

# Pharmaceutics-I

## Unit-5 Notes

# SEMI - SOLIDS

- Semi solid dosage forms are topical (dermatological) preparations used for therapeutic, protectives or cosmetic function.
- They are generally applied over the skin but can also be applied nasally, vaginally or rectally.
- Pharmaceutical semi solid dosage forms generally include : ointments, pastes, creams and gels.
- They contain one or more active pharmaceutical ingredients (API) dissolved or uniformly dispersed in a suitable base.

## Advantages

- It is used externally hence probability of side effects are very less.
- First pass metabolism is avoided.
- Suitable for unconscious patients.
- Suitable dosage form for bitter drugs.
- More stable than liquid dosage form.

## Disadvantages

- No dose accuracy.
- They are bulky to handle
- Application with finger may cause contamination.
- Physio-chemically less stable compared to solid dosage form.
- May cause irritation or allergy in some patients.

## Ideal Properties of Semi Solid Dosage Forms

It can be defined on the basis of 3 parameters :

- Physical Properties
- Physiological Properties
- Application Properties

### Physical Properties

- They should have smooth texture.
- They should be elegant in appearance.
- They should be non-dehydrating.
- They should be non-gritty in nature.
- They should have non-greasy and non-staining properties.
- They should be non-hygroscopic in nature.

### Physiological Properties

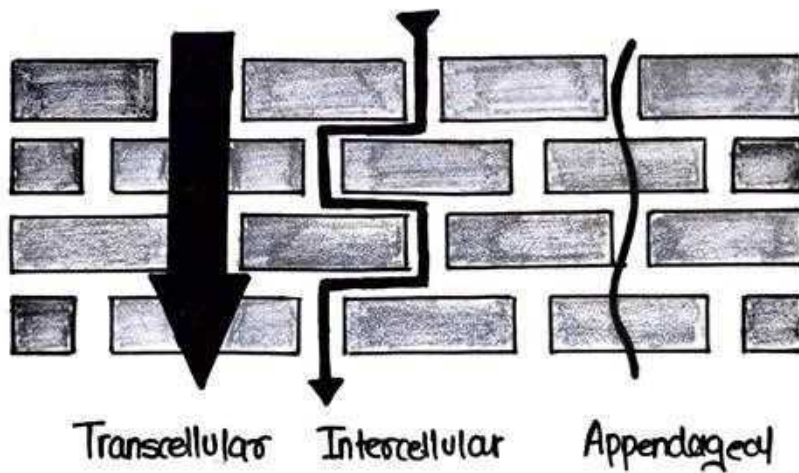
- They should be Non-irritating in nature.
- They should not alter skin membrane
- They should be easily miscible with skin secretion.

### Application Properties

- They should be easily applicable with efficient drug release.
- They should have high aqueous washability.

## MECHANISM OF DRUG PERMEATION

- It can also be known as Dermal Penetration of Drugs
- The skin has two main layers
  - ① Epidermis (outermost layer)
  - ② Dermis (Active part of skin containing hair follicles & blood supply)
- Epidermis itself divides into 5 other parts but the main layer that controls the penetration of drugs is called Stratum Corneum.
- The permeation / penetration of drugs occurs through three major routes:
  - (1) Transcellular
  - (2) Intercellular
  - (3) Appendageal



# FACTORS INFLUENCING DERMAL PENETRATION OF DRUGS

These factors can be further divided into two categories

- ① Biological Factors
- ② Physicochemical Factors

## Biological Factors

Biological factors mainly includes :

- Skin Condition
- Skin Age
- Blood Flow
- Regional Skin Sites
- Skin Metabolism
- Species Difference
- Skin Hydration

### Skin Hydration

- When the amount of water is sufficient or in excess the tissue swells and softens.
- Drugs through this softens tissues easily penetrates the skin.
- Hence, Hydration increases drug penetration.

### Skin Condition

- The penetration of drugs through skin is affected by Age, Disease, Climate and Injury.
- Drug absorption occurs rapidly in children.
- Diseases and Injured skin increases drug penetration
- Drug Penetration is less in healthy skin.

### Skin Age

- The young skin is more permeable than older.
- The skin of the childrens are more sensitive to the toxic effects of drugs.
- Skin Age plays an important role in dermal penetration of drugs.

### Blood Flow

- Blood flow through the skin also affects the dermal penetration of drugs.
- When blood flow is reduced, amount of drug penetration increases.

### Regional Skin Site

- Dermal Penetration of drugs changes with varying of skin thickness.
- Facial skin is generally more permeable compare to other body sites.

### Skin Metabolism

- The skin metabolizes steroid hormones, chemical carcinogens and some other drugs.
- So skin metabolism determines efficacy of drug permeated through skin

### Species Difference

- The condition and thickness of skin varies in different species.
- Mice, rat, rabbits have more hair follicles but they lack sweat glands, so drug penetration is different in their skin compare to human skin.

