Semi-Solids: Topical Dosage Forms

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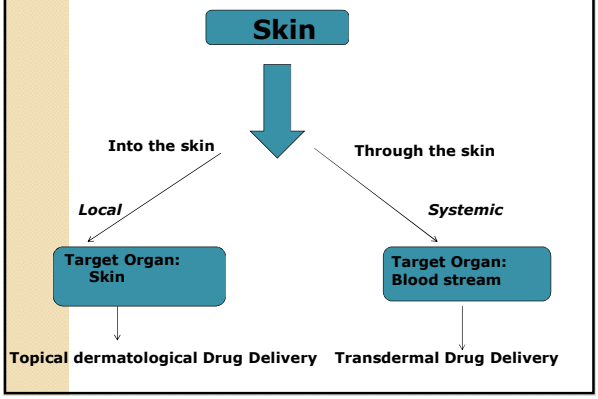
Topical Drug Delivery

- Products can be topically administered via skin or mucous membrane.
- Topical application via skin falls under two categories:



Topical Dermatological Drug Products

- Include:
  - Lotions, topical solutions, foams, aerosols and liniments.
  - **Ointments, creams, gels, and pastes (referred to as Semisolid dosage form).**
- Has OTC and prescription uses.
- **"external use only"** label for products to the skin or the scalp only.

Topical Dermatological Dosage Form

- Most frequently compounded products.
- Used primarily to deliver drug to the skin/ scalp.

Purpose of Topical Dermatological Formulations

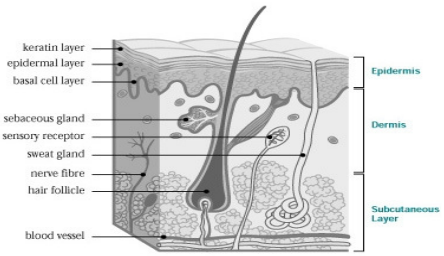
1. Protecting skin from chemical or physical irritant and allowing skin to heal example sunscreens.
2. Emollient effect by hydrating skin through occlusive effect.
3. A vehicle for medications for "local drug effect" such as antifungals and keratolytic.

Skin

- Skin is the largest of the body organs.
- It acts as a barrier to harmful penetration.
- Anatomically it is a stratified organ with three distinct tissue layers

1. Epidermis
2. Dermis
3. Subcutaneous fat layer

Skin section



Factors affecting drug penetration in skin

1. Physicochemical properties of the drug.
2. The vehicle/ base.
3. Method of application.
4. Contact time.
5. The skin conditions.
6. Multiple application.

Semi Solid Dosage Form

- Semisolid dosage forms intended for topical application.
  - Ointments
  - Pastes
  - Gels
  - Creams
  - Lotions

Choice of Dosage forms

- **Ointments**: on dry scaly regions.
- **Pastes**: Applied to area that is intended to be protected.
- **Creams**: applied to moist "weeping regions" miscible with aqueous external phase.
- **Lotions**: applied to intertriginous areas" skin rubbing occurs" under arms, between thighs or fingers due to lubricating effect.

Ointments

Ointments

- Ointment base may be used for their physical effects or as vehicles for medicated ointments.

1. **Non-Medicated ointments**
   1. Used alone as emollient or lubricating.
   2. Used as base for preparation of medicated ointments.
   3. As occlusive to enhance of absorption of drugs.
2. **Medicated ointments**
   1. **Antifungals**
   2. **Steroids**

Ointments

- Ointments are semisolid dosage form intended for external application to the skin or mucous membranes which soften or melt at body temperature, spread readily and should be non-gritty. Why ?

Ointments

- An ointment is typically a preferred dosage form to be used on dry and scaly regions due to

1. Superior emollient property.
2. Superior protective property.
3. Longer residence/ contact time.

Ointment Bases

4 main groups

1. Oleaginous (hydrocarbon bases)
2. Absorption bases
   1. (Anhydrous)
   2. W/O emulsion type
3. Water removable bases (O/W type)
4. Water soluble bases

I-Oleaginous Bases (hydrocarbon base)

- Hydrophobic
- Has **emollient** effect
- Difficult to wash with water
- Greasy and stain clothing
- Mineral oil is levigating agent.
- **Occlusive**: prevent the escape of water
- Do not dry out or change on aging
- Retained on the skin for long periods

Oleaginous Bases:

1-Petrolatum USP (Vaseline).

2-White Petrolatum USP (White Vaseline).

3-Yellow Ointment USP (simple ointment).

4-White Ointment USP.

