

Ophthalmic Preparations



Presented by :
Srikanth A.V.N
Pharmaceutical Technology

Ophthalmic preparations:

- **Definition:** They are specialized dosage forms designed to be instilled onto the external surface of the eye (topical), administered inside (intraocular) or adjacent (periocular) to the eye or used in conjunction with an ophthalmic device.
- The most commonly employed ophthalmic dosage forms are **solutions, suspensions, and ointments**.
- The newest dosage forms for ophthalmic drug delivery are: **gels, gel-forming solutions, ocular inserts , intravitreal injections and implants**.



Drugs used in the eye:

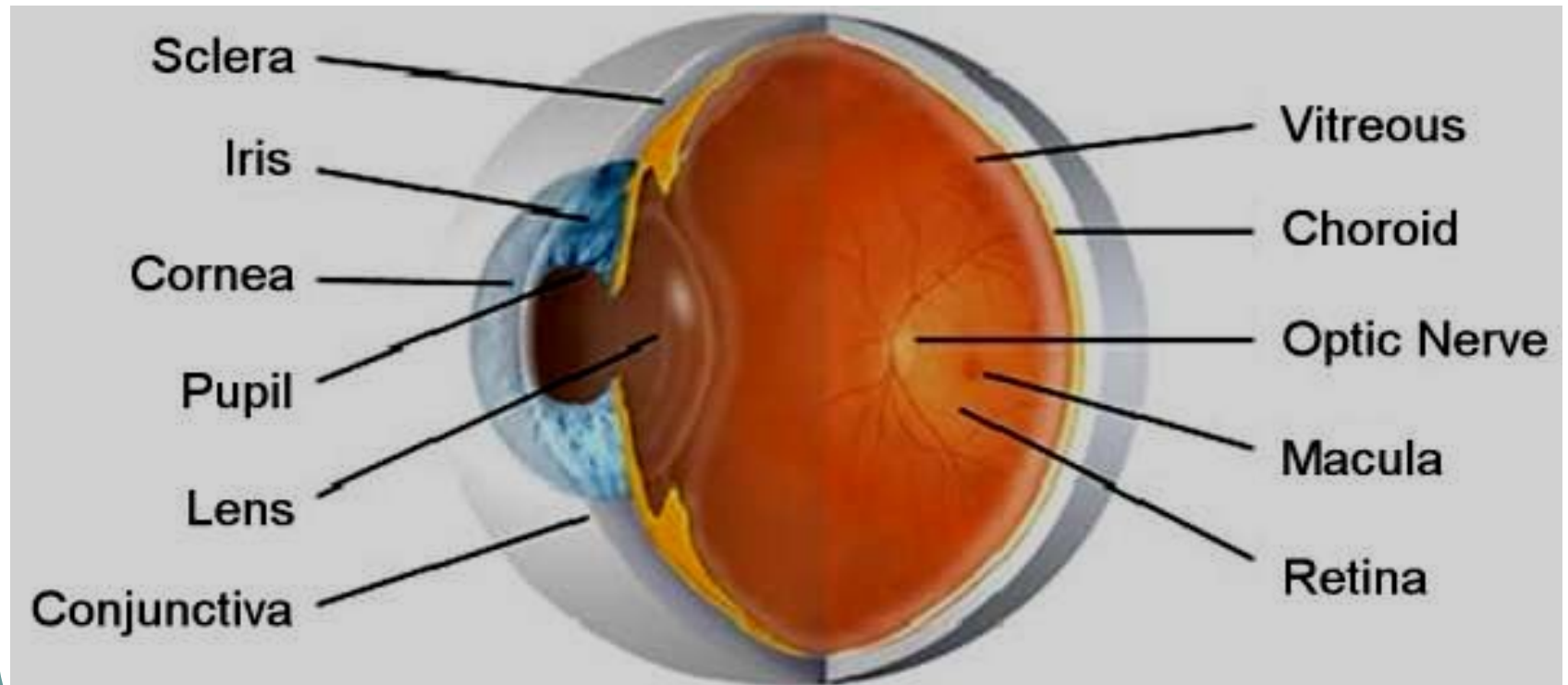
- Miotics e.g. pilocarpine Hcl
- Mydriatics e.g. Atropine
- Cycloplegics e.g. Atropine
- Anti-inflammatories e.g. corticosteroids
- Anti-infectives (antibiotics, antivirals and antibacterials)



Drugs used in the eye:

- **Anti-glucoma drugs** e.g. pilocarpine Hcl
- **Adjuncts** e.g. Irrigating solutions
- **Diagnostic drugs** e.g. sodiumfluorescein
- **Anesthetics** e.g. Tetracaine

Anatomy and Physiology of the Eye:



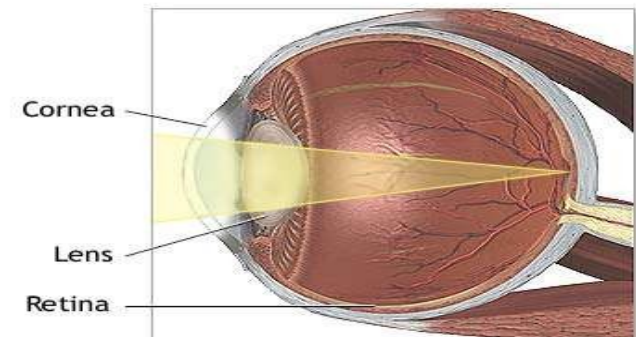
Anatomy and Physiology of the Eye (Cont.)

- **The sclera:** The protective outer layer of the eye, referred to as the “white of the eye” and it maintains the **shape of the eye.**
- **The cornea:** The front portion of the sclera, is transparent and **allows light to enter the eye.**
The cornea is a powerful **refracting surface**, providing much of the eye's focusing power.



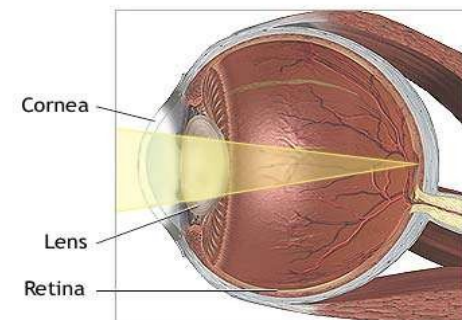
Anatomy and Physiology of the Eye (Cont.)

- **The choroids** is the second layer of the eye and lies between the sclera and the retina.
- It contains the **blood vessels** that provide **nourishment to the outer layers** of the retina.
- **The iris** is the part of the eye that gives it color.
- It consists of **muscular tissue** that responds to surrounding light, making the **pupil opening** in the center of the iris, larger or smaller depending on the brightness of the light.



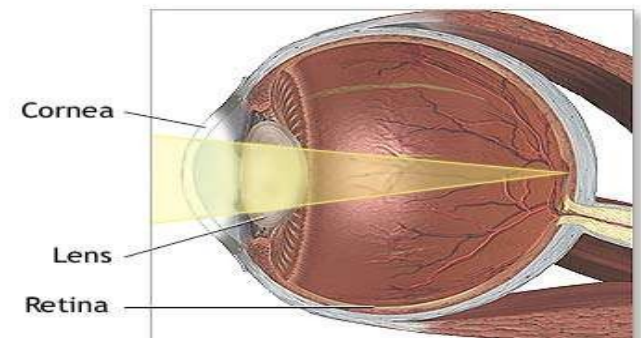
Anatomy and Physiology of the Eye (Cont.):

- **The lens** is a transparent, biconvex structure, encased in a thin transparent covering. The function of the lens is to **refract and focus incoming light onto the retina.**
- **The retina** is the innermost layer in the eye. It converts images into electrical impulses that are sent along the optic nerve to the brain where the **images are interpreted.**
- **The macula** is located in the back of the eye, in the center of the retina. This area produces **the sharpest vision.**



Anatomy and Physiology of the Eye (Cont.):

- The inside of the eyeball is divided by the lens into two fluid-filled sections.
- The larger section at the back of the eye is filled with a **colorless gelatinous mass** called the **vitreous humor**.
- The smaller section in the front contains a clear, **water-like material** called **aqueous humor**.
- The **conjunctiva** is a mucous membrane that begins at the edge of the cornea and lines the inside surface of the eyelids and sclera, which serves to **lubricate the eye**.