## Physiochemical Factors

Physiochemical factors mainly includes :

- Temperature and pH
- Drug Concentration
- Solubility of Drugs
- Diffusion Coefficient
- Molecular Size and Shape

### Temperature and pH

- The increase in temperature increases the dermal penetration of drugs through skin.
- Drug with pH value near 5 easily penetrates the skin.

### Drug Concentration

- The drug penetration is depends upon the concentration gradient.
- Concentration gradient will be higher if concentration of drug will be more across the barrier.

### Solubility of Drugs

- Highly lipid soluble drugs easily penetrates the skin compare to hydrophilic drugs

### Diffusion Coefficient

- The diffusion coefficient of drug depends on the properties of drugs & diffusion medium.

### Size and Shape

- Penetration of drugs is inversely depends on size.
- Small molecules penetrates faster than larger ones.

# PREPARATION OF SEMISOLIDS DOSAGE FORMS

## INGREDIENTS USED IN PREPARATION:

- Bases
- Preservative
- Humectants
- Antioxidants
- Emulsifier
- Gelling agent
- Permeation enhancer
- Buffers

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## BASES

- It is one of the most important ingredient used in formulation of semisolid dosage form. Ointment bases do not merely act as the carriers of the medicaments, but they also control the extent of absorption of medicaments incorporated in them.

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## IDEAL PROPERTIES OF A BASE

They should be:

- Inert, non-irritating and non-sensitizing.
- Compatible with skin pH and the drug.
- Good solvent and/or emulsifying agent.
- Emollient, protective, non-greasy and easily removable.
- Release medicament readily at the site of application.
- Pharmaceutically elegant and pleasant to use.



# ANTIOXIDANTS

**Oxygen** is a highly reactive atom that is capable of becoming part of potentially damaging molecules commonly called "**free radicals.**"

**Free radicals** are capable of attacking the healthy cells of the body, causing them to **lose their structure and function.** To prevent this an antioxidants are added.

E.g. **Butylated hydroxy anisole, Butylated hydroxy toluene**

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## PERMEATION ENHANCERS

- Skin can act as a barrier. With the introduction of various penetration enhancers, penetration of the drug through the skin can be improved.
  
- E.g. Oleic Acid

# EMULSIFIER

- An emulsifier (emulgent) is a substance that stabilizes an emulsion by increasing its kinetic stability.
  - Must reduce surface tension for proper emulsification.
  - Prevents coalescence.
  - Ability to increase the viscosity at low concentration.
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# HUMECTANT

A humectant is a hygroscopic substance, Humectants are used to :

- increase the solubility of the active ingredient
- to elevate its skin penetration.
- elevate the hydration of the skin.

# BUFFERS

Buffers are added for various purpose such as :

- Compatibility with skin.
  - Drug solubility.
  - Drug stability.
  
  - E.g. **sodium acetate, sodium citrate, potassium metaphosphate.**
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## Ideal Properties of Bases

They should be:

- Compatible with skin pH and drug
- Inert ,non irritating and non sensitizing
- Good solvent and/or emulsifying agent
- Emollient , protective , non greasy and easily removable
- Release medicaments easily at the site of administration
- Pharmaceutical elegant and possess good stability.

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## Types of Bases

1. Oleaginous/ Hydrocarbon Bases
2. Absorption/ Emulsifiable Bases
3. Emulsifying Bases
4. Water Soluble Bases

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## 1. Oleaginous ( hydrocarbon) bases:

- They consist of a combination of more than one oleaginous material such as water insoluble hydrophobic oils and fats

Disadvantages:

- Greasy, sticky-non washable
- Retain body heat
- Do not increase absorption
- Prevent drainage on oozing area.
- They are anhydrous, do not absorb water & insoluble in water.
  
- Hydrocarbons: Paraffin wax, Soft paraffin, Liquid paraffin
- Vegetable oils and animal fats: Peanut oil, Coconut oil, Lanolin, Bees wax
- Hydrogenated & sulfated oils: Hydrogenated castor oil, Hydrogenated & sulfated castor oil.
- Acids, Alcohols & Esters: Stearic acid, Stearyl alcohol, Isopropyl Myristicate.
- Silicones: Dimethyl polysiloxanes

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## 2. Absorption (Emulsifiable) base:

Qualities :

- Anhydrous
- Forms w/o emulsion
- Absorbs 50% water
- Due to the presence of sterol emulgent
- Easily removable by water

Classification

1)Non-emulsified bases:

- Absorb water and aqueous solutions to produces w/o emulsions Eg. wool fat, wool alcohol, beeswax, cholesterol.

