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BP504T

Pharmaceutical Dosage Forms II

Unit V — Semisolid Dosage Forms

B.Pharm · Semester V · Theory notes

Syllabus coverage: UNIT V (6 hours).

From-zero teaching standard: every technical term is defined before use.

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CHAPTER 6 — SEMISOLID THEORY: SKIN PERMEATION & ENHANCERS

Chapter 6 · Semisolid Theory: Skin Permeation & Enhancers

Learning Objectives

1. Define semisolid dosage forms and state their purpose.
2. Describe the drug permeation pathways through skin.
3. List the factors affecting percutaneous permeation.
4. Classify permeation enhancers into physical and chemical types with examples.

Key definitions

- Semisolid dosage form: a soft, non-pourable preparation (ointment, cream, gel, paste) applied to skin or mucous membranes for local or systemic effect.
- Percutaneous absorption: movement of drug through the skin into deeper tissues or blood.
- Stratum corneum: the outermost dead-cell layer of skin — the main barrier to drug entry. Think of it as a brick wall: dead cells are the bricks, skin lipids are the mortar.
- Permeation enhancer: an agent or technique that temporarily increases skin permeability so more drug passes through.

Terminology at a glance

Term	Simple meaning
Transepidermal route	Through the skin layers (between or through cells)
Transappendageal route	Through hair follicles and sweat glands (shortcuts)
Partition coefficient	How much the drug prefers oil vs water — decides skin entry
Flux	Amount of drug crossing a unit area of skin per unit time
Occlusion	Covering the skin to trap moisture and boost absorption
Iontophoresis	Driving charged drugs through skin with a small electric current
Sonophoresis	Using ultrasound to push drugs through skin
Microneedles	Tiny needles that painlessly pierce only the top skin layer

Explanations

6.4.1 Definition & purpose

Semisolids treat skin conditions locally (eczema, infections, burns), protect skin (barrier creams, sunscreens), deliver drugs systemically through skin (transdermal patches/gels), and serve cosmetic purposes.

6.4.2 Structure of skin (brief)

Epidermis (outer, includes stratum corneum barrier) -> dermis (blood vessels, nerves) -> hypodermis (fat). The stratum corneum's brick-and-mortar lipid structure blocks most drugs; only small, moderately oil-loving molecules pass easily.

6.4.3 Drug permeation pathways through skin

1. Intercellular (between cells): drug weaves through the lipid mortar between dead cells — the main route for most drugs.
2. Transcellular (through cells): drug passes alternately through cells and lipids — harder, less common.
3. Transappendageal (shunt route): through hair follicles, sebaceous and sweat glands — a shortcut but small total area; important for large/polar molecules and in early time periods.

Simple picture: three doors into a building — the long winding corridor (intercellular), straight through walls (transcellular), and the side service entrance (appendages).

6.4.4 Factors affecting permeation

1. Drug factors: molecular size (smaller is better), partition coefficient (balanced oil/water liking is best — too oily gets stuck in skin lipids, too watery cannot enter), concentration (higher gradient drives more flux), ionization (unionised form penetrates better).
2. Skin factors: thickness and site (thin eyelid skin absorbs more than thick palm), age (baby/elderly skin more permeable), hydration (wet skin absorbs more), damaged/diseased skin (barrier broken -> much higher absorption).
3. Formulation factors: vehicle (ointment bases are occlusive and boost absorption), pH, drug solubility in the base (drug must leave the base to enter skin), enhancers.

6.4.5 Permeation enhancers — chemical

Agents that temporarily loosen the stratum corneum:

- Alcohols/glycols: ethanol, propylene glycol — extract skin lipids, improve drug solubility.
- Surfactants: sodium lauryl sulphate, polysorbates — interact with skin lipids/proteins.
- Fatty acids: oleic acid — disrupts lipid packing.
- Azone-like compounds, DMSO, urea — various lipid/protein interactions.
- Essential oils/terpenes: menthol, eucalyptus oil — mild, pleasant-smelling enhancers.

Caution: enhancers must be non-irritating at use levels and their effect must be reversible.

