Chapter- 19

Semisolid Dosage Forms

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ABSTRACT

Semisolid dosage forms are pharmaceutical preparations that have a consistency between solid and liquid. They are intended for topical application to the skin or mucous membranes, where they provide localized or systemic effects. These forms include ointments, creams, gels, and pastes, each designed to deliver active ingredients effectively while providing protective and soothing properties.

The classification of semisolid dosage forms includes:

1. **Ointments**: Greasy preparations with a high oil content, used for their emollient and protective effects. Example: Hydrocortisone ointment.
2. **Creams**: Emulsions of oil and water, less greasy than ointments, used for moisturizing and medicated purposes. Example: Antifungal creams.
3. **Gels**: Transparent or translucent preparations with a jelly-like consistency, used for localized drug delivery. Example: Diclofenac gel.
4. **Pastes**: Thick, stiff preparations containing a high proportion of solid materials, used for protective and absorbent purposes. Example: Zinc oxide paste.

The mechanisms and factors influencing dermal penetration of drugs include the drug's physicochemical properties (e.g., molecular size, lipophilicity), the formulation's characteristics (e.g., type of base, use of penetration enhancers), and the condition of the skin (e.g., hydration, integrity). Lipophilic drugs and formulations with penetration enhancers tend to penetrate the skin more effectively. The stratum corneum, the outermost layer of the skin, is the primary barrier to drug penetration.

Preparation of ointments involves several steps. First, the base (e.g., petrolatum, lanolin) is melted if necessary. The active ingredients are then incorporated into the base, either by levigation (rubbing on a smooth surface with a small amount of base) or fusion (melting together). The mixture is thoroughly homogenized to ensure uniform distribution of the active ingredients.

Preparation of pastes is similar to ointments but involves a higher proportion of solid materials. The active ingredients are finely powdered and mixed with a small amount of base to form a smooth paste. Additional base is gradually added while mixing to achieve the desired consistency. The final product is typically more viscous and adherent than ointments.

19.1 Introduction

Semisolid dosage forms are a crucial category in pharmaceutical formulations, designed to provide local or systemic effects. These forms include creams, ointments, gels, and pastes. Here's an introduction to each type, along with their characteristics and uses:

1. Creams

a. **Definition**: Creams are emulsions of oil in water (O/W) or water in oil (W/O), which are generally smooth and easily spreadable.
b. **Characteristics**: They are usually white or off-white and can be either oil-based or water-based. They tend to be less greasy compared to ointments.
c. **Uses**: Creams are commonly used for topical applications like moisturizing, delivering medications for skin conditions, or providing a barrier against irritants.

2. Ointments

a. **Definition**: Ointments are thick, greasy preparations that are predominantly oil-based. They are usually made from a mixture of hydrocarbons or waxes and sometimes include an emulsifier.
b. **Characteristics**: Ointments are more occlusive than creams, meaning they provide a barrier that can help retain moisture in the skin and enhance drug absorption.
c. **Uses**: They are used for their protective, emollient, and therapeutic properties. Commonly applied for chronic conditions like eczema or psoriasis.

3. Gels

a. **Definition**: Gels are semisolid systems where the active ingredient is dispersed in a gel-like medium, usually made from a gelling agent such as carbomer or hydroxyethyl cellulose.
b. **Characteristics**: Gels are typically transparent or translucent and are less greasy compared to ointments. They have a more fluid consistency, which allows them to spread easily.
c. **Uses**: Gels are often used for topical delivery of drugs, particularly in cases where a non-greasy application is preferred. They are also used in cosmetic formulations.

4. Pastes

a. **Definition**: Pastes are thick, stiff formulations that contain a higher percentage of solid particles compared to ointments and creams.
b. **Characteristics**: Due to their consistency, pastes provide a protective layer on the skin and are less likely to be absorbed.
c. **Uses**: They are used for their protective and adsorbent properties, often in conditions where a thicker barrier is needed, such as for the treatment of diaper rash or to protect against friction.

Formulation Considerations

a. **Base Selection**: The choice of base (oil-based, water-based, or a combination) affects the texture, absorption, and release characteristics of the semisolid dosage form.
b. **Drug Release**: The release rate of the active ingredient from semisolid dosage forms is influenced by the base, the drug’s solubility, and the formulation’s viscosity.

c. **Stability**: Stability testing is critical to ensure that the semisolid maintains its efficacy and safety throughout its shelf life.

