

## B. Semisolid Dosage Forms Ophthalmic ointment Ointments/Gels Anhydrous

اغلب ointment يكون عبارہ عن  
anhydrous شو يعني ... يعني اغلب الي فيه  
اشياء ما تحب الماء مثل  
petrolatum



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**.

ويكون استخدامه ليلا لانه ممكن يشوش الرؤيا اما كقطرات بقدر استخدمها  
باي وقت فش مشكله

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

لو بدني اوخذ دوا وكان عبارہ عن gel or ointment بدني اوخذ  
بعين الاعتبار اذا هاد sensitive for the moisture or not  
ف اذا كان اه رح اروح طبعا ointment لانه فش فيه ماء

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

بالنسبه لل drop ف contact time جدا قليل لانها بسرعه تختفي اما بالنسبه ointment فبتطول

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

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

حكينا مشكلتها انها تعمل تشويش  
بالؤيا لذلك يفضل وضعها عند النوم

- **Disadvantage:**

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



# Manufacturing Techniques:

Mineral oil and petrol

## Ophthalmic ointment:

اول اشى عن طريق heat وبعدين عن طريق filtered وهو ذائب

- 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.

بحطه ب jacket لانه يحافظ على الحرارة وطبعاً يكون تحت aseptic condition وبعدين اضيف active ingredient وتكون sterile

وبعدين اعمل mixing وبعده diffusion through the filter under aseptic في علبه المخصصه وهي كمان تكون معقمه



## Examples :

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

هون يحكي عن  
انواع  
ointment

## ***B. Semisolid Dosage Forms:***

- ***Ophthalmic gel:***

- Aqueous semisolid dosage forms
- Carbomer

يحتوي على نسبة ماء منيحه ويكون نستخدم معه  
carbomer هو 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.

معنى هاي انو لازم اتاكد انو فش اشني  
يدخل لداخل

The screw cap is made of polyethylene or polypropylene.

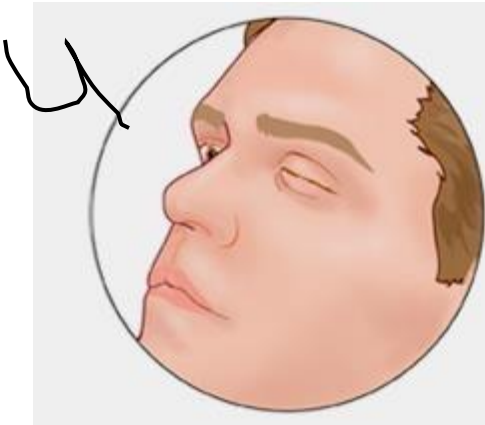
The tube can be a source of particles and must be cleaned carefully before sterilization (by autoclaving or ethylene oxide).

اذا يتحمل الحراره

اذا ما بتحمل الحراره



# How to Use Eye Ointments and Gels Properly?



# C. Solid Dosage Forms

## Ocular Inserts

زي العدسات تكون

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

هاد الي  
بحط فيه  
الدواء

Drug  
reservoir

Transparent  
rate controlling  
membrane

Annual ring  
(surrounds  
reservoir opaque  
white for visibility  
in handling and  
inserting system)

عندي 2 membrane وهن  
يعملو control for  
diffusion drug

وهاي الحلقة الهدف منها تعلمي  
drug حتى يكون واضح لانه الدواء يكون عديم  
اللون هون

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

عندي نوعين منهم soluble non soluble



في جزء منها رح يضل بعيني واطر اشيله  
بعد ما ينتهي مده العلاج

- **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.

نفس الي انشرحو على رسمه قبل سلايدين

- **The rate of drug diffusion is controlled by:**

- The polymer composition
- The membrane thickness
- The solubility of the drug

استخدم لعلاج glaucoma

الفقره هاي تحكي انو طول ما العدسه تحتوي  
على احد هدول المادتين عليهم هايالات بني ما  
رح احتاج اي دوا ثاني غير هالمده 7 ايام

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.**

خذفتكم هاد الاسايد من عندي لاني عارفه  
انكم ما رح تتطلعو عليه



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

## II.Soluble Ocular inserts:

هدول بعد ما يخلص مفعولهم يختفو من  
العين كيف يعني بنوبو

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

### *Types*

- a) **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.

