

# SEMISOLID DOSAGE FORMS

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# SEMISOLID DOSAGE FORMS

## ❖ INTRODUCTION

- Semi-solid dosage forms are dermatological preparations intended to apply externally on the skin to **produce local or systemic effect** e.g. ointments, creams, gels and pastes.
- They contain **one or more active ingredients** dissolved or uniformly dispersed in a suitable base and any suitable excipients such as **emulsifiers, viscosity increasing agents, antimicrobial agents, antioxidants, or stabilizing agents**
- Novel semisolids are non-greasy since they are made up of water washable

## ❖ IDEAL PROPERTIES OF SEMI-SOLID DOSAGE FORMS

### Physical Properties

- (a) They should have smooth texture
- (b) They should be elegant in appearance
- (c) They should be non-dehydrating
- (d) They should be non-gritty in nature
- (e) Possess non-greasy and non-staining property
- (f) They are non-hygroscopic in nature



### Physiological Properties

- (a) They should be non-irritating
- (b) They should not alter skin functioning
- (c) They should be easily miscible with skin secretion
- (d) They should have low sensitization effect

### Application Properties

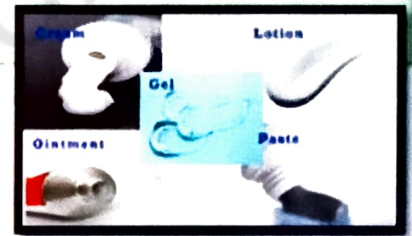
- (a) They should be easily applicable with efficient drug release
- (b) They should possess high aqueous washability

**Different types of semisolid are as given :**

### OINTMENTS

Semisolid systems containing **dissolved or suspended drug** into certain bases that are applied externally, primarily to skin, and also to mucous membranes, e.g. rectum, vagina or eye

<b>PASTES</b>	Semisolids incorporating a high percentage of insoluble particulate solids. Insoluble particulate solids may exceed 50%.
<b>CREAMS</b>	Pastes Creams Semisolid emulsions for external application <b>o/w semisolid emulsions = vanishing creams</b> <b>w/o semisolid emulsion = cold creams</b>
<b>GEL</b>	Semisolid dispersion systems consist of a <b>dispersion of small or large solid molecules in an aqueous liquid vehicle, exhibiting jelly-like consistency</b>
<b>PLASTERS</b>	Solid or semisolid <b>masses spread on backing paper, plastic, or fabric. Non-medicated forms (adhesive plasters)</b> Medicated plasters <b>provide a therapeutic effect</b> at the site of application.



## OINTMENTS

Ointments are semi-solid preparations meant for external application to the skin or mucous membrane. They usually contain a medicament or **medicaments dissolved, suspended or emulsified in an ointment base**. They may contain a suitable antimicrobial preservative. The ointments are mainly used as protective or emollient for the skin.

### Classification of Ointments ;

- (1) According to their therapeutic properties based on penetration
- (2) According to their therapeutic uses



### Ointment classified according to properties based on penetration :

#### Epidermic ointments

- **These ointments are meant for action on epidermis and produce local effect**
- **They are not absorbed.**
- **These types of ointments are mainly used as protectives, antiseptics, local anti-infectives and parasiticides.**

<b>Endodermic ointments</b>	<ul style="list-style-type: none"> <li>• These ointments are meant for <b>action on deeper layers of cutaneous tissues.</b></li> <li>• They are partially absorbed and act as emollients, stimulants and local irritants.</li> </ul>
<b>Diadermic ointments:</b>	These ointments are meant for deep penetration and release the medicaments that pass through the skin and <b>produce systemic effects</b>

