

# Pharmaceutics 1

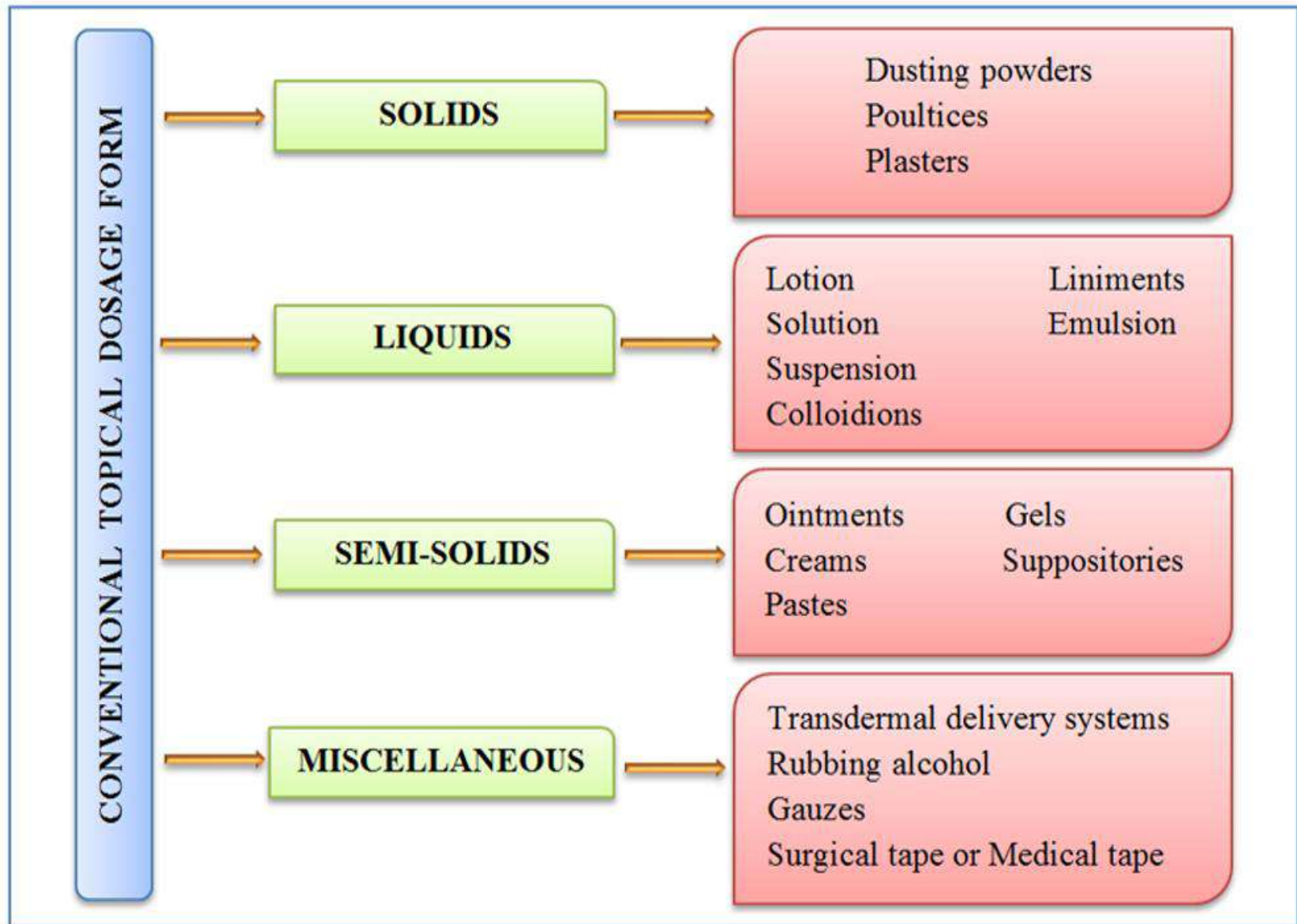
## Chapter 3

### Semisolid dosage form

### Ointments

## Lecture 4





# Semisolid dosage form

- Ointment
- Cream
- Paste
- Gel
- Suppositries
- Other less common semisolid dosage forms



# Ointments

- Ointments are semisolid preparations intended for external application to the skin or mucous membranes.
- Ointments may be medicated or not.
- 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.