6.4.6 Permeation enhancers — physical

Techniques that physically assist delivery:

- Occlusion: covering with an impermeable film/bandage traps moisture, hydrates the stratum corneum and boosts absorption.
- Iontophoresis: small electric current drives charged drug molecules into skin.
- Sonophoresis (ultrasound): sound waves disturb the lipid barrier.
- Microneedles: micro-projections pierce only the stratum corneum painlessly, creating micro-channels.
- Heat: warming increases blood flow and diffusion.

Classifications

- Permeation pathways: intercellular, transcellular, transappendageal.
- Enhancers: chemical (solvents, surfactants, fatty acids, terpenes) vs physical (occlusion, iontophoresis, sonophoresis, microneedles, heat).
- Factors: drug-related, skin-related, formulation-related.

Mechanism / how it works

- Passive diffusion: drug moves down its concentration gradient through the stratum corneum (Fick's law in words: more drug outside + thinner barrier + better partitioning = more flux).
- Enhancer action: lipid extraction/fluidisation (oils move more freely), protein interaction, or creation of new pathways (microneedles, current).

Diagram to draw

1. Skin cross-section: label stratum corneum, epidermis, dermis, hair follicle, sweat gland; arrows for the three pathways.
2. Brick-and-mortar model: dead cells as bricks, lipids as mortar.

Process flow

Factors -> permeation:

Drug properties (size, partition, concentration, ionization) + Skin condition (site, age, hydration, integrity) + Formulation (vehicle, pH, enhancer) -> Flux into skin -> local action or systemic absorption.

One-glance summary

One-glance summary

SKIN PERMEATION — one glance

- Barrier = stratum corneum (brick-and-mortar lipids)
- 3 doors: between cells (main) · through cells · via follicles/glands
- More flux when: small molecule · balanced oil/water liking · high concentration · hydrated/thin/damaged skin · occlusive base
- [EXP] Chemical enhancers: alcohol · PG · surfactants · oleic acid · menthol · urea
- Physical enhancers: occlusion · iontophoresis · ultrasound · microneedles · heat

Tables

Enhancer type	Examples	How it works
Solvents	Ethanol, propylene glycol	Lipid extraction, better drug solubility

Enhancer type	Examples	How it works
Surfactants	SLS, polysorbates	Lipid/protein interaction
Fatty acids	Oleic acid	Disrupts lipid packing
Terpenes	Menthol	Mild lipid disruption
Occlusion	Plastic film, ointment base	Hydrates stratum corneum
Iontophoresis	Electric current	Drives charged drugs in
Microneedles	Micro-projections	Creates micro-channels

Examples

1. Nitroglycerin ointment/patch: systemic delivery through skin for angina.
2. Menthol-containing rub: terpene enhancer + cooling sensation.
3. Occlusive bandage over steroid cream: boosts absorption for stubborn eczema patches.

Think of it this way

- Stratum corneum is a brick wall; enhancers are like loosening the mortar.
- Flux is like water flowing through a sieve — bigger holes (enhanced skin) and more water (higher concentration) mean more flow.

Pharmacy relevance

Pharmacists advise: apply thin layers, do not cover unless told to (occlusion increases absorption and side effects), and warn that broken skin absorbs much more drug.

India context

Topical steroid misuse on the face is common in India; pharmacists play a key role in counselling against prolonged unsupervised use, especially under occlusion.

Key points

1. Semisolids act locally or systemically through skin.
2. Stratum corneum is the main barrier (brick-and-mortar).
3. Three pathways: intercellular (main), transcellular, transappendageal.
4. Flux depends on drug, skin and formulation factors.
5. Enhancers: chemical (solvents, surfactants, fatty acids, terpenes) and physical (occlusion, iontophoresis, ultrasound, microneedles).

Common confusions

- Penetration vs permeation vs absorption: penetration = entry into skin layers; permeation = passage through skin; absorption = reaching blood.
- Occlusion as enhancer: it is a physical method (trapping moisture), not a chemical.

