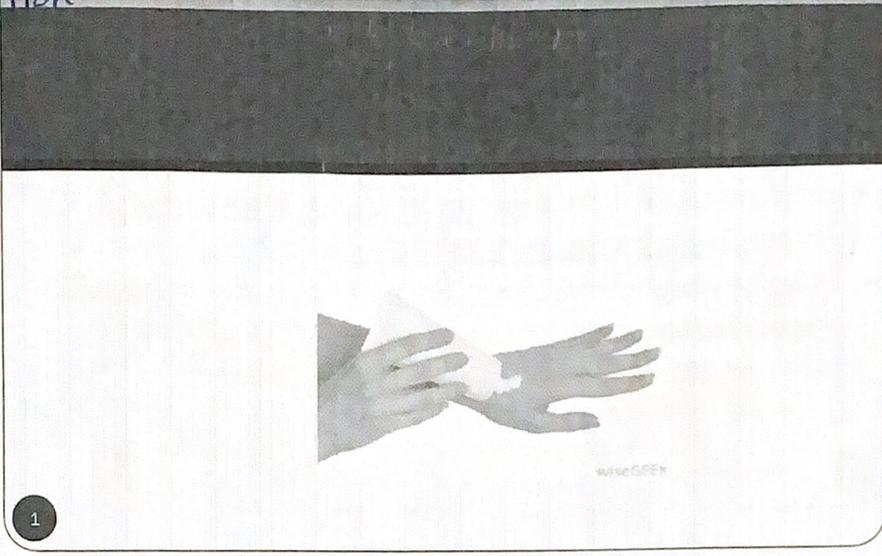


Product that is related to the skin application

# ← Dermatological Formulations: Ointments Creams and Pastes



1

## Dermatological Formulations



← كذا على الجلد

- They are also termed "**semisolids**" because they appear to be solid but still have fluid properties.
- Ointments, creams, pastes and gels are semisolid dosage forms intended for **topical application**.

Topical ←

- They may be applied to the skin, placed on the surface of the eye, or used nasally, vaginally, or rectally.
- Topical applications can be designed for either local effects or systemic absorption

الهدف منه يوصل للدواء ويوصل لمكان عبر ال (Skin)



2

• A **topical dermatological product** is designed to deliver drug into the skin in treating dermal disorders, with the skin as the target organ.

← رقع وجبر الجلد

• A **transdermal** product is designed to deliver drugs through the skin (percutaneous absorption) to the general circulation for systemic effects

← قد يدخل في جداراً

→ (مبنية على ال Emulsion)

• Pharmaceutical **creams** are **semisolid preparations** containing **one or more medicinal agents dissolved or dispersed** in either a **w/o emulsion** or an **o/w emulsion**

← سهل نشرها على الجلد وغسلها

• Many patients and physicians prefer creams to ointments (because they are easier to spread and remove.)

زيتي مائتي

← في الصيدليات رقع

• Pharmaceutical manufacturers frequently manufacture topical preparations of a drug in both cream and ointment bases to satisfy the preference of the patient and physician.

← نلاحظ الدواء نفسه

موجود Cream

+ Ointment

لإرضاء الطرفين

(المرضى والصيد)

3 Dr. Isra Dmour

## Purposes of dermatological formulations:

1. To protect the skin or mucous membranes from **chemical or physical irritants** in the environment thus permit the skin to (rejuvenate and heal)

← مطري

→ (يعمل طبقة عازلة) يتجدد ويلتئم

2. To provide **emollient** (skin softening) and **occlusive effect**

3. To provide a topical vehicle for medications for **local** (anti-infective, anti-pruritic, astringent, <sup>واقعي</sup> keratolytic) or **transdermal/systemic effect** (e.g. nitroglycerin)

→ مقشر

← لتخفيف الحكة بسوية كبيرة لمنع الحطبات

4

## Structure of the skin

- The skin is the **largest and heaviest organ** in the body and accounts for **about 17% of a person's weight**.
- Its major function is to **protect the underlying organ systems** from **trauma**, temperature, humidity, harmful penetrations, moisture, radiation, and microorganisms.
- It is composed of **three layers** of stratified tissue: **epidermis**, **dermis**, and **subcutaneous tissue**. (SC)
- The **thickness of the skin** is 3 - 5 millimeters. The thickness of the skin varies with the different parts of the body. The **thickest parts of the skin** are the **palms and soles** and the **thinnest parts** are the **eyelids and genitals**.

ضربة عينه (مضوض)

Stratum Corneum ← وبقا لهم ال

يمكن رؤية اضرار للدواء من خلالهم

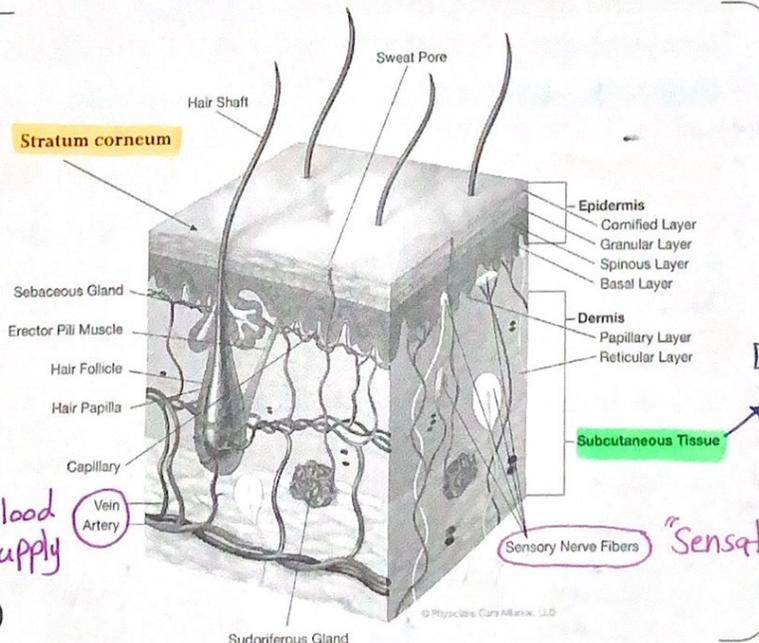
5

Within the structure of the skin are several **skin appendages**: hair follicles, sebaceous glands, sweat glands, and nails.