هون ما نحتاج نشيلهم لانهم بعد بساعه يختفو لحالهم

## II.Soluble Ocular inserts:

هاد يعتبر ocular insert يستخدم لعلاج جفاف العين

**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.

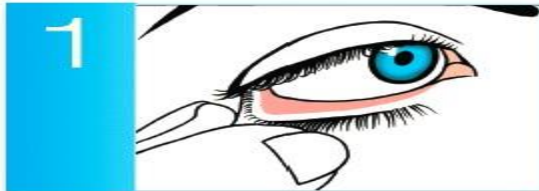
جكينا قبل انو القطرات تحتوي على بوليمر بس ممكن ما يكون فعال بالنسبه لهاد المريض لذلك نستخدم (الموضوع الي نحكي عنه) لانه يحتوي على سيليلوز ويحافظ على رطوبه العين فتره منيحه

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



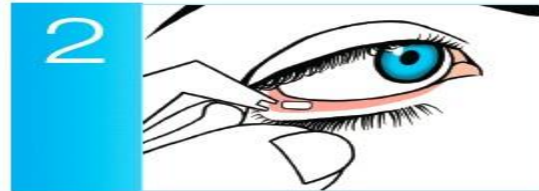
**Prep** Rinse the soft and flexible applicator with hot water. Shake off the excess. Pick up LACRISERT® (hydroxypropyl cellulose ophthalmic insert) by lightly touching it with the grooved tip of the applicator.

### 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*

هسا بدنا نحكي عن الاشكال الدوائيه الي تنحط داخل العين

- 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

ممکن مرکب استخدمه ك  
preservative ما ياتر على العين  
من برا بس من جوا ياتر واي منتج  
صيدلاني يكون مستخدم لداخل  
العين ممنوع يكون multiple  
dosage

## 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. مش للحفظ

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

لازم نعرف انو مهمم يكون iso-osmotic

# *D. Intraocular Dosage Forms*

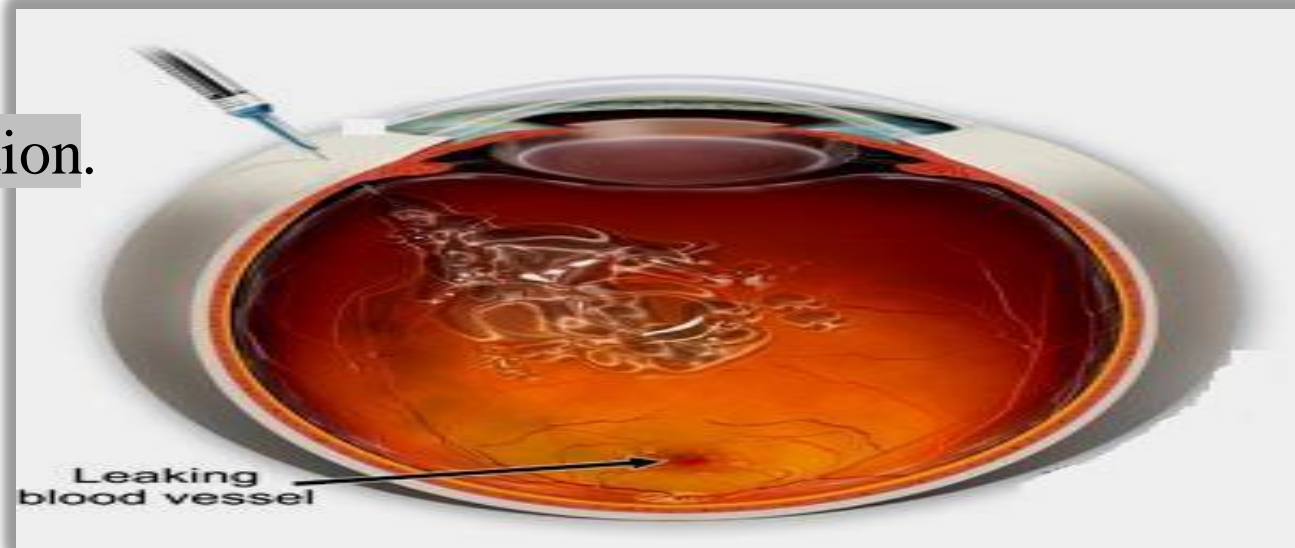
## *2- Intraocular Injections*

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

### 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 .

هي عبارة عن tablet مع  
الي عليهم هايلايت اصفر  
وعليها coated حتى يصير  
اطلاق لدواء ب كله مره  
وحده

