
DERMATOLOGICAL FORMULATIONS: OINTMENTS CREAMS AND PASTES
By solaf

Rationale for Dermatological Formulations– why a treatment is given locally to the skin?

1. To enhance **barrier function** of the skin. → Barrier repair → Skin protection
2. **Targeted delivery** to specific layers of the skin.
   - Fungal infections are in the outermost part of skin.
   - Eczema need to deliver drugs deeper into the skin.

   superficial / Deep
3. To provide a topical vehicle for medications for local (anti-infective, anti-pruritic, astringent, keratolytic). → break keratin, Removes dead cells, Like salicylic acid / Glycolic Acid
4. Fewer side-effects compared with oral delivery of drugs (to treat skin conditions).

Local action, reduce systemic side effect.

Tissue contraction, spreed throughout the body

① How do formulations improve skin's barrier function?

- Sunscreens protect against UV radiation.
- Antibiotics for abrasions protect against infection.
- Emollients improve dry skin conditions.
- Moisturisers protect against drying atmospheric conditions.
- Barrier creams prevent exposure of skin to chemical or physical irritants in the environment thus permit the skin to rejuvenate and heal (hair stylists' creams for instance)

Dermatological Formulations

- Ointments, creams, pastes and gels are semisolid dosage forms intended for topical application.
- They are also termed "semisolids" because they appear to be solid but still have fluid properties
- 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
- A topical dermatological product is designed to deliver drug into the skin in treating dermal disorders, with the skin as the target organ.

➢ 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

➢ Many patients and physicians prefer creams to ointments because they are easier to spread and remove.

oleaginous

washable

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.
- The thickness of the skin is 3 - 5 millimeters. The thickness of the skin varies with the different parts of the body.
- Within the structure of the skin are several skin appendages: hair follicles, sebaceous glands, sweat glands, and nails.

- Stratum corneum is outer layer of epidermis.

dead layer

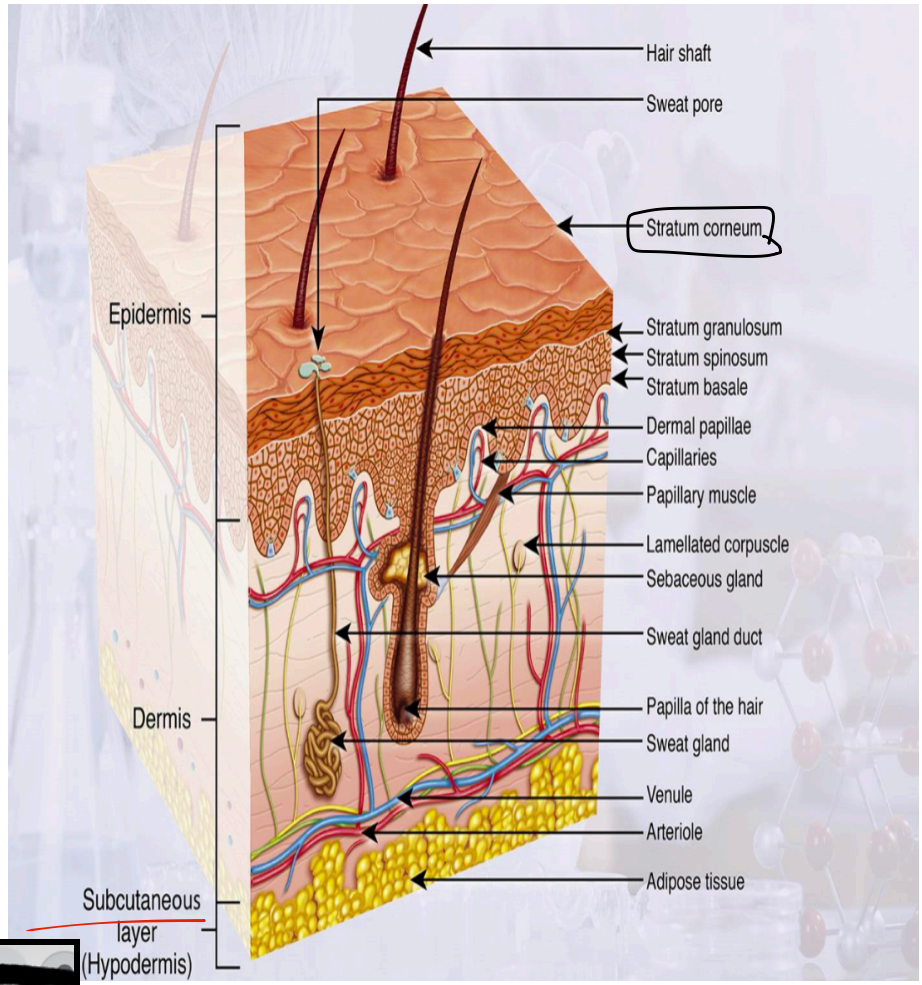
- Blood vessels are present in the dermis but not the epidermis.