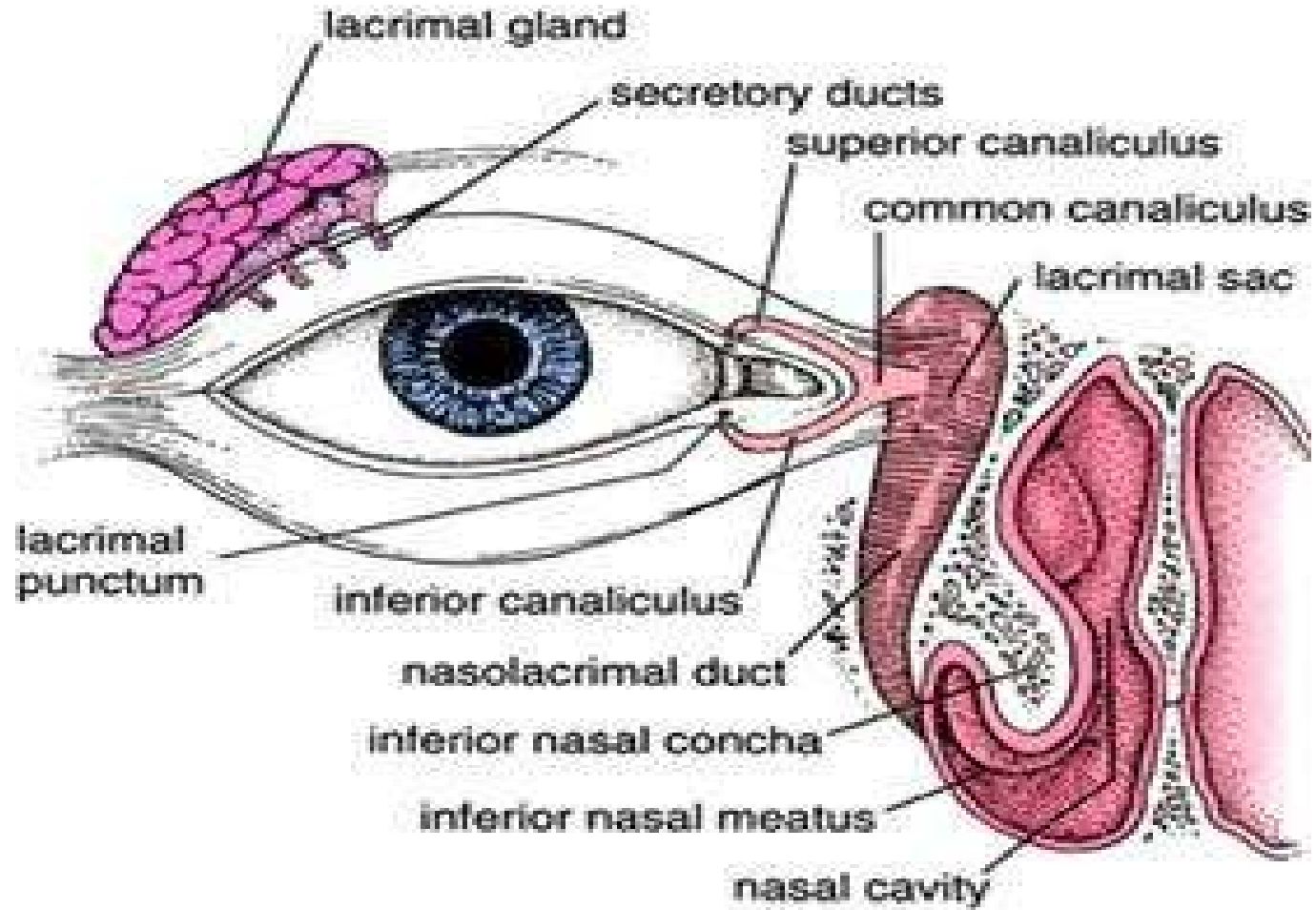
Absorption of drugs in the eye:

Factors affecting drug availability:

- Rapid solution drainage by gravity, induced lachrymation, blinking reflex, and normal tear turnover:
- The normal volume of tears = 7 ul, the blinking eye can accommodate a volume of up to 30 ul without spillage, the drop volume = 50 ul



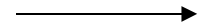
lacrimal nasal drainage:



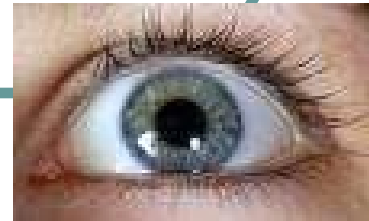
Absorption of drugs in the eye:

- Low corneal permeability (act as lipid barrier)
- Transport of hydrophilic and macromolecular drugs occurs **through** scleral route
- Lipophilic agents of low molecular weight **follow** transcorneal transport by passive diffusion and obey

Ficks's first law of diffusion:



$$J = - D \cdot d C_m / dx$$



Corneal absorption:

J = The flux rate across the membrane

D = diffusion coefficient

- The diffusion coefficient \uparrow , as the molecular size of the drug \downarrow

C_m = concentration gradient

- As the drug solubility \uparrow , the gradient \uparrow , the driving force for drug entry into the aqueous humour \uparrow

.



Corneal absorption:

♣ Drug delivery in ocular therapeutics is a challenging problem.

Poor Bioavailability

Protective Mechanisms
(Short residence time)

- * Blinking
- * Reflex Lacrimation
- * Nasolacrimal Drainage

Anatomy of the eye

- * Barrier properties of the cornea

General safety considerations:

A. Sterility:

- Ideally, all ophthalmic products would be terminally sterilized in the final packaging.
 - Only a few ophthalmic drugs formulated in simple aqueous vehicles are stable to normal autoclaving temperatures and times (121°C for 20-30 min).
- * Such heat-resistant drugs may be packaged in glass or other heat-deformation-resistant packaging and thus can be sterilized in this manner.

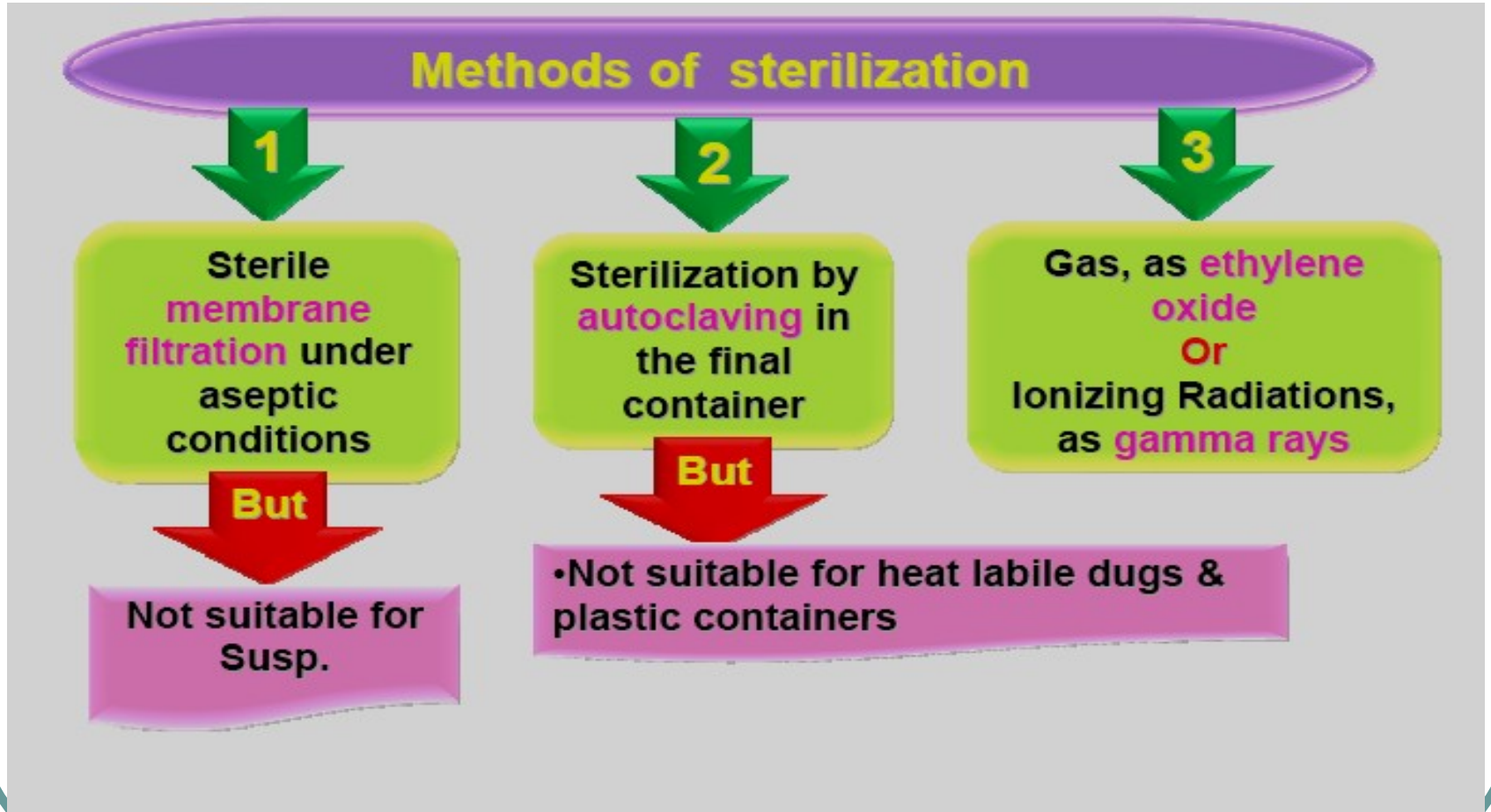


A. Sterility (cont.):

- Most ophthalmic products, however cannot be sterilized by heat due to the active principle or polymers used to increase viscosity **are not stable to heat.**
- Most ophthalmic products are **aseptically manufactured** and filled into previously sterilized containers in aseptic environments using aseptic filling-and-capping techniques.



