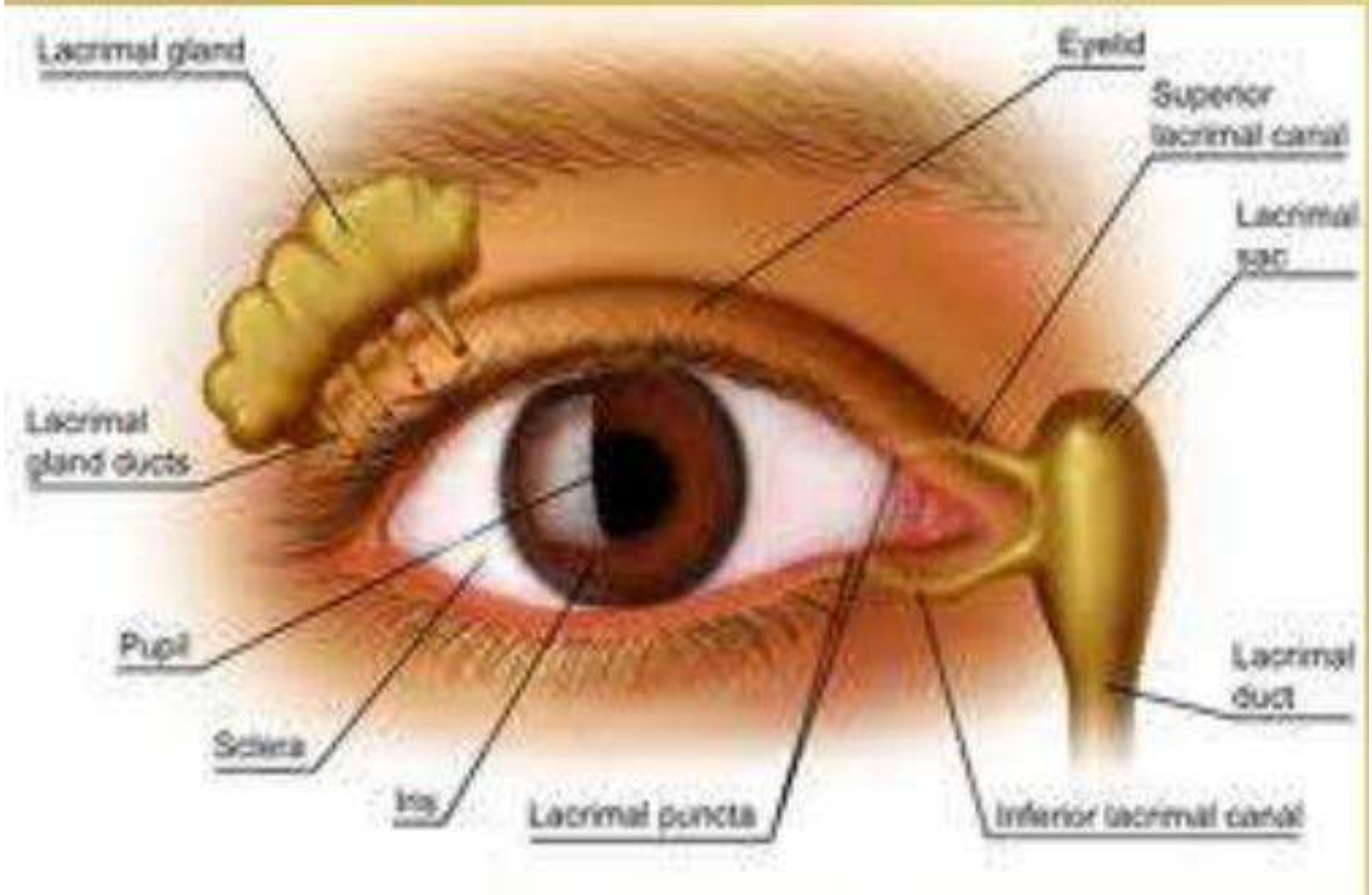