أظافر غدد عرقية غدد دهنية وصلات شعر

ملفات الجلد

5



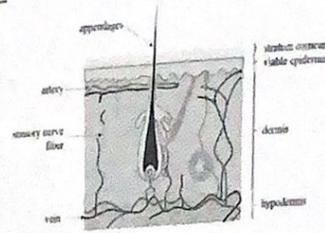
أول طبقة بالجلد وهي من أصعب الطبقات التي يمكن اختراقها الدواء وتعتبر طبقة عازلة للحماية

لما نطحن لأية لانتا توصل إليها عشان فيها vein + arteries.

6

6

## Local and systemic effects of Dermatological Formulations:



حاجز

- It is the stratum corneum that is the barrier to drug penetration through the skin.
- The stratum corneum is approximately 10 microns thick. It can swell to approximately three times its original thickness and absorb about five times its weight in water.
- When the stratum corneum hydrates, it becomes more permeable. Therefore, occlusive dressings are often used to hydrate the stratum corneum and increase the penetration of certain drugs.

عشان أزيد قابلية  
الاختراق فيها  
بعد hydration  
تبيس  
more permeable.

ويمكن عشان أزيد الامتصاص أعطى الجلد فيضا فقط  
على الرطوبة أكثر وتزيد الاختراق.



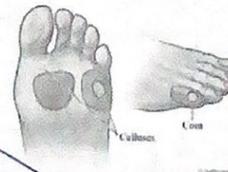
7

## Local and systemic effects of Dermatological Formulations:

الجلد يتقشر  
تزيد الاختراق  
أكثر

- Dermatoses (any skin disease) such as eczema and psoriasis (have disrupted SC) can also increase the absorption of some drugs.
- Dermatological formulations produce a local drug effect either on or in the skin.
- Besides the specific therapeutic action of incorporated active drugs, the formulations also serve as protectants, lubricants, emollients, or drying agents.
- Examples of treatments using dermatological formulations include

- minor skin infections, itching, الحكة
- burns, طلع الحفاضات. diaper rash,
- insect stings and bites, athlete's foot,
- corns, calluses, warts, dandruff,
- acne, psoriasis, and eczema.



رطب  
رطب رطبي (Humectant)

التهاب وكثير  
حروق  
لسعات/عضات  
مسامير اللحم  
كعب الشبان

8

تآكل  
الجلد  
مشرقة

البهق والأكزيما

التهابات  
وفطريات  
للرياضيين

8

## Local and systemic effects of Dermatological Formulations:



مثل لصقات  
النيكوتين  
تأثيرها في الدماع  
(بصيرة عن الجلد)

- Some dermatological formulations are intended to **systemically** deliver a drug.
- The formulation is placed on the skin, and the drug penetrates the epidermis into the dermis and subcutaneous tissues, where it is absorbed into the systemic circulation
- Some dermatological formulations provide continual **percutaneous absorption** (i.e. **transdermal patch**)
- Percutaneous (through the skin) absorption** is the result of three competing processes:
  - the potential of the drug to cross the **stratum corneum**
  - the potential of the drug to leave the formulation
  - the influence of the formulation on the stratum corneum.

dermis ← كذا ما يدخل  
Blood Supply ← عناء  
Systemic re-2 absorption.

(diffusion of the drug) from formula firstly

9

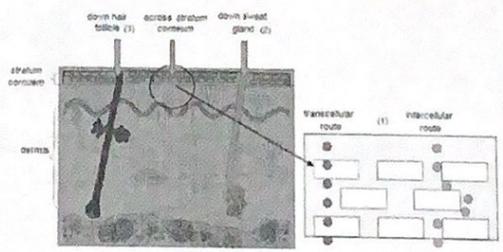
## Transdermal (من سطح الجلد)

### Percutaneous absorption

area ← كلما كانت الـ  
التي رطب عليها الدواء  
أكبر يزيد الامتصاص

- More drug is absorbed when the formulation is applied to a larger surface area
- Formulations or dressing that **increase hydration** of the skin generally **enhance percutaneous absorption** (more hydration, more absorption)
- The greater the amount of **rubbing** the formulation, the greater is the absorption (تزيد الامتصاص → تنشيط الدورة الدموية → توليد الحرارة)
- The **longer** the formulation remains in contact with the skin, the greater is the absorption

Longer time → So more absorption.



10

## Percutaneous absorption:

- The amount of drug that can be absorbed is about 2mg/day
- Thus:

### 1. **percutaneous enhancers** are used:

- Improve the solubility of active drug in the stratum corneum
- Facilitate the drug's diffusion into the systemic circulation

(DMSO, Urea, Triethanolamide, Dimethyl formamide) → Penetration enhancer

### 2. **Mechanical methods:** Force

1- **Phonophoresis** uses **ultrasonic vibrations** to increase the absorption of drugs such as lidocaine, tetracycline into and through the skin

2- **Iontophoresis** uses electrical field to aid in the transportation of local anesthetic and analgesic, peptides and proteins

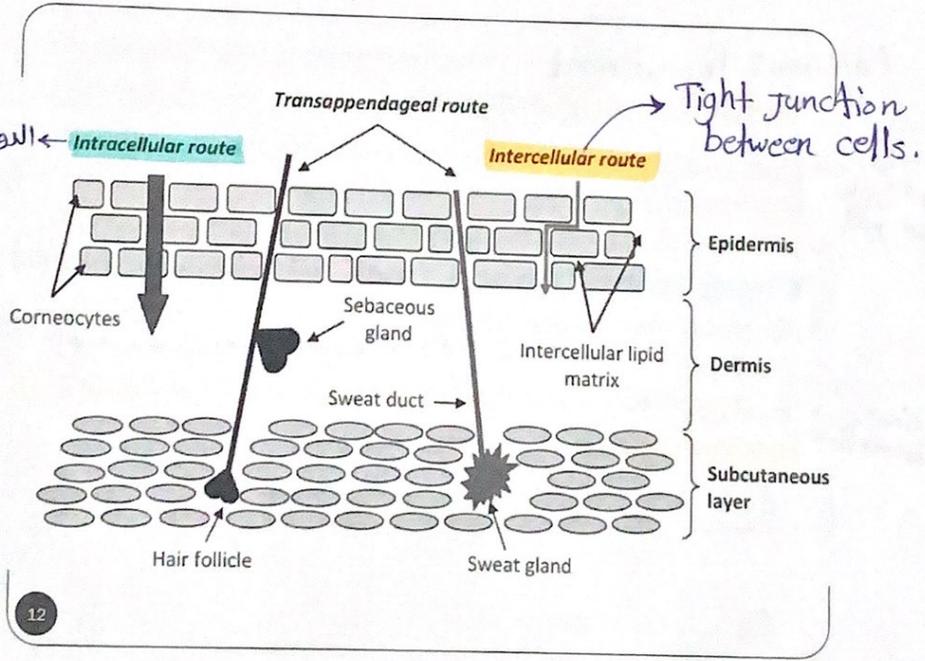
① توضیح نقطه 1  
السكرتیک بواسطة  
الأمواج الصوتية  
(تعرض الجلد لتردد  
محسوس من الأمواج  
فقط ال junction  
بين الخلا وبين  
الأنسجة.  
transient →

