B. Pharmacy 1st Semester - Pharmaceutics 1

UNIT – 5: Semisolid Dosage Forms

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INTRODUCTION

Semisolid dosage forms represent a crucial category of dermatological preparations specifically designed for external application on the skin to produce either local or systemic therapeutic effects. These formulations include ointments, creams, gels, and pastes, each serving distinct therapeutic purposes and offering unique advantages in drug delivery.

These pharmaceutical preparations contain one or more active pharmaceutical ingredients (APIs) that are either dissolved or uniformly dispersed within a suitable base system. The formulation is enhanced with appropriate excipients including emulsifiers, viscosity-increasing agents, antimicrobial preservatives, antioxidants, and stabilizing agents to ensure optimal performance and stability.

Modern semisolid formulations have evolved significantly, with novel preparations being non-greasy and formulated with water-washable bases, addressing traditional limitations of earlier formulations and improving patient compliance and cosmetic acceptability.

DEFINITIONS AND CLASSIFICATION

Definitions



Semisolid Dosage Forms: Dermatological preparations with intermediate consistency between liquids and solids, intended for external application to produce local or systemic effects.

Ointments: Semisolid systems containing dissolved or suspended drugs in specific bases, applied externally primarily to skin and mucous membranes. **Creams**: Viscous semisolid emulsions for external use, typically containing water-soluble bases for easy removal.

Pastes: Semisolid preparations incorporating high percentages (often exceeding 50%) of insoluble particulate solids.

Gels: Semisolid dispersion systems consisting of small or large solid molecules dispersed in aqueous liquid vehicles, exhibiting jelly-like consistency.

Classification of Semisolid Dosage Forms 📋



Туре	Description	Key Characteristics	
Ointments	Drug dissolved/suspended in bases	Applied to skin and mucous membranes	
Pastes	High percentage insoluble solids	Protective, thick consistency	
Creams	Semisolid emulsions	O/W (vanishing) or W/O (cold) types	
Gels	Dispersion in aqueous vehicle	Jelly-like consistency	
Plasters	Solid/semisolid masses on	Medicated or non-medicated	
	backing	forms	
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MECHANISMS AND FACTORS INFLUENCING **DERMAL PENETRATION**

Mechanisms of Dermal Penetration



Dermal penetration of drugs from semisolid dosage forms involves complex processes that determine the extent and rate of drug absorption through the skin layers.

Penetration Pathways:

- Transcellular Route: Drug passes through the cells of the stratum corneum
- Intercellular Route: Drug moves between the cells through lipid-rich pathways
- Appendageal Route: Penetration through hair follicles and sweat ducts

Factors Influencing Dermal Penetration

Drug-Related Factors:

- Molecular weight and size of the drug molecule
- Lipophilicity and hydrophilicity balance (partition coefficient)
- Drug concentration and solubility in the vehicle
- Chemical stability of the active ingredient
- Degree of ionization at physiological pH

Vehicle-Related Factors:

- Type and composition of the base system
- Viscosity and rheological properties
- Presence of penetration enhancers
- pH of the formulation

• Thermodynamic activity of the drug in the vehicle

Skin-Related Factors:

- Thickness and integrity of the stratum corneum
- Hydration status of the skin
- Age and anatomical site of application
- Presence of skin diseases or damage
- Regional variations in skin permeability

Environmental Factors:

- Temperature and humidity conditions
- Occlusion and duration of contact
- Mechanical factors such as rubbing

★ IDEAL PROPERTIES OF SEMI-SOLID DOSAGE FORMS

Physical Properties **

Semisolid dosage forms should exhibit specific physical characteristics to ensure optimal performance and patient acceptance.

- Smooth Texture: The preparation should possess a uniform, smooth consistency without grittiness or lumps that could cause discomfort during application.
- **Elegant Appearance**: The formulation should be visually appealing with consistent color and texture throughout the product lifecycle.

- Non-dehydrating Nature: The base should not draw moisture from the skin, preventing dryness or irritation.
- Non-gritty Consistency: Complete absence of particles that could cause mechanical irritation or discomfort.
- Non-greasy and Non-staining Properties: Modern formulations should not leave greasy residues or stain clothing.
- Non-hygroscopic Characteristics: The preparation should not absorb excessive moisture from the environment, maintaining stability.

Physiological Properties 🦑



The formulation must be compatible with biological systems and skin physiology.

- Non-irritating Formulation: Should not cause inflammation, redness, or discomfort upon application.
- **Preservation of Skin Function**: Must not interfere with normal skin barrier function or physiological processes.
- Compatibility with Skin Secretions: Should mix readily with natural skin secretions without causing adverse reactions.
- **Low Sensitization Potential**: Minimal risk of causing allergic reactions or contact sensitization

Application Properties

Practical aspects of use and drug delivery performance.

