# SEMI- SOLID DOSAGE FORM

## INTRODUCTION

- Pharmaceutical semisolid dosage preparations include :ointments, pastes, cream, plasters, gels and rigid foams.
- 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, anti microbial agents, antioxidants, or stabilizing agents etc..

# DEFINATION

• Semi solids are the topical dosage form used for the therapeutic, protective or cosmetic function. They may be applied to the skin, or used nasally, vaginally, or rectally....

## Advantage of semi-solid dosage form

- It is used externally
- Probability of side effect can be reduce
- First pass metabolism is avoided.
- Local action and Site specific action of drug on affected area.
- Convenient for **unconscious patient** or patient having **difficulty** on oral administration.
- Suitable dosage form for **bitter drugs**.
- More **stable** than liquid dosage form

## **Disadvantages of semi-solid dosage form**

- There is **no dosage accuracy** in this type of dosage form
- The base which is used in the semi-solid dosage form can be **easily oxidized**.
- May cause **staining**
- They are **bulky** to handle.
- Application with finger may cause **contamination**
- May cause **irritation or allergy** to some patients

## **IDEAL PROPERTIES OF SEMISOLIDS**

- PHYSICAL PROPERTIES:
- Smooth texture
- Elegant in appearance
- Non dehydrating
- Non gritty
- Non greasy and non staining
- Non hygroscopic

- PHYSIOLOGICAL PROPERTIES
- Non irritating
- Do not alter membrane / skin functioning
- Miscible with skin secretion
- Have low sensitization index
- APPLICATION PROPERTIES
- Easily applicable with efficient drug release.
- High aqueous wash ability.

## PREPARATION OF SEMISOLIDS DOSAGE FORMS

- INGREDIENTS USED IN PREPARATION
- Bases
- Preservative
- Humectants
- Antioxidants
- Emulsifier
- Gelling agent
- Permeation enhancer
- Buffers

## 1. BASES:

• It is one of the most important ingredient used in formulation of semisolid dosage form. Ointment bases do not merely act as the carriers of the medicaments, but they also control the extent of absorption of medicaments incorporated in them

### • IDEAL PROPERTIES OF A BASE:

- Inert, non-irritating and non-sensitizing.
- Compatible with skin pH and the drug.
- Good solvent and/or emulsifying agent.
- Emollient, protective, non-greasy and easily removable.
- Release medicament readily at the site of application.

## **ANTIOXIDANTS** :

- Oxygen is a highly reactive atom that is capable of becoming part of potentially damaging molecules commonly called "free radicals."
- Free radicals are capable of attacking the healthy cells of the body, causing them to lose their structure and function. To prevent this an antioxidants are added.
- E.g. Butylated hydroxy anisole,
- Butylated hydroxy toluene

## **PERMEATION ENHANCERS**

Skin can act as a barrier. With the introduction of various penetration enhancers, penetration of the drug through the skin can be improved

**Oleic acid** 

## **EMULSIFIER**

- An emulsifier (emulgent) is a substance that stabilizes an emulsion by increasing its kinetic stability.
- - Must reduce surface tension for proper emulsification.
- Prevents coalescence.
- Ability to increase the viscosity at low concentration.

## HUMECTANT

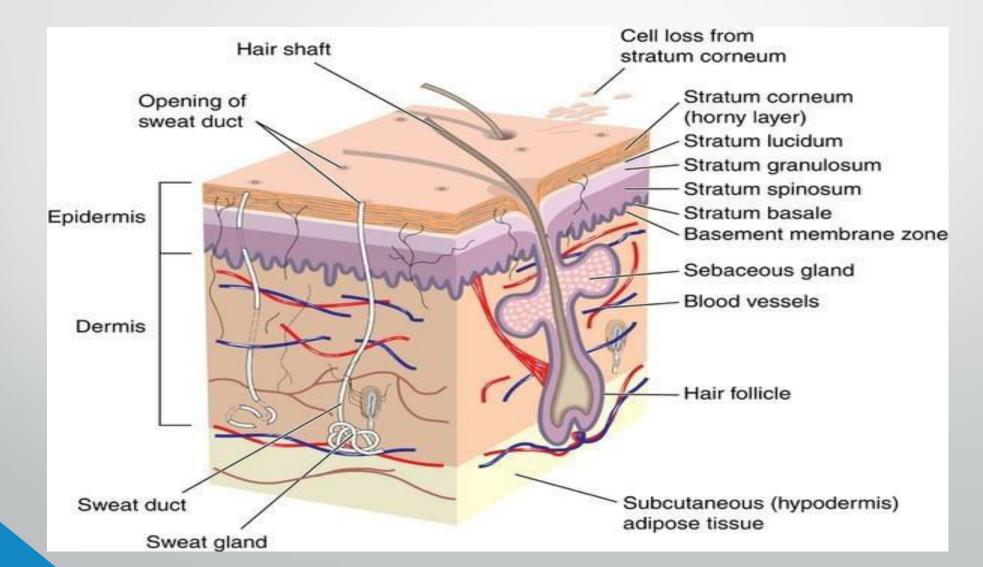
- A humectant is a hygroscopic substance, Humectants are used to :
- increase the solubility of the active ingredient to elevate its skin penetration.
- elevate the hydration of the skin.
- **BUFFERS:**
- Compatibility with skin.
- Drug solubility.
- Drug stability
- E.g. sodium acetate, sodium citrate

