

# تفريغ تعقيم

محاضرة: Ophthalmic part 2

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لجان الرفعات





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

- **Disadvantage:**

Greasy nature → blurring of vision (bed time application).



# .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**.

→ لحفظ على الحرارة

من مكونات المكونات  
منها نسبة في بعض



## Examples :

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

## *B. Semisolid Dosage Forms:*

- *Ophthalmic gel:*
  - Aqueous semisolid dosage forms
  - Carbomer (gelling agent)

## 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.



# Packaging:

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

Filled tubes may be tested for leakers. → *Outside* بصور المواد من خارج *inside* ما يسمح بالتحقق من الداخل

The screw cap is made of polyethylene or polypropylene.

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



لازم تنظيف tube قبل الـ Packaging حتى لا يكون في Partical يسبب Contamination

# How to Use Eye Ointments and Gels Properly?



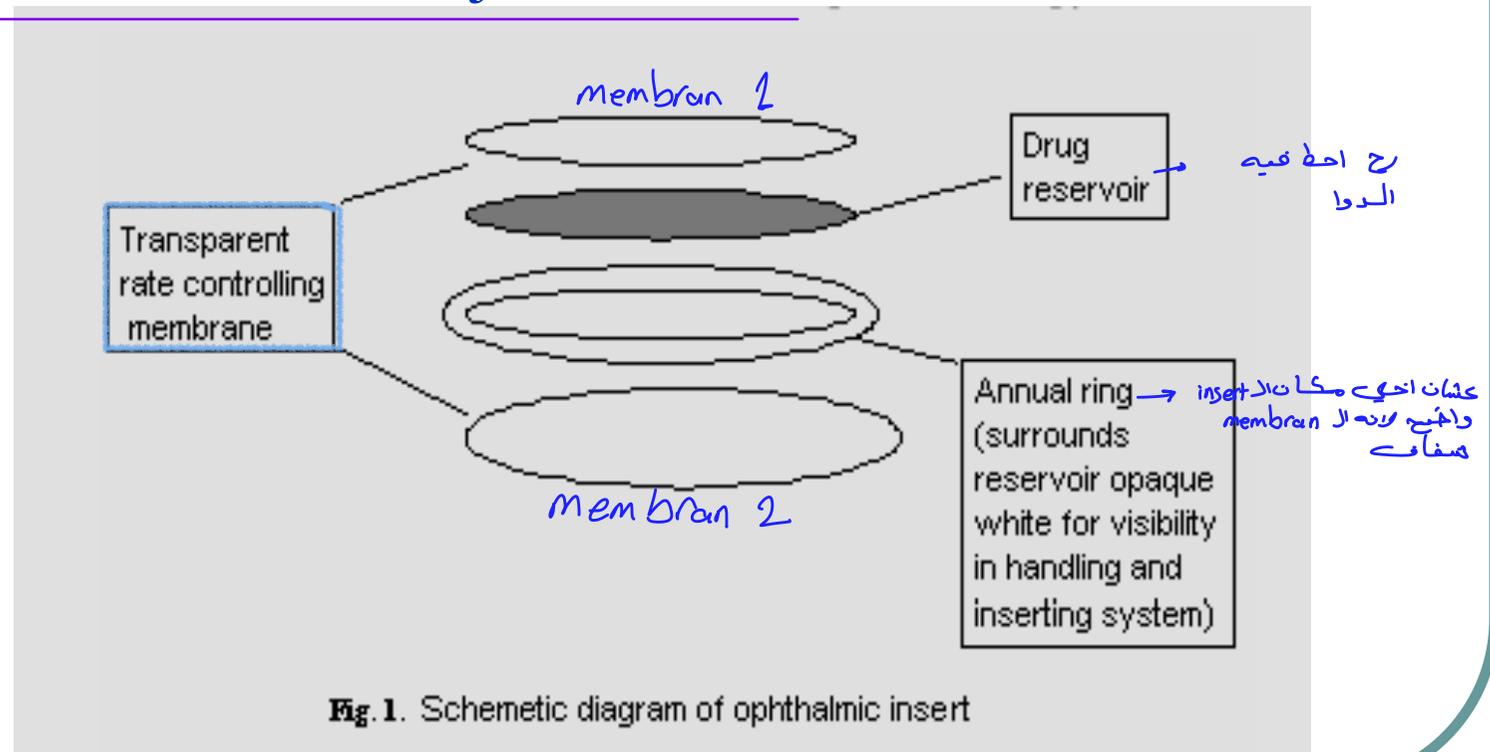
احتیاط سے استعمال کریں



## 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.



## *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. → *يعني بقدر العيب بموتنوع الـ prolonge*

● **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:

- ① **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.
- ② to obtain symptomatic relief with artificial tear solutions.