توضیح نقطه 2: النوعان يكونان كنه  
وسكرتیک نوع opposite charge

11

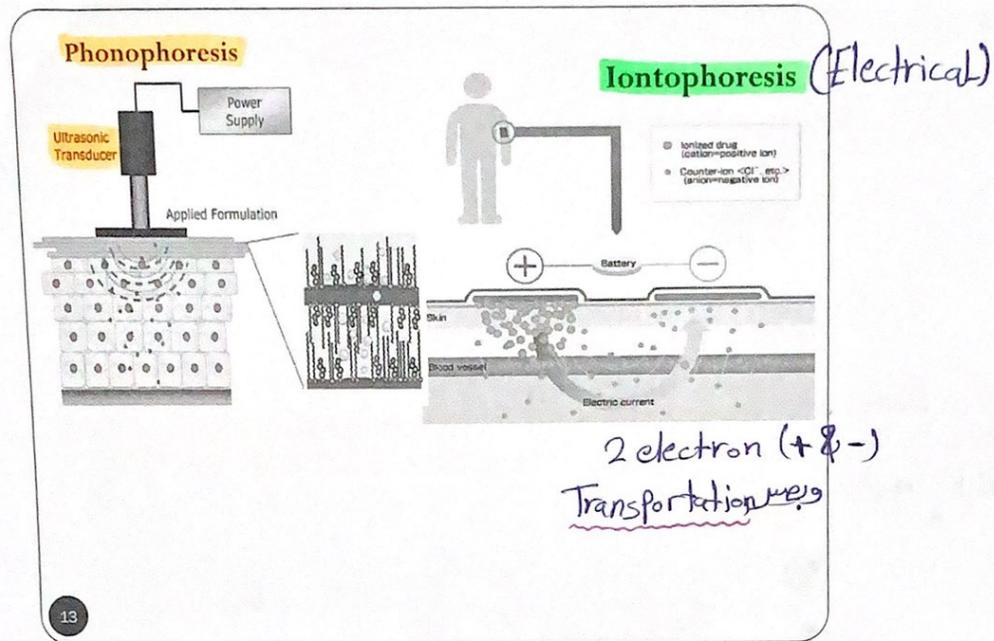
11

البلازما من ال  
Phospholipid  
membrane



12

12



13

Ointments : المرهم



- Ointments are **semisolid preparations intended for external application** to the **skin** or (**mucous membranes**). → Nasal or ophthalmic
- Traditionally the term **ointment** has been used for
  - (i) the general class name for **all external-use semisolids** and
  - (ii) the subclass, **oleaginous semisolids**. → زيته
- USP 31 Chapter (1151) defines ointments very generally as "semisolid preparations intended for external application to the skin or mucous membranes".
- Ointments may be **medicated** or **Unmedicated** ointments
- **Unmedicated** ointments are used for the physical effects they provide as **protectants**, **emollients**, or **lubricants**.
- **Ointment bases**, as described, may be used for their physical effects or **as vehicles** for medicated ointments.

تعريف USP  
 التعريف العام

المادة الرئيسية  
 Ointment بال  
 ووع يتم إدخال  
 الأدوية فيه.

14

## Ointments

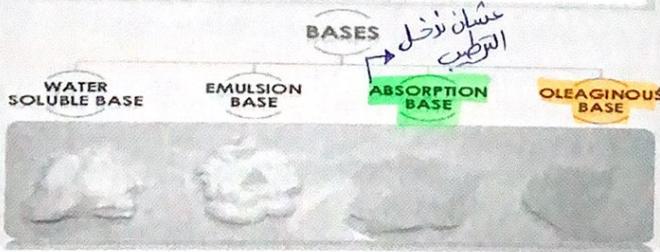
- However, pharmaceutical manufacturers use the word *ointment* more specifically to indicate that a drug is incorporated into an oleaginous ointment base; for example, the name Hydrocortisone Ointment means that hydrocortisone is incorporated into an oil-type semisolid base.
- Thus, the term *semisolid* would be used for naming the general class, and the term *ointment* would be redefined more narrowly as "a viscous oleaginous or polymeric semisolid dosage form", which is consistent with current usage by the pharmaceutical industry

يمكن تلاقى مرهم  
وما يكون دهنى  
وطريقته مثل الكريم

15

15

## CLASSIFICATION OF BASES



عشان تدخل  
التصنيف

مبتدئ على  
الفار ليني  
وليسو بالمرهم  
من عندها

16

16

4/17/2022

عندما نترك من العصار  
إلى العنق تزداد كمية الماء  
(aqueous solution)

\*Surfactant stability important  
for stability of emulsion  
4/17/2022

مستحلب  
emulsifying agent

الجدول  
حفظ

لا تكتسب  
HLB كلما قلت  
تكون أقرب إليها  
تطغى (w/o)  
(hydrophobic)  
ولها تزيدها تكون  
Hydrophilic  
(o/w)  
أقرب إلى hydrophobic  
تبرادة الماء سهل  
الاستنشاق  
قابلية الغسل بالماء  
يكون استعمالها بحت  
(water only)

	Oleaginous Ointment Bases	Absorption Ointment Bases	Water/Oil Emulsion Ointment Bases This is correctly classified as cream	Oil/Water Emulsion Ointment Bases This is correctly classified as cream	Water-miscible Ointment Bases More correctly called gels
Composition	oleaginous compounds	oleaginous base + w/o surfactant	oleaginous base + water (< 45% w/w) + w/o surfactant (HLB ≤ 8)	oleaginous base + water (> 45% w/w) + o/w surfactant (HLB ≥ 9)	Polyethylene Glycols (PEGs)
Water Content	anhydrous	anhydrous	hydrous	hydrous	anhydrous, hydrous, hydrophilic
Affinity for Water	hydrophobic	hydrophilic	hydrophilic	hydrophilic	hydrophilic
Spreadability	difficult	difficult	moderate to easy	easy	moderate to easy
Washability	nonwashable	nonwashable	non- or poorly washable	washable	washable
Stability	oils poor; hydrocarbon s (better)	oils poor; hydrocarbon s (better)	unstable, especially alkali soaps and natural colloids Because Present of more oil.	unstable, especially alkali soaps and natural colloids; (nonionics better)	stable