**Ointment classified according to therapeutic use :**

<b>OINTMENTS</b>	<b>DESCRIPTION</b>
<b>Antibiotic ointments</b>	Used to <b>kill microorganisms</b>
<b>Antifungal ointments</b>	Ointments are used to <b>inhibit or kill the fungi</b>
<b>Anti-inflammatory ointments</b>	Used to relieve <b>inflammatory, allergic and pruritic conditions of the skin</b>
<b>Antipruritic ointments</b>	These ointments are used to <b>relieve itching</b>
<b>Astringent ointments</b>	Causes contraction of the skin and decrease discharges.
<b>Counter-irritant ointments</b>	Ointments are <b>applied locally to irritate the skin</b> , thus reducing or relieving another irritation or deep seated pain.
<b>Ointments used for dandruff treatment</b>	Applied locally to get relief from dandruff. The drugs commonly used are salicylic acid and cetrimide
<b>Ointments for psoriasis treatment</b>	Coal tar, corticosteroid, dithranol and <b>salicylic acid are incorporated with the suitable ointment base</b> for the treatment of psoriasis.
<b>Parasiticide ointments</b>	Ointments destroy or inhibit living infestation, such as lice and ticks, The drugs commonly mixed with ointment bases are benzyl benzoate, hexachloride, sulphur etc.

The ointment base is that substance or part of an ointment, which serves as carrier or vehicle for the medicament.

An ideal ointment base should possess the following properties:-

- (i) It should be **inert, odourless and smooth**
- (ii) It should be **physically and chemically stable**
- (iii) It should be compatible with the skin and with the incorporated medicaments
- (iv) It should be of such a consistency that it spreads and softens when applied to the skin with stress
- (v) It should not retard healing of the wound
- (vi) It should not produce **irritation or sensitization of the skin**

## ❖ CLASSIFICATION OF OINTMENT BASES

1. Oleaginous bases
2. Absorption bases
3. Emulsion bases
4. Water soluble bases



### 1. OLEAGINOUS BASES

- Consist of **water insoluble**, hydrocarbons, vegetable oils, animal fats and waxes.
  - The constituents of **hydrocarbon bases** are **soft paraffin, hard paraffin and liquid paraffin**
- (i) **Petrolatum (soft paraffin)**: It is a **purified mixture of semi- solid hydrocarbons obtained from petroleum**.
- There are two varieties of soft paraffin, one is **yellow soft paraffin** and other is **white soft paraffin**
  - **White soft paraffin is prepared by bleaching yellow paraffin**.
- White soft paraffin is **never used** in the preparation of **ophthalmic ointments** because the **white soft paraffin** may contain small traces of **bleaching agent**

## **(ii) Hard paraffin:**

- It is a **purified mixture of solid hydrocarbons** obtained from **petrolatum**
  - It is **colourless or white translucent, odourless, tasteless wax**
  - It is used to **harden or soften the ointment base**

## **(iii) Liquid paraffin:**

- It consists of a **mixture of liquid hydrocarbons** and obtained from petroleum **by distillation**.
- It is also known as **white mineral oil or liquid petroleum**.
- It is a **colourless, odourless, tasteless and transparent oily liquid**.

**The oleaginous is bases are losing their importance nowadays for the following reasons:-**

- (i) They are **greasy**
- (ii) They are **sticky and are difficult to remove both from skin and clothing**.
- (iii) They **retain body heat** which may produce an uncomfortable feeling of warmth.
- (iv) They **do not help in the absorption of medicaments**
- (v) **prevent evaporation of cutaneous secretions along with perspiration**

## **2. ABSORPTION BASES**

These bases are generally **anhydrous substances** which have the property of absorbing (emulsifying) considerable quantities of water but still retaining their ointment-like consistency.

**The absorption bases are of two types:-**

- (i) **Non-emulsified bases**
- (ii) **Water in oil emulsions**

- ✓ **The non-emulsified bases absorb water and aqueous solutions producing w/o emulsions** e.g., wool fat, wool alcohol, beeswax and cholesterol
- ✓ **The water in oil emulsions are capable of absorbing more water** and have the properties of non-emulsified bases e.g., hydrous wool fat (lanolin)

### **(i) Wool fat:**

- It is the **purified fat-like substance** obtained from the **wool of sheep**
- It is also known as **anhydrous lanolin**



