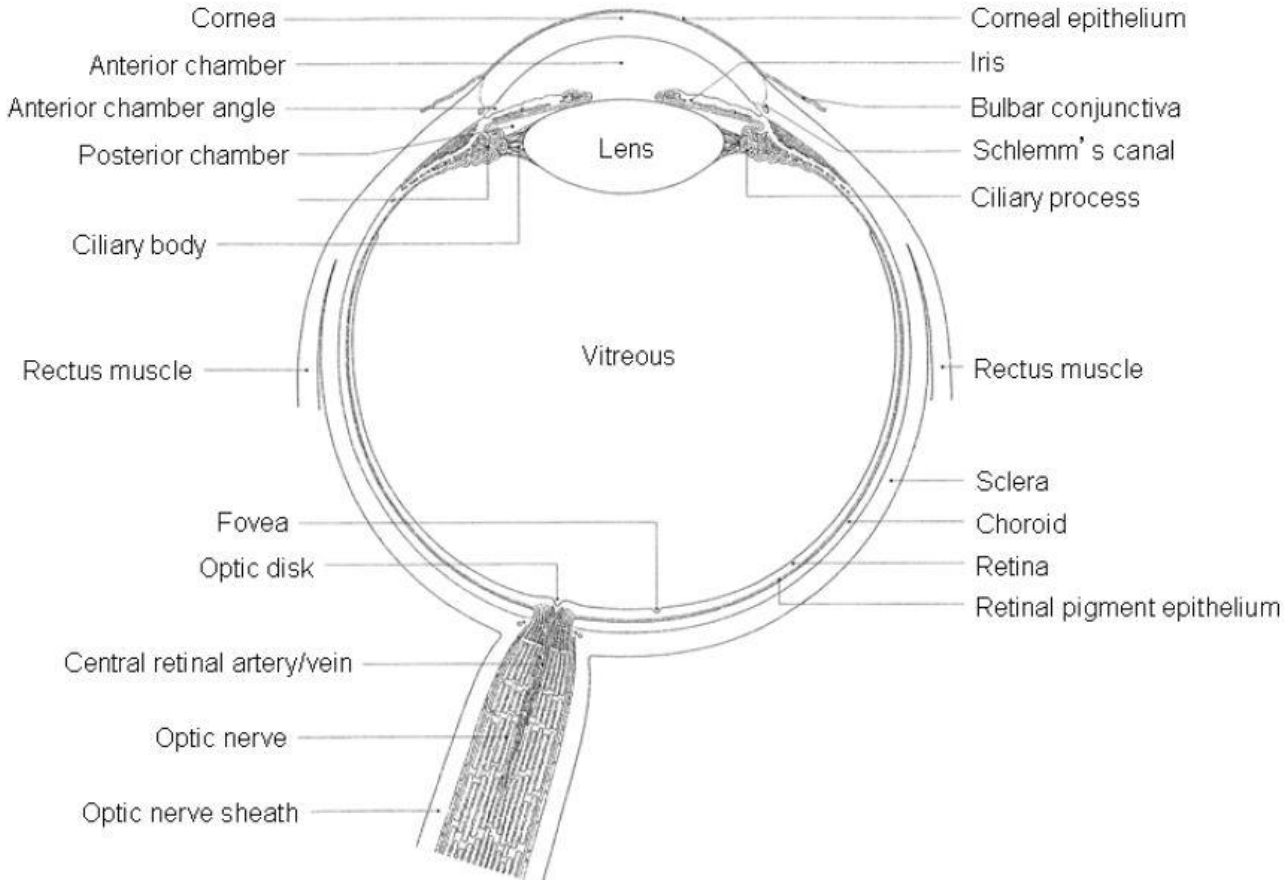
SYSTEMS FOR CONTROLLED DRUG DELIVERY AND DELIVERY MECHANISMS

13. WEEK

OCULAR CONTROLLED RELEASE SYSTEMS

The eye is a complex organ with an unique anatomy and physiology. The structure of eye can be divided into two main parts:

- Anterior segment, and
- Posterior segment.



- Anterior segment of the eye occupies approximately one-third while the remaining portion is occupied by the posterior segment. Tissues such as cornea, conjunctiva, aqueous humor, iris, ciliary body and lens make up the anterior portion.
- Back of the eye or posterior segment of the eye include sclera, choroid, retinal pigment epithelium, neural retina, optic nerve and vitreous humor.
- The anterior and posterior segment of eye is affected by various vision threatening diseases. Diseases affecting anterior segment include, but not limited to glaucoma, allergic conjunctivitis, anterior uveitis and cataract.

- For the treatment of the anterior segment of the eye (cornea, conjunctiva, sclera, anterior uvea), usually topical ocular eye-drops are used.
    - An eye-drop, irrespective of the instilled volume, often eliminates rapidly within five to six minutes after administration, and only a small amount (1–3%) of an eye-drop actually reaches the intraocular tissue.
    - Thus, it is difficult to provide and maintain an adequate concentration of drug in the precorneal area.
    - More than 75% of applied ophthalmic solution is lost via nasolachrymal drainage and absorbed systemically via conjunctiva, hence ocular drug availability is very low.