Advantages

a. **Local Effects**: Many semisolid formulations are used for localized treatment, reducing systemic side effects.
b. **Enhanced Compliance**: They can be more acceptable to patients due to their ease of application and varying textures.

Disadvantages

a. **Limited Systemic Use**: Some semisolid forms may not be suitable for systemic drug delivery due to absorption limitations.
b. **Messiness**: Ointments and pastes can be greasy, which might affect patient compliance.

19.2 Definitions of Semisolid Dosage Forms

1. Creams

a. **Definition**: Creams are semisolid emulsions consisting of a mixture of oil and water. They can be classified into two types:
   i. **Oil-in-Water (O/W)**: Where oil droplets are dispersed in a continuous water phase.
   ii. **Water-in-Oil (W/O)**: Where water droplets are dispersed in a continuous oil phase.
b. **Characteristics**: Creams are smooth, non-greasy, and easy to spread. They have a balanced consistency that allows them to be absorbed quickly by the skin.
c. **Uses**: They are used for both cosmetic and therapeutic purposes, such as moisturizing, delivering medication to the skin, or treating conditions like dermatitis and eczema.

2. Ointments

a. **Definition**: Ointments are thick, greasy semisolid preparations that are predominantly oil-based. They consist of a base (like petrolatum or lanolin) that may be combined with active ingredients and sometimes emulsifiers.
b. **Characteristics**: Ointments are more occlusive and greasy compared to creams. They create a barrier on the skin, which can help to retain moisture and protect against irritants.
c. **Uses**: Commonly used for their protective, emollient, and therapeutic properties. They are suitable for treating dry, scaly skin conditions and delivering medications over a prolonged period.

3. Gels

a. **Definition**: Gels are semisolid systems in which a gelling agent (such as carbomer, hydroxyethyl cellulose, or agar) is used to form a network that traps the active ingredients in a gel-like medium.
b. **Characteristics**: Gels are usually clear or translucent, less greasy, and have a fluid consistency that allows for easy application. They can be quickly absorbed and leave minimal residue.

c. **Uses**: They are used for topical delivery of medications, especially when a non-greasy or less occlusive formulation is preferred. Gels are often used in cosmetic products and for treating conditions like acne or muscle pain.

4. Pastes

a. **Definition**: Pastes are thick, viscous semisolid formulations that contain a high proportion of solid particles suspended in a base. The base can be either oil-based or a mixture of oil and water.
b. **Characteristics**: Due to their high solid content, pastes are stiff and form a protective layer on the skin. They are less likely to spread compared to ointments or creams.
c. **Uses**: Pastes are used where a thicker barrier is needed, such as for protecting the skin from irritation or treating conditions like diaper rash or dermatitis.

19.3 Classification of Semisolid Dosage Forms

Semisolid dosage forms can be classified based on their composition, consistency, and intended use. Here's a detailed classification:

1. Based on Composition

1.1. Emulsions

a. **Creams**:
   i. **Oil-in-Water (O/W)**: Water is the continuous phase, and oil is dispersed as droplets. This type is less greasy and more easily absorbed.
   ii. **Water-in-Oil (W/O)**: Oil is the continuous phase, and water is dispersed as droplets. This type is more occlusive and greasy, providing better moisture retention.

1.2. Oleaginous Bases

a. **Ointments**:
   i. **Hydrocarbon Bases**: Composed of pure hydrocarbons (e.g., petrolatum). These are highly occlusive and provide a protective barrier.
   ii. **Absorption Bases**: Contain emulsifying agents that allow the addition of water. They can absorb more water, making them less greasy.
   iii. **Water-Removable Bases**: Often referred to as creams, they are similar to O/W emulsions but are generally easier to wash off.

1.3. Gels and Jellies

a. **Gels**:
   i. **Aqueous Gels**: Contain water as the main solvent, gelling agents (e.g., carbomer, agar), and sometimes active ingredients.
   ii. **Hydroalcoholic Gels**: Contain both water and alcohol, which can help dissolve some drugs and act as a vehicle for topical application.
   iii. **Organic Gels**: Use organic solvents like oils combined with gelling agents.

1.4. Pastes

a. **Pastes**:
   i. **Zinc Oxide Paste**: Contains a high proportion of zinc oxide, providing a protective layer on the skin.

ii. **Antiseptic or Medicinal Pastes**: Formulated with active ingredients to treat specific conditions like fungal infections or irritations.