# Ointment bases

- Ointment bases are generally classified by the USP into four groups:
  - (a) oleaginous bases,
  - (b) absorption bases,
  - (c) water-removable bases,
  - (d) water-soluble bases.



# CLASSIFICATION OF BASES

## BASES

WATER  
SOLUBLE  
BASE

EMULSION  
BASE

ABSORPTION  
BASE

OLEAGINOUS  
BASE



- In the formulation of a vehicle for topical drug application, **many factors** must be considered in formulating a dosage form or delivery system that will release the drug readily when placed in contact with the skin.
- Drug stability,
- Intended product use,
- Site of application, and
- Product type
- Further, **the release characteristics of the vehicle** depend on the physical-chemical properties of the specific drug substance to be delivered to the skin.



- Drug release from a vehicle is
- a function of the drug's concentration and
- Solubility in the vehicle, and
- The drug's partition coefficient between the vehicle and the skin.
  
- A vehicle optimized for delivery of hydrocortisone may be quite inappropriate for delivery of a different steroid





- The selection of the optimum vehicle based on the USP classification *per se* may require compromises.
- For example, stability or drug activity might be superior in a hydrocarbon base; however, patient acceptability is diminished because of the greasy nature of the base.
- The water solubility of the polyethylene glycol bases (PEG bases ) may be attractive, but the glycol(s) may be irritating to traumatized tissue.



- For some drugs, activity and percutaneous absorption may be superior when using a hydrocarbon base; however, it may be prudent to minimize percutaneous absorption by the use of a less occlusive base.
- In other instances, activity and percutaneous absorption may be enhanced by using a hydrophilic base.



# (a)Oleaginous bases

- Are also termed hydrocarbon bases.
- On application to the skin,
  - a. They have an emollient effect,
  - b. Protect against the escape of moisture,
  - c. Are effective as occlusive dressings,
  - d. Can remain on the skin for long periods without drying out,
  - e. Because of their immiscibility with water are difficult to wash off.



F-Petrolatum USP is a tasteless, odorless,

G-unctuous material with a melting range of 38°C to 60°C;

(The wide melting range permits some latitude in  
vehicle selection, and the USP permits addition of  
waxy materials as an aid in minimizing temperature  
effects)

H-its color ranges from amber to white (when decolorized).



I-Petrolatum often is used externally, without modification or added medication, for its emollient qualities.

(Hydrocarbon bases, being occlusive, increase skin hydration by reducing the rate of loss of surface water. )

J-Petrolatum used as an ointment base has a high degree of compatibility with a variety of medicaments.

K-Bases of this type are occlusive

L-nearly anhydrous and thus provide optimum stability for medicaments such as antibiotics.



- Water and aqueous preparations may be incorporated, but only in small amounts and with some difficulty.
- Petrolatum,
- White petrolatum,
- White ointment,
- Yellow ointment
- All are examples of hydrocarbon ointment bases.
- When powdered substances are to be incorporated into hydrocarbon bases, liquid petrolatum (mineral oil) may be used as the levigating agent.