Common mistakes

1. Applying thick layers thinking "more is better" (thin, uniform layers work best).
2. Covering steroid creams with plastic wrap without medical advice.
3. Using skin products on broken/infected skin without caution.

Mnemonics

- "I-T-T" — Intercellular, Transcellular, Transappendageal pathways.
- "O-I-S-M-H" — Occlusion, Iontophoresis, Sonophoresis, Microneedles, Heat (physical enhancers).

Exam summary

Semisolid dosage forms deliver drugs via skin. The stratum corneum's brick-and-mortar structure is the main barrier. Drugs cross by intercellular, transcellular or transappendageal routes. Flux is governed by drug properties, skin condition and formulation. Chemical enhancers (solvents, surfactants, fatty acids, terpenes) and physical methods (occlusion, iontophoresis, ultrasound, microneedles) improve delivery.

One-minute revision

Barrier = stratum corneum. 3 pathways: between/through cells, via follicles. Flux: small + balanced + concentrated + hydrated skin. Enhancers: chemical (alcohol, SLS, oleic acid, menthol) + physical (occlusion, current, ultrasound, microneedles).

Exam questions

Short answers:

1. Define semisolid dosage form and state two purposes.
2. Name the three permeation pathways through skin.
3. List four factors affecting percutaneous absorption.
4. Classify permeation enhancers with two examples each.
5. What is occlusion? How does it enhance absorption?

Long answers:

1. Describe the structure of skin and the pathways of drug permeation, with the factors affecting permeation.
2. Discuss permeation enhancers with suitable examples.

MCQs:

1. The main skin barrier is the: (a) Dermis (b) Stratum corneum (c) Hypodermis (d) Muscle — Answer: (b)
2. The major permeation pathway for most drugs is: (a) Transcellular (b) Intercellular (c) Transappendageal (d) Oral — Answer: (b)
3. Which is a physical enhancer? (a) Oleic acid (b) Menthol (c) Iontophoresis (d) Ethanol — Answer: (c)
4. Occlusion enhances absorption by: (a) Cooling (b) Hydrating the stratum corneum (c) Drying (d) Colouring — Answer: (b)
5. Unionised drugs penetrate skin: (a) Better (b) Worse (c) Equally (d) Never — Answer: (a)

Viva:

1. Why do ointments generally give better absorption than creams?
2. Name one risk of applying drugs to damaged skin.

Application-based:

1. A patient covers a potent steroid cream with cling film overnight to "make it work faster." Counsel the patient.

References

CHAPTER 7 — SEMISOLID TYPES: OINTMENTS, CREAMS, GELS, PASTES, SUPPOSITORIES & ADVANCES

Chapter 7 · Semisolid Types: Ointments, Creams, Gels, Pastes, Suppositories & Advances

Learning Objectives

1. Classify ointment bases and explain base selection.
2. Describe formulation, manufacturing and evaluation of ointments, creams, gels/jellies and pastes.
3. Describe formulation, manufacturing and evaluation of suppositories and pessaries.
4. Give an overview of xerogels and emulgels with applications.

Key definitions

- Ointment: a greasy semisolid for external use, with the drug dissolved or dispersed in a suitable base.
- Cream: a soft semisolid emulsion (o/w or w/o) for external use; less greasy than ointments.
- Gel/jelly: a transparent/translucent semisolid with a three-dimensional polymer network trapping liquid.
- Paste: a stiff ointment containing a high proportion of solid powder (less greasy, more absorbent).
- Suppository: a solid dosage form for insertion into body cavities (rectum, vagina — pessary), which melts/dissolves at body temperature to release the drug.
- Xerogel: a gel dried to remove liquid, leaving a porous solid network (re-hydratable).
- Emulgel: an emulsion incorporated into a gel base — combines emulsion and gel advantages.