OLEAGINOUS BASES

Oleaginous Bases:
1- Petrolatum USP

- Petrolatum= yellow petrolatum=petroleum jelly
- Mixture of semisolid hydrocarbons obtained from petroleum
- High degree of compatibility with a variety of medicaments.
- Yellowish to light amber
- 38-60^{0}C Melting point
- Commercial ***Vaseline***

Oleaginous Bases:
2- White Petrolatum USP

- Wholly or partially decolorized, purified mixture of semisolid hydrocarbons from petroleum.
- White Petroleum Jelly =white Soft Paraffin
- Used for the same purpose as petrolatum
- More esthetically pleasing due to its color.
- not water washable, occlusive
- Also known as **white petroleum Jelly**
- Commercial ***White Vaseline***

Oleaginous Bases:
3-Yellow Ointment USP (simple ointment)

Petrolatum with 5% yellow beeswax

Yellow wax	50 g
Petrolatum	950 g

- Prepared by melting the wax on water bath
- then adding the petrolatum until mixture is uniform or melt them together
- mix and allow to congeal.
- Has slightly greater viscosity than plain petrolatum.

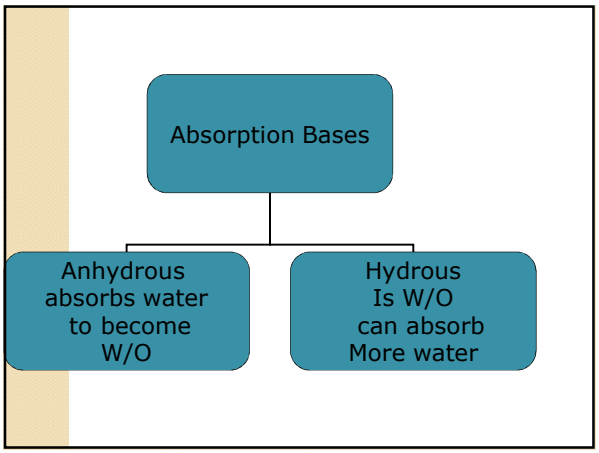
Oleaginous Bases
4-White Ointment USP

White petrolatum with 5% white beeswax

White wax	50 g
White Petrolatum	950 g

- Prepared by melting the white wax on water bath
- then adding the white petrolatum until mixture is uniform or melt them together
- mix and allow to congeal.

II- ABSORPTION BASES



I- Anhydrous Absorption Bases

- Anhydrous absorption bases absorb water to become w/o emulsion
  - Emollient
  - Occlusive
  - **Anhydrous**
  - **Absorbs water**
  - **Not water washable**
  - Greasy and stain clothing
  - e.g. Hydrophilic Petrolatum
  - e.g. Anhydrous Lanolin (Lanolin USP)

1. Hydrophilic Petrolatum:
   Commercial product: ***Aquaphor*** products (takes up 3 time of water per weight.
2. Anhydrous Lanolin (Lanolin USP)

Anhydrous Absorption bases

- **I- Hydrophilic Petrolatum USP**

Cholesterol	30 g emulsifying agent
Stearyl alcohol	30 g emulsifying agent
White wax	80 g
White petrolatum	860 g

  - Melt Stearyl alcohol and white wax on steam bath
  - add cholesterol till dissolves completely
  - then add white petrolatum and mix
  - remove from heat, stir until mix congeals

Commercial product: ***Aquaphor*** products (takes up 3 time of water per weight.

Hydrophilic Petrolatum
Aquaphor

Anhydrous Absorption bases

- **2- Anhydrous Lanolin USP**
- From sheep wool
- Contains sterols & aliphatic alcohols
- Purified wax like substance
- Mixes with up to twice its weight in water
- Wool fat= refined wool fat
- They changed the name to lanolin
- Modified Lanolin USP: has less lanolin alcohols, less detergents and pesticide residues.

2- (Hydrous Absorption Bases) (w/o)

- Prepared by adding water to an anhydrous absorption base. They are W/O emulsions that can absorb more water also called Hydrous Absorption bases or hydrated emollient base.
  1. Emollient
  2. Occlusive
  3. **Contain water to start with**
  4. **Absorb additional water**
  5. Greasy and stain clothing
  - Examples:
    1. Hydrous Lanolin
    2. Cold cream(cleansing creams)
    - **Commercially Eucerin & Nivea cream**

Hydrous Lanolin
Eucerin

Cold Cream

Hydrous Absorption bases (w/o)

1. **Hydrous Lanolin**
   - Wool fat (anhydrous lanolin) with 25-30% water added becomes "lanolin"
   - Additional water may be incorporated
   - Hydrous Wool fat= Lanolin or hydrous Lanolin
2. **Cold cream (cleansing cream)**
   - w/o emulsion
   - e.g. Petrolatum Rose Water Ointment, nivea cream
   - Both hydrous & anhydrous bases not used often for drugs:
     - w/o system more difficult to deal with than o/w
     - Decreased patient acceptance due to greasiness.