A. Sterility (cont.):



B. Ocular toxicity and irritation:

- **Albino rabbits** are used to test the ocular toxicity and irritation of ophthalmic formulations.
- The procedure based on the examination of the **conjunctiva, the cornea or the iris.**
- ***E.g. USP procedure for plastic containers:***
 - 1- Containers are cleaned and sterilized as in the final packaged product.
 - 2- Extracted by submersion in saline and cottonseed oil.
 - 3- Topical ocular instillation of the extracts and **blanks** in rabbits is completed and **ocular changes examined.**



C.Preservation and preservatives:

- Preservatives are included **in multiple-dose eye solutions** for maintaining the product sterility during use.
- Preservatives not included **in unit-dose package**.
- The use of preservatives is **prohibited** in ophthalmic products that are used at the of **eye surgery** because, if sufficient concentration of the preservative is contacted with the corneal endothelium, the cells can become damaged causing clouding of the cornea and **possible loss of vision**.
So these products should be packaged in sterile, unit-of-use containers.
- The most common organism is **Pseudomonas aeruginosa** that grow in the cornea and **cause loss of vision**.

C.Preservation and preservatives:

Ophthalmic products may be packaged in multiple-dose containers when intended for the individual use of one patient

1st
Dose



Other doses may
cause infection to eye



We add preservative to prevent the growth or to destroy, microorganisms accidentally introduced when the container is opened during use

C.Preservation and preservatives:

Examples of preservatives:

1- Cationic wetting agents:

- Benzalkonium chloride (0.01%)
- It is generally used in combination with 0.01-0.1% disodium edetate (EDTA). **The chelating, EDTA has the ability to render the resistant strains of PS aeruginosa more sensitive to benzalkonium chloride.**

2- Organic mercurials:

- Phenylmercuric nitrate 0.002-0.004%
- phenylmercuric acetate 0.005-0.02%.



C.Preservation and preservatives:

3-Esters of p-hydroxybenzoic acid:

- Mixture of 0.1% of both methyl and propyl hydroxybenzoate (2 :1)

4- Alcohol Substitutes:

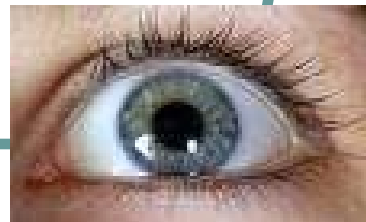
- Chlorobutanol(0.5%). Effective only at pH 5-6.
- Phenylethanol (0.5%)

Manufacturing considerations:

A. Manufacturing Environment:

The environment should be **sterile and particle-free** through:

- *Laminar-flow* should be used throughout the manufacturing area.
- Total particles per cubic foot of space should be minimum.
- **Relative humidity controlled to between 40 and 60%.**
- **Walls, ceilings and floors** should be constructed of materials that are hard, non flaking, smooth and non-affected by surface cleaners or disinfectants.

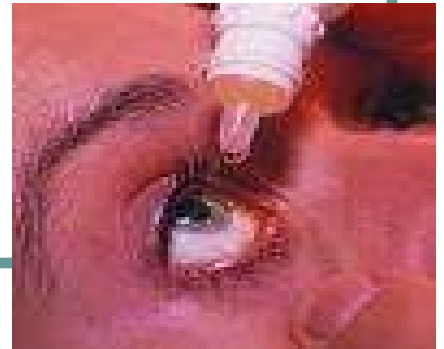


A. Manufacturing Environment:



A. Manufacturing Environment:

- **Ultraviolet lamps** provided in flush-mounted fixtures to maintain **surface disinfection**
- **Separate entrance** for personnel and equipment should be provided through specially designed air locks that are maintained at negative pressure relative to the aseptic manufacturing area and at a positive pressure relative to the noncontrolled area



A. Manufacturing Environment:



. *Manufacturing Techniques:*

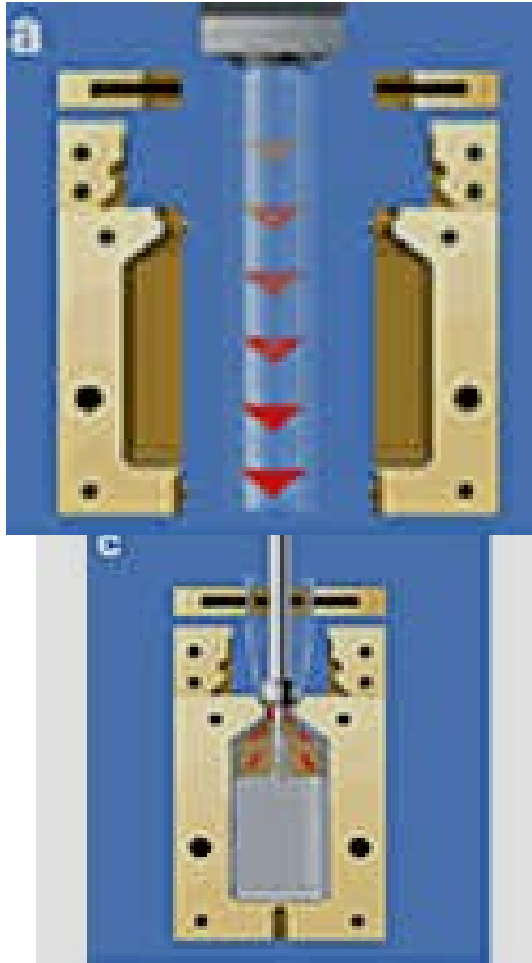
- *Unpreserved formulations of active drug (s):*

The blow/fill/seal method

It is used for manufacture of **unpreserved ophthalmic products** , especially for artificial tear products.

In this first step is : To **extrude** polyethylene resin **at high temperature and pressure** and **to form the** container **by blowing the polyethylene resin** into mold with compressed air. The product is vented out, and finally the container is **sealed on the top**.

The blow /fill/seal method:



C. Equipment:

All tanks, valves, pumps and piping must be of best available Grade of corrosion – **resistant stainless steel.**

All products-contact surface should be polished either mechanically or be electropolishing to provide a surface as Free as possible **from scratches or defects.**

Care should be taken in the design of such equipment to Provide adequate means of **cleaning and sanitization.**