The insert is composed of 5 mg of Hydroxypropyl cellulose → ال Cellulose مع يحاطه  
in a rod-shaped form about 1.27 mm diameter by about 3.5 mm → ال الماء بالهوية لفترة منبحة  
long. → هيك عملت hydration



**Prep** Rinse the soft and flexible applicator with hot water. Shake off the excess. Pick up LACRISERT® (hydroxypropyl cellulose ophthalmic insert) by lightly touching it with the grooved tip of the applicator.

### 3 Simple Steps for Placement



#### Pocket

Gently grasp the outer corner of the lower eyelid between your thumb and index finger and pull out to create a "pocket".



#### Place

Place LACRISERT® by gently brushing it on the inside of the "pocket".



#### Pull up and over

Pull the lower lid up and over the LACRISERT®, then release. Allow LACRISERT® to settle comfortably in the "pocket".

## *D. Intraocular Dosage Forms*

- They are Ophthalmic products that introduced into the **interior structures** of the eye primarily during ocular surgery.
- Parenteral-type products
- **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**

زیر الـ Preservative! کی حکینا عنها فوقه  
انه مهتوج تدخل لانسجه العین الداخليه

## D. Intraocular Dosage Forms: 1- Irrigating Solutions



Used during surgery to maintain hydration, ocular volume, and clarity of the cornea. It also removes blood and cellular debris

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

It contains the five essential ions: **sodium, potassium, calcium, magnesium and chloride.**

It also contains oxidized glutathione, dextrose, and 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

الدكتورة حكة  
بالفيديو مشن مهم  
تحفظوا المكونات  
هم انفس الfunction

## *D. Intraocular Dosage Forms*

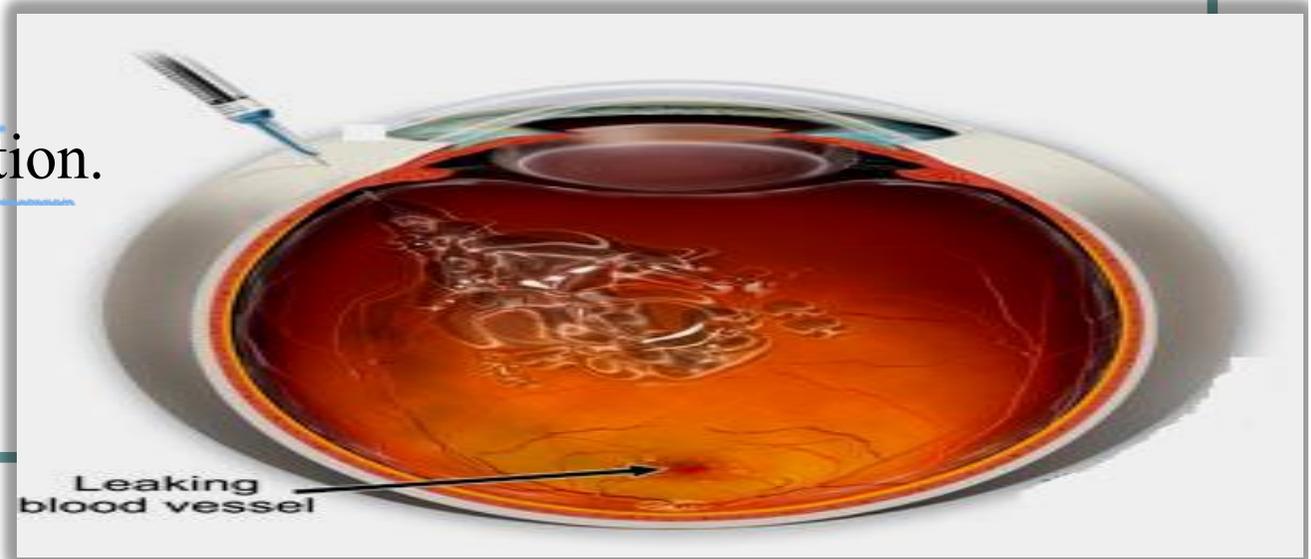
### *2- Intraocular Injections*

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 (e.g. sodium hyaluronate)

And

an antiviral agent  
for intravitreal injection.