# Hydrocarbon bases

## 1. Petrolatum, USP

Yellow petrolatum/petrolatum jelly

Vaseline (Chesebrough-Ponds/Unilever) (vahser-elaion)

Melts at 38-60°C

## 2. White petrolatum, USP

Decolored petrolatum,

White petroleum jelly/white vaseline

## 3. Yellow ointment, USP

Yellow wax (5%, w/w), petrolatum (95%)

## 4. White ointment, USP

White wax/white petrolatum



# Examples (A) Oleagenous bases

## Yellow Ointment, USP.

- This ointment has the following formula for the preparation of 1000 g:
- Yellow wax 50 g + Petrolatum 950
- Yellow wax is the purified wax obtained from the honeycomb of the bee *Apis mellifera*.
- The ointment is prepared by melting the yellow wax on a water bath, adding the petrolatum until the mixture is uniform, then cooling and stirring until congealed.
- Also called simple ointment, it has a slightly greater viscosity than plain petrolatum.

## 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.





# Paraffins wax



# Vaseline ointment and cream



- A gelled mineral oil vehicle (Plastibase) represents a unique member of this class of bases that comprises refined natural products:
- When approximately 5 percent of low-density polyethylene is added to liquid petrolatum and the mixture is then heated and subsequently shock-cooled, a soft, unctuous, colorless material resembling white petrolatum is produced.



# Plastibases

A-The mass maintains unchanged consistency over a wide temperature range.

B-It neither hardens at low temperatures nor melts at reasonably high temperatures.

C-Its useful working range is between  $-15^{\circ}\text{C}$  and  $60^{\circ}\text{C}$ .

D-Excessive heat (above  $90^{\circ}\text{C}$ ), will destroy the gel structure.



- On the basis of *in vitro* studies, drugs may be released faster from a gelled mineral oil vehicle than from conventional petrolatum.
- This quicker release has been attributed to easier diffusion of drug through a vehicle with lower microscopic viscosity (i.e., a vehicle that is essentially a liquid) than through petrolatum.
- Despite the advantages that hydrocarbon or oleaginous vehicles provide in terms of stability and emolliency, such bases have the considerable disadvantage of greasiness.



## (B) Absorption bases,

- Particularly the emulsion bases, impart excellent emolliency and a degree of occlusiveness on application.
- The anhydrous types can be used when the presence of water would **cause stability problems with specific drug substances (e.g., antibiotics)**. Absorption bases also are greasy when applied and are difficult to remove. Both of these properties are, however, less pronounced than with hydrocarbon bases.
- Commercially available absorption bases include Aquaphor (Beiersdorf) and Polysorb (Fougera). Nivea Cream (Beiersdorf) is a hydrated emollient base.
- Absorption bases, either hydrous or anhydrous, are seldom used as vehicles for commercial drug products. The W/O emulsion system is more difficult to deal with than the more conventional oil-in-water (O/W) systems, and there is, of course, reduced patient acceptance because of greasiness



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### Semisolid dosage form

#### Bases of Ointments

## Lecture 5



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# Examples on (B) Absorptive

## 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
- It is prepared by melting the stearyl alcohol and white wax on a steam bath, adding the cholesterol with stirring until dissolved, adding the white petrolatum, and allowing the mixture to cool while stirring until congealed



# Ingredients of Hydrophilic Petrolatum



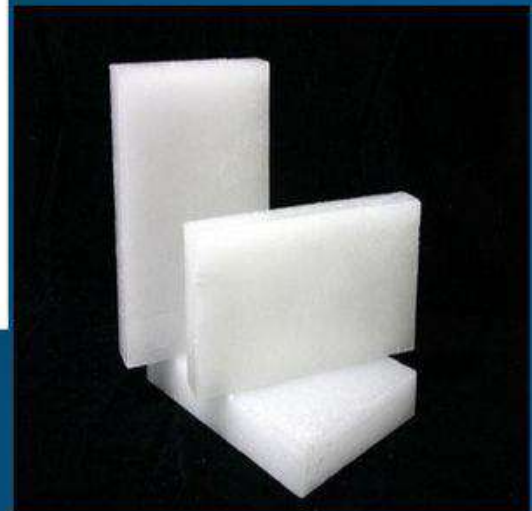
White Petrolatum



Stearyl Alcohol



Cholesterol



White Wax



- A commercial product, **Aquaphor**, a variation of hydrophilic petrolatum, has the capacity to **absorb up to three times** its weight in water and **useful to help incorporate a water-soluble drug, e.g., tobramycin sulfate, into a oleaginous ointment base.**
- This concept is used in the preparation of **ophthalmic ointments.**