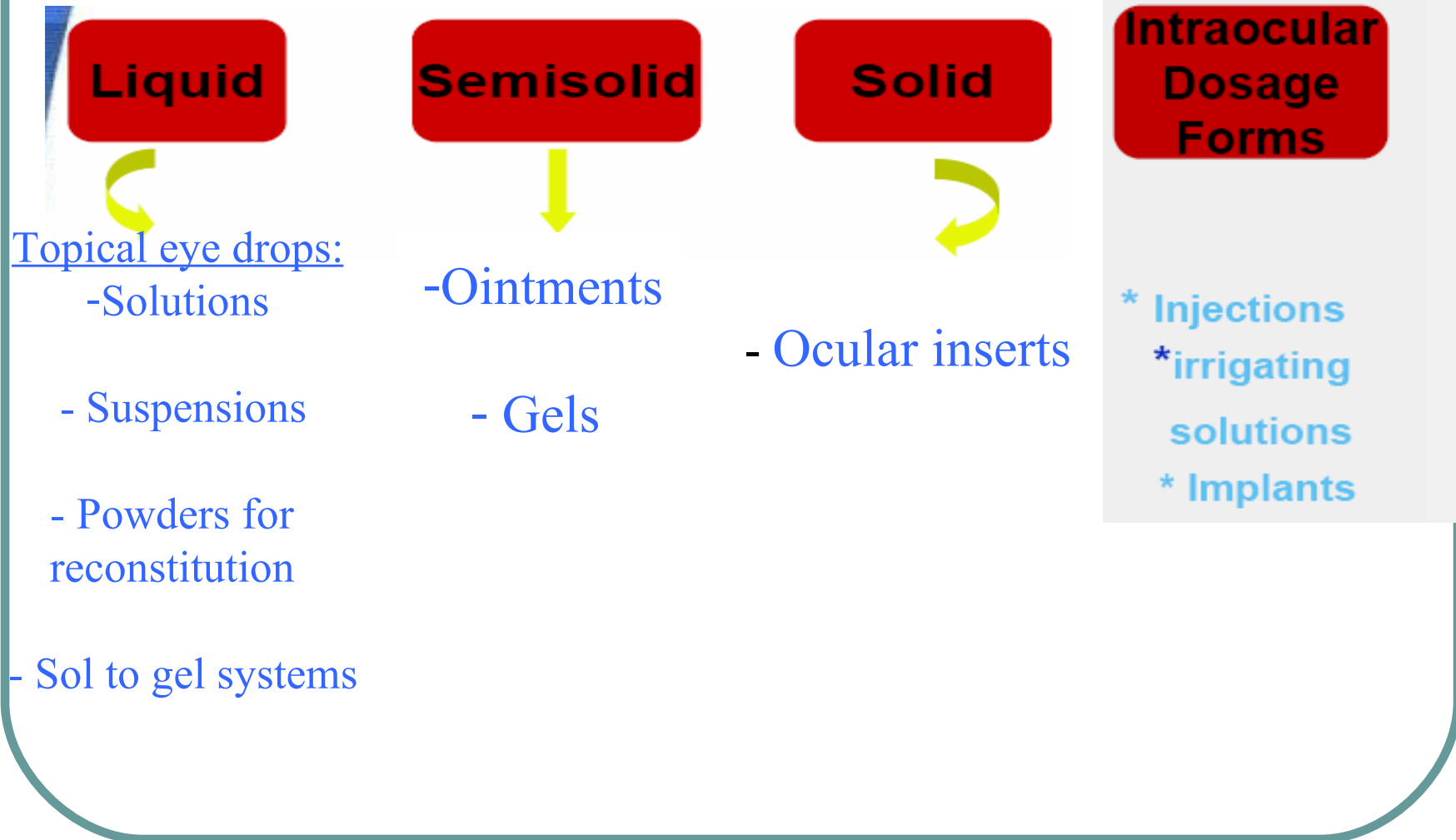
Ideal ophthalmic delivery system:

Following characteristics are required to optimize ocular drug delivery system:

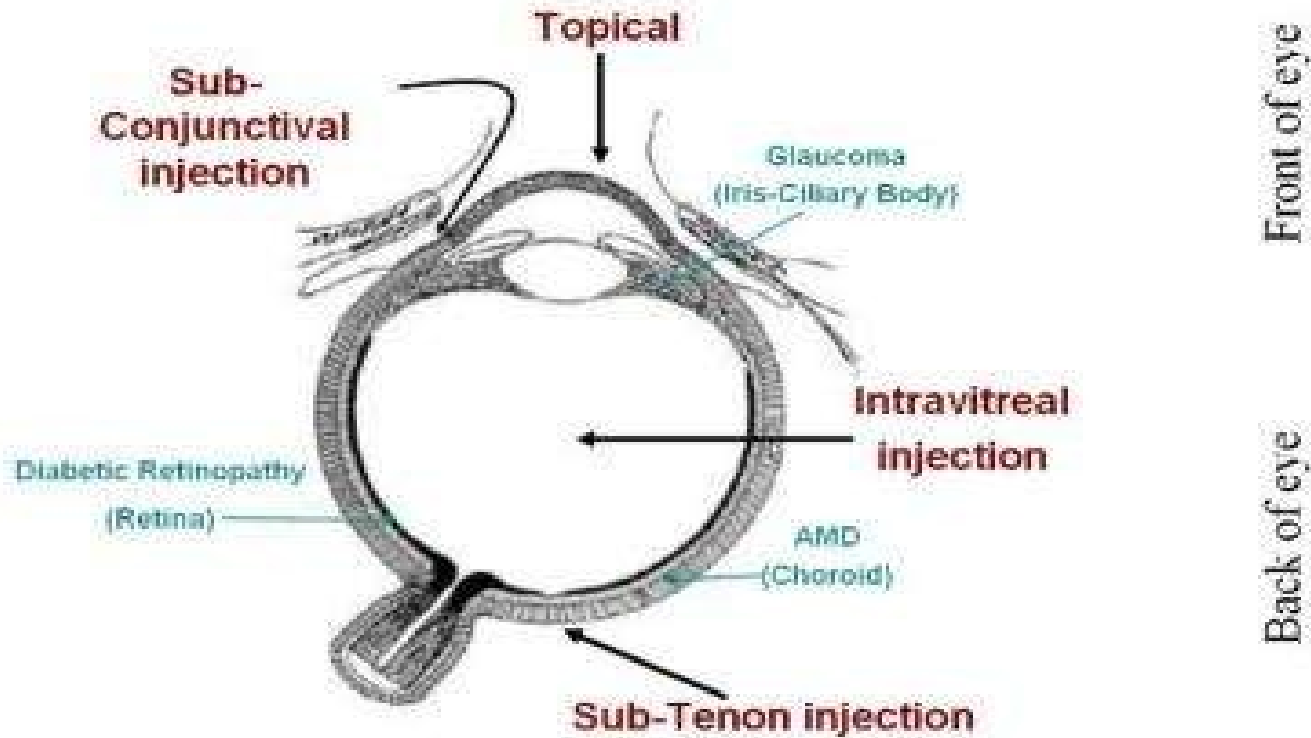
- Good corneal penetration.
- Prolong contact time with corneal tissue.
- Simplicity of instillation for the patient.
- Non irritative and comfortable form
- Appropriate rheological properties



Classification Of Ocular Drug Delivery Systems:



Routes of Ocular Delivery



A. Topical Eye drops:

1- Solutions:

- Ophthalmic solutions are sterile solutions, essentially free from foreign particles, suitably compounded and packaged for instillation into the eye.



A. Topical Eye drops:



● *Administration:*

- Pull down the eyelid
- Tilting the head backwards
- Look at the ceiling after the tip is pointed close to the lower cul-de-sac
- Apply a slight pressure to the rubber bulb or plastic bottle to allow a drop to fall into the eye.
- Do not squeeze lids

To prevent contamination:

- Clean hands
- Do not touch the dropper tip to the eye or tissue



1- Solutions:

-Nearly all the major ophthalmic therapeutic agents are water soluble salts

The selection of the appropriate salt depend on :

- solubility
- ocular toxicity
- The effect of pH, tonicity, and buffer capacity
- The intensity of any burning sensation
- The most commonly used salts are: hydrochloride, Phosphates, nitrates



Examples of topical eye drops:

- Atropine sulphate eye drops.
- Pilocarpine eye drops .
- Silver nitrate eye drops.
- Zinc sulphate eye drops.

B. Manufacturing Techniques:

- *Aqueous ophthalmic solution:*

- * Manufactured by dissolution of the **active ingredients** and a portion of the excipients into **all portion of water**.

The sterilization of this solution done by **heat or by sterilizing Filtration** through sterile depth or membrane filter media Into a sterile receptacle.

This sterile solution is then mixed with the additional required Sterile components such as **viscosity –imparting agents, Preservatives** and so and the solution is brought to final Volume with **additional sterile water**.



Disadvantages of eye solutions:

- 1-The very short time the solution stays at the eye surface.
The retention of a solution in the eye **is influenced by viscosity.**
- 2- Its **poor bioavailability** (a major portion i.e. 75% is lost via naso lacrimal drainage).



2- suspensions:

* If the **drug is not sufficiently soluble**, it can be formulated as a suspension.

A suspension may also be desired to improve **stability**, **Bioavailability**, and **efficacy**.

The major topical ophthalmic suspensions are the **steroid anti-inflammatory agents**.

An ophthalmic suspension should use the drug in a microfine form; usually 95% or more of the particles have a Diameter of **10 μ m** or less.



Examples :

- Prednisolone acetate suspension.
- Besifloxacin suspension.
- Blephamide suspension.
- Fluorometholone .

B. Manufacturing Techniques:

- *Aqueous suspensions:*

Are prepared in much the same manner, except that
Before bringing to the final volume with additional
sterile water .