Terminology at a glance

Term	Simple meaning
Base	The vehicle/carrier in which the drug is incorporated
Occlusive base	Base that blocks water loss from skin (e.g., petrolatum)
Displacement value	Amount of base displaced by 1 g of drug in suppository moulds
Bloom strength	Measure of gelatin gel firmness (for gelatin-based pessaries)
Syneresis	Liquid separating out of a gel on storage
Spreadability	How easily a semisolid spreads on skin

Explanations

7.4.1 Ointment bases — classification & selection

1. Oleaginous (hydrocarbon) bases: soft paraffin, hard paraffin, liquid paraffin — occlusive, greasy, anhydrous; good for dry, scaly skin; poor drug release for water-soluble drugs.
2. Absorption bases: wool fat (lanolin), beeswax — can absorb water to form w/o emulsions.
3. Water-miscible/washable bases: emulsifying ointment — wash off easily, less greasy.
4. Water-soluble bases: macrogols (PEGs) — non-greasy, water-washable, good drug release.

Base selection rules:

match base to purpose — dry lesions need occlusive greasy bases; weeping/oozing lesions need non-greasy, absorbent bases (pastes/creams); drug solubility in the base should allow the drug to leave the base and enter skin; consider stability, compatibility and patient acceptability.

7.4.2 Ointments — formulation, manufacturing, evaluation

- Formulation: drug + base + (antioxidants, preservatives if water present, stiffening agents).
- Manufacturing: (a) trituration — mixing drug powder into a small portion of base on an ointment slab, then diluting geometrically; (b) fusion — melting bases together, adding drug, stirring while cooling.
- Evaluation: appearance/homogeneity, pH (where applicable), viscosity/consistency, spreadability, drug content uniformity, tube extrudability, microbial limits, stability.

7.4.3 Creams — formulation, manufacturing, evaluation

- Formulation: o/w or w/o emulsion system — oil phase, water phase, emulsifiers, preservatives, drug.
- Manufacturing: heat both phases, add one to the other with stirring, homogenise, cool with stirring, add drug/flavour at the right stage.
- Evaluation: appearance, type test (o/w vs w/o), pH, viscosity, spreadability, phase separation/centrifugation test, drug content, microbial limits.

7.4.4 Gels/jellies — formulation, manufacturing, evaluation

- Formulation: gelling agent (carbomer, HPMC, xanthan, gelatin) + water/glycol + drug + preservative; neutraliser for carbomers.

- Manufacturing: disperse gelling agent in water with stirring (avoid lumps), allow hydration, add drug solution, adjust pH/consistency, deaerate.
- Evaluation: clarity, pH, viscosity, spreadability, syneresis, drug content, microbial limits.

7.4.5 Pastes — formulation, manufacturing, evaluation

- Formulation: high solid content (powder like zinc oxide, starch) in a greasy base — stiff, less greasy, absorbent, stays in place.
- Manufacturing: trituration/fusion like ointments, ensuring uniform powder distribution.
- Evaluation: stiffness/consistency, homogeneity (no gritty lumps), drug content, adhesion.

7.4.6 Suppositories and pessaries — formulation, manufacturing, evaluation

- Bases: (a) oleaginous — cocoa butter (theobroma oil), hard fat; melt at body temperature; (b) water-soluble/mis

...[truncated 10599 chars]cible — macrogols (PEGs), glycerinated gelatin; dissolve in body fluids.

- Formulation: drug + base + (surfactants for wetting, preservatives where needed); displacement value used to calculate how much base to use so each mould gives the correct drug dose.
- Manufacturing methods: (a) hand moulding/rolling (small scale); (b) fusion/melt-pour — melt base, incorporate drug, pour into cooled moulds, trim; (c) compression moulding.
- Evaluation: appearance, weight variation, melting point/range, disintegration/dissolution time, drug content uniformity, mechanical strength (breaking test), liquefaction time.

Worked numerical — displacement value:

A suppository mould makes 2 g suppositories with cocoa butter. The drug's displacement value is 1.5 (1 g drug displaces 1.5 g base... simplified teaching version: base needed = mould capacity (drug weight ÷ displacement value)). For 10 suppositories each containing 0.5 g drug:

- Step 1: total drug = 10 × 0.5 g = 5 g.
- Step 2: base displaced by drug = 5 g ÷ 1.5 = 3.33 g.
- Step 3: total mould capacity = 10 × 2 g = 20 g.
- Step 4: base required = 20 3.33 = 16.67 g.
- Answer: weigh 16.67 g of base.