# Lanolin, USP (Anhydrous lanolin)

- It is obtained from the wool of sheep (Ovis aries), is a purified waxlike substance that has been cleaned, deodorized, and decolorized.
- It contains not more than 0.25% water Additional water may be incorporated into lanolin by mixing.
- Modified Lanolin, USP, is lanolin processed to reduce the contents , of free lanolin alcohols and any detergent and pesticide residues.



# Lanolin



Lansinoh®

#1 Brand

Recommended by Doctors  
and Lactation Consultants  
in the USA

# Lanolin Nipple Cream



Soothes & protects sore nipples



Safe for baby, relief for mom



100% natural



 Care

NET WT. / PESO NETO 1.41 OZ (40g)



## (c) Water-Removable (Water-Washable) Bases

- Water-removable bases are O/W emulsion bases, commonly referred to as *creams*, and represent **the most commonly used type of ointment base.**
- By far the majority of commercial dermatologic drug products are formulated in an emulsion (or cream) base.
  - Emulsion bases are washable
  - are removed easily from skin or clothing.
  - Emulsion bases can be diluted with water, although such additions are **uncommon.**





- Nonetheless, emulsion bases typically include antimicrobial preservatives, stabilizers (such as antioxidants, metal chelating agents, or buffers), and humectants (e.g., glycerin or propylene glycol), in addition to the emulsifiers, in order to ensure stability and efficacy.



- Soaps and detergents (i.e., emulsifiers) have, overall, a damaging effect on the skin. ???☆☆
- Both anionic and cationic surfactants can cause damage to the stratum corneum in direct proportion to concentration and duration of contact.
- Nonionic surfactants appear to have much less effect on the stratum corneum.



# • Examples on (C ) Water removable base

## • Hydrophilic Ointment, USP,

- has the 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



# Water-removable bases

- Water-washable bases, O/W emulsion

## **Hydrophilic ointment, USP**

Methylparaben	0.25 g
Propylparaben	0.15
SDS	10
Propylene alcohol	120
Stearyl alcohol	250
White petrolatum	250
Water	370

**Vanishing cream:** o/w emulsion contains a large % of water and humectant. An excess of stearic acid in the formula helps to form a thin film when the water evaporates.



## (d) Water-Soluble Bases

- Soluble ointment bases, as the name implies, are made up of **soluble components** or may include gelled aqueous solutions.
- The latter often are referred to as gels, and in recent years have been formulated specifically to maximize drug availability.
- Major components, and in some instances the only components, of water-soluble bases are the polyethylene glycols (PEGs).
- Patch tests have shown that these compounds are innocuous, and long-term use has confirmed their lack of irritation.



- PEGs are relatively inert, nonvolatile, water-soluble or water-miscible liquids or waxy solids identified by numbers that are an approximate indication of molecular weight.
- Polyethylene glycol 400 is a liquid superficially similar to propylene glycol, while polyethylene glycol 6000 is a waxy solid.
- Polyethylene glycols of interest as vehicles include the 1500, 1600, 4000, and 6000 products, ranging from soft, waxy solids (polyethylene glycol 1500 is similar to petrolatum) to hard waxes.



- Polyethylene glycols, particularly 1500, can be used as a vehicle *per se*;  
however, better results often are obtained by using blends of high- and low-  
molecular-weight glycols, as in polyethylene glycol ointment NF.
- The water-solubility of polyethylene glycol vehicles does not ensure availability of drugs contained in the vehicle.
- Because hydrated stratum corneum is an important factor in drug  
penetration, the use of polyethylene glycol vehicles, which are anhydrous  
and nonocclusive, actually may hinder percutaneous absorption due to  
dehydration of the stratum corneum ???????★



# Examples on (d ) Water soluble base

- Polyethylene Glycol Ointment, NF
- PEG is a polymer of ethylene oxide and water represented by the formula  $\text{H}(\text{OCH}_2\text{CH}_2)_n\text{OH}$ , 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.