- Application of the w/o emulsions helps dissolve and remove cellular debris and lipophilic sebum.
- Addition of large quantity of water produces a phase inversion
- w/o ——→ o/w
- o/w emulsion is water washable.

WATER REMOVABLE BASES

III. Water removable bases

- **O/W emulsions**
- Also called "Water-washable Bases" creams.
- External phase is _____.
- Easily water washable bases.
- Can be diluted with water or aqueous solutions.
- **Non greasy**
- **Must be preserved**
- Cosmetically elegant.
- **Hydrophilic ointment** is an example

Water removable bases

- Three phases: oil phase, emulsifier, aqueous phase
- Oil (internal phase): typically petrolatum and /or liquid petrolatum with a higher MW alcohol, like cetyl or stearyl alcohol.
- Emulsifying agents especially soaps & detergents(anionic & cationic surfactants) can damage /dry skin (SC). Nonionic surfactants to a lesser extent.

Hydrophilic Ointment

Methyl paraben	**0.25 g**	**preservative**
Propyl paraben	**0.15 g**	***preservative***
Sodium Lauryl Sulfate	**10g**	***emulsifying agent***
Propylene glycol	**120 g**	***aqueous phase***
Stearyl alcohol	**250 g**	***oily phase***
White petrolatum	**250 g**	***oily phase***
Purified water	**370 g**	***aqueous phase***
Total about 1000 g		

- **Aqueous phase= external phase**
- **Oily phase= internal phase**
- **Propylene glycol=** humectant *

WATER SOLUBLE BASES

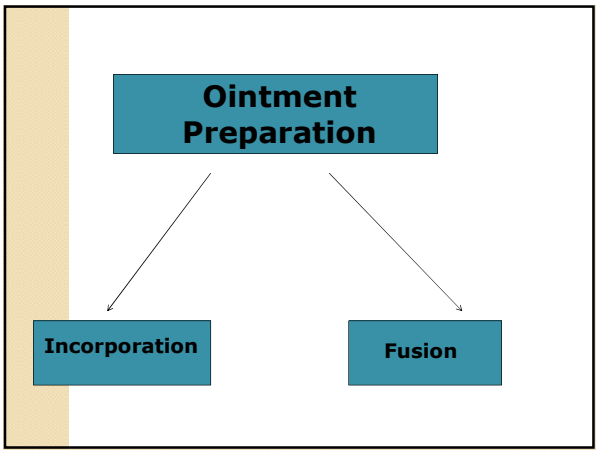
IV. Water- Soluble Bases

- Contain only water soluble components
- May include gelled aqueous solutions
- **Water washable, lipid free, greaseless**
- No oleaginous component
- for non-aqueous or solid substance incorporation.
- **Non-occlusive and may dehydrate SC**
- **High drug solubility in the base may lead to poor bioavailability.**
- Major component is PEG (polyethylene glycol)
- Example : PEG ointment NF:

- Aqueous gel vehicles containing water, propylene glycol and or PEG and gelled with a carbomer or a cellulose derivative are also classed as water-soluble bases. Referred to as gels.

PEG ointment NF

- PEG : polymer of ethylene oxide and water.
- Many grades
- Depend on the average molecular weight
- 200-8000
- The greater the molecular weight the more viscous the PEG
- General formula
  - PEG 3350 400g
  - PEG 400 600g



Ointment Preparation

1. Incorporation: "mix together". For insoluble drugs.
2. Fusion: For soluble drugs, all or some components of an ointment are melted/liquified at temperatures not exceeding 75°C and drug is added to the molten base then cooled with constant stirring until congealed.

Solid Incorporation

- Trituration: Crystalline form reduced to powders with the use of mortar and pestle.
- Then the powder is incorporated into the ointment base by Levigation to form a paste.
- "Levigation" (reduction of particle size in suspending agent compatible with the ointment base).
- Please provide examples of levigating agents(discussed earlier).

Solid Incorporation

- Levigating agent: mineral oil, glycerin or propylene glycol.
- Geometric dilution: The levigated solid is geometrically diluted with the ointment base to form the final product.
- Use 2 spatulas and slab in small scale.

Levigating Agents

- Mineral oil is the best choice for oleaginous bases.
- Water soluble or miscible levigating agents are: Water, glycerin, alcohol, or propylene glycol.
- Oil soluble levigating agent is Mineral oil.
- w/o base ?

Incorporation

- Solids may be dissolved in solvent before incorporation into base (use mortar).
- Pulverization by intervention: Gummy materials (like camphor) are dissolved in solvent then solvent is spread and allowed to evaporate, leaving a thin film.