يتم حقنها داخل  
vitreous cavity  
وهون يحكيلنا انو يضل  
الدوا يطلق داخل العين  
لمده 8 اشهر تقريبا



# E. Miscellaneous

هاي كمان طريقه عشان ازيد من  
ادخال الدواء الى العين يتم استخدام  
direct current

## 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.

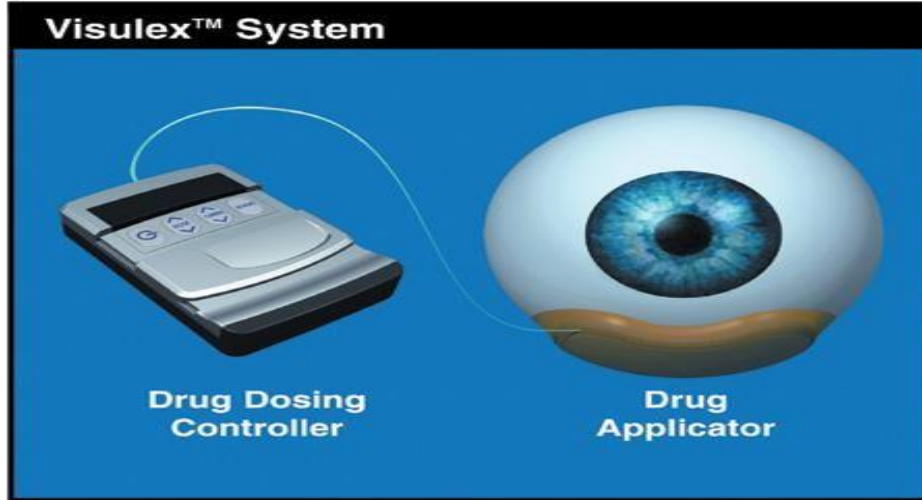
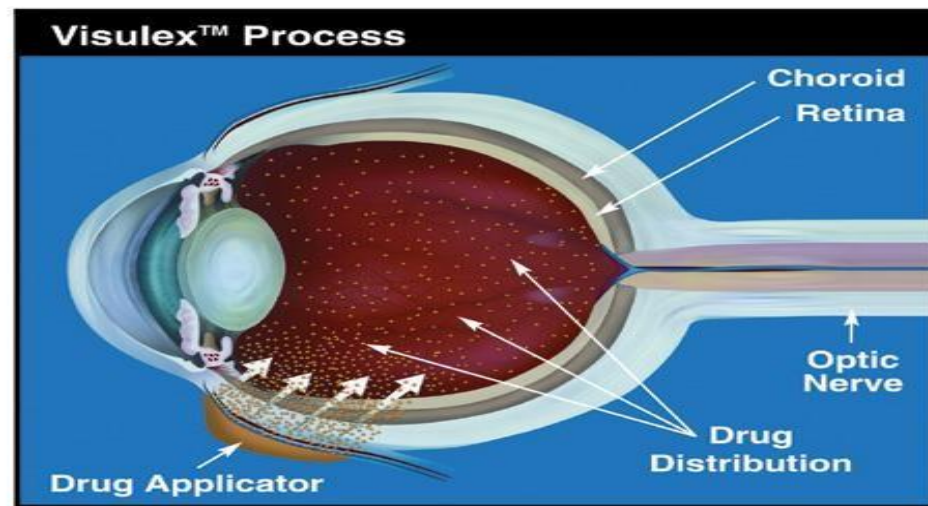