OH group  
PEG فقط  
PEG+water  
تغير على وجود الماء  
والسائل للPEG  
كلما زاد السائل يكون  
more liquid (easy)

السبب  
stable on PH  
alkali + acid  
وغيره

	Oleaginous Ointment Bases	Absorption Ointment Bases	Water/Oil Emulsion Ointment Bases This is correctly classified as cream	Oil/Water Emulsion Ointment Bases This is correctly classified as cream	Water-miscible Ointment Bases More correctly called gels
Drug Incorporation Potential	solids or oils (oil solubles only)	solids, oils, and aqueous solutions (small amounts)	solids, oils, and aqueous solutions (small amounts)	solid and aqueous solutions (small amounts)	solid and aqueous solutions
Drug Release Potential*	poor	poor, but > oleaginous	fair to good	fair to good	good
Occlusiveness	yes	yes	sometimes	no	no
Uses	protectants, emollients (+/-), vehicles for hydrolyzable drugs	protectants, emollients (+/-), vehicles for aqueous solutions, solids, and non-hydrolyzable drugs	emollients, cleansing creams, vehicles for solid, liquid, or non-hydrolyzable drugs	emollients, vehicles for solid, liquid, or non-hydrolyzable drugs	drug vehicles
Examples	White Petrolatum, White Ointment	Hydrophilic Petrolatum, Anhydrous Lanolin, Aquabase™, Aquaphor®, Polysorb®	Cold Cream type, Hydrous Lanolin, Rose Water Ointment, Hydrocream™, Eucerin®, Nivea®	Hydrophilic Ointment, Dermabase™, Velvachol®, Unibase®	PEG Ointment, Polybase™

قاعدة: كلما كان  
ال drug وال vehicle  
ال reaction بينهم  
عالية (Release)  
يكون لو يبرح  
ال (Release)  
يكون ← Prolong  
توجه لا لاي  
(high interaction)

Stable water!

hydrolyzable: more susceptible  
to water hydrolysis.  
(فبرج عال Oleaginous)

Occlusiveness  
يقلل الحد  
ويحافظ على  
طوبه

## Oleaginous ointment Bases

بتزول

- **Petrolatum, USP**, is a purified mixture of semisolid hydrocarbons obtained from petroleum.
- vary in color from yellowish to light amber.
- It melts at **38°C to 60°C** and may be used alone or in combination with other agents as an ointment base.
- Petrolatum is also known as yellow petrolatum (and) petroleum jelly.
- A commercial product is **Vaseline®**.



الـ range كبير فيدل على وجود خليط من المواد

19

19

## Oleaginous ointment Bases

- **White Petrolatum, USP**, is a purified mixture of semisolid hydrocarbons from petroleum that has been **wholly or nearly decolorized**.
- It is used for the same purpose as petrolatum, but because of its lighter color, it is considered more esthetically pleasing by some pharmacists and patients.
- White petrolatum is also known as white petroleum jelly.
- A commercial product is **White Vaseline®**.

سحب من اللون  
white  
بعد yellow

note: د. اسراء يحب  
الاصفر وما يتقنع  
بالأبيض ^^

يتلف عن الـ vaseline  
باللون قديم



20

20

### Oleaginous ointment Bases

نفس الـ Petrolatum  
بس ما فوقه wax  
(Bees wax) تسمى  
كان 1000 Petrolatum  
أخذنا 50 وبقينا  
بالهم 50 wax

• **Yellow Ointment, USP:** This ointment has the following formula for the preparation of 1000 g:

- Yellow wax 50 g
- Petrolatum 950 g
- Yellow wax is the purified wax obtained from the honeycomb of the bee Apis mellifera.



خشب النحل

21

21

### Oleaginous ointment Bases

نفس الـ white wax  
عن الـ yellow Ointment  
(سحبنا اللون من شمع  
النحل)

• **White Ointment, USP.** This ointment differs from yellow ointment by substitution of white wax (bleached and purified yellow wax) and white petrolatum in the formula.



نفس الـ Hydrocarbon bases  
(مسمى آخر)  
• **Hydrocarbon bases**, known also as "oleaginous ointment bases"

نضاف عليهم كمية قليلة جداً من الماء

- Only small amounts of an (aqueous component) can be incorporated into these bases
- Hydrocarbon bases serve to keep medicaments in prolonged contact with the skin and act as occlusive dressings.

يقلل نسبة غاربه جداً  
و يحافظو على رطوبته  
الجلد فيسمح للأدوية  
أن تدخل

22

22

## Absorption Ointment Bases

Hydrophilicity  
 ← Polar group  
 ← OH group

Hydrophilic Petrolatum, USP, has the following formula for the preparation of 1000 g:

- Cholesterol 30 g
  - Stearyl alcohol 30 g
  - White wax 80 g
  - White petrolatum 860 g
- white Ointment



23

23

## Absorption ointment Bases

تستخرج من صوف الأغنام  
 عشان تزيد  
 النقاوة باله

• **Lanolin, USP (Anhydrous lanolin)** obtained from the wool of sheep (*Ovis aries*), is a purified wax-like substance that has been (cleaned, deodorized, and decolorized.)

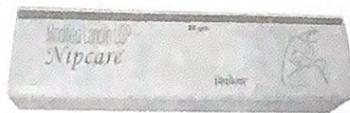
تظف وتنزع الرائحة  
 منه واللون

• It contains not more than 0.25% water.

• **Modified Lanolin, USP** is lanolin processed to reduce the contents of free lanolin alcohols and any detergent and pesticide residues.

مزيلات

عشان  
 حشره



24

24

### Absorption ointment Bases

- Permit the incorporation of aqueous solutions with the formation of a (water-in-oil) emulsion (e.g., Hydrophilic Petrolatum and Anhydrous Lanolin, both USP),
- Cholesterol and Stearyl alcohol are added as emulsifiers
- **Hydrophilic Petrolatum, USP**,
  - has the following formula for the preparation of 1000 g:
  - Cholesterol 30 g w/o emulsifying agent
  - Stearyl alcohol 30 g o/w emulsifying agent
  - White wax 80 g
  - White petrolatum 860 g **oil phase**

سواء فاتي سيعاين  
أو فاتي وايتير سيعاين  
(homogenize) فاعلا

#### > Lanoline Absorption base

Rx	Lanolin alcohol	10%
	<b>fatty</b> Lanolin	25%
	Mineral oil	30%
	Purified water	35%

25

### Water/Oil Emulsion Bases

(not-water washable)

- Are more correctly called "creams".
- Consists of water-in-oil emulsions that permit the (incorporation of additional quantities of aqueous solutions) (Cold cream type, USP).