The solid that is to be suspended is previously rendered sterile
by – heat ,exposure to ethylene oxide ,ionizing radiation
(gamma), sterile filtration.

The particle size should be monitored.

3- Gel-Forming Solutions

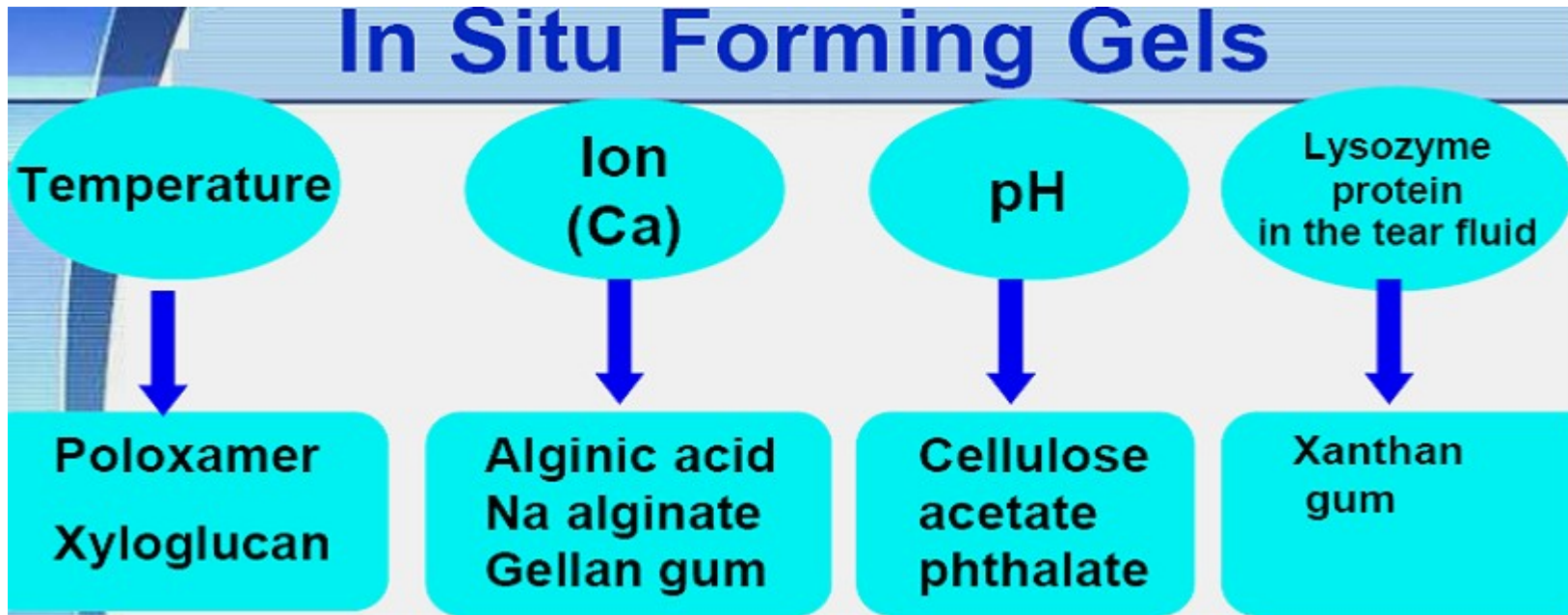
* Solution that are liquid in the container and thus can be instilled as eye drops but forms gel on contact with the tear fluid and provide **increased contact time** with the possibility of **improved drug absorption** and **Duration** of therapeutic effect.

* liquid-gel phase transition-dependent delivery system vary according to the **particular polymer(s) employed** and their mechanisms for triggering the Transition to a gel phase in the eye.

* Take the advantage of **changes** in **temperature**, **pH**, **ion sensitivity**, **lysozymes** upon contact with **tear fluid**.



3- Gel-Forming Solutions



Different mucoadhesive polymers were added to poloxamer

1. Carbopol 940

2. Hydroxypropylmethyl cellulose (HPMC)

3. Hydroxyethyl cellulose (HEC)

Inactive Ingredients in Topical Drops:

The inactive ingredients in ophthalmic solution and Suspension dosage forms are necessary to perform one or more of the Following functions:

Adjust concentration and tonicity

5. Buffer and adjust pH,
6. Stabilize the active ingredients against decomposition ,
7. Increase solubility,
8. Impart viscosity
9. And act as solvent.



1- Tonicity and Tonicity-Adjusting Agents:

The pharmacist should adjust the tonicity of an ophthalmic solution correctly (i.e., exert an osmotic pressure equal to that of tear fluid, generally agreed to be **equal to 0.9% NaCl**).

A range of 0.5-2.0% NaCl equivalency **does not cause a marked pain response** and a range of about 0.7-1.5% should be acceptable to most persons.

Commonly tonicity adjusting ingredients include : NaCl, KCl, buffer salts, dextrose, glycerin, propylene glycol, mannitol



Isotonicity

Lacrimal fluid is isotonic with blood having an isotonicity value corresponding to that of 0.9% NaCl solution

Ideally, an ophthalmic solution should have this isotonicity value

But

The eye can tolerate isotonicity from 0.6% to 2% NaCl without marked discomfort

Some ophthalmic solutions are necessarily hypertonic in order to enhance absorption and provide a concentration of the active ingredient strong enough to exert an effective action.

2- pH Adjustment and Buffers:

pH adjustment is very important as pH affects

- 1- To render the formulation **more stable**
- 2- The **comfort, safety** and activity of the product.

Eye irritation \longrightarrow increase in tear fluid secretion \longrightarrow

Rapid loss of medication.

- 3- To enhance aqueous **solubility** of the drug.
- 4- To enhance the **drug bioavailability**
- 5- To maximize preservative **efficacy**



2- pH Adjustment and Buffers:

Ideally , every product would be buffered to a pH of 7.4 (the normal physiological pH of tear fluid).

When necessary they are buffered adequately to maintain Stability within this range for at least 2 years.

If buffers are required there capacity is controlled to be As low as possible(low buffer capacity) thus enabling the Tear to bring the pH of the eye back to the physiological range .

pH & buffer

Normal tears have a pH of about 7.4 and possess some buffer capacity.

So

Any formulation having different pH than 7.4 will be neutralized by normal buffer of tears.

But

Most alkaloidal salts precipitate as the free alkaloid at this pH. And many drugs are chemically unstable at pH levels approaching 7.4.

So

For this reason, the buffer system should be selected that is nearest to the physiological pH of 7.4 & does not cause precipitation of the drug or its rapid deterioration.

3- *Stabilizers & Antioxidants:*

- * Stabilizers are ingredients added to a formula to **decrease the rate of decomposition** of the active ingredients.
 - * **Antioxidants** are the principle stabilizers added to some ophthalmic solutions , primarily those containing epinephrine and other oxidizable drugs.
 - * **Sodium bisulfite or metabisulfite** are used in concentration up to 0.3% in epinephrine hydrochloride and bitartrate solutions.
- The several antioxidant system have been developed :-

These consists of **ascorbic acid and acetylcysteine** and **sodium thiosulfate** .

4- Surfactants:

The order of surfactant toxicity is :

anionic > cationic >> nonionic .

- **several nonionic surfactants** are used in relatively low Concentration to aid in dispersing steroids in suspensions and to achieve or to improve solution clarity.
- Those principally used are the sorbitan ether esters of oleic acid (**polysorbate or tween 20 and 80**).

5- Viscosity-Imparting Agents:

Polyvinyl alcohol, methylcellulose, hydroxypropyl methylcellulose, hydroxyethylcellulose, and carbomers, are commonly used to increase the viscosity of solution and suspensions (to retard the rate of setting of particles)

They **increase the ocular contact time** , there by **decreasing** the **drainage rate**, increase the mucoadhesiveness and **Increasing** the **bioavailability** .

Disadvantage : produce **blurring vision** as when dry, form a dry film on the eye lids. make filtration more difficult .

commercial viscous vehicles are :

- **polyvinyl alcohol (liquifilm)**
- **hydroxypropyl methylcellulose (isopto)**

6- Vehicles:

Ophthalmic drop (using purified water USP) as the solvent.

Purified water meeting USP standards may be obtained by :
Distillation, deionization, or reverse osmosis.

Oils have been used as vehicles for several topical eye drops products that are extremely sensitive to moisture.

When oils are used as vehicles in ophthalmic fluids, they must be of the highest purity.



Packaging:

- Eye drops have been packaged almost entirely in plastic dropper bottles

The main advantage of the Drop-Trainer are:

- convenience of use by the patient
- decreased contamination potential
- lower weight
- lower cost
- The plastic bottle and dispensing tip is made of *low-density polyethylene (LDPE) resin*, which provides the necessary flexibility and inertness.
- The cap is made of harder resin than the bottle.