- To increase ocular bioavailability and prolong the retention time on the ocular surface, numerous ophthalmic dosage forms such as viscous solutions, suspensions, emulsions, ointments, aqueous gels, and polymeric inserts, have been investigated for topical application to the eye.
- In general, topical applied drugs do not reach the posterior segment of the eye (retina, vitreous, choroid), therefore, systemic administration, periocular or intraocular injections of drugs are normally applied in clinical therapeutics.

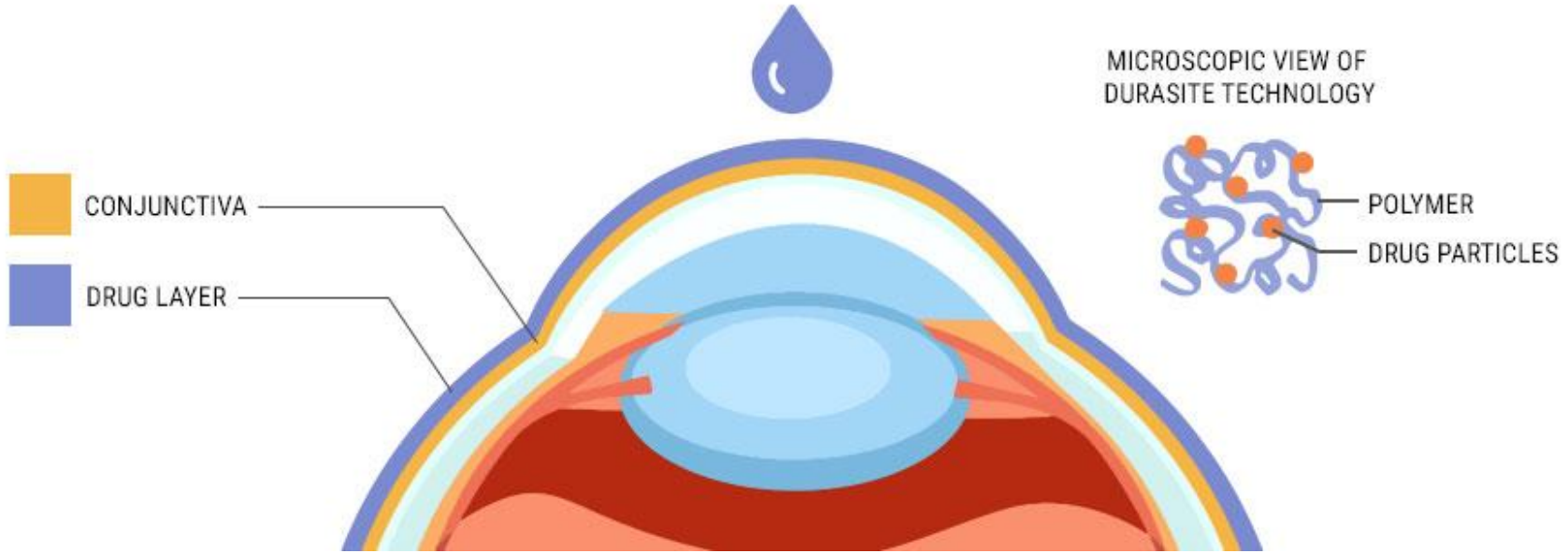
- However, the unique anatomy and physiology of the eye and its protective barriers prevent the administrated drugs from penetrating into the target tissues. Currently there is also rapidly growing interest in drug delivery systems to the posterior segment of the eye. This trend is toward a polymeric depot system implanted or injected directly into the vitreous, to obtain long-term, sustained release of drugs.

Drug Delivery Systems to Anterior Segment of Eye

❖ Eye Drops:

To prolong the retention time of topically applied drugs, anterior drug delivery systems for eye-drops utilizing interaction between drug carrier (excipients) and physiological environment of cornea and/or subconjunctiva are being developed.