Fusion

- Melting, mixing , cooling , congealing.
- Heat sensitive and volatile substances are added last.
- Solutions and levigated solids may be added to the congealed base.
- In porcelain dish or beaker, industry: steel-jacketed kettles.

Creams

- Semisolid dosage form containing one or more medicinal agent dissolved or dispersed in either a w/o emulsion or an o/w emulsion or water washable bases.
- Topical, vaginal, rectal creams...
- Easier to spread and easier to remove than ointments
- Pharmaceutical creams are classified as water-removable bases in the USP and are described under Ointments.

Creams

1. Vanishing Cream: o/w emulsion
   - containing large percentage of water and stearic acid or other oleaginous components
   - upon application water evaporates leaving a thin residue film of the stearic acid or other oleaginous component.
2. Cold Cream: w/o emulsion

Gels

- The United States Pharmacopoeia (USP) defines gel as a semisolid being either a suspension of small inorganic particles or a large organic molecule interpenetrated in a liquid medium.
- Rendered jelly like by the addition of a gelling agent.
- Not tacky
- Spread readily
- Easily removed from skin
- Most are clear ⟶ patient compliance

Gelling Agents

- A number of polymers are used to provide the structural network that is the essence of a gel system

1. **Cellulose derivatives** such as methylcellulose, hydroxypropyl methylcellulose (HPMC),and other derivatives
2. **Polysaccharides(natural)** such as xanthan gum ,tragacanth, alginates, and carrageenan.
3. **Acrylic polymers(synthetic)** such as Carbomer that form gels at concentrations as low as 0.5%.
4. **Colloidal dispersed solids** such as silica and clays.

Classification of Gels

- Gels can be classified in two ways

1. by the nature of the solvents
   1. A hydrogel is a water-based gel
   2. an organogel has a non- aqueous solvent system
2. by the number of phases that comprise them
   1. Single Phase
   2. Two Phase called magma e.g Milk of magnesia

Miscellaneous Semi-Solids

Lotions *
Pastes*
Plasters
Liniments
Collodions
Glycerogelatin

Lotions

- Lotions are suspensions of solids in an aqueous medium.
- Intended to be applied to unbroken skin with no friction
- Prepared by triturating the ingredients to a smooth paste and then adding the remaining liquid phase with trituration.
- Larger scale use of High-speed mixers or colloid mills produce better dispersion.
- e.g. Calamine Lotion, USP

Calamine Lotion, USP

- Calamine 80g
- Zinc Oxide 80g
- Glycerin 20ml
- Bentonite Magma 250 ml
- Calcium Hydroxide qs 1000ml

Pastes

- The USP defines pastes as semisolids dosage forms that contain one or more drug substances intended for topical application
- Prepared by fusion or incorporation
- Contain a larger percentage of solid material than ointments (thicker and stiffer)
- Will not soften and flow after application
- Should not be applied to hairy parts
- Used to absorb serous secretions.

Triamcinolone Acetonide Dental paste

- Zn oxide paste 25% ZnO with white petrolatum
- Triamcinolone Acetonide Dental paste=Kenalog® in Orabase

Plasters

Reading

- Plasters are intended for external application
- Adhesive material made of rubber base or resin
- May be medicated (10-40% salicylic acid for corns)
- Or unmedicated for the mechanical protection or support.

Liniments

Reading

- **Liniments** are of a similar viscosity to lotions (being significantly less viscous than an ointment or cream) but unlike a lotion a **liniment** is applied with friction, that is a **liniment** is always rubbed in.

Liniments

Reading

- **Liniments** are typically sold to relieve pain and stiffness, such as from sore muscles or from arthritis.
- These **liniments** typically are formulated from alcohol, acetone, or similar quickly evaporating solvents, and contain counterirritant aromatic chemical compounds such as benzoin resin or capsaicin.

Collodions

Reading

- **Collodions** are liquid preparation containing pyroxylin, a partially nitrated cellulose, in a mixture of ethyl ether and ethanol.
- Applied to the skin by means of a soft brush or other applicator and when ether or ethanol have evaporated leaving on the skin an adherent, flexible, water-repellent film of pyrolixin containing the medicament.

Collodions

Reading

- Salicylic acid Colloidon contains 10% w/v salicylic acid in Flexible Colloidon USP and is used as a keratolytic agent in the treatment of warts and corns.
- Made flexible by addition of castor oil and camphor.

Packaging

- Some Ointments can be packed in jar or tube
- Jars may be transparent or light resistant
- 0.5 ounce- 1 lb
- Ophthalmic, nasal, vaginal, rectal are packed in tubes
- Jars and tubes need to be compatible with the cream/ointment.
- Tubes are light, cleaner, inexpensive, convenient, compatible with most products 1.5-120g.
- Aluminum or plastic.

Packaging

Questions