### (ii) Hydrous wool fat:

- It is the **purified fat like substance**
- Obtained from **wool of sheep**
- It is also known as **lanolin**
- It is **insoluble in water but soluble in ether and chloroform.**
- Hydrous wool fat is a **mixture of 70% w/w wool fat and 30% w/w purified water**

### (iii) Wool alcohol:

- It is obtained from **wool fat by treating it with alkali**
- It contains not **less than 30% of cholesterol**
- It is used as an **agent** for the preparation of **w/o emulsion.**

### (iv) Beeswax :

- It is purified wax **obtained from honey comb of bees**
- It is available as **yellow beeswax and white beeswax.**
- White beeswax is obtained by **bleaching the yellow beeswax**
- It is used as a stiffening agent in pastes and ointments

### These bases have following advantages -

- (1) These bases are **compatible with large number** of medicaments
- (2) These bases can **absorb a large quantity of water or aqueous substances**
- (3) These bases are relatively **heat stable**
- (4) These bases are **quite greasy**, but these can be **easily removed from the skin** as compared to oleaginous bases

## 3. EMULSION BASES

- These bases are semisolid or have a **cream-like consistency**. Both **o/w and w/o emulsions are used as ointment base**
- The oil in water type of emulsion bases are more popular because these can be easily removed from the skin or clothes by washing with water
- The w/o type of bases are **greasy and sticky**
- The emulsifying ointment is prepared from **emulsifying wax, white soft paraffin and liquid paraffin**

## 4. WATER SOLUBLE BASES

- These are commonly known as "grease- less ointment bases"
- The water-soluble bases consist of water soluble Ingredients, such as, **polyethylene glycol polymers which are popularly known as "carbowaxes"**
- Tragacanth, gelatin, pectin, cellulose derivatives, bentonite, magnesium-aluminium silicate and sodium alginate are also used as water soluble bases

### ❖ METHODS OF PREPARATION

#### 1. Trituration method

#### 2. Fusion method

#### 3. Emulsification Method:

(a) Preparation of oil and aqueous phases

(b) Mixing of the phases

(c) Cooling the emulsion

(d) Homogenization

#### 4. Chemical reaction method.

#### Trituration method

- Most commonly used method for preparation of ointments
- The method is **used when the base is soft** and the **medicament is insoluble in the base**
- So for uniform mixing of medicament in the base, it becomes necessary to reduce the medicament to fine powder

#### Fusion method

- When an ointment base contains a number of solid ingredients of different melting points, such as white beeswax, Stearic acid, hard paraffin and cetyl alcohol, it is **necessary to melt them in decreasing order** to their melting point
- This means, that the **Sub- stance with highest melting point** should be **melted first**, then the substance with next melting point and so on
- This will **avoid the overheating** of substances having low melting points



<b>Fusion method</b>	<ul style="list-style-type: none"> <li>• The medicament is incorporated slowly to the melted mass, stirred thoroughly until the mass cools down and homogeneous product is formed.</li> <li>• In case any liquid ingredient or aqueous substance is also to be incorporated, that should be heated to almost to the same temperature as the melted bases.</li> </ul>
<b>Emulsification method</b>	<ul style="list-style-type: none"> <li>• In this method, <b>the fats, oils and waxes</b> are melted together on a water bath at a temperature of <b>70°C</b></li> <li>• The aqueous solution of all of the heat stable water soluble components is also heated almost at the same temperature as that of the melted bases.</li> <li>• The solution is slowly added to the melted bases with continuous stirring until the product cools down and semi-solid mass known as ointment is prepared</li> <li>• Important to heat the aqueous liquid to almost the same temperature as that of the melted bases</li> <li>• Otherwise high melting point fats and waxes will immediately get solidified when a cold aqueous solution is mixed with it</li> <li>• Emulsifying agent is needed to make a stable emulsion</li> </ul>
<b>Chemical reaction method</b>	<ul style="list-style-type: none"> <li>• Certain chemical reactions are involved in the preparation of several ointments.</li> <li>• For example, <b>iodine ointment</b>. Iodine may be present in free form or in combined form with the ointment base</li> </ul>