Phase سيعاين  
water-ال سيعاين

← Why is it called cold cream?

- What is the role of borax in this formula?

Sodium borate

#### Rx 20 gm cold cream USP

Ingredients	Master formula	Scaled formula
Spermaceti (Cetyl esters wax)	125gm	
White wax (Bees Wax)	120gm	
Mineral oil	560gm	
Sodium borate	5gm	
Purified water to make	1000gm (add 190 ml)	20gm

fatty part

26

emulsifier: mixture of Sodium borate (Base) with Spermaceti (acid)

emulsifying agent و Salt مبيج

because It gives Cooling Sensation  
بعد ما تبسب عليه  
وتبخر الماء له

سائل قابل للإزالة

### Oil/Water Emulsion Bases

(water removable base)

- oil-in-water emulsions (e.g., Hydrophilic Ointment, USP), and **are more correctly called "creams"** لأصناف
- They also are described as "**water-washable**" because they may be readily washed from the skin or clothing with water an attribute that makes them **more acceptable for (cosmetic purposes)**
- **Advantages of the water removable bases**

Oleaginous ←

A. Some medicaments may be **more effective in these bases than in hydrocarbon bases.**

B. they may be **diluted with water**

التخفيف

يسهلوا ويخففوا  
الاصح ←

C) they favor the absorption of **serous discharges** in dermatological conditions.



27

\* توزع زبدة A و B لا يسهل حواء soluble (water miscible)

27 في w/o أو water miscible في w/o (oleogenous) Hydrocarbon → quick release / w/o Slow release

### Water-Removable Bases (o/w emulsion bases)

مثال للتوزيع

- **Hydrophilic Ointment, USP:**
- following formula for the preparation of about 1000 g:

*Ingredient Amount (grams)*

- Methylparaben 0.25
- Propylparaben 0.15
- Sodium lauryl sulfate 10.00
- Propylene glycol 120.00
- Stearyl alcohol 250.00
- White petrolatum 250.00
- Purified water 370.00

Preservative ←

Surfactant ←

Co solvent ←

emulsifying agents ←

vehicle ←

28

تكون وتختلط بالماء

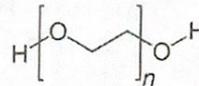
### Water Miscible Ointment Bases

غير دهنية

- Water-miscible Bases—This group of so-called “greaseless ointment bases” comprises **water-soluble constituents**.
- **Polyethylene Glycol Ointment** NF is the **only** pharmacopeial preparation in this group.
- Bases of this type offer many of the advantages of the **water-removable bases** and in addition, **contain no water-insoluble substances** such as **petrolatum, anhydrous lanolin, or waxes**.
- **They are more correctly called (Gels)**.

➤ Example : Polyethylene Glycol Ointment, NF:  
 ➤ The general formula for preparation of 1,000 g of PEG ointment is

Rx	PEG 3350	400 g
	PEG 400	600 g



Polymer ← المادة الرئيسية فيها

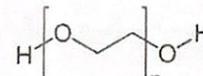
grades

PEG سيجي على شكل رقم  
 مثل 400 و 600  
 بس لا تعرف انه

29

لما الرقم يكون  
 أقل من ألف ← liquid  
 وفوق ألف ← solid  
 أو بين ألف ← semi solid

### Water-Miscible Ointment Bases



- PEG is a polymer of ethylene oxide and water represented by the formula  $H(OCH_2CH_2)_nOH$ , in **which n represents the average number of oxyethylene groups**.
- The numeric designations associated with PEGs refer to the **average molecular weight of the polymer**.
- PEGs having average molecular weight **below 600** are **clear, colorless liquids**.
- those with molecular weight **above 1,000** are **waxlike white materials** and those with molecular weight **in between** are **semisolids**.
- **The greater the molecular weight, the greater the viscosity**

الرقم العلاقة بال (M.w)

600

كل ما تزيد ال M.w  
 تزيد اللزوجة  
 Solid يصير hard

30



400 liquid  
 600 Semisolid  
 3350 Solid

30

على أي أساس ربح اختيار ال Base

## SELECTION OF THE APPROPRIATE BASE

- A. Stability of the drug in the ointment base
- B. Desired release rate of the drug substance from the ointment base
- C. Desirability of <sup>سريع</sup>topical or <sup>مغلق</sup>percutaneous drug absorption
- D. Desirability of occlusion of moisture from the skin
- E. Washable with water or not
- F. Characteristics of the surface to which it is applied: an ointment is generally applied to dry, scaly skin; a cream is applied to weeping or oozing surfaces

ببك ال release سريع  
water miscible  
في سائل أو مائجة

ويكون في hydrocarbon أو w/o

بسهولة PEG water  
بفضل الماء  
أما الفازلين به هياوون

متشعب وجاف  
مثل الأكريليك  
hydrocarbon  
(الفازلين)



في تقرحات  
بسبب الله إلهي  
بعض القروح  
(سائل)

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## SELECTION OF THE APPROPRIATE BASE

- Oleaginous (hydrophobic) bases release drugs slowly and (unpredictably) because water cannot penetrate the base sufficiently to dissolve the drug
- Water miscible and hydrophilic bases tend to release drugs more rapidly and more predictably because water can penetrate into the base
- Once the drug has been released from the base the penetration through skin is influenced by the <sup>1</sup>area to which the ointment is applied, the <sup>2</sup>condition of the skin, the <sup>3</sup>location, and method of <sup>4</sup>application

بسرعة drug بمرجات  
متفاوتة وغير منظمة  
(عشوائية)

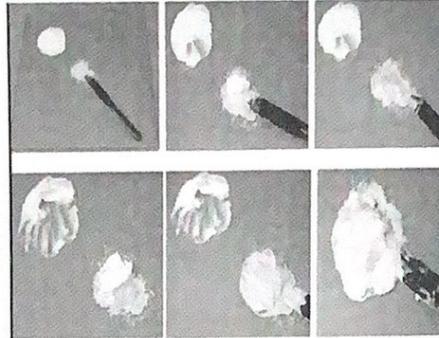
بسرعة دواء بكميات محددة  
ومحسوبة (منظمة)