- The greater the molecular weight, the greater the viscosity. The NF lists the viscosity of PEGs ranging from average molecular weight of 200 to 8,000.
- The general formula for preparation of 1,000 g of PEG ointment is
  - **PEG 3350..... 400 g**
  - PEG 400..... 600 g
- Combining PEG 3350, a solid, with PEG 400, a liquid, results in a very pliable semisolid ointment.



- If a firmer ointment is desired, the formula may be altered to contain up to equal parts of the two ingredients.
- When aqueous solutions are to be incorporated into the base, substitution of 50 g of PEG 3350 with an equal amount of stearyl alcohol is advantageous in rendering the final product firmer.



# Consistency and spreading



# Preparation

Ointment preparation or manufacture depends on the type of vehicle and the quantity to be prepared.

The objective is the same (i.e., to disperse the drug uniformly throughout the vehicle).

Normally, the drug materials are either in finely powdered form or in solution before being dispersed in the vehicle.



# Preparation of ointments

Ointments are prepared by two general methods

(a) Incorporation

(b) Fusion

Depending primarily on the nature of the ingredients



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# (1)Mortar and pestle



# (2) Ointment slab

## OINTMENT SLAB

- An ideal surface for mixing compounds because of its nonabsorbent surface.



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# (2) Ointment slab



# (a) 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 (1) a mortar and pestle, or a spatula may be used to rub the ingredients together on (2) an ointment slab (a large glass or porcelain plate or pill tile).
- Some pharmacists use (3) nonabsorbent parchment paper to cover the working surface; being disposable, the paper eliminates cleaning the ointment slab.
- If using an ointment parchment pad, it is best to not allow too long a contact of the ointment with the parchment, as it may soften and tear.



- Others will use (4) an ointment mill, an electronic mortar and pestle, or a device called an “Unguator” which allows a pharmacist to place the ingredients in a plastic ointment jar with a special lid that allows for a mixing blade to be used to mix the ingredients in the dispensing container.
- These devices can be controlled manually or via computer software.



# (4) Unguator



# Incorporation of Solids

- When preparing an ointment by spatulation, the pharmacist works the ointment with a stainless steel spatula having a long, broad blade and periodically removes the accumulation of ointment on the large spatula with a smaller one.
- If the components of an ointment react with metal (as does iodine), hard rubber spatulas may be used.
- The ointment is prepared by thoroughly rubbing and working the components together on the hard surface until the product is smooth and uniform.



- The ointment base is placed on one side of the working surface then the powdered components, previously reduced to fine powders then thoroughly blended in a mortar, on the other side.
- A small portion of the powder is mixed with a portion of the base until uniform.
- Geometric dilution is continued until all portions of the powder and base are combined and thoroughly and uniformly blended.
- It often is desirable to reduce the particle size of a powder or crystalline material before incorporation into the ointment base so the final product will not be gritty.
- This may be done by 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) should be physically and chemically compatible with the drug and base.
- 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.
- Solids soluble in a common solvent that will affect neither the stability of the drug nor the efficacy of the product may first be dissolved in that solvent (e.g., water or alcohol) and the solution added to the ointment base by spatulation or in a mortar and pestle.



# The mortar and pestle method

- Is preferred when (1) large volumes of liquid are added, because the liquid is more captive than on an ointment slab.
- For(2) incorporating a gummy material, such as camphor, pulverization by intervention can be used.
- The material is dissolved in a solvent and spread out on the pill tile.
- The solvent is allowed to evaporate, leaving a thin film of the material onto which the other ingredient or ingredients are spread.
- The material is then worked into the ingredients by trituration with a spatula.