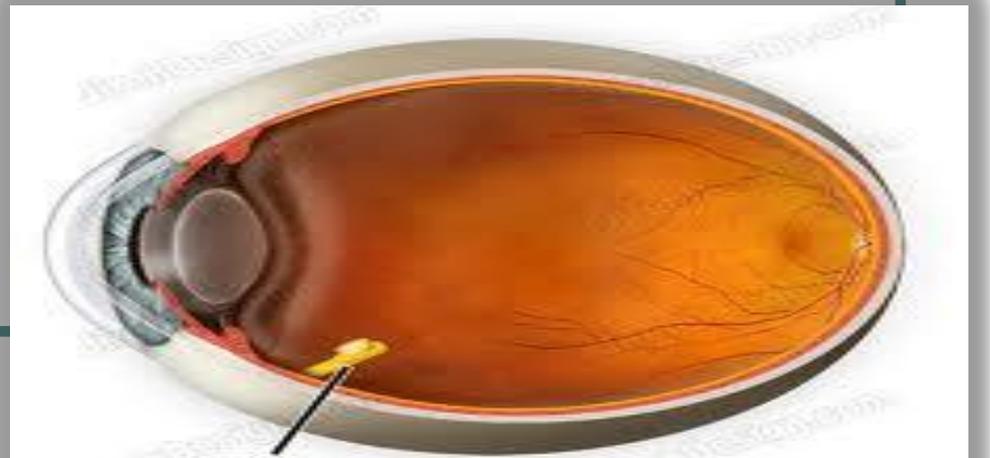
## D. Intraocular Dosage Forms

### 3- Intravitreal Implant → زراية

#### 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 → طرف اخرى

### 1- Ocular iontophoresis:

- Iontophoresis is the process in which direct current drives ions into cells or tissues.
- The solution is in contact with the cornea by means of an eye cup bearing an electrode
- 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.

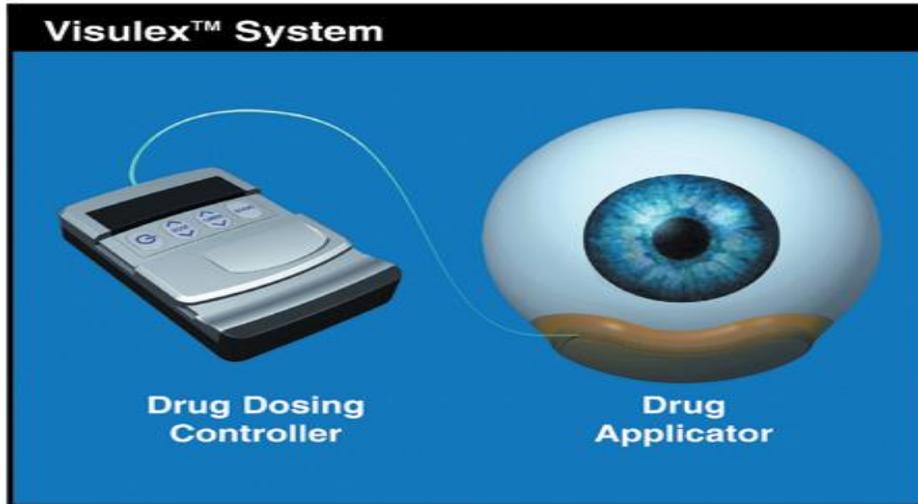
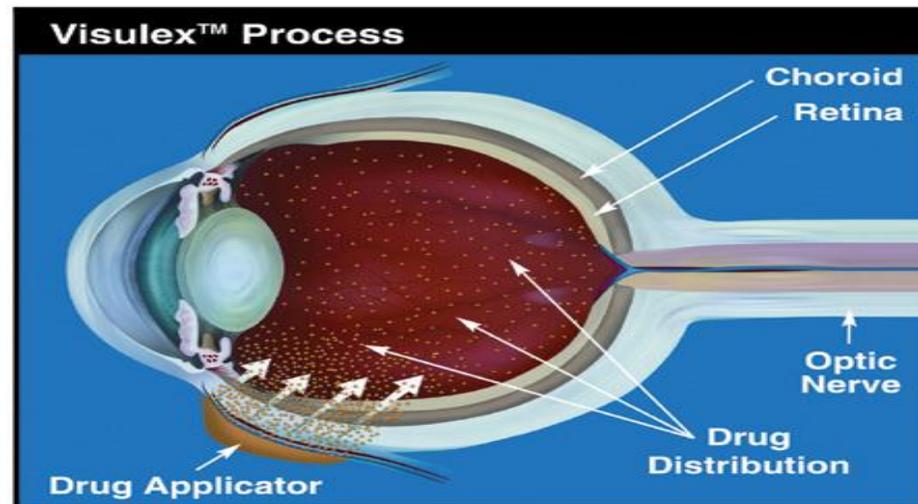


