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PHARMACEUTICS – I

UNIT 5

TOPIC :

- **Semisolid dosage forms :** Definitions, classification, mechanisms and factors influencing dermal penetration of drugs. Preparation of ointments, pastes, creams and gels. Excipients used in semi solid dosage forms. Evaluation of semi solid dosages forms

Semi-Solid Dosage Forms

- Semisolid dosage forms are pharmaceutical products that exist in a state between solid and liquid.
- These formulations are intended primarily for external application on skin or mucous membranes for local or systemic effects.
- They offer prolonged contact of the drug with the target site and are often used for dermal, rectal, vaginal, and nasal routes.

Classification of Semisolid Dosage Forms:

Dosage Form	Description	Example
Ointments	Greasy, viscous preparations with drug in a suitable base; used for emollient, protective or therapeutic purposes.	White ointment, Sulphur ointment
Creams	Emulsified systems (oil-in-water or water-in-oil) that are less greasy and more patient-acceptable than ointments.	Hydrocortisone cream, Cold cream
Gels	Semisolid systems with a liquid phase trapped in a polymer matrix; transparent or translucent.	Diclofenac gel, Aloe vera gel
Pastes	Contain large amounts of insoluble solids in a base; more absorptive and less greasy than ointments.	Zinc oxide paste
Lotions	Fluid semisolids or suspensions/emulsions; used when low viscosity is needed for spreading.	Calamine lotion

Mechanisms of Dermal Penetration of Drugs

→ Drugs must penetrate the stratum corneum (outermost skin layer) to exert their effects.

Pathways of Drug Penetration

1. **Transcellular (Intracellular) Pathway:**
   - Drug passes directly through the keratinocytes.
2. **Intercellular Pathway:**
   - Drug moves through the lipid matrix between skin cells.
3. **Appendageal Route:**
   - Drug enters via sweat glands or hair follicles (minor route).

Mechanism

- **Passive diffusion** is the main mechanism, governed by **Fick's Law**:

  Flux – D.K. ΔC / h

  - D = Diffusion coefficient
  - K = Partition coefficient
  - ΔC = Concentration gradient
  - h = Membrane thickness

Factors Influencing Dermal Penetration:

Factor	Details
Drug physicochemical properties	Molecular size (smaller is better), lipophilicity (enhances stratum corneum penetration), degree of ionization (non-ionized drugs penetrate better).
Vehicle/Formulation	Type of base affects release (e.g., hydrophilic vs lipophilic); use of penetration enhancers like alcohols or surfactants.
Skin condition	Damaged or hydrated skin increases permeability.
Site of application	Thinner skin (eyelids) is more permeable than thicker skin (palms, soles).
Application area	Larger area provides more absorption surface.
Duration of contact	Longer contact enhances absorption.

Preparation of ointments, pastes, creams and gels.

Ointments

- Ointments are semisolid preparations intended for external application to the skin or mucous membranes. They have an oleaginous or greasy base, making them occlusive and emollient.

Methods of Preparation

- There are two primary methods:

A. Fusion Method (for heat-stable ingredients):

Steps:

1. All ointment base ingredients (e.g., waxes, oils) are melted together in a beaker using a water bath.
2. The drug (if heat stable) is dissolved or dispersed in the melted base.
3. The mixture is stirred continuously while cooling to prevent separation and to ensure uniformity.
4. Transferred to a container while still soft.

Used for: Ointments with oleaginous bases or waxy materials (e.g., white ointment).

B. Incorporation Method (for heat-sensitive drugs):

Steps:

1. The base is prepared or taken in a mortar or on an ointment slab.
2. The drug is levigated (finely ground and blended) using a levigating agent (e.g., mineral oil for oily bases or glycerin for water-soluble bases).

3. The levigated drug is gradually incorporated into the base using geometric dilution.
4. Mixed until uniform.

Used for: Thermolabile or insoluble drugs.