32

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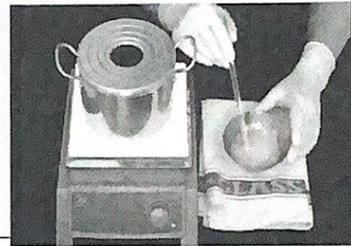
## PREPARATION OF OINTMENTS

- Ointments are prepared by two general methods,
- (a) *incorporation*
- (b) *fusion*



incorporation

fusion



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## Incorporation

الدمج و التفتيح  
mixing & milling

trituration → mortar & Pestle  
levigation → Tile & Slab

- The components are mixed until a uniform preparation is attained.
- On a small scale, as in extemporaneous compounding, the pharmacist may mix the components using a mortar and pestle, or a spatula may be used to rub the ingredients together on an ointment slab (a large glass or porcelain plate or pill tile).
- Others will use an ointment mill

تفتيح كبير للتفتيح ←



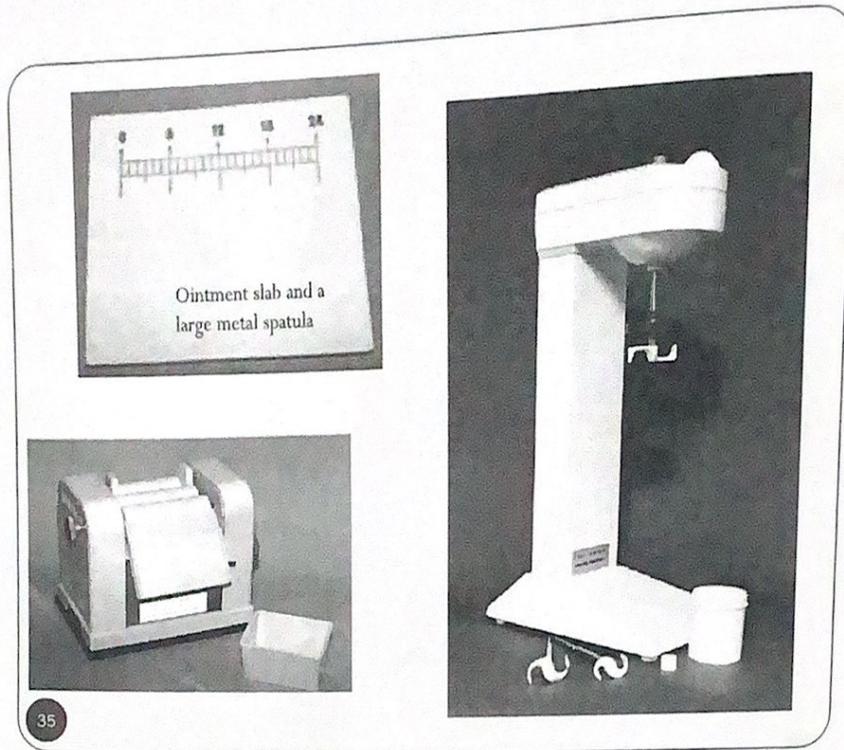
Trituration



levigation

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### Incorporating a drug into an ointment base:

بمطحنين صغيرين فيعملونهم  
(grinding) طحن

مطحون + خلط

أخذ البودرة وأذوبها  
بمطول وأعمل  
Solution

1. Insoluble powders that are added into ointment base should be in the finest possible state of subdivision:
  2. Powder form used instead of crystalline form
  3. Triturate the powder in a mortar & pestle
  4. Levigating agents (miscible with the ointment base)
5. Some powders are incorporated into ointment base by dissolving the solid in a low vapor pressure solvent or oil that can be taken up by the ointment base

كلما كان مطحون أكثر يكون أفضل



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### Incorporating a drug into an ointment base:

قبل إضافة الدواء على ال Base

- levigating or mixing the solid material in a vehicle in which it is insoluble to make a smooth dispersion.
- The levigating agent (e.g. mineral oil) for bases in which oils are the external phase, or glycerin for bases in which water is the external phase. or alcohol
- The levigating agent should be about equal in volume to the solid material.
- A mortar and pestle are used for levigation. This allows both reduction of particle size and dispersion of the substance in the vehicle.
- After levigation, the dispersion is incorporated into the ointment base by spatulation or with the mortar and pestle until the product is uniform.

تقليل حجم الجسيمات

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### heat stable / لا يتم التواء / thermo-labile (thermosensitive)

يسهل فيه حرارة Fusion

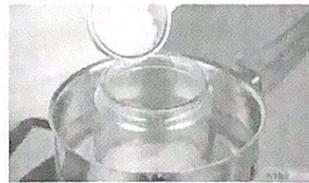


ما يستعمل في Fusion

- By the fusion method, all or some of the components of an ointment are combined by being melted together and cooled with constant stirring until congealed. (التماثل بعد البرودة)
- Components not melted are added to the congealing mixture as it is being cooled and stirred.
- On a small scale, fusion may be conducted in a porcelain dish or glass beaker.
- On a large scale, it is carried out in large steam jacketed kettles.

بسخن المادة التي لها حرارة عالية (أعلى م.م) وليس أثناء الحرارة بالتدريج وأندرج بإضافة المواد

تهدئة mixture بتخلي الوقت ساخن



المواد Volatile يضافها بالآخر ما يسخن أعرضها للحرارة العالية.

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# Fusion

بعد ما يتصلب يمرره  
على الكاشيتا ريس  
more fine

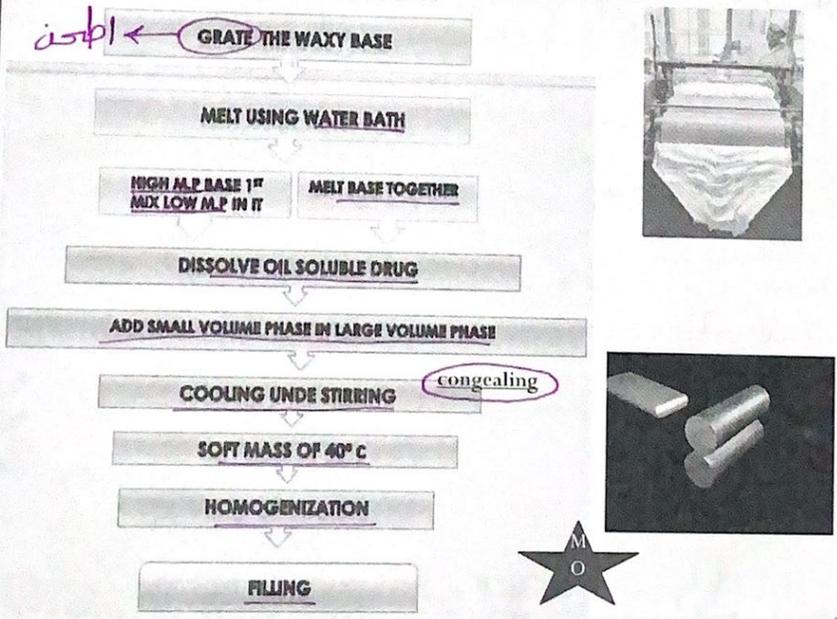
- Once congealed, the ointment may be passed through an ointment mill (in large-scale manufacture) or rubbed with a spatula or in a mortar to ensure a uniform texture.
- The materials with the highest melting points are heated to the lowest required temperature to produce a melt.
- The additional materials are added with constant stirring during cooling of the melt until the mixture is congealed.
- In this way, not all of the components are subjected to the highest temperature.