Easy Application: Should spread smoothly and uniformly with minimal effort.

- **Efficient Drug Release**: Must provide optimal drug release characteristics for therapeutic efficacy.
- **High Aqueous Washability**: Easy removal with water, improving patient compliance and hygiene.

OINTMENTS

Ointments represent one of the most traditional and widely used semisolid dosage forms in pharmaceutical practice. These preparations are specifically designed for external application to the skin or mucous membranes, serving various therapeutic purposes from protection to drug delivery.

Classification of Ointments

Based on Penetration Properties ©

Туре	Penetration	Action	Uses	
Epidermic	Surface only	Local effect	Protectives, antiseptics, anti- infectives	
Endodermic	Partial absorption	Deeper tissue action	Emollients, stimulants, irritants	
Diadermic	Deep penetration	Systemic effects	Transdermal drug delivery	
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Epidermic Ointments: These formulations are designed to act primarily on the epidermis, producing localized effects without significant absorption into deeper tissues. They serve as protective barriers, antiseptics, local anti-infective agents, and parasiticides.

Endodermic Ointments: These preparations penetrate into the deeper layers of cutaneous tissues through partial absorption. They function as emollients, providing moisturization, or as stimulants and local irritants for therapeutic purposes.

Diadermic Ointments: These advanced formulations are engineered for deep penetration, allowing medicaments to pass through the skin and produce systemic therapeutic effects, essentially functioning as transdermal drug delivery systems.

Based on Therapeutic Uses 💉

Ointments can be classified according to their specific therapeutic applications:

- Antibiotic Ointments: Formulated to eliminate pathogenic microorganisms
- Antifungal Ointments: Designed to inhibit or destroy fungal infections
- Anti-inflammatory Ointments: Used to manage inflammatory, allergic, and pruritic skin conditions
- Antipruritic Ointments: Specifically formulated to relieve itching sensations
- Astringent Ointments: Cause skin contraction and reduce discharge production
- Counter-irritant Ointments: Applied locally to create irritation that reduces deeper pain
- Parasiticide Ointments: Destroy or inhibit parasitic infestations

Classification of Ointment Bases 🥕

The ointment base serves as the carrier or vehicle for the medicament, and its selection significantly influences the performance of the final product.

1. Oleaginous Bases 📱

Oleaginous bases consist of water-insoluble hydrocarbons, vegetable oils, animal fats, and waxes. The primary constituents include soft paraffin, hard paraffin, and liquid paraffin.

Petrolatum (Soft Paraffin): A purified mixture of semisolid hydrocarbons obtained from petroleum. Available in two varieties - yellow soft paraffin and white soft paraffin, with the white variety prepared by bleaching the yellow form.

Hard Paraffin: A purified mixture of solid hydrocarbons obtained from petrolatum, appearing as a colorless or white translucent, odorless, tasteless wax used to adjust consistency.

Liquid Paraffin: A mixture of liquid hydrocarbons obtained from petroleum distillation, also known as white mineral oil, appearing as a colorless, odorless, tasteless, and transparent oily liquid.

Limitations of Oleaginous Bases:

- Greasy texture and appearance
- Difficult removal from skin and clothing
- Heat retention causing discomfort
- Poor drug absorption facilitation

• Prevention of natural cutaneous secretion evaporation

2. Absorption Bases

These bases are anhydrous substances capable of absorbing considerable quantities of water while maintaining ointment-like consistency.

Types:

- Non-emulsified Bases: Absorb water to form w/o emulsions
- Water-in-Oil Emulsions: Capable of absorbing additional water

Key Components:

- Wool Fat (Anhydrous Lanolin): Purified fat-like substance from sheep wool
- Hydrous Wool Fat (Lanolin): Contains 70% wool fat and 30% purified water
- Wool Alcohol: Obtained from wool fat, contains minimum 30% cholesterol
- Beeswax: Purified wax from honeycomb, available as yellow or white varieties

Advantages:

- Compatibility with numerous medicaments
- High water absorption capacity
- Relative heat stability
- Easier removal compared to oleaginous bases

3. Emulsion Bases 🔼

These bases possess semisolid or cream-like consistency, utilizing both o/w and w/o emulsion systems.

Oil-in-Water (O/W) Emulsions: More popular due to easy removal with water washing, non-greasy characteristics.

Water-in-Oil (W/O) Emulsions: More greasy and sticky, but provide better occlusion and prolonged contact.