### ❖ ADDITIVES USED IN OINTMENTS

**preservatives, antioxidants**(to prevent oxidative decomposition ), **chelating agents** (catalytic oxidative degradation of trace element) and **perfumes** **Methyl paraben or propyl paraben may be incorporated as preservative** to prevent the microbial growth in ointment during its storage for a long period. To prevent the loss of moisture from the preparation, **the humectant such as, glycerin, propylene glycol or sorbitol may be added.**

## ❖ EVALUATION OF OINTMENTS

### Drug content

- Required quantity of ointment is weighed
- The medicament is extracted by using suitable solvent and its content is determined as per procedure given in the pharmacopoeia

### Rate of release of medicament from bases

two methods are used to study-

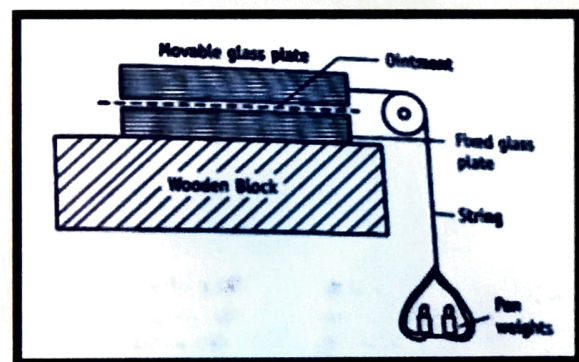
- (i) **Agar cup plate method**
- (ii) **Diffusion method**

### Rate of penetration of base or medicament

- Determined by rubbing the weighed quantity of base into defined area skin for a fixed time.
- The difference in weight shows the total base penetrated in a particular fixed time and from this observation, penetration rate of base is calculated.
- The unabsorbed collected material is analyzed to find out the content of medicament remained.
- The difference between the initial and final drug content will show the total amount of drug penetrated in a particular fixed time.
- From this observation **penetration rate of medicament** is calculated

### Consistency of the preparation

The **consistency of ointments can be studied by sliding a glass plate** over the ointment spread evenly on another glass plate which is fixed on a wooden surface as shown in figure



### Absorption of medicament into blood stream

- After rubbing a specified amount of ointment under standard conditions the assay of drug content is done either from blood, urine, faeces or tissues at different intervals.
- The method is not applicable in case the drug content in the ointment is very less

### Irritant effect

- The **test is performed on the skin and eyes of rabbits** or also on human skin.
- The observation is made daily for a week. Lesions on cornea, iris and conjunctiva suggest irritant effect. Patches on the skin within 2 weeks at the site of application suggests irritation effect of the ointment

## CREAMS

These are viscous semi-solid emulsions which are **meant for external use**. They usually contain a **water soluble base** due to which they can be **easily removed from the skin**. They are of softer consistency and have light weight in comparison to true ointments when applied to the skin, creams leave no visible evidence of their presence on the skin

### Types of Creams -

The creams are of two types:-

- (1) Aqueous creams [o/w]
- (2) Oily creams

### Aqueous creams [o/w]

**In aqueous creams**, the emulsions are **oil-in-water** type. These creams are relatively **non-greasy**. These creams are further divided into three types depending on the type of emulsifying agent used for preparing them.

- (a) Anionic emulsifying wax creams
- (b) Cationic emulsifying wax cream
- (c) Non-ionic emulsifying wax cream



## Oily Creams

In oily creams, the emulsions are **w/o type**. These creams are greasy. The oily creams are further divided into two types depending on the type of emulsifying agent used for preparing w/o emulsion

- (a) Sterol creams
- (b) Soap cream

## PASTES



Pastes are semi-solid preparations intended for **external application** to the skin. The pastes are generally **very thick and stiff**.

They **do not melt at ordinary temperature** and thus form a protective coating over the area where they are applied.