Pastes

- Pastes are semisolid formulations containing a **high proportion of insoluble solids** (usually 20–50%) dispersed in a fatty or aqueous base. They are **thicker, less greasy**, and **more absorptive** than ointments.

Method of Preparation

Incorporation Method (preferred method):

Steps:

1. Solid ingredients are finely powdered and sieved.
2. The powder is mixed with a small portion of base and levigated thoroughly to form a smooth, uniform mixture.
3. Remaining base is added in portions using geometric dilution.
4. Paste is homogenized to ensure uniformity.

Levigating agents: Glycerin, liquid paraffin, or water (depending on base).

Example: Zinc Oxide Paste – contains zinc oxide and starch in white soft paraffin.

Creams

- Creams are emulsion-based semisolid dosage forms—either oil-in-water (O/W) or water-in-oil (W/O)—used for skin application.

Method of Preparation

Emulsification Method

Steps:

1. **Separate the oil and water phases:**
   - Oil-soluble components (e.g., emulsifiers, oils) are melted and combined.
   - Water-soluble components (e.g., preservatives, humectants) are dissolved in water.
2. Both phases are heated separately to 70–75°C to ensure uniform mixing.
3. The aqueous phase is added to the oil phase with continuous stirring (or vice versa, depending on emulsion type).
4. The emulsion is cooled gradually with constant stirring to room temperature.
5. The active drug (if heat-sensitive) may be added during the cooling phase.
6. Stabilizers, emulsifiers, and preservatives must be compatible and used in correct concentrations.

Example: Vanishing cream (O/W) or cold cream (W/O)

Gels

- Gels are semisolid systems in which a liquid phase (water or alcohol) is immobilized within a three-dimensional polymeric matrix, giving a jelly-like consistency.

Method of Preparation

Steps:

1. **Dispersion of Gelling Agent:**
   - Weigh and slowly add the gelling agent (e.g., Carbopol, HPMC, Xanthan gum) into purified water or hydroalcoholic base.
   - Stir continuously to prevent lump formation. This may take several hours to hydrate.
2. **Neutralization (if required):**
   - If using Carbopol, neutralize with triethanolamine or sodium hydroxide to adjust pH (~6–7), which causes gelation.
3. **Addition of Active Drug and Excipients:**
   - Drug is dissolved (or suspended) and incorporated into the gel base.
   - Add humectants (e.g., glycerin), preservatives (e.g., parabens), and colorants (if needed).
4. **Final Mixing:**
   - Gently mix until a homogeneous, smooth gel is obtained.
   - Avoid air entrapment.

Example: Diclofenac sodium gel, Lidocaine gel

Excipients Used in Semisolid Dosage Forms:

Category	Examples	Function
Bases	Petrolatum, Lanolin, PEGs	Vehicle for drug; affect drug release
Gelling Agents	Carbopol, HPMC, Xanthan gum	Provide gel structure
Emulsifiers	Cetostearyl alcohol, Span, Tween	Stabilize emulsions (creams)
Humectants	Glycerin, Propylene glycol	Retain moisture, improve skin hydration
Preservatives	Parabens, Benzalkonium chloride	Prevent microbial growth
Antioxidants	BHT, BHA, Tocopherol	Prevent oxidation of drug and base
Penetration Enhancers	DMSO, Urea, Oleic acid	Increase drug permeation through skin
Buffering Agents	Sodium phosphate, Citric acid	Maintain pH stability

Evaluation of Semisolid Dosage Forms

Parameter	Purpose / Description
Appearance	Color, homogeneity, absence of lumps or grittiness
pH	Should match skin pH (~4.5–6.5) for compatibility
Viscosity/Rheology	Affects spreadability and stability
Spreadability	Ease of application; measured by glass slide method
Drug Content Uniformity	Ensures uniform distribution of drug in the base
In vitro Drug Release	Performed using Franz diffusion cells
Microbial Testing	Assess preservative efficacy and sterility (if needed)
Stability Studies	Accelerated and long-term stability tests for shelf-life