4. Water-Soluble Bases 💎

Commonly known as "greaseless ointment bases," these consist of water-soluble ingredients such as polyethylene glycol polymers (carbowaxes), tragacanth, gelatin, pectin, cellulose derivatives, bentonite, magnesium-aluminum silicate, and sodium alginate.

Methods of Preparation

1. Trituration Method 🛒

This is the most commonly employed method for ointment preparation, particularly suitable when the base is soft and the medicament is insoluble in the base. The process requires reduction of the medicament to fine powder for uniform distribution throughout the base matrix.

2. Fusion Method 🤚

Utilized when the ointment base contains multiple solid ingredients with different melting points. The technique involves melting components in

decreasing order of their melting points, starting with the highest melting point substance to avoid overheating of thermolabile components.

The medicament is incorporated slowly into the melted mass with thorough stirring until cooling occurs and a homogeneous product is formed. Any liquid ingredients or aqueous substances must be heated to similar temperatures as the melted bases.

3. Emulsification Method 6

This method involves melting fats, oils, and waxes together in a water bath at 70°C. The aqueous solution containing heat-stable, water-soluble components is heated to the same temperature as the melted bases. The aqueous phase is slowly added to the oil phase with continuous stirring until cooling produces a semisolid mass.

Temperature equilibration is crucial to prevent immediate solidification of high melting point components when cold aqueous solutions are added. Emulsifying agents are essential for stable emulsion formation.

4. Chemical Reaction Method 🕸

Certain ointment preparations involve chemical reactions during the manufacturing process. This method is employed when the active ingredient is formed or modified through chemical interactions within the formulation matrix.

Additives Used in Ointments 🥕

Preservatives: Methyl paraben and propyl paraben are incorporated to prevent microbial growth during extended storage periods, ensuring

product safety and stability.

Antioxidants: Added to prevent oxidative decomposition of active ingredients and base components, maintaining therapeutic efficacy and product integrity.

Chelating Agents: Prevent catalytic oxidative degradation caused by trace metal elements, enhancing product stability.

Humectants: Glycerin, propylene glycol, or sorbitol may be added to prevent moisture loss from the preparation, maintaining optimal consistency and preventing drying.

Perfumes: Added to improve organoleptic properties and patient acceptance.

Evaluation of Ointments

Drug Content Analysis

A specified quantity of ointment is weighed accurately, and the medicament is extracted using an appropriate solvent system. The drug content is then determined following pharmacopoeial procedures to ensure compliance with labeled potency.

Rate of Release Studies 🧑

Two primary methods are employed:

 Agar Cup Plate Method: Utilizes agar plates with cups to measure drug diffusion Diffusion Method: Measures drug release through diffusion cells or membranes

Penetration Rate Determination

The rate of penetration is determined by rubbing a weighed quantity of base into a defined skin area for a fixed time period. The weight difference indicates total base penetration, allowing calculation of penetration rates. Unabsorbed material is analyzed for remaining drug content to determine medicament penetration rates.

Consistency Testing \

Consistency evaluation involves sliding a glass plate over ointment spread evenly on another fixed glass plate, measuring the force required for specific displacement distances.

Absorption into Bloodstream

After applying specified amounts under standard conditions, drug content assays are performed on blood, urine, feces, or tissue samples at various time intervals. This method is limited when drug concentrations are very low.

Irritation Studies

Testing is performed on rabbit skin and eyes, or human skin under controlled conditions. Daily observations for one week assess lesions on cornea, iris, and conjunctiva, while skin patches within two weeks indicate potential irritation effects.

CREAMS

Creams represent viscous semisolid emulsions specifically formulated for external application. These preparations typically contain water-soluble bases, enabling easy removal from the skin surface. Creams possess softer consistency and lighter weight compared to traditional ointments, leaving minimal visible evidence after application.

Types of Creams 🎨



Aqueous Creams (O/W Type)

Oil-in-water emulsion creams are relatively non-greasy and are further classified based on the emulsifying agent employed:

- Anionic Emulsifying Wax Creams: Utilize negatively charged emulsifying agents
- Cationic Emulsifying Wax Creams: Employ positively charged emulsifying systems
- Non-ionic Emulsifying Wax Creams: Use neutral emulsifying agents

Oily Creams (W/O Type)

Water-in-oil emulsion creams possess greasy characteristics and are classified into:

- **Sterol Creams**: Utilize sterol-based emulsifying systems
- **Soap Creams**: Employ soap-based emulsification mechanisms



Pastes are semisolid preparations intended specifically for external skin application. These formulations are characteristically thick and stiff, maintaining their consistency at ordinary temperatures and forming protective coatings over application areas.