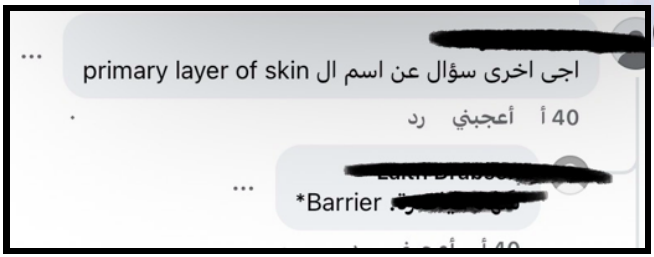
appendages in the Dermis

- Sweat glands, hair follicles and sebaceous glands originate in the dermis.

- The subcutaneous layer is fatty tissue that acts as "cushion" for the skin.

لعتقهن الصدمات





Local and systemic effects of Dermatological Formulations:

- 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 as serve as protectants, lubricants, emollients, or drying agents.
- Examples of treatments using dermatological formulations include minor skin infections, itching, burns, diaper rash, insect stings and bites, athlete's foot, corns, calluses, warts, dandruff, acne, psoriasis, and eczema.

CORNS CALLUSES

* therapeutic effect for skin disorders

Local and systemic effects of Dermatological Formulations:

target → other parts in the body

- 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 * epidermis → dermis → subcutaneous → Blood circulation (skin → blood)
- Some dermatological formulations provide continual percutaneous absorption (i.e. transdermal patch) → لصقات على الجلد — nicotine patch ← — إمتصاص عبر الجلد
- Percutaneous (through the skin) absorption is the result of three competing processes:

- the potential of the drug to leave the formulation
- the potential of the drug to cross the stratum corneum
- the influence of the formulation on the stratum corneum.

خصائص لازم تكون موجودة في الدواء عشان يطلع من الفورمولا و يتخطى عبر الجلد

Lipophilic

1. drug leaves the patch
2. crosse the stratum corneum
3. enters the systemic circulation

Percutaneous absorption

Which of the following increases transdermal absorption
1-decrease hydration
2- use dressing
3-applications on small eras
الجواب : ٢

- 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
- The greater the amount of rubbing the formulation, the greater is the absorption
- The longer the formulation remains in contact with the skin, the greater is the absorption

بعض الادوية بيكون شكلها زي بلاستر/غطاء بنحطها فوق المواد
•occlusive dressing
بتمنع فقدان الماء ↑ hydration
ointment او بنحطه -

باختصار

- Percutaneous absorption increases with larger application area, increased skin hydration, rubbing, and prolonged contact time.

Occlusive vs non-occlusive topical formulations

- Occlusive means that **the formulation prevents water movement out of the body**. So an occlusive preparation increases skin hydration and moisture content by "locking in" the water present in the body

- Good for dry skin but bad for infected skin
- Enhances skin barrier as forms a "shield" on skin
- Good penetration of drugs through the skin

Ointments

- Traditionally the term *ointment* has been used for (i) the general class name for all external-use semisolids and (ii) the subclass, oleaginous semisolids.