Packaging:

A special plastic ophthalmic package made of **polypropylene** is introduced. The bottle is filled then sterilized by steam under pressure at 121°C.

Powder for reconstitution also use glass containers , owing to their heat-transfer characteristics, which are necessary during the freeze-drying processes.



Packaging:

- The glass bottle is made sterile by dry-heat or steam autoclave sterilization.
- Amber glass is used for light-resistance.



B. *Semisolid Dosage Forms: Ophthalmic Ointments and Gels:*

The ointment vehicles used in ophthalmology is mixture of **Mineral oil and petrolatum base** .

The mineral oil is used to modify melting point and modify **consistency**.

Petrolatum vehicle used as a ocular **lubricate** to treat dry Eye syndromes.

They are mostly used as adjunctive **night time** therapy, While eye drops administered during the day

It is suitable for moisture sensitive drugs and has longer **Contact time** than drops.



B. Semisolid Dosage Forms: Ophthalmic Ointments and Gels:

- *Chlorobutanol and methyl- and propylparaben* are the most commonly used **preservatives** in ophthalmic ointments.
- **Disadvantage:**

Their are **greasy** nature ,blurring of vision.



.Manufacturing Techniques:

- ***Ophthalmic ointment:***

- The ointment base is sterilized by heat and appropriately filtered while molten to remove foreign particulate matter

It is then placed into a **sterile steam jacket kettle** to maintain the ointment in a molten state under aseptic conditions, and the previously sterilized active ingredient (s) and excipients are added aseptically.

- The entire ointment **may be passed through a previously sterilized colloid mill** for adequate dispersion of the insoluble components . After the product is compounded in an aseptic manner ,it is **filled into a previously sterilized container.**



Examples :

- Chloramphenicol ointment.
- Tetracycline ointment.
- Hydrocortisone ointment.

B. Semisolid Dosage Forms: Ophthalmic Ointments and Gels:

- **Packaging:**

Ophthalmic ointment are packaged in :

1. **Small collapsible tin tube** usually holding 3.5g of product. the pure tin tube is compatible with a wide range of drugs in petrolatum-based ointments.
2. **Aluminum tubes** have been used because of their lower cost and as an alternative should the supply of tin.



Packaging:

3. Plastic tubes made from flexible LDPE resins have also been considered as an alternative material.

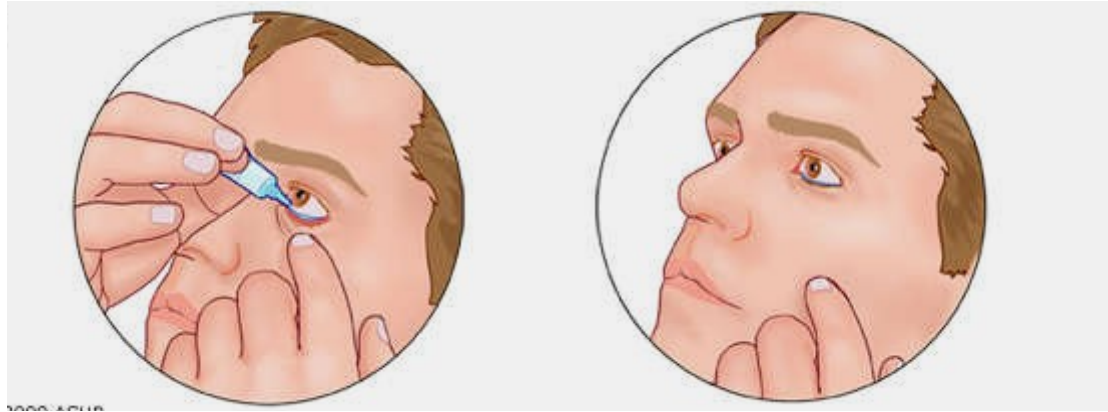
Filled tubes may be tested for leakers.

The screw cap is made of polyethylene or polypropylene.

The tube can be a source of metal particles and must be cleaned carefully before sterilization (by autoclaving or ethylene oxide).



How to Use Eye Ointments and Gels Properly?



C. Solid Dosage Forms

Ocular Inserts

- **Ophthalmic inserts** are defined as sterile solid or semisolid preparations, with a thin, flexible and multilayered structure, for insertion in the conjunctival sac.

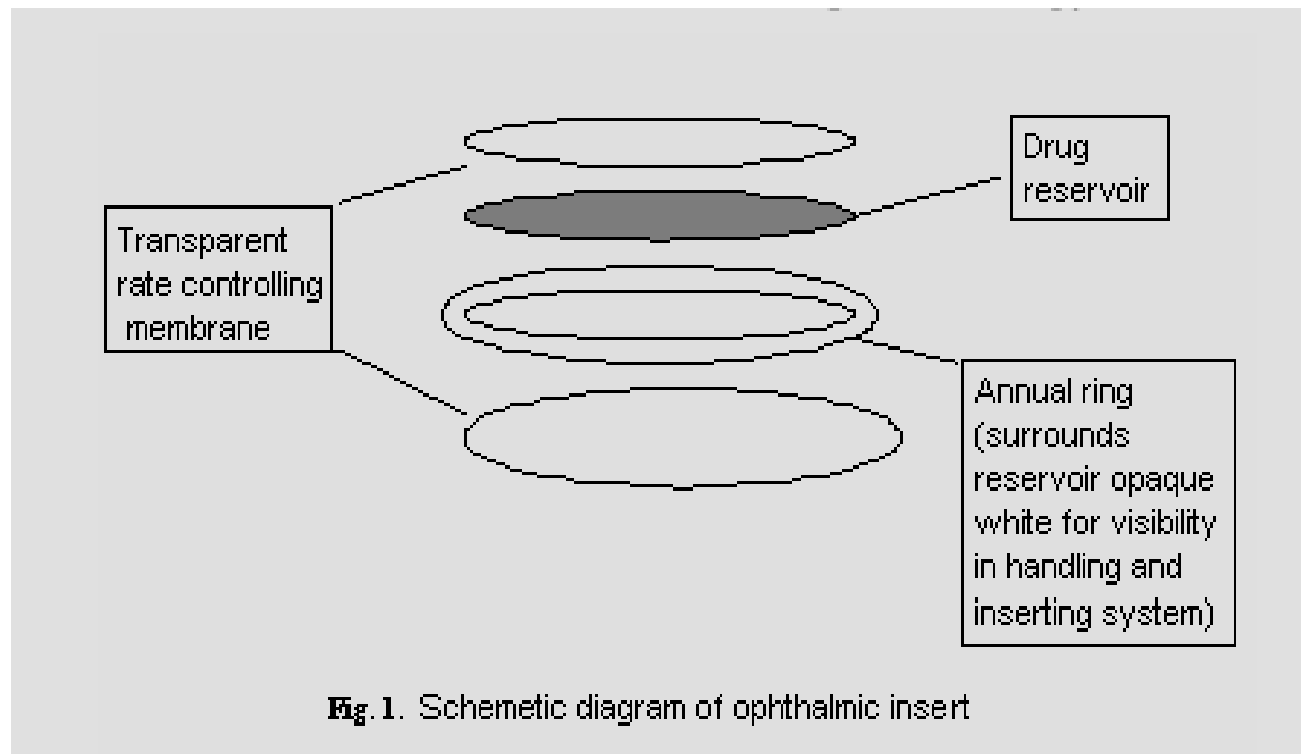


Fig. 1. Schematic diagram of ophthalmic insert

C. Solid Dosage Forms

Ocular Inserts

- ***Advantages:***
- Increasing contact time and improving bioavailability.
- Providing a **prolong drug release** and thus a better efficacy.
- Reduction of adverse effects.
- Reduction of the number administrations and thus better patient compliance.



C. Ocular Inserts

I. Insoluble inserts:



- ***Insoluble insert*** is a multilayered structure consisting of a drug containing core surrounded on each side by a layer of **copolymer membranes** through which the **drug diffuses** at a constant rate.
- **The rate of drug diffusion is controlled by:**
 - The polymer composition
 - The membrane thickness
 - The solubility of the drug

e.g. The Ocusert® Pilo-20 and Pilo-40 Ocular system

- Designed to be placed in the inferior cul-de-sac between the sclera and the eyelid and to release **pilocarpine** continuously at a steady rate for **7 days for treatment of glaucoma**.