لما ريس اعرقه على  
المواد لاهي حرارة



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## Fusion Method



# PASTES



- Pastes are **semisolid** preparations intended for application to the skin. They generally **contain a larger proportion of solid material** (such as 25%) than ointments and therefore are stiffer.

فيه كثير لهاد عشان هيلك لما اخط  
العجوز على الفرسة ما يبسط  
بفضل ثابت

متناسك أكثر

- Stiffer than ointments

فوهة امتصاصه تحت  
الجلد أقل

- The stiffness reduce the percutaneous absorption potential of any drug incorporated in the paste

- They are used for their :

- A. protective action      التقيحات
- B. ability to absorb serous discharge from skin lesions
- C. ability to remain in place longer than ointments

بفضل بكتانه فترة  
أطول

(E.g. Zinc Oxide paste USP, Carboxymethylcellulose Sodium Paste USP, Triamcinolone Acetonide Dental Paste USP.)

من حفظ



Pharmacopieal  
or official

## COMPENDIAL REQUIREMENTS FOR OINTMENTS

Ointments and other semisolid dosage forms must meet USP tests for

- a) microbial content,
- b) minimum fill,
- c) packaging,
- d) storage,
- e) labeling.

كل مستحضرات العين

**ophthalmic** ointments must also meet tests for **sterility** and **metal particles content**.

بيون استثناء سواء  
drop, gel, ointment...

لازم تكون معقمة  
(Sterile)

مبدأه : مثلاً عندي 10 علب معجون نزيل عنهم ال Label أو أي ملصقات  
 ووزنهم ← ① weight / ثم نفس العلب هياي بفضها من محتواها  
 ووزنهم ← ② weight / ثم نطرحهم من بعض لنجد كمية المعجون  
 بالداخل

$$\text{weight ① (All)} - \text{weight ②} = \text{minimum fill (filled) (empty)}$$

بعضكم بقية علبه  
 المعجون ؟

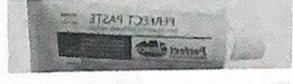
**MINIMUM FILL**

The USP's minimum fill test is determination of the net weight or volume of the contents of filled containers to ensure proper contents compared with the labeled amount.

الهدف اعرف انه هل  
 بقية العلبه صح  
 وانه الى جولاها  
 صحه ومطابقه  
 لوزنها عال Label

**Minimum Fill (USP)**

- Select a sample of 10 filled containers and remove any labeling that might be altered in weight while removing the contents of the containers.
- Clean and dry the outer surfaces of the containers and weigh each container.
- Remove quantitatively the contents from each container. If necessary, cut open the container and wash each empty container with a suitable solvent, taking care to ensure that the closure and other parts of the container are retained.
- Dry and again weight each empty container together with its parts which may have been removed.
- The difference between the two weights is the net weight of the contents of the container.



1	2	3	4	5
6	7	8	9	10

W1-W2

تم توضيحه في  
 أعلى السلايد

**MICROBIAL CONTENT**

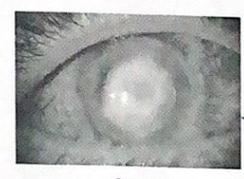
- With the exception of ophthalmic preparations, topical applications are not required to be sterile.
- They must, however, meet acceptable standards for microbial content, and preparations prone to microbial growth must contain antimicrobial preservatives.
- Dermatologic products should be examined for *P. aeruginosa* and *S. aureus*, and those intended for rectal, urethral, or vaginal use should be tested for yeasts and molds.

هدول النوعين من  
 البكتيريا لازم اتأكد  
 لانهم مش موجودين  
 بالمواد وظهورها للعين  
 بسبب وعين وعيانش  
 وتلف بأنسجه  
 العين.

Fungi فطريات

(Sterility) تعني خسه

أي نوبكتيري ← non-sterile



P. aeruginosa

بكتيريا  
 بتعمل على بالعين  
 خلال 3 أيام  
 (عافاكم الله)

وهي باقي التخصيرات في microbial-Content  
 مسموح فيه لحد معين عادي.  
 غير العين

### PACKAGING SEMISOLID PREPARATIONS

- Topical dermatologic products are packaged in either jars, tubes, or syringes whereas (ophthalmic, nasal, vaginal, and rectal semisolid) products are almost always packaged in tubes or syringes.
- The so-called ointment jars are made of clear or opaque glass or plastic
- Ointment tubes are made of aluminum or plastic



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ال tube بي ايها  
not-collapsible



بجملها lining (طلاء) مع جوا  
عشان يمتصوا  
التقليل بين الامتصاص  
والدواء

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بعض بعد ما اذوبها  
تقل زيده وما تخرج  
لو ضوعها الطيب وهو الطيب عشان ما يدخل  
فيها الهواء ويتلف

بعض بعد ما اذوبها  
تقل زيده وما تخرج  
لو ضوعها الطيب وهو الطيب عشان ما يدخل  
فيها الهواء ويتلف

### PACKAGING, STORAGE, AND LABELING

- Semisolid preparations must be stored in well-closed containers to protect against contamination and in a cool place to protect against product separation in heat
- light-sensitive preparations are packaged in opaque or light-resistant containers.
- **In addition to the usual labeling requirements** for pharmaceutical products, the USP directs the labeling for certain ointments and creams include the type of base used (e.g., water soluble or water insoluble).