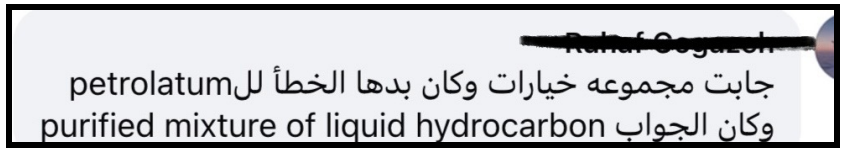
- *USP 31* Chapter 〈1151〉 defines ointments very generally as "semisolid preparations intended for external application to the skin or mucous membranes".

- **Two types** of ointments for the skin. **First type** is composed of **hydrocarbons** from petroleum or other oils which are **not water soluble.**
  - Soft paraffin is most common ingredient but liquid paraffin (mineral oil) or hard paraffin used to thin or thicken formulation as needed

Oleaginous ointment Bases

Petrolatum, USP

مثل الفازلين



- ***It 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.

Oleaginous ointment Bases

➢ ***White Petrolatum, USP*** → decolorized

- ***It 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. افضل جمالياً

- White petrolatum is also known as white petroleum jelly.
- A commercial product is White Vaseline

Oleaginous ointment Bases

➢ ***Yellow Ointment, USP:*** → petrolatum + yellow wax

- ***This ointment has*** the following formula for the preparation of 1000 g: 95% → petrolatum

- Yellow wax 50 g 5% → yellow wax

- Petrolatum 950 g

- Yellow wax is the purified wax obtained from the honeycomb of the bee *Apis mellifera.*

Oleaginous ointment Bases

➢ ***White Ointment, USP.*** → bleached

- ***This ointment differs*** from yellow ointment by substitution of white wax (bleached and purified yellow wax) and white petrolatum in the formula. or decolarization

Oleaginous ointment Bases

- Hydrocarbon bases, known also as "oleaginous ointment bases"
  - 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.

Absorption Ointment Bases

water absorbing bases.

➢ ***Hydrophilic Petrolatum, USP,***

- ***It has the following*** formula for the preparation of 1000 g:

1. Cholesterol 30 g
2. Stearyl alcohol 30 g
3. White wax 80 g
4. White petrolatum 860 g

(o/w) as emulsifying agent

oleaginous

* Hydrocarbon bases:
  - 👉 "only small amounts of water can be incorporated"
* Absorption bases:
  - 👉 "can incorporate aqueous solutions forming W/O emulsion"

وسؤال عن anhydrous lanolin لأي base بتبع
والجواب كأنه كان absorption ointment bases

Absorption ointment Bases

امثلة

- ***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.

wool wax

- It contains not more than 0.25% water. خالية (anhydrous)

نعدله ← لنسخة نظف واصفى اكثر

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

اللي ناتج من غسل الصوف

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

water droplets within the oil

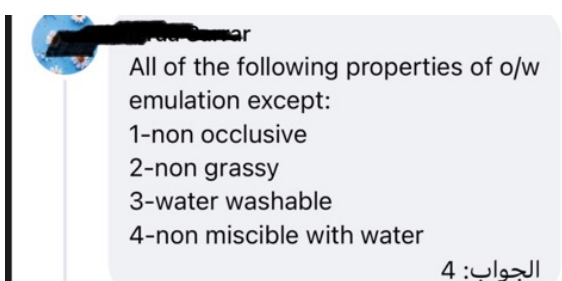
Water/Oil Emulsion Bases

- **Are more correctly called "creams"**.
- Consists of water-in-oil emulsions that permit the incorporation of additional quantities of aqueous solutions (Cold cream type, Hydrous Lanolin, USP).
- http://www.cosmeticsandskin.com/aba/cold-cream.php: refer to this article for the history of cold cream
- Why is it called cold cream? because the evaporation of its water content from the skin produces a cooling
- What is the role of borax in this formula?