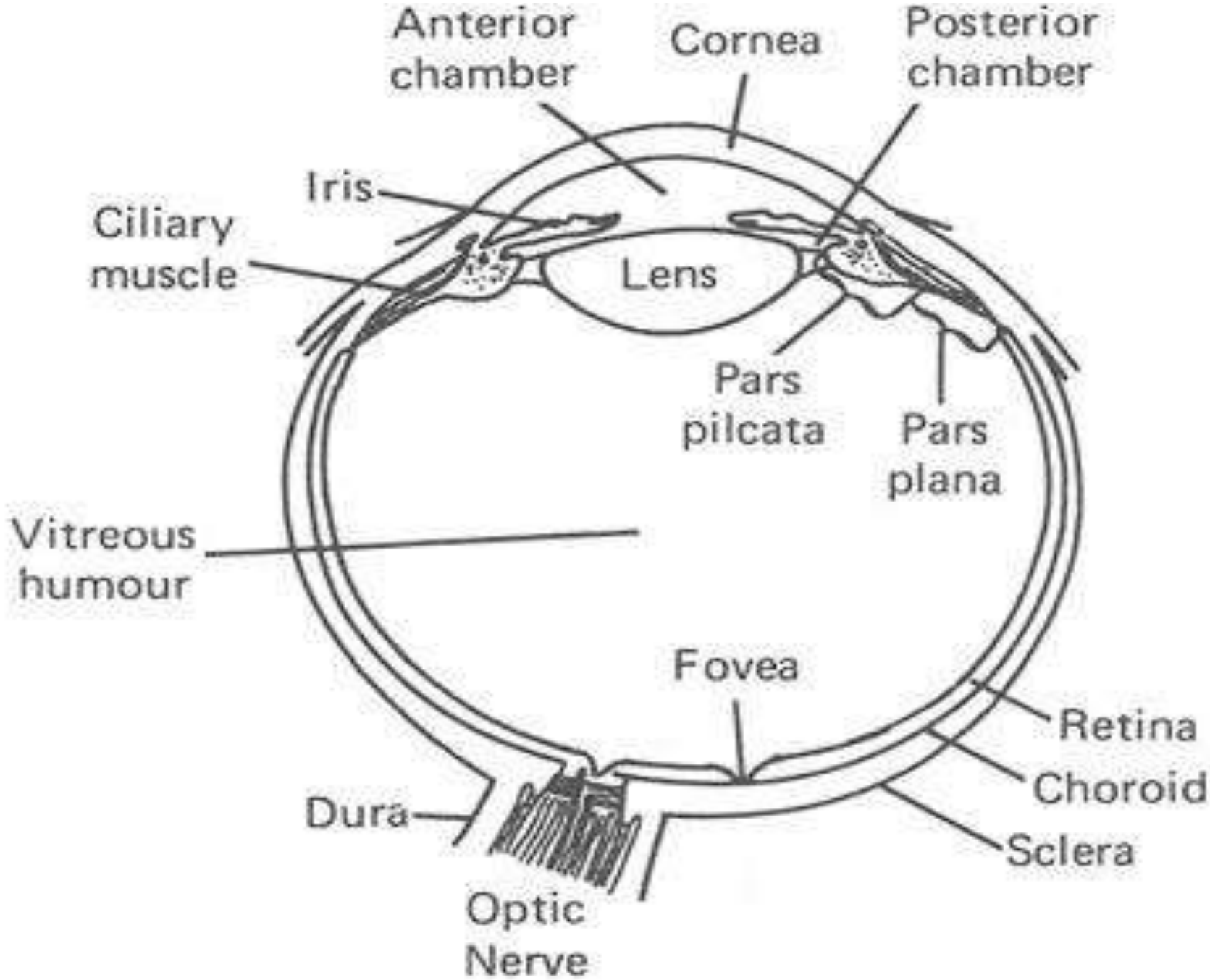
CHAPTER 10