## Roles of incorporation of Liquids.

1-Liquid substances or solutions of drugs, as described above, are added to an ointment only after due consideration of an ointment base's capacity to accept the volume required.

2-For example, as noted previously, only very small amounts of an aqueous solution may be incorporated into an oleaginous ointment, whereas hydrophilic ointment bases readily accept aqueous solutions.



**3-When it is necessary to add an aqueous preparation to a hydrophobic base, the solution first may be incorporated into a minimum amount of a hydrophilic base and then that mixture added o the hydrophobic base.**

**4-However, all bases, even if hydrophilic, have their limits to retain liquids, beyond which they become too soft or semiliquid.**

**5-Alcoholic solutions of small volume may be added easily to oleaginous vehicles or emulsion bases.**



# • Incorporation of Drug by Levigation

1-The incorporation of a drug powder in small quantities of an ointment (i.e., 30–90 g) can be accomplished by using a spatula and an ointment tile (either porcelain or glass).

2-The **drug material is levigated thoroughly with a small quantity of the vehicle or a miscible liquid component of the formulation (e.g., propylene glycol; light mineral oil) to form concentrate.**

3-The concentrate then is diluted geometrically with the remainder of the base. If the drug substance is water soluble, it can be dissolved in water and the resulting solution incorporated into the vehicle by use of a small quantity of lanolin, if the base is oleaginous. @@@



4-Generally speaking, an amount of anhydrous lanolin equal in volume to the amount of water used will suffice.

5-On a larger scale, mechanical mixers (e.g., Hobart mixers and pony mixers) are used. The drug substance in finely divided form usually is added slowly or sifted into the vehicle contained in the rotating mixer.

6-When the ointment is uniform, the finished product may be processed through a roller mill to ensure complete dispersion and reduce any aggregates.

7-An alternative procedure involves preparing and milling a concentrate of the drug in a portion of the base. The concentrate then is dispersed in the balance of the vehicle, using a mixer of appropriate size.

9- Occasionally, the base may be melted for easier handling and dispersing. In such cases the drug is dispersed and the base slowly cooled, using continuous agitation to maintain dispersion.



## 2. Methods

### a. Trituration:



- Wedgwood and porcelain mortars and pestles have rough interior surfaces. However, they should not be used for powders that may stain their porous surfaces. In addition, a portion of the powder mixture is lost within their rough surfaces, and therefore, they should not be used for powders of very small quantity.
  - ideal for decreasing particle size
  - e.g. dyes
  - e.g. potent drugs



- In such situations, clear glass mortars and pestles, which have smooth, nonporous interior surfaces, may be used
  - not as effective at decreasing particle size



# TRITURATION METHOD-

- **TRITURATION METHOD :**

- Used for finely divided insoluble powder particles or liquids.
- Insoluble powders are added by geometric dilution.
- Liquids are added by making well in centre.
- Air pocket formation avoided.
- Mortar and pestle used when we have large quantities.
- Involved use of glass slab when small quantities are used.





# (b)Fusion

- By the fusion method, all or some of the components of an ointment are combined being melted together and cooled with constant stirring until congealed.
- Components not melted are added to the congealing mixture as it is being cooled and stirred.
- Naturally, heat-labile substances and any volatile components are added lastly when the temperature of the mixture is low enough not to cause decomposition or volatilization of the components.



- Substances may be added to the congealing mixture as solutions or as insoluble powders levigated with a portion of the base.
- 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.
- Medicated ointments and ointment bases containing components such as beeswax, paraffin, stearyl alcohol, and high-molecular-weight PEGs, which do not lend themselves well to mixture by incorporation, are prepared by fusion.



- By this general process, 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.
- In preparation of ointments having an emulsion base, the method of manufacture often involves both melting and emulsification.



