms are inserted, and the receptor section, which is filled with 7.4 tear fluid to trigger the tear fluid in the eye. A membrane, which might be an egg membrane or a permeable dialysis membrane, divides the two compartments. The instrument is turned on, and the temperature and RPM are changed. Tear fluid is put in the receptor compartment and ocuserts in the donor compartment. After a predetermined amount of time (up to six hours) and after creating an appropriate dilution, 1 milliliter of the sample is removed. Using a UV spectrophotometer, the sample is examined (44).

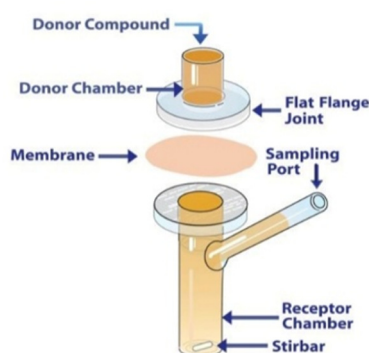


Figure No. 9: Franz diffusion cell

8. Percentage Moisture Absorbance

This is carried out to check the physical stability and integrity at wet condition. The prepared ocuserts were accurately weighed and placed in desiccators containing 100ml of saturated solution of Aluminium chloride and it was kept for 3 days. The ocuserts are taken out and reweighed after 3 days (42).

The percentage of moisture absorbed by the ocuserts was calculated using the following formula:

Percentage moisture absorption = $\frac{\text{Final weight} - \text{initial weight}}{\text{initial weight}} \times 100$

9. Accelerated Stability Study

To make sure that the drug products remain suitable for use until the end of their expiration date, stability studies are conducted in accordance with ICH guidelines. Ocuserts are wrapped in aluminum foil and kept in a glass bottle at 40 degrees Celsius and 75% relative humidity (RH) in the stability chamber. Samples are tested for drug content after 0, 7, 15, 21, and 30 days, respectively, and are assessed for drug concentration, color, folding endurance, etc (41).

10. Sterility Testing

The direct inoculation approach was used to test the sterilized ocuserts for sterility.

- *Culture media:* Soy bean digest casein medium and alternative thioglycolate medium were utilized as culture media for fungus and bacteria, respectively. The media were prepared in accordance with IP 2014, placed in a 20 ml boiling test tube, securely sealed with cotton, and autoclaved for 20 minutes at 121°C and 15 lb/inch gauge pressure to sterilize them.

- *Inoculation and incubation:* The formulation was aseptically added to the test tube with the appropriate media, and a positive and negative control were made for each medium at the same time. For a minimum of 14 days, the bacterial and fungal inoculation media were incubated at 300–350°C and 200–250°C, respectively, in an incubator (41).

List of users for various over-the-counter medications

In 1973, Alza Corporation in the United States introduced pilocarpine ocuserts to the market. It was the first pilocarpine administration system that was comparatively successful in treating ocular hypertension. A pilocarpine-alginate reservoir is encased in thin ethylene-vinyl acetate sheets to form pilocarpine ocuserts. Pilocarpine can be administered by the devices at a rate of 20 µg or 40 µg per hour. For seven days, it continually and steadily releases pilocarpine (14)



Figure No. 10: Pilocarpine ocuserts (Pilo -20 & Pilo- 40)

Conclusion

There is a need to concentrate more on non-invasive continuous drug release for eye problems in both categories because the hurdles are greater for the eyes than the skin (45). Extending the medications' ocular residence period has been the primary goal of innovative ocular drug delivery methods developed over the past 20 years [7]. Ocuserts should be able to reduce systemic exposure while maintaining a sustained, effective medication concentration at the intended site. Such systems produce output that makes them user-friendly

and comfortable. Ocuserts can be evaluated using a variety of factors and are made using a variety of methods (45). Ocuserts are innovative methods that adhere to ethical standards in the era of ocular medicine administration. Although ocuserts have several benefits for treating eye-related issues, only a small number of them are commercially accepted [7]. Future research is underway to determine the therapeutic efficacy of these systems in humans using pharmacokinetic and pharmacodynamics; this formulation is seen as promising. Other medications that are sold as ocuserts include Ofloxacin, Norfloxacin, Moxifloxacin, Acyclovir, Timolol, and Aceclofenac. However, these are not well-liked. Many studies on drug delivery using ocuserts have been carried out recently (14).

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