The Ocular Route of Administration. Advantages and disadvantages. Factors affecting ocular absorption. Mechanisms of Absorption.


Lacrimal gland
Eyelid
Superior lacrimal canal
Lacrimal sac
Lacrimal gland ducts
Pupil
Sclera
Iris
Lacrimal puncta
Inferior lacrimal canal
Lacrimal duct


Anterior chamber
Cornea
Posterior chamber
Iris
Ciliary muscle
Lens
Pars pilcata
Pars plana
Vitreous humour
Fovea
Retina
Choroid
Sclera
Dura
Optic Nerve

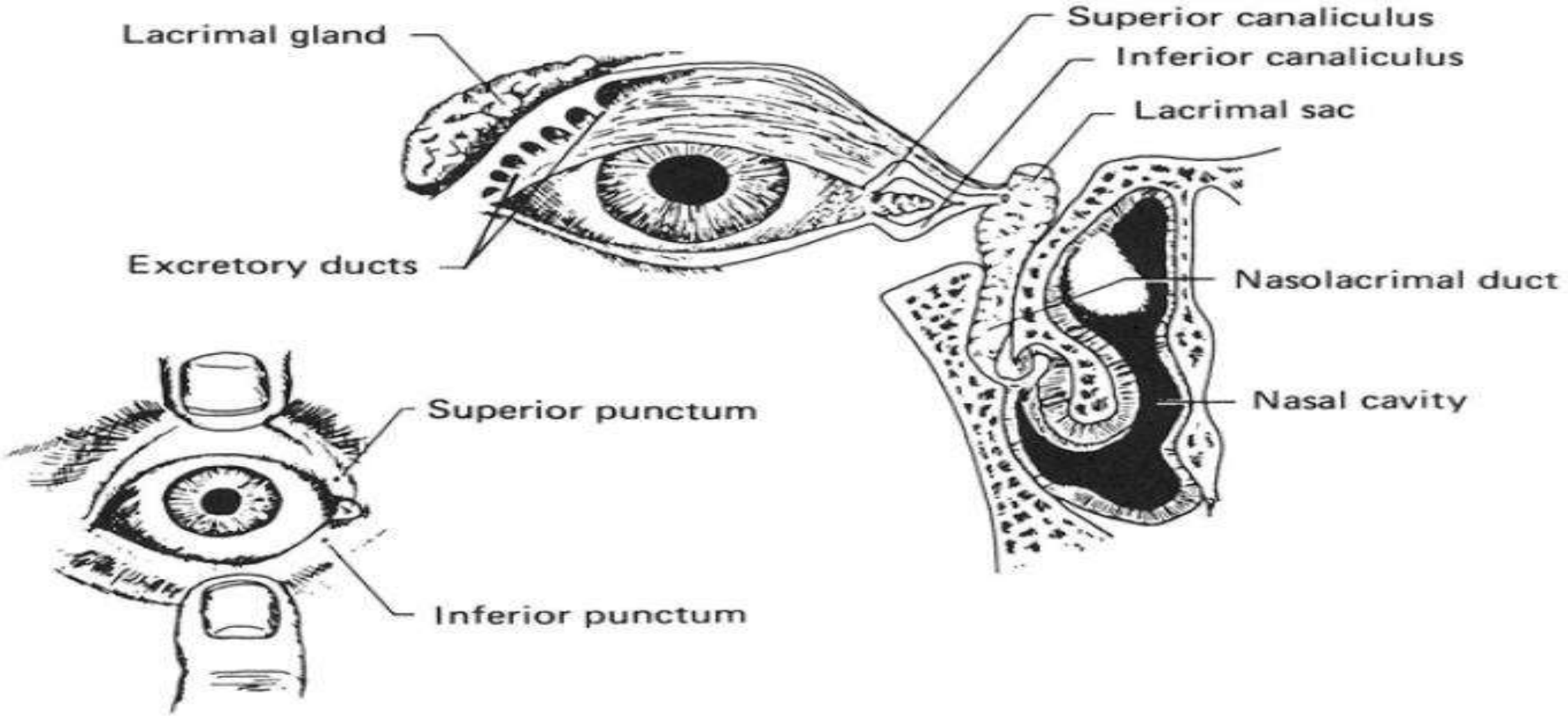


Figure: **Diagrams of parts of the eye of importance in medication. The superior and inferior punctae are the drainage ports for solutions and tear fluids. Medicaments can drain via the canaliculi into the nasolacrimal duct and then to the nasal cavity from whose surfaces absorption can occur.**

❖Local drug administration

- Miotics (Small size of pupil).
- Mydriatics (Dilation of pupil).
- Anti-inflammatories.
- Anti Infectives (Moxifloxacin ophthalmic solution0.5%).
- Surgical adjuvants (Mitomycin C).
- Diagnostic agents (Angiography or Angioscopy).