Oil/Water Emulsion Bases

- Oil-in-water (external) emulsions (e.g., Hydrophilic Ointment,USP), and **are more correctly called "creams"**. → vanishing cream
- 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.
- Some medicaments may be more effective in these bases than in hydrocarbon bases. Other advantages of the water removable bases are that they may be diluted with water and that they favor the absorption of serous discharges in dermatological conditions.

* في الحالات اللي بتكون الجرح بطلع افرازات سائلة (مائية)
← سلاح قادر على امتصاصها



Water-Removable Bases
(o/w emulsion bases)

➢ Following formula for the preparation of about 1000 g:

Ingredient Amount (grams)

1. Methylparaben 0.25
2. Propylparaben 0.15
3. Sodium lauryl sulfate 10.00
4. Propylene glycol 120.00
5. Stearyl alcohol 250.00
6. White petrolatum 250.00
7. Purified water 370.00

preservative

→ emulsifing agent

→ cosolvent

→ humectant (يسحب ماء رطوبة)

→ co emulsifing agent

→ oil phase (internal)

→ external (continuous phase)

* الكمية حسب شكل واحد نحوش شو يعمل

[redacted]

Polyethylene Glycol Ointment NF is the only pharmacopeial preparation in water miscible group

Water Miscible Ointment Bases

- 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**.

Water-Miscible Ointment Bases

➢ ***Polyethylene Glycol Ointment, NF***

- ***PEG is*** a polymer of ethylene oxide and water represented by the formula H(OCH2CH2)*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 wax like white materials; and those with molecular weight in between are semisolids

OINTMENT BASES

1) Hydrocarbon
   - Petrolatum
   - White Petrolatum
   - Yellow Ointment
   - White Ointment
2) Absorption
   - Hydrophilic Petrolatum
   - Anhydrous Lanolin
3) W/O cream
   - Cold Cream,
   - Hydrous Lanolin

Water-Removable (O/W)
- Hydrophilic Ointment

4) Water-Miscible Gel
- PEG Ointment

SELECTION OF THE APPROPRIATE BASE

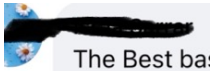
1. Desired release rate of the drug from the ointment base → Slow release → Hydrocarbon; Fast release → O/W cream/gel
2. Desirability of topical or percutaneous drug absorption
3. Desirability of occlusion of moisture from the skin

Need occlusion / dry skin ➡ Hydrocarbon ointment

Non occlusion —>Gel

4. Stability of the drug in the ointment base
5. Desire for a base easily removed by washing with water → o/w
6. 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

وجابت سؤال عن لما تكون حالة الجلد dry and scaly ايش المركب الي بستخدمه
Oleaginous ointment



The Best base for release sold and oleaginous drug
1-absorption base
2-W/o
3-O/W
4-water -miscible base
مش متأكدة من صيغة السوال
الجواب: 4

SELECTION OF THE APPROPRIATE BASE

1. Oleaginous (hydrophobic) bases release drugs slowly and unpredictably because water cannot penetrate the base sufficiently to dissolve the drug

2. Water miscible and hydrophilic bases tend to release drugs more rapidly and more predictably because water can penetrate into the base

3. Once the drug has been released from the base the penetration through skin is influenced by the area to which the ointment is applied, the condition of the skin, the location, and method of application

PREPARATION OF OINTMENTS

→ oleaginous
→ absorption base → w/o
→ creams o/w / w/o
→ water miscible (Gel)