- The water-immiscible components such as the oil and waxes are melted together in a steam bath to about 70°C to 75°C. Meantime, an aqueous solution of the heat-stable, water-soluble components is prepared and heated to the same temperature as the oleaginous components.
- Then the aqueous solution is slowly added, with mechanical stirring, to the melted oleaginous mixture.
- The temperature is maintained for 5 to 10 minutes and the mixture is slowly cooled and stirred until congealed.
- If the aqueous solution is not at the same temperature as the oleaginous melt, some of the waxes will solidify on addition of the colder aqueous solution to the melted mixture



# • Compendial requirements for ointments

- Ointments and other semisolid dosage forms must meet USP tests for microbial content, minimum fill, packaging, storage, and labeling.
- As discussed later in this chapter, 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.
- Preparations that contain water tend to support microbial growth to a greater extent than water-free preparations.



- Among the preservatives used to inhibit microbial growth in topical preparations are (methylparaben, propylparaben, phenols, benzoic acid, sorbic acid, and quaternary ammonium salts). Microbial limits are stated for certain articles in the USP.
- For example,
- Betamethasone Valerate Ointment, USP, must *meet the requirements of the tests for absence of Staphylococcus aureus and Pseudomonas aeruginosa.*
- These particular microbes have special importance in dermatologic preparations because of their capacity to infect the skin, which for patients being treated for a skin condition, is already compromised.



- This involves the testing of
- raw materials,
- use of acceptable water,
- in-process controls, and
- final product testing.
  
- The USP states certain products should be routinely tested for microorganisms because of the way they are used.
  
- Thus, 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, common offenders at these sites of application.





## • 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.

## • Packaging, storage, and labeling

- Ointments and other semisolid preparations are packaged either in large-mouth ointment jars or in metal or plastic tubes.
- 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.
- When required, 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).



# Ointment jar and tubes



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## Additional standards

- In addition to the USP requirements, manufacturers often examine semisolid preparations for viscosity and for in vitro drug release to ensure within-lot and lot-to-lot uniformity .
- In vitro drug release tests include diffusion cell studies to determine the drug's release profile from the semisolid product.



## Packaging of 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. Some are colored green, amber, or blue.



- In commercial manufacture and packaging of topical products, the jars and tubes are first tested for compatibility and stability for the intended product.
- This includes stability testing of filled containers at room temperatures (e.g., 20°C) as well as under accelerated stability testing conditions (e.g., 40°C and 50°C).
- They are
- light in weight,
- relatively inexpensive,
- convenient for use, and
- compatible with most formulative components,
- and they provide greater protection against external contamination and environmental conditions than jars (5).



- Ointment tubes are made of aluminum or plastic. When the ointment is to be used for ophthalmic, rectal, vaginal, aural, or nasal application, they are packaged with special applicator tips.
- 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), and various plastic, foil, and/or paper laminates, sometimes 10 layers thick



# Differences between types of plastic

- **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, PET offers transparency and a high degree of product chemical compatibility.
- **Laminates** provide an excellent moisture barrier because of the foil content, high durability, and product compatibility (5).
- These qualities and flexibility make plastic and plastic laminate tubes preferable to metal tubes for packaging of pharmaceuticals.
- The cylindrical bodies of plastic tubes are made by extrusion and then joined to the shoulder, neck, and tip piece, which is made by molding.



# Filling Ointment Jars

- Ointment jars are filled on a small scale in the pharmacy by carefully transferring the weighed amount of ointment into the jar with a spatula.
- The ointment is packed on the bottom and along the sides of the jar, avoiding entrapment of air.
- The jar size should allow the ointment to reach near the top of the jar but not so high as to touch the lid when closed.





- Through the adept use of the spatula, some pharmacists place a curl in the center of the surface of the ointment.
- Ointments prepared by fusion may be poured directly into the ointment jar to congeal in it.
- This must be done cautiously to prevent stratification of the components.
- In large-scale manufacture of ointments, pressure fillers force the specified amount of ointment into the jars



# The end of chapter