FIGURE 2

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

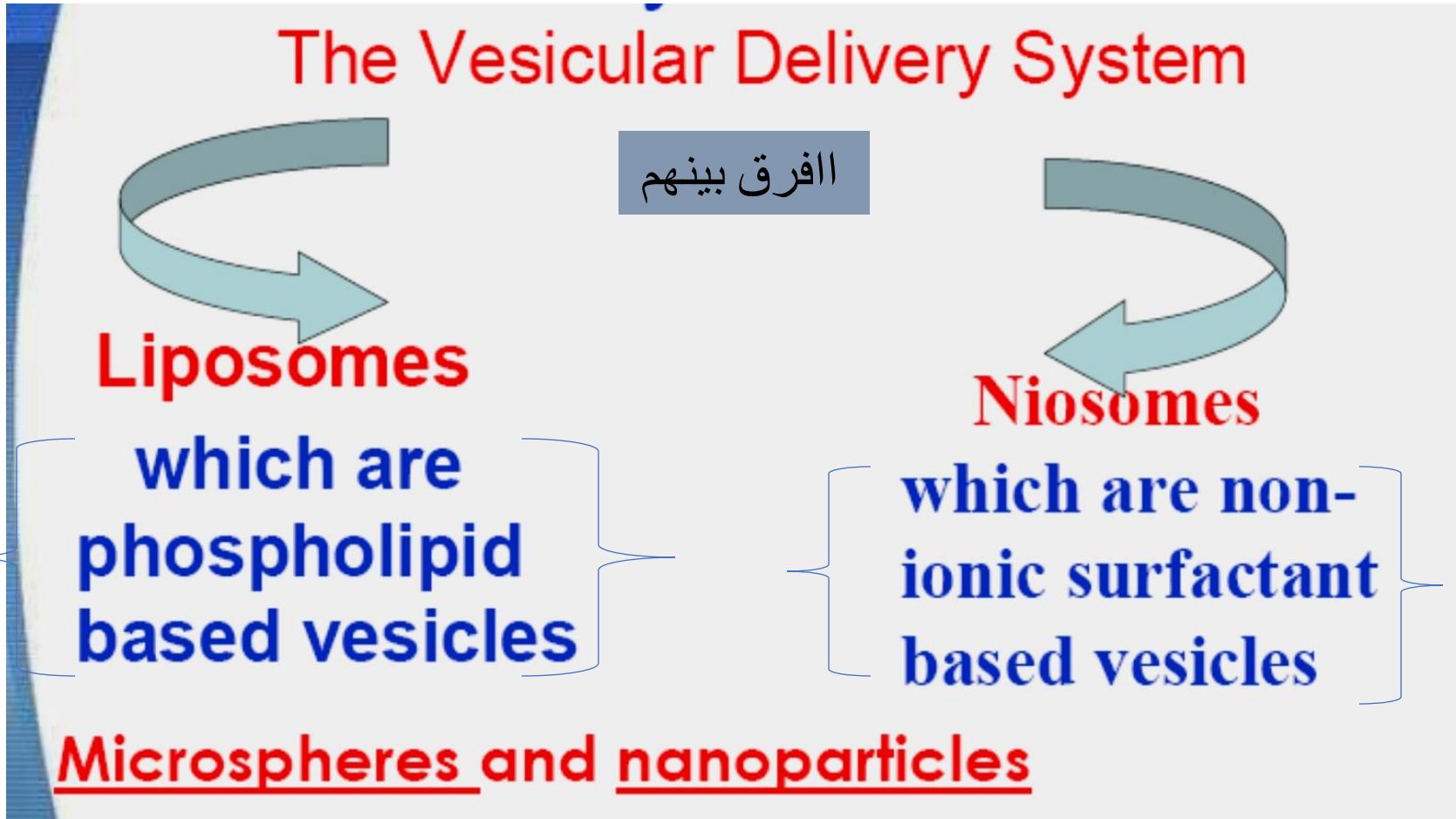


هاد  
يساعد على  
حركه  
الايونات  
وتخل لجوا

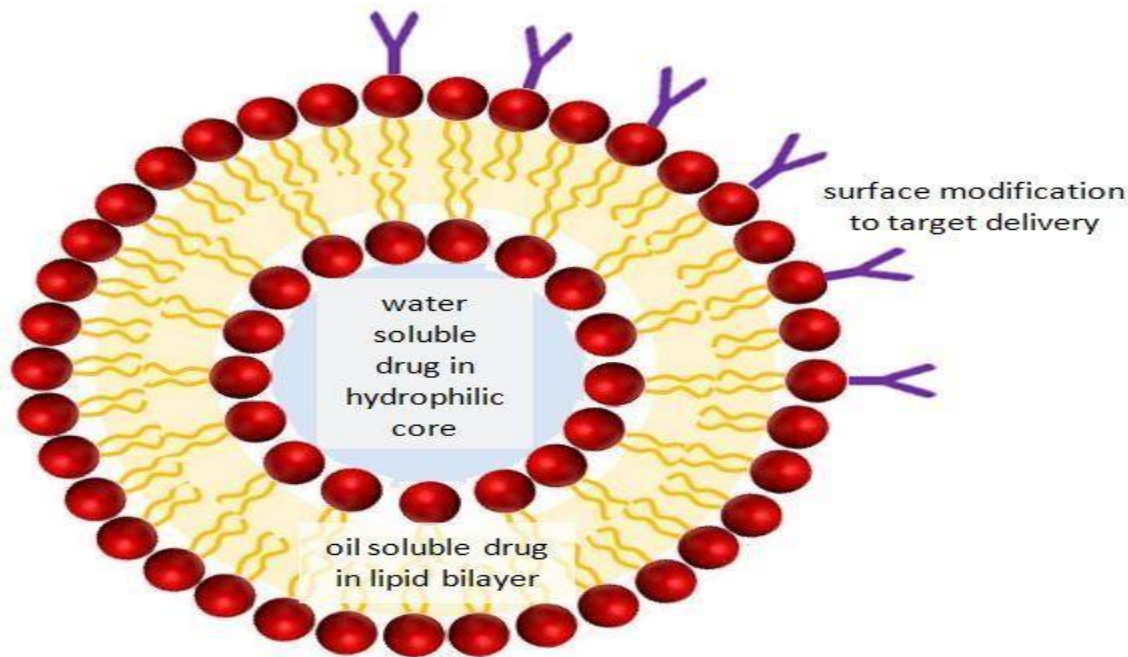


## *E. Miscellaneous*

### 2- The vesicular delivery system

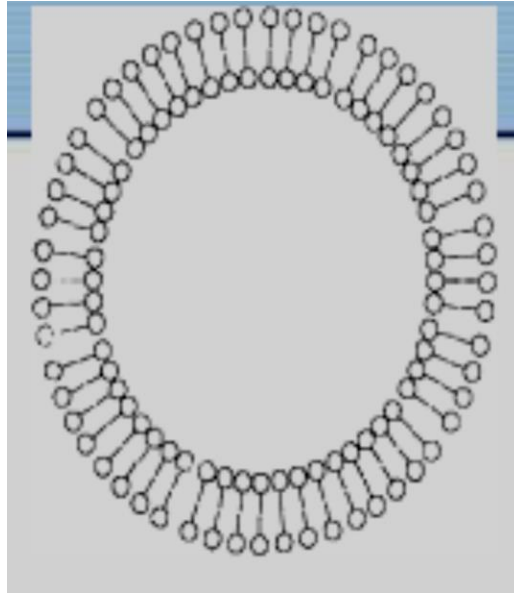


Liposome's are microscopic and submicroscopic vesicles consists of one or more concentric sphere of Lipid bilayers separated by Water or aqueous buffer compartments .



# 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**



# 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 can efficiently penetrate the cornea of of the eye.
- They have low toxicity because of their non-ionic nature

# OTC products for dry eyes

- Causes:

ممکن تصیر  
لاسیاب معینه

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

Mucin → natural lubricating component of the tears

ممکن یكون مشكله بتصنیع های

# OTC products for dry eyes

هاي الاشياء  
الي  
نستخدمهم  
لللاج

## ● Products:

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

هدول زي مبالابricant

**Dosage forms:** solutions, gels, ointments

# OTC products for dry eyes

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

- Contain:

هدول الاشياء الي استخدمهم جوا vehicle

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

- ✓ **protect and lubricate of conjunctiva and cornea**

لانه ممكن تكون مشكله ب tear

- ✓ **Thicken the tear film**

- ✓ **Decrease the rate of tear loss**

بقلل منه لاني بحط اشئ يكوون water soluble

# Contact Lenses & Care Solutions:

هدول يتسجلو لما يدخلو على البلد  
انهم medical device

- **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:

الي باللون الاصفر مش حفظ

متى ما حظيتها فالمنطقه الي محطوطه فيها  
ما رح يوصلها اوكسجين لهيك الها وقت  
معين وبعدين اشيلها