## **Antimicrobial preservatives**

•To inhibit the growth of contaminating microorganisms, So require the addition of chemical antimicrobial preservatives to the formulation

•-E.G. para-hydroxybenzoates (parabens), phenols, benzoic acid, sorbic acid, quaternary ammonium salts and other compounds.

## **Anatomy of skin**



The skin is very effective as a selective penetration barrier. The epidermis provides the major control element for drug penetration

### **STRUCTURE OF SKIN :**

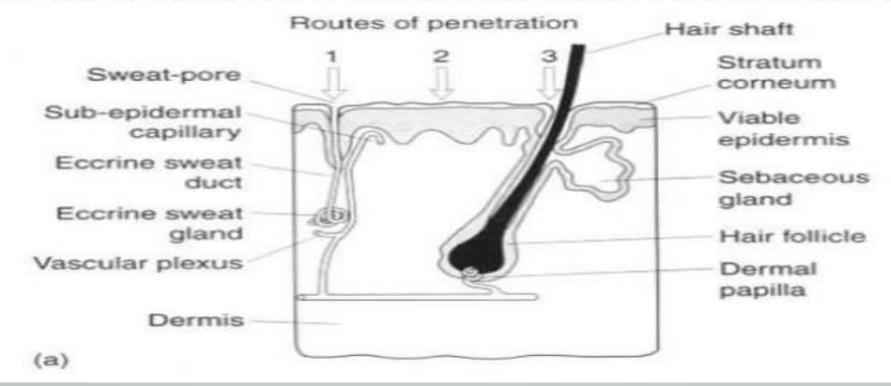
- The skin has three main layers: the epidermis, dermis and hypodermis.
- **Epidermis** is the outermost layer. It consists of:
- (a) The *basal layer* (innermost) is one cell thick layer. Its cells divide constantly and the daughter cells are steadily pushed towards the surface.
- (b) The *prickle cell layer*: The cells in this region are linked by tiny bridges or prickles.
- (c) The *granular layer*: When they reach this region, the upwardly moving cells become granules and begin to synthesize the inert protein keratin.
- (d) The *horny layer* (stratum corneum). This is the outermost layer and the cells are heavily keratinized and dead. The dead cells sloughs off gradually.

- **Dermis** is the middle and the main part of the skin. The dermis is made up of protein collagen and elastin.
- Dermis contains the following structures:
- (a) Blood vessels, lymphatics and nerves.
- (b) Epidermal appendages e.g. hair follicles, sebaceous glands and sweat glands.
- **Hypodermis**, the innermost layer, consists of adipose tissues. It gives physical protection and thermal insulation to underlying structures