7.4.7 Advances — xerogels and emulgels

- Xerogels: gels from which the liquid has been removed by drying, leaving a porous solid matrix; they re-swell on contact with moisture. Overview: light, stable, easy to store/transport; on application they hydrate and release drug in a controlled manner. Applications: wound dressings, controlled topical delivery.
- Emulgels: emulsion droplets entrapped in a gel network — combines the drug-loading of emulsions (oily drugs) with the elegant, non-greasy, easily spreadable feel of gels. Overview: thixotropic, good spreadability, better patient acceptance than ointments. Applications: topical NSAIDs, antifungals, cosmetic–dermatological products.

Simple analogy: emulgel is like fruit pieces suspended in jelly — the goodness of both in one spoon.

Classifications

- Ointment bases: oleaginous, absorption, water-miscible, water-soluble.
- Suppository bases: oleaginous (cocoa butter) vs water-soluble (PEG, glycerinated gelatin).
- Semisolids by greasiness: ointments (most) > creams > gels (least).

Mechanism / how it works

- Drug release from ointment: drug partitions from base into skin; occlusive bases hydrate skin and boost flux.
- Gel formation: polymer chains hydrate and cross-link into a 3-D network trapping water.
- Suppository action: base melts (cocoa butter) or dissolves (PEG) at body temperature, releasing drug for local action or rectal absorption.

Diagram to draw

1. Ointment base selection flowchart: dry/scaly lesion -> oleaginous; weeping lesion -> paste/cream; need washability -> PEG/emulsifying base.
2. Suppository mould: cavities, base plate; label displacement.
3. Emulgel structure: gel network with oil droplets trapped inside.

Process flow

Ointment by fusion:

Weigh bases -> melt together -> add drug (dissolved/dispersed) -> stir while cooling -> IPQC (homogeneity, pH, viscosity) -> fill tubes -> seal -> label -> QC -> pack. Suppository by fusion: Calibrate mould -> melt base -> incorporate drug -> pour into cooled moulds -> solidify -> trim -> remove -> wrap -> QC (weight variation, melting range, content) -> pack.

One-glance summary

One-glance summary

SEMISOLID TYPES — one glance

- [LAB] Ointments: greasy · occlusive · bases: paraffin/lanolin/PEG · trituration or fusion
- Creams: o/w or w/o emulsions · less greasy · type test matters
- [VEHICLE] Gels: polymer network + water · clear · non-greasy · watch syneresis
- Pastes: high powder content · stiff · absorbent · stays put
- Suppositories: melt/dissolve in body cavity · cocoa butter vs PEG · displacement value for dosing
- Advances: xerogels (dried gels, re-swell) · emulgels (emulsion-in-gel, elegant)

Tables

Dosage form	Key base	Greasiness	Best for
Ointment	Soft paraffin/lanolin/PEG	High	Dry, scaly lesions
Cream (o/w)	Emulsion base	Low	General, cosmetic elegance
Gel	Carbomer/HPMC + water	None	Oily skin, hairy areas

Dosage form	Key base	Greasiness	Best for
Paste	Powder + greasy base	Medium	Weeping lesions, stays in place
Suppository	Cocoa butter/PEG	—	Rectal/vaginal delivery

Test	Ointment	Cream	Gel	Suppository
Spreadability				—
Viscosity				—
Drug content				
Microbial limits				
Weight variation	—	—	—	
Melting range	—	—	—	
Syneresis	—	—		—

Examples

1. Antifungal ointment: occlusive base keeps drug on the skin longer.
2. Burns cream (o/w): cooling, non-greasy, easy to apply on painful skin.
3. Diclofenac emulgel: elegant gel for joint pain — the advance over greasy rubs.
4. Glycerin suppository: local laxative action in the rectum.