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## PACKAGING, STORAGE, AND LABELING

- **Tubes of aluminum** generally are coated with an epoxy resin, vinyl, or lacquer to eliminate any interactions between the contents and the tube. *طلاء دافني Liming*
- **Plastic tubes** are made of high- or low-density polyethylene (HDPE or LDPE) or a blend of each, polypropylene (PP), polyethylene terephthalate (PET) *لبنة / سلاط على سلاطها*
- LDPE is soft and resilient (strong), and it provides a good moisture barrier. *حاجتي*
- HDPE provides a superior moisture barrier (but) is less resilient. *سلاط*
- PP has a high level of heat resistance, and PET offers transparency and a (high degree of product chemical compatibility). *لا يتفاعل مع اللي جوالها*



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## PACKAGING, STORAGE, AND LABELING

- Packaging should keep the formulation clean during repeated use and as free from air exposure and microbial contamination as feasible
- Tubes, jars, applicators, syringes, patches, pump dispensers
- **Jars** does not meet the above requirements, thus a tongue depressor can be used to remove the required quantity of formulation and keep the formulation free from hand contamination
- **Pastes** are generally packed in ointments jars



الجبسة اللي يفهم فيها الطبي في المريض



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استعمال الجبسة  
عشان أخفف من  
اللونيات أنتك ضغط  
العين  
وليس المستحضر  
باليد

أكدت بالاحضو الشية باخر العلب للمراهم والمعجون  
 صيرت يتم تعبئتهم من الأسفل  
 عكس مكان الغطاء  
 ويتم تعبئهم من الأسفل  
 لعلهم) بملكات.

### Filling Ointment Tubes

- Tubes are filled from the open back end of the tube, opposite from the cap end.
- Ointments prepared by fusion may be poured while still soft but viscous directly into the tubes with caution (to prevent stratification) of the components.
- On a small scale, as in the extemporaneous filling of an ointment in the pharmacy, the tube may be filled manually or with a small-scale filling machine

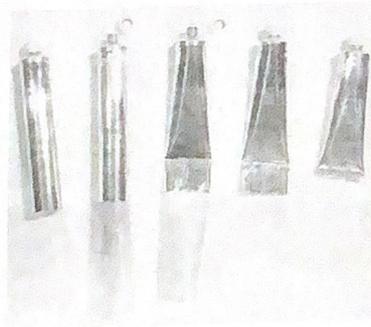
بعض المادة وهي للشفية  
 لأنه لو عسرتها وهي  
 باردة رططها فيها  
 خطوط (غير متجانسة)

لما أعين المادة وهي  
 فيها سهولة أسهل  
 (بأشرو بعد ال fusion)



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أنسكال فلتنة  
 (filling machine)



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كيف نفسد على تلف المادة

### Observing formulations for evidence of instability

• Instability of various dermatological formulations can be identified by :

- 1. A separation of components
- 2. Discoloration *تغير اللون*
- 3. Development of rancid odor *رائحة الفاسد*
- 4. Dryness
- 5. Crystal growth
- 6. Shrinkage *انكماش حجمها نتيجة تبخر الماء منها*
- 7. Microbial contamination
- 8. Additional instability signs for ointments:
  - Excessive bleeding (i.e. separation of excessive amounts of liquids)
  - Formation of granules or grittiness

*يطلق منها سائل اسود* ← 1

*انكماش حجمها نتيجة تبخر الماء منها* ← 6

*المذيبات Solvent وفقدانها* ← 8

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*لعمل صدمات على الجلد وبشكل صحيح الجلد*

### Observing formulations for evidence of instability

قاعدة: Anhydrous more stable than hydrous

- Anhydrous formulations tend to be more stable than hydrous products
- Anhydrous formulation can have a 6 month beyond use date (BUD) if incorporated drug is stable for that period
- For formulations containing water it is recommended that no more than a (2 week) supply be dispensed if no preservative is used

*14 days (hydrous) مائتي*

*لو ضيفنا Preservative بتقصي المدة أكثر*

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### Ophthalmic ointments

الظلمة الرئيسي  
Sterility

- **Ophthalmic ointments** are semisolids for application to the eye.
- Special precautions must be taken in the preparation of ophthalmic ointments.
- They are manufactured from sterilized ingredients under rigidly **aseptic conditions**, must meet the requirements under Sterility Tests and must be (free of large particles.) → to prevent pain of eye
- The medicinal agent is added to the ointment base either as a <sup>1</sup> solution or as a <sup>2</sup> micronized powder.

بقوم ال drug والمواد  
وال Tube ...  
aseptic  
no sepsis  
ظروف لا يوجد فيها  
Contamination  
أما (anti-septic)  
(مقوم الديدان)  
Contamination

بأخذ عينة من  
الophthalmic  
ويزرعها ويفحصه  
أي نمو بكتيري  
فيكون sterile

Grinding/reduction  
to size of micron  
بمسح حجم الجسيمات بالمايكون  
لتجنب تهيج العين.

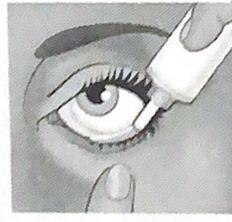


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### Ophthalmic ointments

- The USP directs that ophthalmic ointments must be packaged in **collapsible ointment tubes**.
- These tubes have an elongated narrow tip to facilitate application of a narrow band of ointment to the eye.
- The patient should be advised that blurred vision will occur as the ointment spreads over the eye and not to be alarmed.
- If the ointment is to be administered only once daily, it is often preferable to do so at bedtime, when vision impairment will be inconsequential.

لما يضطه يفضل تحمله  
مثل ما هو عشان  
ما يدخل هوا  
يكون عندي تطوعه للاستعمال  
بتركب عال Tube عشان  
أبعد محتويات الدواء عن  
أنتحية العين وما تتلف  
محتويات الدواء.



أفضل وقت لإعطائه ال ointment  
في العين هو عند النوم لأنه  
يسبب غباش في العين

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## Ophthalmic ointments

- It is important to emphasize to the patient that ocular products if handled improperly can become contaminated by bacteria that cause ocular infections, which may lead to serious consequences.
- Thus every effort must be made to avoid touching the tip of the tube to the eye, eyelid, fingertip, or any other surface, and the ointment should be used by only one person.



بعض العين

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## Summary

- Differences in emollient and occlusive effects and ease of application and removal between products is a factor of the base used and product type.
- As noted earlier, oleaginous bases provide greater occlusion and emollient effects than do hydrophilic or water-washable bases.
- Pastes offer even greater occlusion and are more effective than ointments at absorbing serous discharge.
- Creams, usually oil-in-water emulsions, spread more easily than ointments and are easier to remove.
- Water-soluble bases are non-greasy and are easily removed.

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