2. Based on Consistency

2.1. Soft and Spreadable

a. **Creams**: Usually have a lighter consistency and are easy to spread over large areas of the skin.
b. **Gels**: Typically smooth and non-greasy, making them easy to apply and suitable for a wide range of conditions.

2.2. Thick and Protective

a. **Ointments**: Have a thicker, greasier consistency, providing a protective barrier and often used for localized treatment.
b. **Pastes**: Very thick and less spreadable, offering a more substantial barrier and protection for the skin.

3. Based on Application and Use

3.1. Therapeutic

a. **Topical Medications**: Used for localized treatment of conditions like eczema, psoriasis, acne, or pain relief (e.g., corticosteroid creams, antifungal ointments).
b. **Protective Agents**: Provide a barrier to protect the skin from irritants and moisture loss (e.g., diaper rash pastes, barrier creams).

3.2. Cosmetic

a. **Moisturizers**: Creams and gels used to hydrate and maintain skin health.
b. **Anti-Aging Products**: Specialized creams and gels formulated to reduce wrinkles and improve skin texture.

3.3. Specialty Applications

a. **Transdermal Systems**: Gels or creams designed for controlled release of medication through the skin into the bloodstream.
b. **Opthalmic and Otic Formulations**: Specially designed semisolids for application in the eyes or ears.

19.4 Mechanisms and Factors Influencing Dermal Penetration of Drugs

Dermal penetration of drugs from semisolid dosage forms is a complex process influenced by various mechanisms and factors. Understanding these can help optimize drug delivery through the skin. Here's a detailed overview:

Mechanisms of Dermal Penetration

1. **Stratum Corneum Penetration**
    a. **Barrier Function**: The stratum corneum (outermost layer of the skin) acts as the primary barrier to drug penetration. Drugs must traverse this layer to reach deeper skin layers.

b. **Lipid Matrix**: The stratum corneum is composed of lipid bilayers and keratinocytes. Drugs can penetrate via:
    i. **Intercellular Route**: Through the lipid matrix between cells.
    ii. **Transcellular Route**: Directly through the cells.
    iii. **Follicular Route**: Via hair follicles and sebaceous glands, which can bypass the stratum corneum.

2. **Drug Partitioning**
    a. **Partition Coefficient**: The drug's ability to partition between the semisolid formulation and the skin is crucial. Drugs with high lipophilicity often penetrate better as they can dissolve in the lipid-rich stratum corneum.
    b. **Solubility**: A drug's solubility in the semisolid formulation affects its availability and absorption. Drugs need to be in solution to diffuse through the skin layers.

3. **Diffusion**
    a. **Fick's Law of Diffusion**: Drug diffusion through the skin follows Fick's Law, which states that the rate of drug diffusion is proportional to the concentration gradient and surface area, and inversely proportional to the thickness of the skin.
    b. **Concentration Gradient**: Higher concentrations in the semisolid formulation lead to a greater gradient and, consequently, increased diffusion into the skin.

4. **Release from the Dosage Form**
    a. **Drug Release Rate**: The rate at which the drug is released from the semisolid dosage form impacts penetration. Faster release rates typically lead to higher drug concentrations in the skin.
    b. **Formulation Factors**: The nature of the semisolid (e.g., gel vs. ointment) affects drug release and penetration. For example, gels with higher water content may allow for quicker drug release compared to oil-based ointments.

Factors Influencing Dermal Penetration

1. **Physicochemical Properties of the Drug**
    a. **Molecular Size**: Smaller molecules generally penetrate the skin more easily than larger ones.
    b. **Lipophilicity/Hydrophilicity**: Lipophilic drugs penetrate better through the lipid-rich stratum corneum, while hydrophilic drugs may require specialized formulations or enhanced delivery methods.

2. **Formulation Factors**
    a. **Base Composition**: The choice of semisolid base (e.g., oil-based ointment vs. water-based cream) affects drug release and skin permeability.
    b. **Additives**: Enhancers or penetration enhancers (e.g., alcohol, surfactants) can increase drug permeability by altering the stratum corneum's barrier properties.

3. **Skin Condition**
    a. **Hydration**: Well-hydrated skin can be more permeable than dry skin. Certain semisolid formulations can increase skin hydration, enhancing drug absorption.
    b. **Skin Integrity**: Damaged or compromised skin (e.g., due to abrasion or inflammation) may have altered permeability compared to intact skin.