Think of it this way

- Choosing an ointment base is like choosing clothes for weather — greasy "winter coat" for dry skin, light "cotton" (gel) for oily skin.
- Displacement value is like knowing how much water your bag displaces in a full bucket — so the mould still fills exactly.

Pharmacy relevance

Pharmacists compound ointments, advise on thin application, storage (gels away from heat), and counsel on suppository insertion and retention.

India context

Combination steroid–antifungal creams are widely used in India; pharmacists counsel against prolonged unsupervised use, and emulgels are popular for musculoskeletal pain.

Key points

1. Base selection matches the lesion: dry -> occlusive ointment; weeping -> paste/cream.
2. Ointments: trituration or fusion; evaluated for homogeneity, spreadability, viscosity, content.
3. Creams are emulsions — type test and phase separation matter.
4. Gels: polymer network; watch syneresis and pH.

5. Suppositories: cocoa butter (melts) vs PEG/gelatin (dissolves); displacement value ensures correct dose.
6. Advances: xerogels (dried, re-swellable), emulgels (emulsion-in-gel elegance).

Common confusions

- Cream vs ointment: cream is an emulsion (contains water), less greasy; ointment is greasy with little/no water.
- Gel vs jelly: both are polymer networks; "jelly" is often used for firmer, sometimes oral/vaginal products — in this syllabus they are grouped together.
- Suppository vs pessary: suppository = rectal (sometimes general term); pessary = vaginal.

Common mistakes

1. Using a greasy ointment on a weeping/oozing lesion.
2. Forgetting displacement value and under-filling suppository drug content.
3. Storing cocoa-butter suppositories in heat (they melt).

Mnemonics

- "O-A-W-W" — Oleaginous, Absorption, Water-miscible, Water-soluble bases.
- "Dry-Greasy, Wet-Pasty" — base selection rule.

Exam summary

Semisolid types are chosen by lesion and purpose. Ointment bases (oleaginous, absorption, water-miscible, water-soluble) are selected by the dry-vs-weeping rule and made by trituration or fusion. Creams are o/w or w/o emulsions; gels are polymer networks; pastes carry high powder loads. Suppositories use cocoa butter (melting) or PEG/gelatin (dissolving) bases with displacement-value calculations. Xerogels and emulgels are modern advances combining stability and elegance.

One-minute revision

Dry lesion -> greasy ointment; weeping -> paste/cream. Bases: O-A-W-W. Trituration/fusion. Creams = emulsions. Gels = polymer network. Suppository: cocoa butter melts, PEG dissolves; displacement value for dose. Xerogel = dried gel; emulgel = emulsion in gel.

Exam questions

Short answers:

1. Classify ointment bases with one example each.
2. State the base-selection rules for ointments.
3. Differentiate cream and ointment.
4. What is displacement value? Why is it needed?
5. Write a short note on emulgels.

Long answers:

1. Describe the formulation, manufacturing and evaluation of ointments.

2. Describe the formulation, manufacturing and evaluation of suppositories, including the displacement-value calculation.

MCQs:

1. An occlusive ointment base is: (a) PEG (b) Soft paraffin (c) Gelatin (d) Water — Answer: (b)
2. Cocoa butter suppositories release drug by: (a) Dissolving (b) Melting at body temperature (c) Evaporation (d) Chewing — Answer: (b)
3. A paste differs from an ointment by its: (a) Colour (b) High powder content (c) Smell (d) Price — Answer: (b)
4. Syneresis is seen in: (a) Tablets (b) Gels (c) Capsules (d) Syrups — Answer: (b)
5. Emulgel combines: (a) Tablet + capsule (b) Emulsion + gel (c) Syrup + elixir (d) Two gels — Answer: (b)

Viva:

1. Why are suppositories stored in a cool place?
2. When would you choose a gel over an ointment?

Application-based:

1. A mould produces 2.5 g suppositories; each must contain 250 mg drug with displacement value 2.0. Calculate the base needed for 20 suppositories. (Steps: drug = 5 g; displaced base = 5/2 = 2.5 g; mould capacity = 50 g; base = 47.5 g.)

References