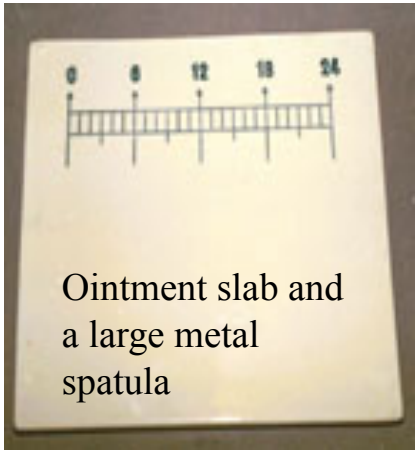
1. Incorporation

- 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

* small scale
Mortar + pestle
or
spatula + slab

* Large scale
(industrial

* Geometrical Mixing → ointment + drug



Ointment slab and a large metal spatula

Incorporating a drug into an ointment base:

- Insoluble powders that are added into ointment base should be in the finest possible state of subdivision:
  - Powder form used instead of crystalline form
  - Triturate the powder in a mortar & pestle
  - Levigating agents (miscible with the ointment base)
  - 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

* Mineral oil (for oleaginous bases)
* Glycerin (for water-miscible bases)

- 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 ethanol
- The levigating agent should be about equal in volume to the solid material. 1:1 ratio
- 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.

2. Fusion

Melt → Mix → Cool

- 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. يتجمد
- Components not melted are added to the congealing mixture as it is being cooled and stirred. * Heat-sensitive ingredients added during cooling

العقاقير التي تتأثر بالحرارة تضاف بعد التسخين

- On a small scale, fusion may be conducted in a porcelain dish or glass beaker. water path :
- On a large scale, it is carried out in large steam jacketed kettles.

Fusion

- 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.

small scale

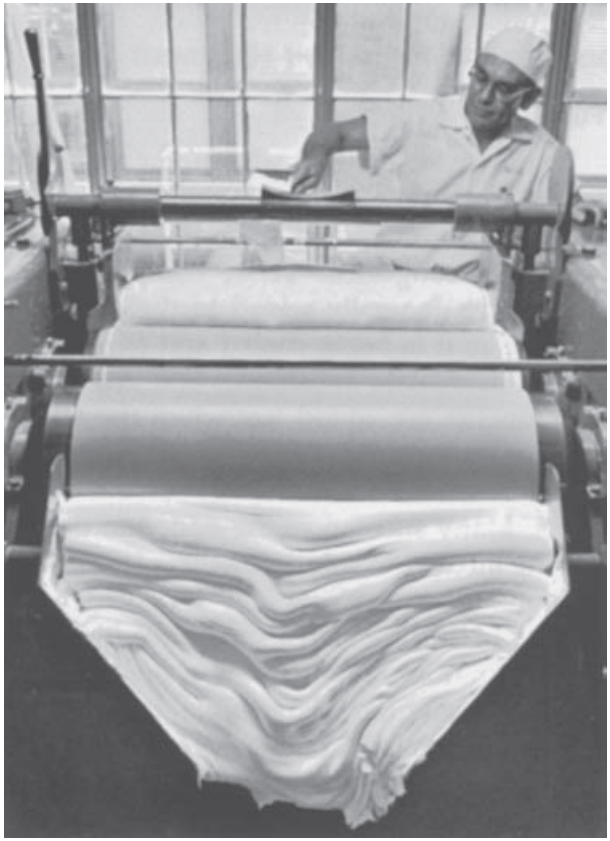
- The materials with the highest melting points are heated to the lowest required temperature to produce a melt. The additional materials are added with constant stirring during cooling of the melt until the mixture is congealed. In this way, not all of the components are subjected to the highest temperature.

heated first

wax → 70°C
petrolatum → 50°C

لو سخنت كل المواد على اعلى حرارة
المواد اللي ال melting point الها قليلة
decomposition لي يصيرلها

1. The highest melting point first
2. Turn off or reduce the heat.
3. Add other materials during cooling and stirring



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.