C. Ocular Inserts

I. Insoluble inserts:



Photograph of patient with Ocusert (pilocarpine) in place in lower cul-de-sac of right eye

II. Soluble Ocular inserts:

- **Soluble inserts** consists of all monolytic polymeric devices that at the end of their release, the device dissolve or erode.

Types

- Based on natural polymers e.g. collagen.
- b) Based on synthetic or semi synthetic polymers e.g. Cellulose derivatives – Hydroxypropyl cellulose, methylcellulose or Polyvinyl alcohol, ethylene vinyl acetate copolymer.
- The system soften in 10-15 sec after introduction into the upper conjunctival sac, gradually **dissolves within 1h** , while releasing the drug.
- **Advantage:** Being **entirely soluble** so that they do not need to be removed from their site of application.

II.Soluble Ocular inserts:

Lacrisert is a sterile ophthalmic insert use in the treatment of **dry Eye syndrome** and is usually recommended for patients unable to obtain symptomatic relief with artificial tear solutions.

The insert is composed of 5 mg of Hydroxypropyl cellulose in a rod-shaped form about 1.27 mm diameter by about 3.5 mm long.

D. Intraocular Dosage Forms

- They are Ophthalmic products that introduced into the **interior structures** of the eye primarily during ocular surgery.
- **Requirements for formulation:**
 - 1- sterile and pyrogen-free
 - 2- strict control of **particulate matter**
 - 3- **compatible** with sensitive internal tissues
 - 4- packaged as **preservative-free single dosage**

D. Intraocular Dosage Forms:

1- Irrigating Solutions

It is a balanced salt solution was developed for **hydration and clarity of the cornea during surgery.**

It contains the five essentials ions:

sodium,potassium,**calcium**,magnesium and **chloride**.

It also contains citrate acetate ions, and a potential source of bicarbonate.

It is formulated to be **iso osmotic** with aqueous humor and has a neutral to slightly alkaline physiological pH.

They must be non-pyrogenic, therefore requiring sterile water for injection(WFI) as the vehicle

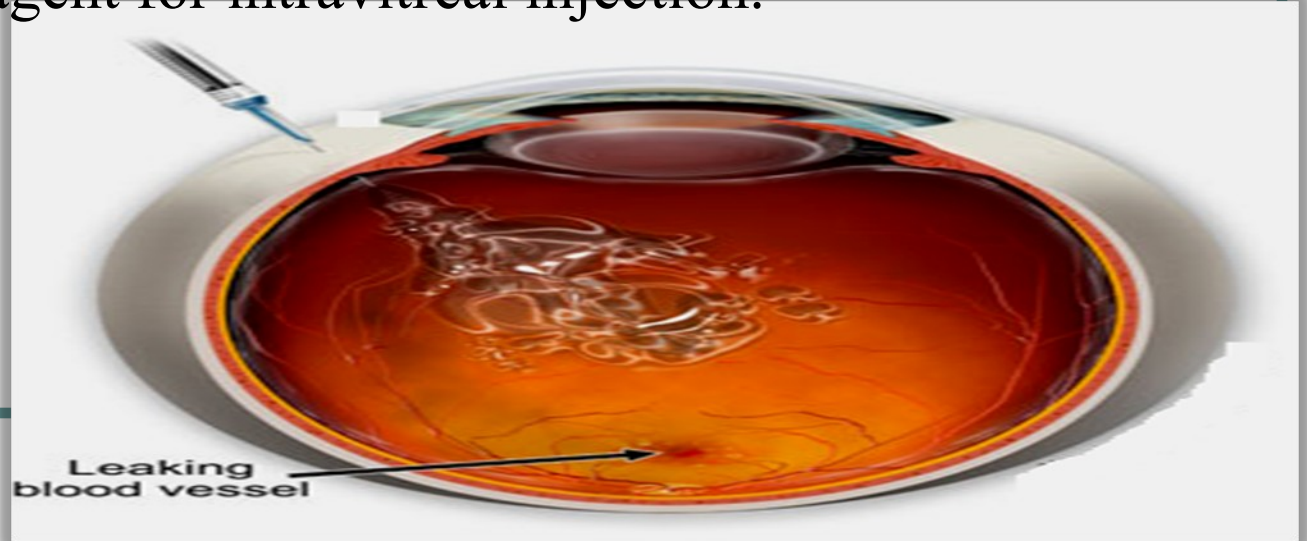


D. Intraocular Dosage Forms

2- Intraocular Injections

The ophthalmologist use available **parental dosage forms** to deliver **Anti-infective, corticosteroids, and anesthetic products** to achieve higher therapeutic concentrations intraocularly than can ordinarily Be achieved by topical or systemic administration.

FDA approved intraocular injection include miotics, viscoelastics and an antiviral agent for intravitreal injection.



D. Intraocular Dosage Forms

3- Intravitreal Implant

Intravitreal implant

An intravitreal sterile implant containing ganciclovir or antineoplastic agents is a **tablet** of ganciclovir with **Magnesium stearate** and is coated to retard release with **Polyvinyl alcohol** and **ethylene vinyl acetate polymers**.

Such that the device when surgically implanted in the Vitreous cavity release drug over a 5 to 8 month period .



E. Miscellaneous

1- Ocular iontophoresis:

- Iontophoresis is the process in which direct current drives ions into cells or tissues.
- If the drug molecules carry a positive charge, they are driven into the tissues at the anode; if negatively charged, at the cathode.
- Ocular iontophoresis offers a drug delivery system that is **fast, painless, safe**, and results in the delivery of a high concentration of the drug to a specific site.
- Iontophoresis is useful for the treatment of bacterial **keratitis**, Iontophoretic application of **antibiotics** may enhance their bactericidal activity and reduce the severity of disease

Iontophoresis

FIGURE 1

A unique dose controller and drug applicator work together to form the Visulex™ system.

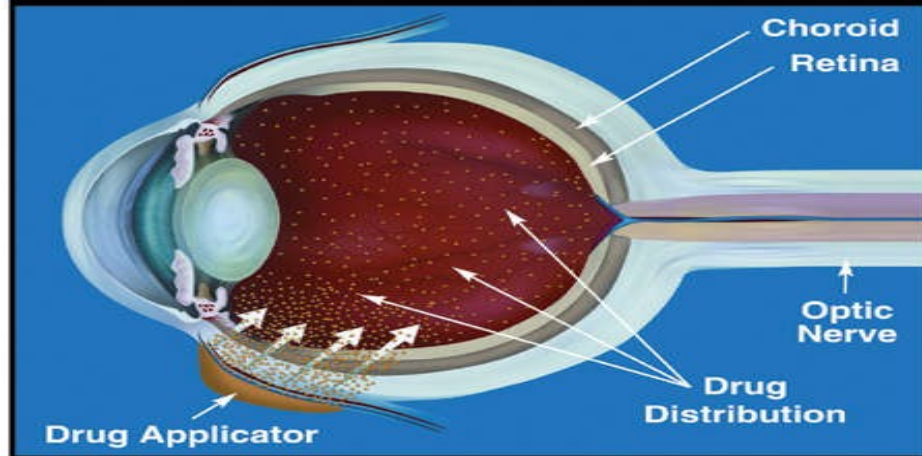
Visulex™ System



FIGURE 2

The Visulex™ applicator selectively transports drug ions into the vitreous.