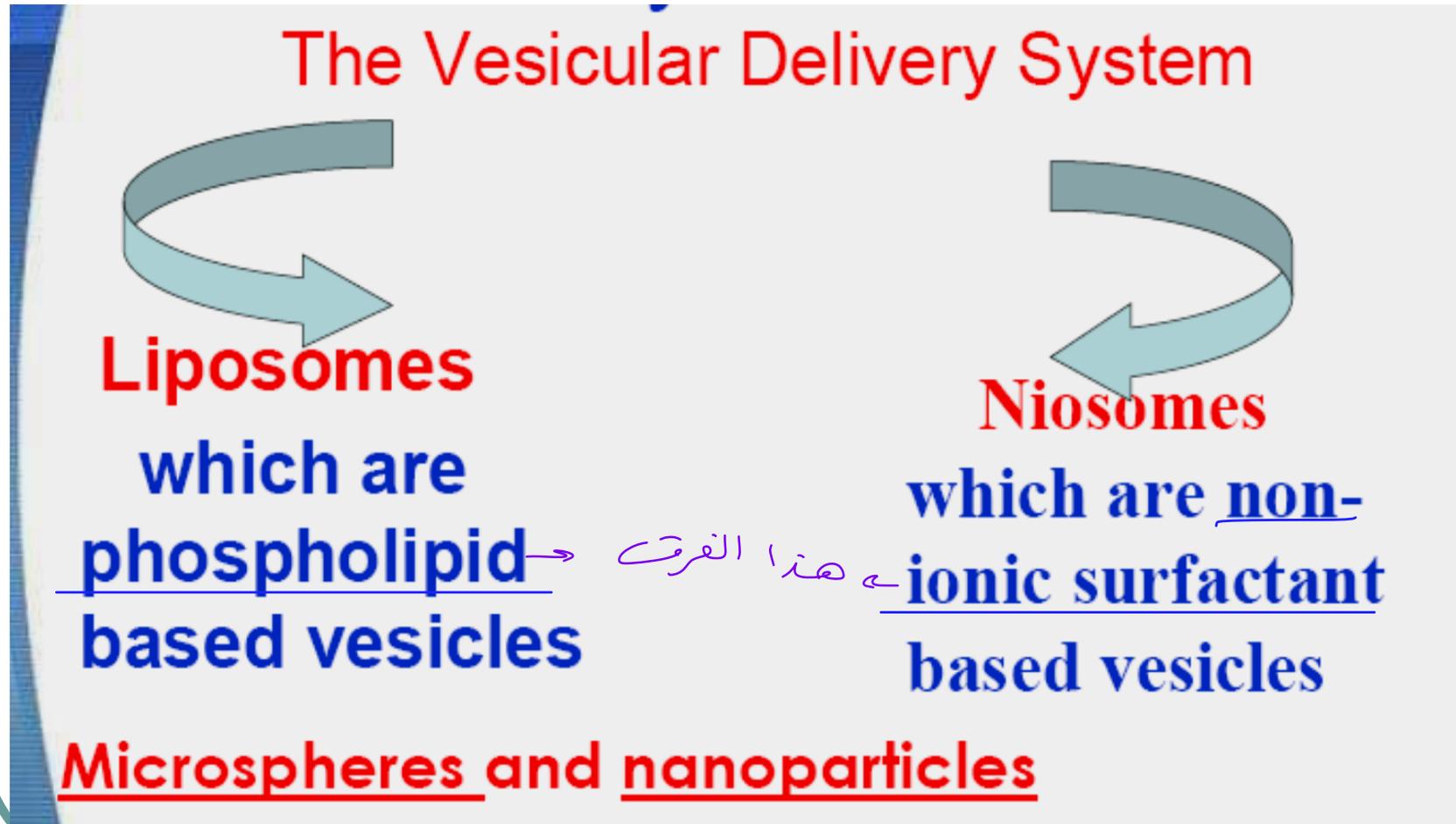
FIGURE 2

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



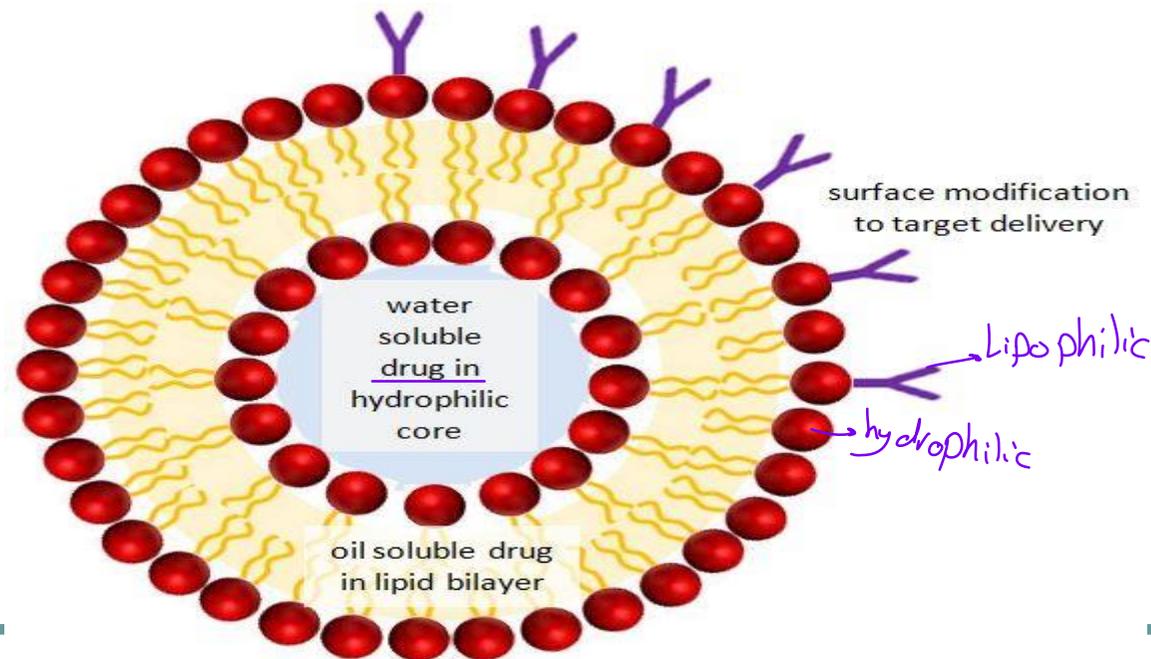
## *E. Miscellaneous*

### 2- The vesicular delivery system



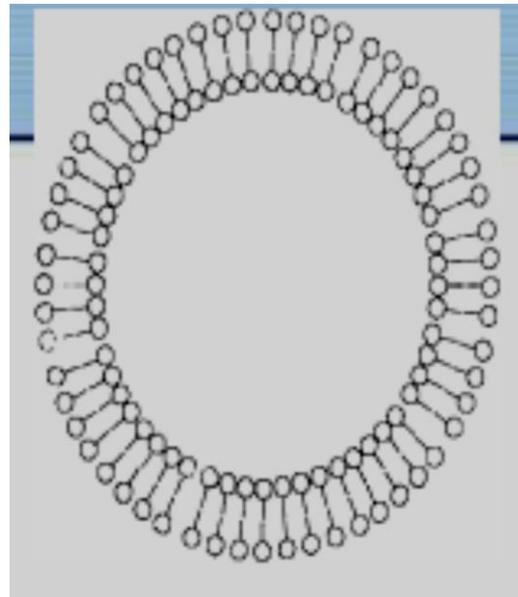
# Liposomes

Liposome's are microscopic and submicroscopic vesicles consists of one or more concentric sphere 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 surfactant in aqueous media resulting in closed **bilayer structures**