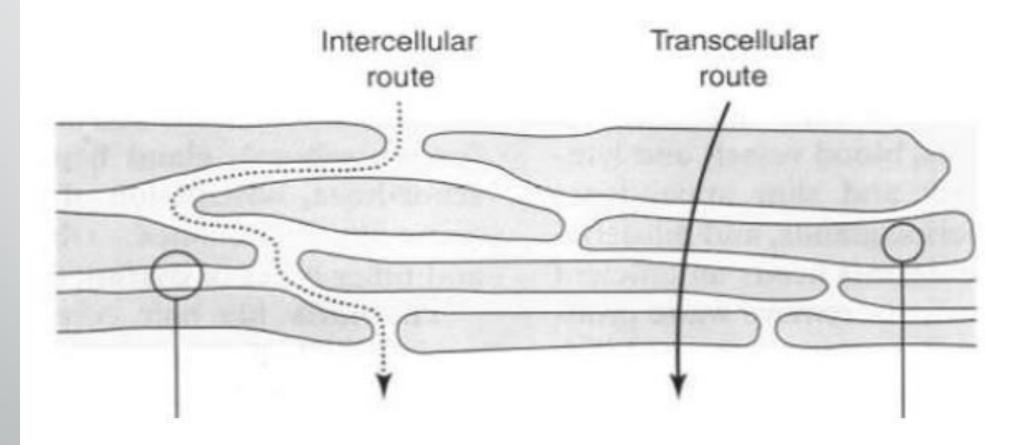
### Mechanism of drug penetration through skin

Three potential entry MACRO ROUTES to the viable tissue:

- 1. Via the sweat ducts
- 2. Across the continuous stratum corneum
- 3. Through the hair follicles with their associated sebaceous glands.



### **MICRO ROUTES**



- Low molecular weight molecules penetrate through stratum conium to some extent.
- Particles of 3-10  $\mu$  penetrate through hair follicle and particles less than  $3\mu$  penetrate through stratum conium.
- Hair follicle route may be important for ions and large polar molecules.
- Topically applied agents such as steroids, hexachlorophene, griseofulvin, sodium fusidate and fusidic acid may form a depot or reservoir by binding within the stratum corneum.
- Once drug permeates through horny layer it readily enters living tissue and systemic circulation.
- The average residence time of drug in dermis may be 1 min before it is washed away by blood.
  - NSAIDS reach far down to muscles to form depots.

### Factors influencing dermal penetration of drugs

### I. Biological factors:

- 1. Skin condition
- 2. Skin age
- 3. Blood flow
- 4. Regional skin site
- 5. Skin metabolism
- 6. Species difference.

### II. Physicochemical

### factors:

- 1. Skin hydration
- 2. Temperature and pH
- 3. Diffusion coefficient
- 4. Drug concentration
- 5. Partition coefficient
- Molecular size and shape.

- A. Factor associated with the skin
- (a) *Hydration of the horny layer*
- The hydration of keratinized cells is raised by covering the area with a moistureproof plastic film to prevent evaporation of perspiration. Hydration increases the drug penetration.
- (b) *Thickness of the horny layer*
- The horny layer is thickest on palms and soles and thinnest on the face; penetration rate increases with decreased thickness of horny layer.
- (c) *Skin condition*
- The permeability of the skin is affected by age, disease, climate and injury. For xample, absorption occurs rapidly in children and if the dermis is exposed by a wound or burn.

### **B.** Factors associated with the medicament

### (a) Solubility of the drug

• Highly lipid soluble molecules enters through hair follicles. Moderately lipid soluble molecules penetrates directly across the horny layer.

### (b) Dissociation constant (pKa)

- If a drug is ionized in the surrounding pH of the dermis then the penetration of the ionic species are restricted by electrostatic interactions. Degree of ionization depends on the pKa of the drug.
- e.g. Methyl salicylate and methyl nicotinate penetrate much faster than salicylic acid and nicotinic acid respectively.

### (c) Particle size

• Reducing the particle size increases the dissolution of a poorly soluble drug in suspension and thus increases the release rate from the vehicle.

### (d) Crystal structure

• The metastable polymorph is much more soluble than its stable form, so the release of drug in metastable state is much more faster than stable form.

- Drugs held firmly by the vehicle exhibit slow rate of release .
- Drug held loosely by the vehicle shows faster rate of release.
- The vehicles may enhance the penetration of a drug in one or more of the following ways:-
- a) By ensuring good contact with the surface of the body
- b) By increasing the degree of hydration of the stratum corneum
- c) By penetrating the epidermis
- d) By directly altering the permeability of the skin

### **Contact with body surface :-**

- Sticky bases such as soft paraffin, Paraffin ointment B.P.C., Simple ointment B.P. etc. adheres well to the skin but are difficult to apply evenly and remove completely.
- Creams are easier to apply and remove. Oil in water (o/w) creams mix with sebum and are more suitable for weeping or wounded surface.