## 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



ممکن استخدمها ليوم  
فقط وفي منها لاكثر  
من يوم وتكون غالبيتها  
ماء

# 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 انو يكون الهم فتره معينه خلالها ما يخربو
- 2 resistant to absorption of medications and environmental contaminants متى ما حطيتاه اتوقع اني حميت المنطقه من ايملوثات
- 3 visual acuity

### *Disadvantages:*

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

ما بنفع البسهم لفترات طويله  
وممكن بسهوله يطلعو من العين



# Contact Lenses & Care Solutions:

- Advantages of soft contact lenses:

1- worn for longer periods

2- do not dislodge easily

بقدر البسها لفتترات  
طويله وما بتطلع من  
العين بسهولة

## Disadvantages:

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

مشكلتهم انو بسرعه  
يصير الهم جفاف

@post\_404

خلي بالك علي نفسك يا حب عشان في  
ارتفاع في درجات الحرارة والحاجات  
الكلوه بتسيح



"soft" lens | "hard" lens

# Wetting solutions

بالمختصر بنضيف طبقة  
hydrophobic فوق hydrophilic

- Lubricating and cushioning preparations designed to furnish the hydrophilic coating over the hydrophobic lens surface
- Include:
  - Viscosity imparting agent (polymer)
  - 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)

@post\_404

هه صدقت نفسك ولا ايه يا خوخو قوم  
ذاكر يا سقوطة وبلاش مرقعه

# 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)

حتى يعمل  
degradatio  
البروتينات

الهدف من عمليه cleaning

ليش فاش لانيونيك  
بيهيچ العين

# 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)

يكون تراكيذه  
قليله surfactant



# Disinfecting systems

تبع characteristic هاد يعتمد على عده شغلات منها  
العدسه  
adsorption ممكن عملهم disinfecting في كثير  
يعني عملهم adsorption عليها

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

حتى ما يصير adsorption على hydrophilic  
lens

## Soaking or storage solutions

هسا انا عندي عدسه وبطلت  
استعملها هل اتركها حتى تخرب  
لاا

لذلك في محاليل مصممه  
لحفظها ومن خصائصهم

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

حتى يحسن من  
preservative capacity

# Rewetting solutions or lubricating drops

الهدف منها

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

مثلا اذا عيونكم وجعتكم لا  
سمح الله وانتم بتحطو  
هاي العدسات بحط عليها  
من هاي القطرات حتى  
ازيد ترطيب العين





# Multipurpose solutions

- 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

بس الي عليه مربع ومكتوب فيه او هايلاط  
لازم نعرفه باقي التفاصيل الدكتور ه حكت  
مش مهمه

هاد بهمني ل  
ointment ممنوع  
يكون في metal لانه  
irritant in عمل  
corneal

## • Metal Particles

لو نفتح الفارماكوبيا رح نلافي  
فيها فصل كامل يشرع عن كل  
اشي يخص العيون

- 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.

بجيب 2 ointment tube و بفضيهم ب petri dish و بقطهم بدرجه  
حراه 85 يعني حتى بذوب وبعدين اعملهم cooling in room  
temperature و بستنى يصير solidification

# 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 :

حكت الدكتو ره المطلوب تكون  
انو عارفين فش metal  
ointment داخل 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 :

طبعاً نسمة وجوده تكون limits  
ف اذا كانت زيها تمام اذا لا يكون  
الشغل غلط

- 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.

بجيب plotting paper  
وبجيب 10 seal container يكونو مسكرا صح وبنضف السطح تبعهم وبحط  
container على blotting وهاي كيف فاين المطبخ الي يمتصل الزيت منيح وبحطه  
على درجه حراره 60 لمدة 8 ساعات

# Leakage test :

إذا طلع زيت وامتصته  
الورقه هاد يكون sing of  
leakage

- 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

الي عليهم اكس  
حكت ما رح  
تدخل  
بتفاصيلهم

- 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 :

sterility of لازم اتأكد من  
ophthalmic قبل ما يزل  
على السوق

- 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

وَأَنْ لَيْسَ لِلْإِنْسَانِ إِلَّا مَا سَعَى

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وهيك نقدر نحكي الحمد لله خلصنا تفرغ ثاني اطول تشابتر  
ربنا يوفقكم وينور دربكم وتجييو علامات عاليه  
ادعولنا 