❖Systemic drug delivery :

➢ **Not encouraged, eye damage.**

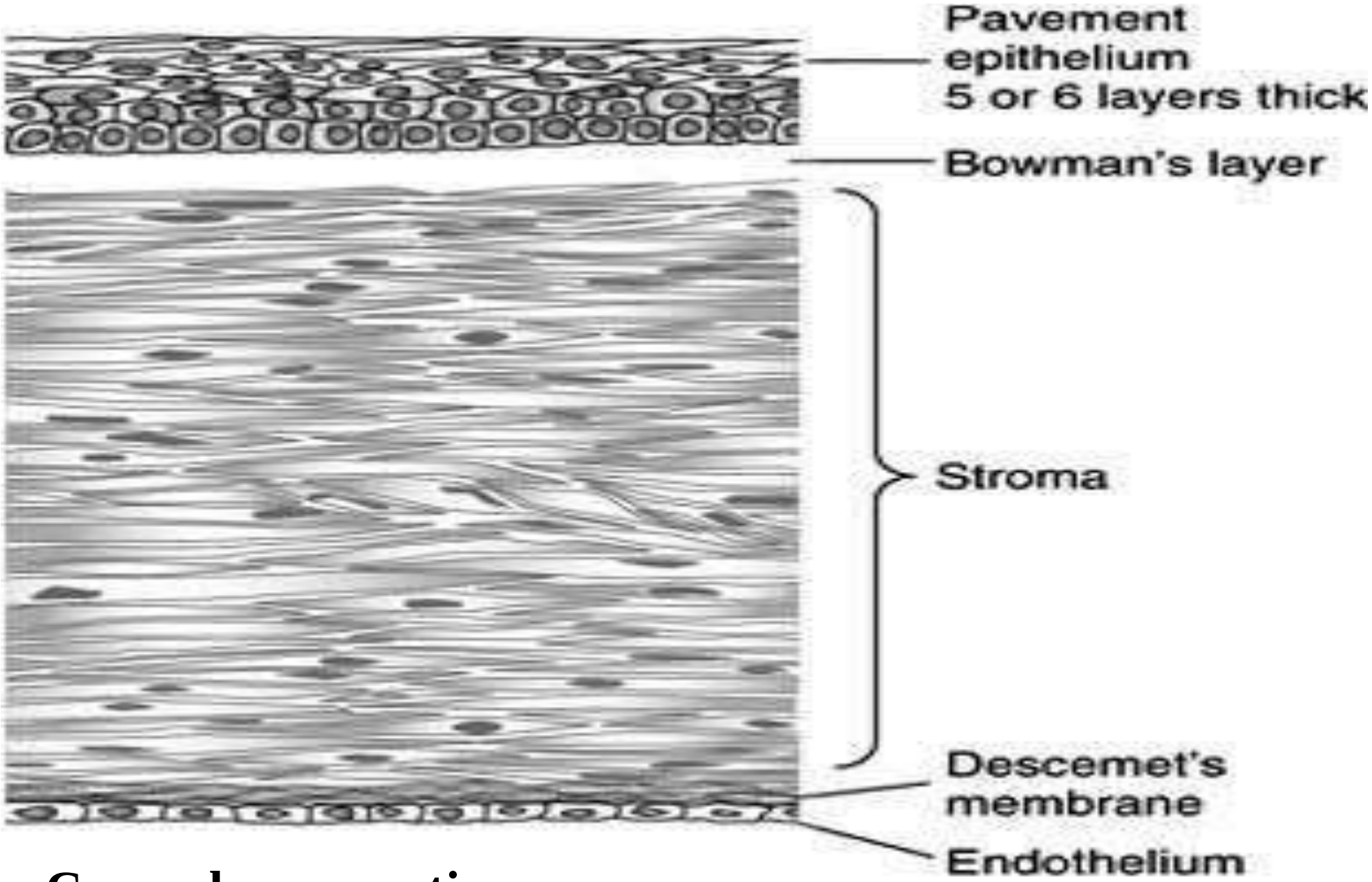
- The absorbing surface is the cornea. And the Drug absorbed by the conjunctiva enters the systemic circulation.
- The cornea, consists of three parts:

1. **The epithelium. (10%)**
2. **The stroma. (90%)**
3. **The endothelium.**

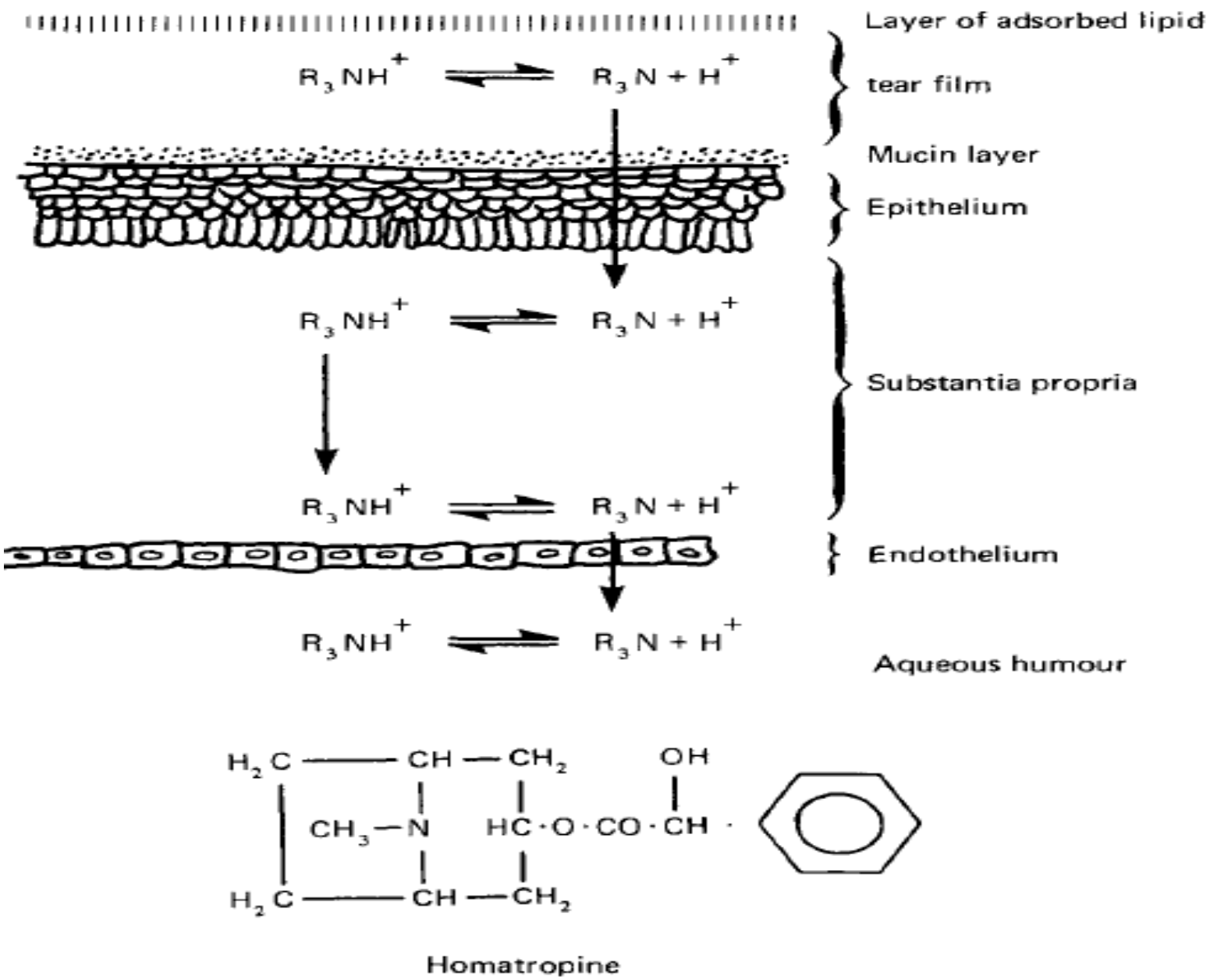
- Both **the endothelium** and the **epithelium** have a high lipid content and, they are penetrated by drugs in their unionized lipid-soluble forms.

- The **stroma** lying between these two structures has a high water content. **(90%)**

- Thus drugs that have to pass the corneal barrier successfully must be both lipid-soluble and water-soluble to some extent.