الفرق عن ointment

- Stiffer than ointments
- The stiffness reduce the percutaneous absorption potential of any drug incorporated in the paste
- They are used for their :

More solid → more stiffness → less absorption

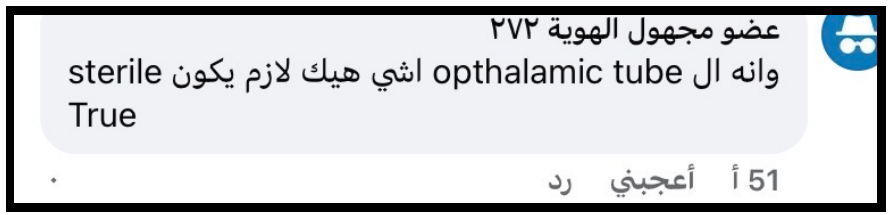
- protective action
- and ability to absorb serous discharge from skin lesions
- and ability to remain in place longer than ointments

↑ stiffness

- E.g. Zinc Oxide paste USP, Carboxymethycellulose Sodium Paste USP, Triamcinolone Acetonide Dental Paste USP.

COMPENDIAL REQUIREMENTS FOR OINTMENTS

- Ointments and other semisolid dosage forms must meet USP tests for microbial content, minimum fill, packaging, storage, and labeling.
- Ophthalmic ointments must also meet tests for sterility and metal particles content.



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

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.

لو مكتوب بالعبوة 30g لازم فعلياً تكون 30g

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

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).

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.

- Plastic tubes are made of high- or low-density polyethylene (HDPE or LDPE) or a blend of each, polypropylene (PP), polyethylene terephthalate (PET)

- LDPE is soft and resilient, and it provides a good moisture barrier. HDPE provides a superior moisture barrier but is less resilient. PP has a high level of heat resistance, and PET offers transparency and a high degree of product chemical compatibility.

* Aluminum → coated to avoid reactions
* LDPE → flexible + moisture barrier
* HDPE → best moisture barrier
* PP → heat resistant
* PET → transparent + chemically compatible

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

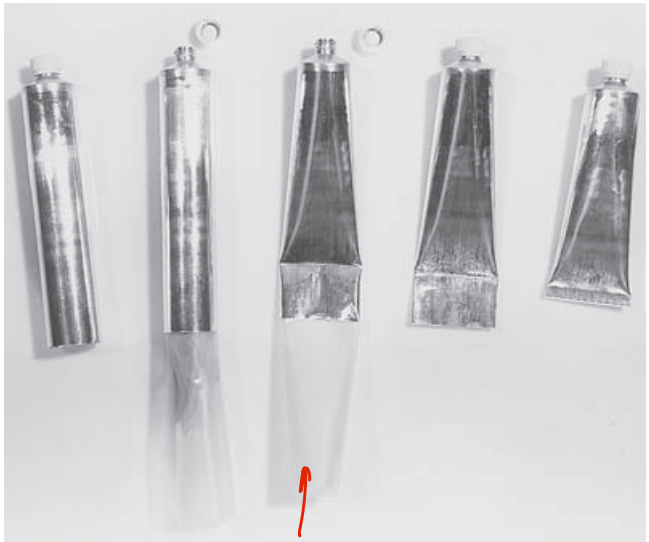
Filling Ointment Tubes

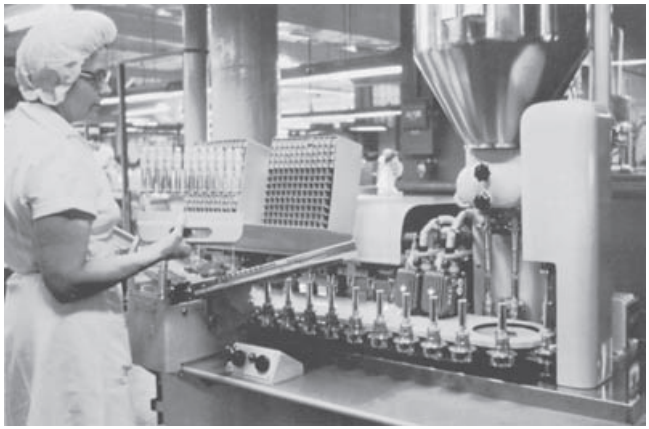
- Tubes are filled from the open back end of the tube, opposite from the cap end.