# OTC products for dry eyes

- Causes:

- Decreased tear production → *بسیب عضوی*
- Increased tear evaporation rate
- Abnormality in tear film that decreases its natural capacity to protect and lubricate the epithelial tissues

← ممکن ہوتے ہیں  
تینا مسئلہ

**Mucin** → natural lubricating component of the tears

# OTC products for dry eyes

- Products:

- Artificial tears
- Ocular lubricants
- Demulcents
- Emollients (petrolatum, mineral oil, lanolin is added to ointment to impart water miscibility)

Dosage forms: solutions, gels, ointments

# OTC products for dry eyes

- The products are the essential viscous vehicle component of therapeutic ophthalmic products

- Contain:

Water soluble polymers (hydroxypropyl methylcellulose, CMC, glycerin, PEG, Polysorbate 80, PVA, povidone)

- ✓ protect and lubricate of conjunctiva and cornea
- ✓ Thicken the tear film
- ✓ Decrease the rate of tear loss

# Contact Lenses & Care Solutions:

- **Medical devices**
- **Types of contact lenses (polymer type, lens characteristic):**
  - 1- Hard contact lenses.
  - 2- Soft contact lenses.
  - 3- Rigid gas permeable (RGP) contact lenses.



# 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

# Wetting solutions

- Lubricating and cushioning preparations designed to furnish the hydrophilic coating over the hydrophobic lens surface
- Include:
  - Viscosity imparting agent
  - Surfactant: it is more important for hard contact lenses to facilitate wetting of lens and spreading of tears
  - preservative

**equate**<sup>®</sup>

Quality  
Guaranteed

## Contact Lens Conditioning Solution

For Rigid Gas Permeable  
Contact Lenses

- Disinfects,  
cushions and wets

Sterile  
3.5 FL OZ (105 mL)

# Cleaning solutions

- Cleansers are based on surface activity, enzyme action, or abradant action (softer than the lens)
- Tablet or liquid
- To remove surface contaminants- lipids, proteins, organic salts
- Contain surfactant (nonionic or amphoteric)

# Cleaning solutions

- Daily and weekly cleansers
- Weekly cleansers may contain proteolytic enzymes like subtilisin or pancreatin or concentrated surfactants
- Daily cleansers use less aggressive surfactant (less toxic if carried over into the eyes) or may contain a nontoxic enzyme (SuperClens)

تركيز ال surfactant  
اقل من ال اسبوعي



# Disinfecting systems

→ Characteristic of soft lens  
Lens

- Sorption characteristic of hydrophilic lens → many preservatives are unsatisfactory
- Quaternary disinfectant covalently bonded to a relatively high MWt polymer

# Soaking or storage solutions

السائل الذي يري اعطه  
على العدسة لما يري  
استخدمها

- Storage, hydration and disinfecting of hard or RGP lenses
- Chlorhexidine
- Quaternary/polymer compound
- Enhanced by sodium edetate → Preservative capacity لا حسنة اد
- Rinse off lens before insertion

# Rewetting solutions or lubricating drops

- To rewet hard or RGP lenses
- To reinforce the wetting capacity of the normal tear film
- Mimics tear composition



viscosity imparting agent *فيها*



# Multipurpose solutions

بالتالي صالحة للحدسات  
تجمع اكثر من  
Purpos

- By combining the actions of two or more solutions
- Simplify the regimens, improve compliance
- For soft contact lenses: cleaning and disinfection
- For hard and RGP lens: cleaning, disinfection, wetting



# Evaluation tests

Ointment لاهمني

## • Metal Particles

حک انه اهم انوع يعرفوا انه  
لستخدمة عشان اشوف اذا في Metal Particle  
بال Ointment او لا .  
صفت التفاصيل مش كثير مهمة (عني د. سحر)

- 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  $85^{\circ}\text{C}$  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  $30\times$  magnification.**

رہتی رح  
نیزوفے

## 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 μm 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.
- Classical plotting paper method
- Ten sealed containers are selected, and their exterior surfaces are cleaned.
- They are horizontally placed over **absorbent blotting paper** .
- Maintained at  $60 \pm 3$  ° 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  $\mu$  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 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

- Remington: Essential of Pharmaceutics by Linda Felton: pg 541-563
- 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

لا تنسوا زيارتنا ايهم من دعائكم