Pastes serve primarily as antiseptic, protective, or soothing dressings, often applied to lint before skin application for enhanced therapeutic delivery.

Types of Bases Used for Paste Preparation 🧱



Soft paraffins and liquid paraffin serve as commonly utilized bases for paste preparation, providing excellent occlusive properties and prolonged contact time.

2. Water Miscible Bases

Emulsifying ointment serves as the primary water-miscible base, while glycerin provides additional water-miscible properties for specific paste formulations.

3. Water Soluble Bases 💎

Suitable combinations of high and low molecular weight polyethylene glycols are blended to achieve desired consistency that softens or melts upon skin contact. These bases offer complete water solubility for easy removal.

GELS/JELLIES

Jellies are transparent or translucent, non-greasy semisolid preparations designed for external application to skin or mucous membranes. These formulations may be prepared from natural gums such as tragacanth, pectin, and sodium alginates, or from synthetic derivatives including methyl cellulose and sodium carboxymethyl cellulose.

Types of Jellies 🍵



Primarily used on mucous membranes and skin for spermicidal, local anesthetic, and antiseptic properties. Following water evaporation, jellies provide local cooling effects and residual protective films.

2. Lubricating Jellies

Specifically formulated for lubrication of diagnostic and surgical equipment including surgical gloves, cystoscopes, fingerstalls, catheters, and rectal thermometers. These preparations should be thin, transparent, and watersoluble.

3. Miscellaneous Jellies

Various specialized gel formulations serving specific therapeutic or diagnostic purposes beyond the primary categories.

EXCIPIENTS USED IN SEMISOLID DOSAGE FORMS

Active Pharmaceutical Ingredient (API)

The active pharmaceutical ingredient represents the therapeutically active component responsible for producing the desired pharmacological effect

in the target tissue or system.

Preservatives



Essential components added to prevent microbial growth and ensure product safety during storage and use. Common preservatives include:

- P-hydroxybenzoates (parabens)
- Phenol and phenolic compounds
- Benzoic acid and derivatives
- Sorbic acid
- Methyl paraben and propyl paraben
- Quaternary ammonium compounds
- Mercury compounds (limited use due to toxicity concerns)

Humectants

Glycerin, propylene glycol, and sorbitol are incorporated to prevent moisture loss from the preparation, maintaining optimal consistency and preventing formulation drying during storage and use.

Emulsifying Agents 6

Polysorbates, anionic emulsifying agents, and other surfactants are added when emulsion formation is required for proper formulation stability and drug delivery.

Antioxidants

Incorporated to protect active ingredients from oxidative degradation, maintaining therapeutic potency and extending product shelf life.

Organoleptic Agents 🎨

- Coloring Agents: Amaranth, brilliant blue, and other approved colorants for aesthetic appeal
- Flavoring Agents: Vanilla, strawberry, raspberry, and other flavors to improve palatability when appropriate



EVALUATION OF SEMISOLIDS

Comprehensive Evaluation Parameters

Parameter	Description	Method	
Appearance	Visual assessment of color, texture, odor	Organoleptic evaluation	
Viscosity	Flow characteristics measurement	Brookfield viscometers	
Drug Content	Active ingredient quantification	Pharmacopoeial assays	
Skin Irritation	Safety assessment on skin	Animal model studies	
Eye Irritation	Ophthalmic safety evaluation	Ocular irritation tests	
Spreadability	Application ease measurement	Slide method under load	

Detailed Evaluation Methods



Comprehensive visual observation encompassing odor evaluation, color consistency, texture analysis, and application feel assessment. This includes evaluation of grittiness, greasiness, stickiness, smoothness, stiffness, and tackiness characteristics.

Viscosity Measurement 📊

Rheological properties are determined using Brookfield viscometers under controlled temperature and shear rate conditions, providing quantitative flow behavior data.

Drug Diffusion Studies 🦑

Drug content determination through pharmacopoeial assay procedures, ensuring therapeutic equivalence and regulatory compliance.

Skin Irritation Studies 🐇

Comprehensive safety evaluation to assess potential skin irritation, rash formation, or erythema development, typically conducted using appropriate animal models under controlled conditions.

Eye Irritation Studies <a>®

Specialized testing for ophthalmic preparations to evaluate potential ocular irritation or erythema, conducted using established animal model protocols.

Spreadability Testing

Quantitative measurement of gel spreadability by placing the formulation between two slides under specific load conditions, determining the ease of application and coverage characteristics. This comprehensive evaluation ensures that semisolid dosage forms meet all required quality, safety, and efficacy standards before clinical use, providing assurance of therapeutic reliability and patient safety.