2)W/O emulsions:

- Absorb more water than non-emulsified bases.
- Eg. Hydrous wool fat (lanolin)

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## 2. Absorption (Emulsifiable) base:

**Advantages of Absorption bases**

- Compatible with most of the medicaments
- Absorb large quantity of water or aqueous substances
- Relatively heat stable
- Easily spreadable
- Less occlusive and good emollients
- Aqueous substances can be incorporated

**Disadvantages**

- Undesirable due to greasy nature
- Chances of microbial contamination.

### 3. Emulsion bases:

Ability to absorb water, serum discharges and forms o/w and w/o emulsions.

According to the type of emulsion these bases are classified as either W/O or O/W.

**W/O**- greasy, sticky. Ex: Sulfur & zinc ointments

**O/W**- easily removed from skin. Ex: vanishing cream.

#### Advantages Of Emulsion bases

- Miscible with exudates from lesions
- Does not interfere with skin function
- Good contact with skin because of surfactant content
- High cosmetic acceptability.
- Easy removable from the hair.

#### Disadvantages of Emulsion bases

- W/o emulsion greasy and sticky
- Its acceptance is less
- Difficult to remove from body and clothing.

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### 4. Water soluble Bases: (Grease less Base)

As the name 'greaseless' suggests, these bases are oil free. They show complete solubility in water. They are hydrous as well as anhydrous in nature.

Carbo waxes 200,300...1500. (For viscous liquids)

Carbo waxes 1540, 3000.. 6000(For Viscous solids)

Pectin, Tragacanth & Cellulose derivatives (Form plants)

Gelatin (Animal)

Silica Gel, Bentonite (Chemical)

For low viscosity - Glycerin, Glyceryl mono stearate.

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### *Methods of Preparation of Ointments & Creams*

- Trituration
- Fusion
- Chemical reaction
- Emulsification

### *Methods of Preparation of Pastes*

- Trituration
- Fusion

### *Method of Preparation of Gels*

- General method

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## **1. TRITURATION METHOD**

- Widely used method
- For extemporaneous preparation of ointments.
- When the base is soft and medicament is solid insoluble Small amount of liquid to incorporated in the base

### **Advantage**

Involves mixing as well as size reduction

### **Procedure:**

- Reduce the solid medicament to fine powder
- Medicament is mixed with small amount of base on ointment slab with a stainless steel spatula until a homogeneous product is formed.
- Add remaining quantities of base with uniform mixing
- Incorporate any liquid ingredient if present

(mortar and pestle to be used in case of large quantity of liquid)





## 2. FUSION METHOD:

Suitable when ointment base contains number of solid ingredients of different melting points.

### Procedure:

- Ointment base are melted in decreasing order of their melting point.
- Highest melting point should be melted first, low melting point next.
- This avoids over heating of substances of low melting point
- Incorporate medicament slowly to the melted mass
- Stir thoroughly until mass cools down and homogeneous product is formed.
- Liquid ingredients or aqueous substance should be heated to the same temperature as the melted bases before addition.
- If not, wax or solids will cool down quickly and get separated

### Precautions:

- Stirring is done continuously- homogeneous mass
- Vigorous stirring should be avoided to prevent entrapment of air
- Rapid cooling should be avoided to get a uniform product.
- To remove the dust or foreign particles strain through muslin cloth

# *Fusion method*



### 3. CHEMICAL REACTION METHOD

Preparation of some ointment involves chemical reactions

Eg – (a) Iodine ointment (iodine free form)

(b) Iodine ointment (iodine combined form with ointment base)

#### *(a) Ointments containing free iodine*

Iodine is slightly soluble in fats and vegetable oils.

Readily soluble is potassium iodide solution in water due to formation of polyiodides (KI. I<sub>2</sub>, KI. 2I<sub>2</sub>, KI. 3I<sub>2</sub>)

Poly iodides are readily soluble in water, alcohol and glycerin.

These solutions may be incorporated with the molten absorption type ointment base.

#### *(b) Ointments containing combined iodine*

Fixed oils and many fats obtained from vegetable and animal sources contain unsaturated constituents. Iodine combines with double bonds

Free iodine is not available, So ointments appear dark, greenish black in colour

Leaves no stain when rubbed into the skin, Hence known as non-staining iodine ointment

#### 4. EMULSIFICATION METHOD

- Facts, oils and waxes are melted together to a temperature and 70°C.
- Aqueous solution of the heat stable, water soluble compounds is also heated to the same temperature.
- Aqueous Solution is slowly added to the melted bases, with continuous stirring until cool.

**Emulsifying agent** is needed to make a stable emulsion

Water soluble soaps are commonly used as emulsifier for semisolid o/w emulsions.

Combination of triethanolamine stearate soap and cetyl alcohol is used in o/w emulsion

Bees wax and divalent calcium ions used in w/o emulsion.