They are used mainly as **antiseptic protective or soothing dressings** which are often spread on lint before being applied

**The following types of bases are used for the preparation of pastes:-**

- (1) Hydrocarbon bases
- (2) Water miscible bases
- (3) Water soluble bases

1. **Hydrocarbon bases:** Soft paraffins and liquid paraffin are commonly used bases for the preparation of pastes
2. **Water miscible bases:** Emulsifying ointment is used as a **water miscible base** for the preparation of pastes.
  - **Glycerine** is also used as water miscible base for the preparation of pastes
3. **Water soluble bases:** Suitable combination of high and low molecular weight **polyethylene glycols are mixed together** to get product of desired consistency which soften or melt when applied to the skin. These **bases are water soluble**. Water soluble dental paste containing neomycin sulphate is prepared with macrogol base.



## JELLIES

- Jellies are **transparent or translucent non-greasy, semisolid** preparations meant for external application to the skin or mucous membrane.
- They may be prepared from **natural gums, such as tragacanth, pectin,** sodium alginates or from **synthetic derivatives of natural substances,** such as **methyl cellulose** and **sodium carboxymethyl cellulose** .

### Types of Jellies

There are three types of jellies:-

- (1) Medicated jellies
- (2) Lubricating jellies
- (3) Miscellaneous jellies



#### Medicated jellies

- Chiefly **used on mucous membrane** and skin for their spermicidal, local anaesthetics, and antiseptic properties
- After evaporation of water, jellies provide a local cooling effect and residual film gives protection.
- After evaporation of water, jellies provide a local cooling effect and residual film gives protection

#### Lubricating jellies

- Lubrication of **diagnostic equipment** such as, surgical gloves, cystoscopes, fingerstalls, catheters, rectal thermometers etc.
- These **jellies should be thin, transparent and water soluble**

## POULTICES

Poultices are **soft, viscous wet masses of solid substances** applied to the skin for their fomentation action in order to **provide relief from pain or reduce inflammation or to act as a counterirritant**. Poultices are also known as cataplasms. Poultices were used to prepare in ancient times to drain infectious material from the diseased tissues



## ❖ EXCIPIENTS USED IN SEMISOLID DOSAGE FORMS

<b>API</b>	<ul style="list-style-type: none"> <li>Active pharmaceutical ingredient is any part of drug which produces any effect.</li> </ul>
<b>Preservatives</b>	<ul style="list-style-type: none"> <li>To stop microbial growth preservatives are added.</li> <li>Preservatives for ointment includes: p-hydroxy benzoates, phenol, benzoic acid, sorbic acid, methyl paraben, propyl paraben, quaternary ammonium compounds, mercury compounds etc.</li> </ul>
<b>Humectants</b>	Glycerin, propylene glycol and sorbitol may be added to prevent the loss of moisture from the preparation.
<b>Emulsifying agents</b>	Like <b>polysorbate</b> , anionic emulsifying agents etc. are added if required
<b>Antioxidant</b>	<b>Antioxidant</b> may be incorporated to protect the active ingredients from oxidation.
<b>Organoleptic agents</b>	Colouring agent ( <b>amaranth, brilliant blue etc.</b> ) flavouring agent ( <b>vanilla, strawberry, raspberry</b> ) are added.

## ❖ EVALUATION OF SEMISOLIDS

PARAMETER	DESCRIPTION
<b>Appearance</b>	Observed for visual appearance, odour, color, texture and feel upon application, such as grittiness, greasiness, stickiness, smoothness, stiffness and tackiness
<b>Viscosity</b>	Measured by using <b>Brookfield viscometers</b>
<b>Drug diffusion study</b>	Drug content is determined by performing <b>Pharmacopoeial assay</b>
<b>Skin irritation studies</b>	To check the skin irritation, or any other rashes or erythema. Generally carried out on animal models
<b>Eye irritation studies</b>	For ophthalmic preparations, to check the irritation or erythema in eye. Generally carried out on animal models
<b>Spreadability</b>	Spreadability is measured by placing gel in between which is under the direction of certain load