Corneal cross-section



Homatropine

Figure: **Diagrammatic representation of the tear film and the penetration of a base through the cornea. In this example R3N represents homatropine.**

➢ADVANTAGES

1. Easily administered.
2. Quick absorption and action.
3. Suitable of absorption of both the hydrophilic and lipophilic drugs
    1. lipophilic → Passive transport
    2. Hydrophilic→ aqueous pores of epithelium
4. Buffering effect of tears to the pH in case of drugs those are not stable in alkaline pH.
5. Less visual and systemic side effects.
6. Small amount of drugs undergoes metabolism → small loss by action of proteases that are specific for peptidases.
7. Better patient compliance.

➢DISADVANTAGES

1. Complicated preparation (Special equipment's and considerations → isotonicity, sterilization,…
2. Low bioavailability of aqueous ophthalmic solutions due to → tear turn over, drainage,…
3. Variation in applicable dose.
4. Irritation and toxicity (large doses → some drug enters nasopharynx).
5. Multiple doses due to short contact time (ophthalmic solutions).
6. Ophth Susp. → some large particles can not be avoided → irritation→ tear drainage → loss of drug.
7. For Local effect not for systemic effect (small surface area and absence of blood vessels).
8. Drainage of the drug through nasolacrimal apparatus→ significant systemic effect from certain potent ophth. Medications.
9. Expensive.

➢Factors Affecting the availability of the ocular administration route:

Biological Factors

1. Thickness of membrane
2. pH of the media 7.4
3. Metabolism
4. Tear turnover
5. Blinking of the eye ocular clearance
6. Age of the patient.

Physicochemical factors

1. Particle size.
2. Mwt and partition coefficient of drug.
3. Drug charge.
4. pH and pKa.

Dosage form factors

1. Excipients →

-Surfactant
-Antioxidants (Stabilizer)
-Tonicity adjusting agents
- Antibacterial agents

2. Dosage form used →

1. Semisolid → ointment
2. Liquid:
   → Solutions
   → Suspension ≤ 10µ
3. Solid:

Ocusert (Reservoir → sustained delivery to the eye).

➢Factors affecting ocular permeation:

1. Tonicity:

- The eye can tolerate solutions having an isotonicity rangr equivalent to 0.6-2% w/v NaCl
- Hyper-tonicity → Stinging for the eye.
- Hypo-tonicity → Corneal permeability increasing.

2. pH of the eye and pKa of the drug:

- pH range of eye (7.4) thus the drug to be administered should be basic in nature (H.H.B equation for weak bases ionized/ un ionized = 10^{pKa-pH})
- If the pH of the drug solution is 5→ increasing tear flow→ draining → decreasing drug concentration.
- If the pH of the drug solution > 11 → drug irritates eye → decreasing absorption.
- Importance of the pH:

A. Drug stability.

B. Comfort, safety & activity of the drug.

3. Viscosity:

- Viscosity affects the corneal absorption since:
  A. Reduces surface tension of the tear film.
  B. Increases ocular contact time with the drug → decreasing drainage.
- Ex : Methyl cellulose polymer → increasing viscosity → increases the contact time.

4. Particle size → Noyes-Whitney equation.

5. Age of the patient

- Age → thickness of mucosal layer.
- Infants → thinner mucosal layer→ more permeability of the drug than adults→ precaution in deciding administered dose.

6. Draining of the tears:

- The main function of the drainage system is the protection of the eye from the foreign bodies.
- At normal conditions tear drainage is about **60%** of the administered dose.
- Increase in the tear drainage→ drug removal from the eye.

7. Surface active agents:

A. Decrease surface tension.
B. Increase the corneal permeability.
C. Adjust viscosity.

- Ex: Benzalkonium chloride has surfactant properties and may well have some effect on corneal permeability, although its primary purpose is as a bacteriostatic and bactericide.
- Chlorhexidine acetate and cetrimide, both of which are surface-active.

- A wide range of drug types are placed in the eye:

  - Antimicrobials, Antihistamines, Decongestants,
  - Mydriatics, Miotics and Cycloplegic agents.

- Drugs are usually applied to the eye in the form of **drops** or **ointments** for local action.
- The absorbing surface is the cornea.
- Drug absorbed by the conjunctiva enters → The systemic circulation.

Ocusert

- The Ocusert therapeutic system is a flat, flexible, elliptical device designed to be placed in the inferior cul-de-sac between the sclera and the eyelid to release Pilocarpine continuously at a steady rate for 7 days.

1. **P-20** (20 micrograms/hour)
2. **P-40** (40 micrograms/hour)