Visulex™ Process



E. Miscellaneous

2- The vesicular delivery system

The Vesicular Delivery System



Liposomes

which are
phospholipid
based vesicles



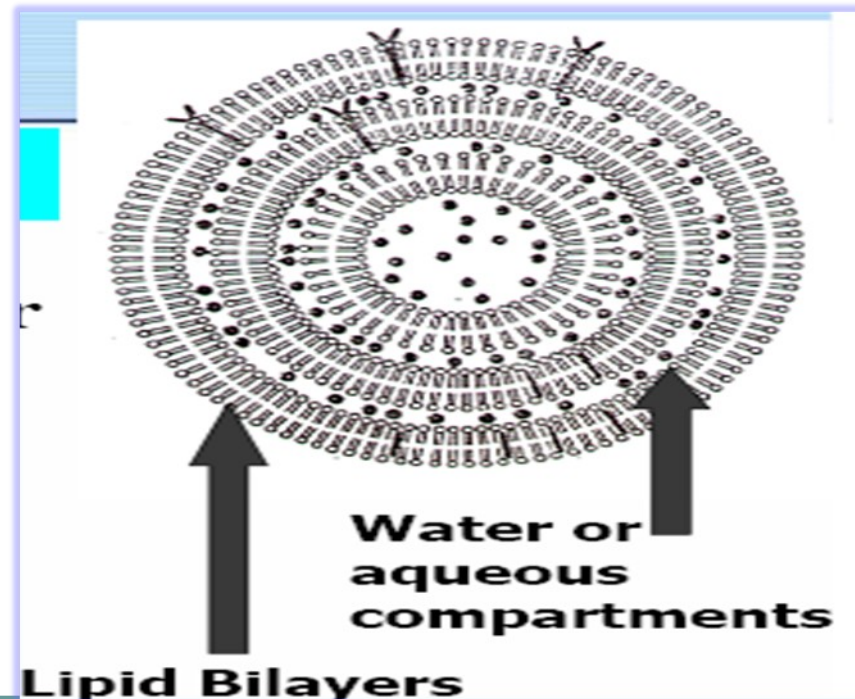
Niosomes

which are non-
ionic surfactant
based vesicles

Microspheres and nanoparticles

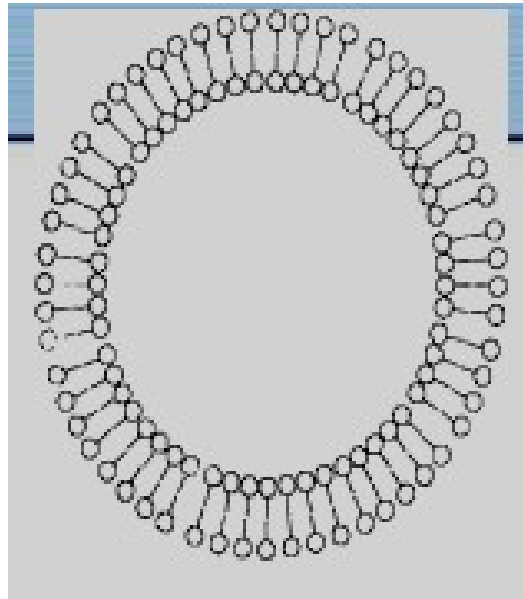
Liposomes

Liposomes are microscopic and submicroscopic vesicles consisting of one or more concentric spheres of **Lipid bilayers** separated by **Water or aqueous buffer** compartments.



Niosomes

They are **non-ionic surfactant** based vesicles , formed from the self assembly of non-ionic amphiphiles in in aqueous media resulting in closed **bilayer structures**



Advantages of Niosomes and liposomes

- Sustained release of active compounds.
- Protect drugs from degradation
- Biocompatible, biodegradable and non-immunogenic.
- can entrap both hydrophilic and lipophilic drugs
- The bilayer of can efficiently penetrate the cornea of of the eye.
- They have low toxicity because of their non-ionic nature

Contact Lenses & Care Solutions:

- **Types of contact lenses:**

1- Hard contact lenses.

2- Soft contact lenses.

3- Rigid gas permeable (RGP).



Contact Lenses & Care Solutions:

1- Hard contact lenses

- Made of rigid plastic resin **polymethylmethacrylate**
- Impermeable to oxygen and moisture

2- Soft contact lenses

- Made of hydrophilic transparent plastic, **hydroxyethylmethacrylate**
- Contain 30 – 80% water so are permeable to oxygen
- Have two types: daily wear and extended wear



Contact Lenses & Care Solutions:

3- Rigid gas permeable (RGP)

- Take the advantages of both soft and hard lenses, they are hydrophobic and oxygen permeable.

Advantages of hard contact lenses and RGP lenses:

- 1- strength durability
- 2- resistant to absorption of medications and environmental contaminants
- 3- visual acuity

Disadvantages:

- 1- require adjustment period of the wearer
- 2- more easily dislodged from the eye



Contact Lenses & Care Solutions:

- **Advantages of soft contact lenses:**

- 1- worn for longer periods
- 2- do not dislodge easily

Disadvantages:

- 1- have a shorter life span and the wearer must ensure that the lenses do not dry out



"soft" lens | "hard" lens

Care of contact lenses:

- **Products for soft contact lenses:**

Cleaners

- To remove lipid and protein debris

- **formulation:**

- 1- **viscolizing surface-active agent:** to enable gentle friction with fingertips

- 2- **antibacterial-fast acting:** benzalkonium chloride



Products for soft contact lenses:

- *Rinsing and storage solutions*
 - Facilitate lens hydration,
 - Inactivation of microbial contamination and prevent the lens from drying out



Products for soft contact lenses:

- *Rinsing and storage solutions:*
- **Formulation:**
- 0.9% NaCl (isotonic)
- Antibacterial- 3% hydrogen peroxide for 30 min followed by inactivation with sodium pyruvate.



Products for hard contact lenses:

- *Rinsing and storage solutions*

- For cleaning, microbial inactivation and hydration

Formulation:

- surface-active agent
- Antimicrobial:

(0.01% benzalkonium chloride + 0.1% sodium edetate)



Products for hard contact lenses:

Wetting solutions

- To achieve rapid wetting by the lachrymal fluid and promote comfort
- Facilitate insertion of the lens
- Provide lubrication



Products for hard contact lenses:

Buffering solutions :

- Hypromellose eye drops B.P.C:
- Buffered to pH 8.4 TO 8.6 with boric acid and borax
- These solutions better tolerated by eye as more alkaline or acid preparations causes fogging effect.

Evaluation tests

- Metal Particles

- This test is required only for ophthalmic ointments.
- The presence of metal particles will irritate the corneal or conjunctival surfaces of the eye.
- It is performed using 10 ointment tubes.
- The content from each tube is completely removed onto a clean 60 - mm - diameter **Petri dish** which possesses a flat bottom.

Metal particles :

- The lid is closed and the product is heated at 85 ° C for 2 h.
- Once the product is melted and distributed uniformly, it is cooled to room temperature.
- The lid is removed after solidification.
- The bottom surface is then viewed through an **optical microscope at 30× magnification**.

Metal particles :

- The viewing surface is illuminated using an external light source positioned at 45° on the top.
- The entire bottom surface of the ointment is examined, And the number of particles $50\ \mu\text{m}$ or above are counted using a calibrated eyepiece micrometer.
- The USP recommends that the number of such particles in 10 tubes should not exceed 50, with not more than 8 particles in any individual tube.

Metal particles :

- limits are not met, the test is repeated with an additional 20 tubes.
- In this case, the total number of particles in 30 tubes should not exceed 150, and not more than 3 tubes are allowed to contain more than 8 particles .

Leakage test :

- This test is mandatory for ophthalmic ointments, which evaluates the intactness of the ointment tube and its seal.
- Ten sealed containers are selected, and their exterior surfaces are cleaned.
- They are horizontally placed over **absorbent blotting paper** .
- Maintained at 60 ± 3 ° C for 8 h.

Leakage test :

- The test passes if leakage is not observed from any tube.
- If leakage is observed, the test is repeated with an additional 20 tubes.
- The test passes if not more than 1 tube shows leakage out of 30 tubes .

Sterility Tests :

- Ophthalmic semisolids should be free from anaerobic and aerobic bacteria and fungi.
- Sterility tests are therefore performed by the:
 1. Membrane filtration technique .
 2. Direct - inoculation techniques.

Sterility Tests

- In the **Membrane filtration method** :
- A solution of test product (1%) is prepared in isopropyl myristate and allowed to penetrate through **cellulose nitrate** filter with pore size less than **0.45 μ m**.
- If necessary, gradual suction or pressure is applied to aid filtration.

Sterility Tests :

- The membrane is then washed three times with 100 - mL quantities of sterile diluting and rinsing fluid and transferred aseptically into **fluid thioglycolate (FTG)** and **soybean – casein digest medium (SBCD)** .
- The membrane is finally incubated for 14 days.
- Growth on FTG medium indicates the presence of anaerobic and aerobic bacteria.

Sterility Tests :

- **Soybean casein digest** medium indicates fungi and aerobic bacteria
- Absence of any growth in both these media establishes the sterility of the product.

Sterility Tests

- In the **Direct - inoculation technique** :
- **1 part** of the product is diluted with **10 parts** of sterile diluting and rinsing fluid with the help of an emulsifying agent
- Incubated in **Fluid thioglycolate (FTG)** and **soybean – casein digest medium (SBCD)** media for 14 days .

Sterility Tests :

- In both techniques, the number of test articles is based on the batch size of the product.
- If the batch size is less than 200 the containers, either 5% of the containers or 2 containers (whichever is greater) are used.
- If the batch size is more than 200, 10 containers are used for sterility testing .

References

- Dispensing for pharmaceutical by Cooper and Gunn's
pg: 634-661
- Modern dispensing pharmacy : N K Jain pg: 13.3-14.9
- Text of pharmaceutical formulation : B.M Mithal
pg: 268-278