4. **Application Site**
    a. **Skin Thickness**: Different areas of the body have varying skin thicknesses and permeability. For instance, the skin on the palms and soles is thicker compared to other areas.
    b. **Temperature**: Higher skin temperatures can increase drug penetration by enhancing blood flow and altering skin permeability.

5. **Duration and Frequency of Application**
    a. **Contact Time**: Prolonged contact with the semisolid formulation allows for more extended drug exposure and potentially greater penetration.
    b. **Frequency of Application**: Regular application can maintain higher drug levels in the skin and improve overall absorption.

6. **Occlusion**
    a. **Occlusive Dressings**: Applying semisolid formulations under occlusive dressings (e.g., plastic wrap) can enhance penetration by preventing evaporation, increasing hydration, and maintaining higher drug concentrations.

19.5 Preparation of Ointments

The preparation of ointments involves a series of steps designed to mix active ingredients with a suitable base to produce a stable, effective semisolid product. Here's a detailed overview of the process:

1. Selection of Ingredients

1.1. Active Ingredients

a. **Pharmacologically Active Substances**: These are the primary agents intended to provide therapeutic effects (e.g., corticosteroids, antibiotics, antifungals).

1.2. Base

a. **Oleaginous Bases**: Pure hydrocarbons or oils (e.g., petrolatum, lanolin). They are non-water-soluble and provide an occlusive barrier.
b. **Absorption Bases**: Contain emulsifiers that can incorporate additional water (e.g., hydrophilic petrolatum).
c. **Water-Removable Bases**: Similar to emulsions, they are generally easier to wash off and are less greasy (e.g., hydrophilic ointment).
d. **Water-Soluble Bases**: Composed mainly of water-soluble materials and often used for specific applications (e.g., polyethylene glycol ointment).

1.3. Auxiliary Agents

a. **Emulsifiers**: For bases that require emulsification (e.g., cetyl alcohol, stearyl alcohol).
b. **Preservatives**: To prevent microbial growth and prolong shelf life (e.g., parabens, benzyl alcohol).
c. **Stabilizers**: To maintain the stability of the formulation (e.g., antioxidants like ascorbic acid).

2. Preparation Methods

2.1. Simple Mixing

a. **Process**: Blend the active ingredient(s) with the base using a mortar and pestle or an ointment mill.
b. **Application**: Suitable for homogeneous mixtures where the active ingredient is soluble in the base or can be easily dispersed.

2.2. Fusion Method

a. **Process**: Heat the base until it melts, then add the active ingredient(s) and mix thoroughly until a uniform mixture is obtained. The mixture is then allowed to cool and solidify.
b. **Application**: Commonly used for bases that are solid at room temperature (e.g., paraffin-based ointments).

2.3. Emulsification Method

a. **Process**: Combine oil and water phases separately, then mix them together using an emulsifier to form an emulsion. Add the active ingredient(s) to the emulsion.
b. **Application**: Used for creams or ointments requiring an emulsified base (e.g., O/W or W/O emulsions).

2.4. Mechanical Mixing

a. **Process**: Utilize equipment like high-shear mixers or homogenizers to achieve a fine, uniform mixture of active ingredients and the base.
b. **Application**: Suitable for large-scale production where consistency and uniformity are critical.

3. Quality Control

3.1. Homogeneity

a. **Process**: Check the uniform distribution of active ingredients throughout the ointment. This can be done through visual inspection and laboratory testing.

3.2. Viscosity

a. **Process**: Measure the ointment's consistency to ensure it is appropriate for application. This can be done using viscometers.

3.3. pH

a. **Process**: Test the pH of the ointment to ensure it is suitable for its intended application, especially for products designed for skin use.

3.4. Microbial Testing

a. **Process**: Perform tests to ensure the ointment is free from microbial contamination, especially if the formulation contains water or other ingredients prone to microbial growth.

4. Packaging and Storage

4.1. Packaging

a. **Process**: Transfer the prepared ointment into appropriate containers (e.g., tubes, jars) that protect it from contamination and degradation.

b. **Considerations**: Containers should be airtight and resistant to moisture and light if necessary.

4.2. Storage

a. **Process**: Store the ointment under conditions that maintain its stability (e.g., temperature-controlled environments, away from direct light).

b. **Considerations**: Follow specific storage instructions based on the formulation and active ingredients.

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