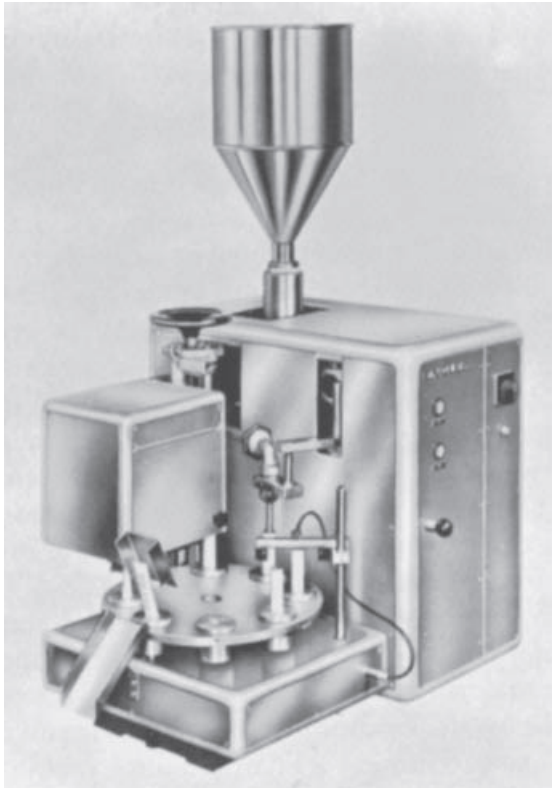
- Ointments prepared by fusion may be poured while still soft but viscous directly into the tubes with caution to prevent stratification of the components.

Ointment tubes are filled during the cooling phase while the mass is still soft and viscous, before complete congealing.

- 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







Evidence of instability

Instability of various dermatological formulations can be identified by :

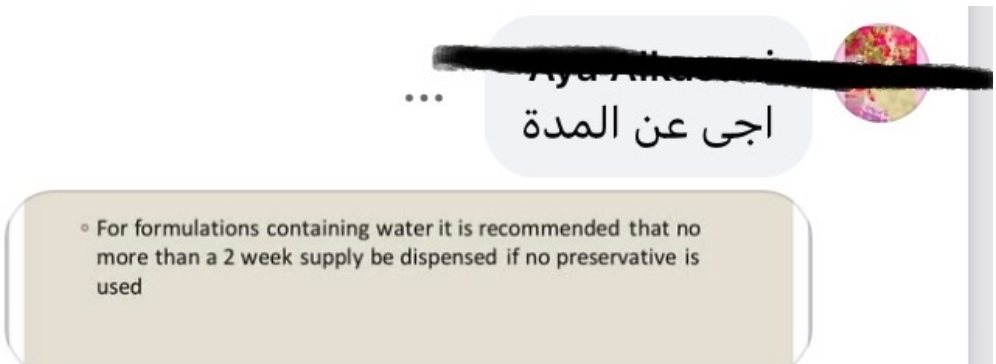
- A separation of components
- Discoloration
- Development of rancid odor
- Dryness
- Crystal growth
- Shrinkage
- Microbial contamination

◦ Additional instability signs for ointments:

- Excessive bleeding (i.e. separation of excessive amounts of liquids
- Formation of granules or grittiness

Evidence of instability

- Anhydrous formulations tend to be more stable than hydrous products
- Anhydrous formulation can have a 6 month beyond use date 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



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. but less percutaneous absorption
- Creams, usually oil-in-water emulsions, spread more easily percutaneous than ointments and are easier to remove. cosmetically acceptable
- Water-soluble bases are nongreasy and are easily removed.

	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
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
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™