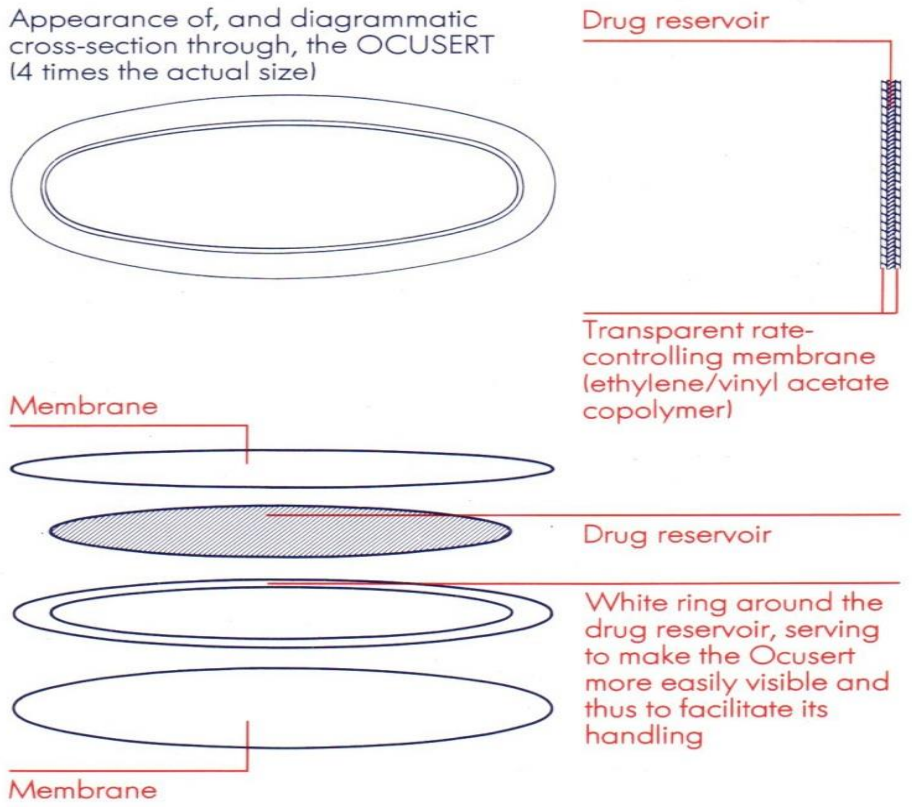
- **Durasite® DDS** (InSite Vision Inc., Alameda, CA, U.S.) is based on a polycarbophil aqueous solution. Polycarbophil is polyacrylic acid cross-linked with divinyl glycol, and forms hydrogen-bonding with the mucus, and corneal and conjunctival epitheliums, which are all negatively charged, to extend the effects of drug to several hours.



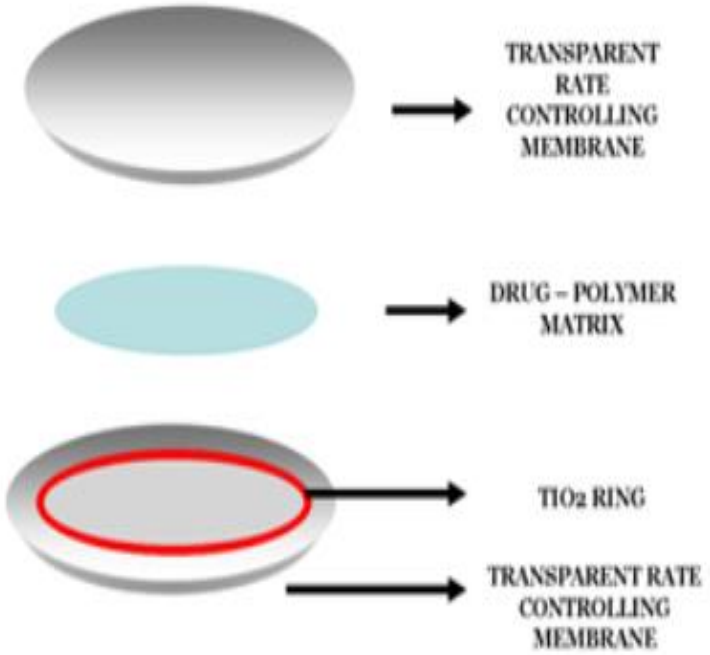
❖ Cul-de sac Inserts:

- **Ocusert®** was the first controlled-release polymer system to be used clinically. It was developed by ALZA Corporation. It was designed to improve therapy for glaucoma, one of the world's leading causes of blindness. The conventional treatment for this disease was for the patient to use eyedrops containing pilocarpine (which reduces intraocular pressure) four times a day.

- These eyedrops were often painful and patient compliance was sometimes poor. The Ocusert ® was designed to deliver pilocarpine continuously over a one-week period. The implant was placed in the lower eyelid's conjunctival cul-de-sac, where it floated in the tear film.



- The Ocusert ® is a reservoir system which utilizes a membrane composed of ethylenevinyl acetate copolymer as a rate-limiting barrier.



- **Lacrisert®** was the second ocular controlled-release system. It was recently introduced for use as artificial tears. The system is a hydroxypropylmethyl cellulose rod which is inserted with a special device beneath the tarsus of the lower eyelid.

- The rod slowly dissolves over a one day period, providing continuous lubrication and tear film stability to the eye. This system has received approval by the Food and Drug Administration and was introduced clinically in 1981.

Drug delıvery systems to POsterıor segment of eye

- Intravitreal Implants:
  - **Durasert™ Technology System** (pSivida Corp., Watertown MA, U.S.) uses a drug core with one or more surrounding polymer layers, and delivers drugs for predetermined periods of time ranging from days to years. The drug release is controlled by permeability of the polymer layers.

- Using the Durasert™ system, an antiviral drug, ganciclovir loaded intravitreal implant (Vitrasert®, Bausch & Lomb Inc., Rochester, NY, U.S.) for the treatment of cytomegalovirus retinitis, has been developed as the first intravitreal drug delivery system that avoids systemic side effects and does not involve frequent intravitreal injections. This implant is made of EVA and PVA, and releases ganciclovir by passive diffusion through a small opening in EVA at the base of the device for 6–8 months.