### **Hydration of stratum corneum :-**

- An occlusive layer reduces evaporation of water from skin, increasing hydration of the horny layer and, therefore, promotes penetration of medicament.
- e.g. hydrocarbons, wool fat and isopropyl myristate containing ointments produce occlusive films on the skin. Water in oil (o/w) type creams have some occlusive effects.

#### **Penetration of the epidermis :-**

- Bases miscible with the sebum penetrate into the regions of the skin in which sebum is found.
- e.g. Woolfat (originating from sebaceous glands of sheep) penetrates into the skin.
- Vegetable oils penetrate more slowly and liquid paraffin does not penetrate at all.

## **1-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. They are mainly used as:
- Emollients
- Protective
- Therapeutic
- Prophylactic purpose

## **Classification of ointments**

#### Ointments may be classified as follows:-

- 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 intended to produce their action **on the surface of the skin** and produce local effect, they are not absorbed.
- They acts as protectives, local anti-infectives, antiseptics and parasiticides

#### **Endodermic ointments**

• These ointments are intended to release the medicaments that **penetrate into the skin**. They are partially absorbed and acts as emollients, stimulants and local irritants.

#### **Diadermic ointments**

• These ointments are intended to release the medicaments that pass through the skin and produce **systemic effects.** 

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. It can absorb about 50% of its weight of water. So it is used in ointments where the proportion of water or aqueous liquids to be incorporated in hydrocarbon base is too large. It is an important constituent of simple ointment base and eye ointment base.

(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. It is used alone as emollient and as an ingredient of several other ointments.

(iii) Wool alcohol : It is obtained from wool fat by treating it with alkali and separating the fraction containing cholesterol and other alcohols. It contains not less than 30% of cholesterol. It is used as an emulsifying agent for the preparation of w/o emulsion. It is also used to improve the texture, stability and emollient properties of o/w emulsions.

(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. texture, stability and emollient properties of o/w emulatoria.

(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 may be used in their anhydrous form or in emulsified form.

These bases are quite greasy, but these can be easily removed from the skin as compared to oleaginous bases. the skill as compared to oreaging

3. Emulsion Bases : These bases are semisolid or have a creamlike 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 "greaseless ointment bases". The water-soluble bases consist of water soluble ingredients, such as, polyethylene glycol polymers which are popularly known as "carbowaxes". The carbowaxes are water soluble, non-volatile and inert substances. Depending upon the molecular weight, carbowaxes are available in different consistencies i.e., liquids, semisolids and solids. Their molecular weight varies from 200 to 8000. By mixing different carbowaxes, ointments of varying consistencies can be obtained.

# SELECTION OF DERMATOLOGICAL VEHICLES There are large number of ointment bases which are available in the market. These have already been discussed. But non of the above discussed ointment base, fulfils all the requirements of an ideal ointment base. Following are the factors which govern the selection of an ideal base for ointments:---

(A) Dermatological factors(B) Pharmaceutical factors

#### preparation of Ointments

The ointments can be prepared by any one of the following meth-

- 1. Trituration method
- 2. Fusion method
- 3. Chemical reaction method
- 4. Emulsification method

1. Trituration method : It is the most commonly used method for the 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. The following procedure is used to get a uniform ointment:—

(1) Finely powder the solid medicaments.

(2) Weigh the required quantity of an ointment base. Triturate the solid medicaments with a small amount of the base on an ointment slab with the help of a stainless steel ointment spatula until a homogenous product is formed.

- Following procedure used to get uniform ointment:
- 1. Finely powder the solid medicaments
- 2. Weigh the required quantity of an ointment base. Triturate the solid medicaments with a small amount of the base on an ointment slab with the help of a stainless steel ointment spatula until a homogenous product is formed.
- 3. Add remaining quantities of the base until the medicaments are uniformly mixed with it. Incorporate any liquid ingredient if present.

## Example 8.1 Prepare and dispense 100 g of simple ointment.

Rx5 gWool fat5 gHard paraffin5 gCetostearyl alcohol5 gWhite soft paraffin85 g

Method : Melt hard paraffin and cetostearyl alcohol on water bath. To this incorporate wool fat and white soft paraffin. Stir until all ingredients are melted. Examine the contents for any foreign particles. Decant or strain if required. Stir the mixture thoroughly until cold. Pack it in an ointment jar, label and dispense.

Example 8.2 Prepare and dispense 100 g of sulphur ointment I.P.

2. 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 substance 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. The medicament is incorporated slowly to the melted mass, stirred thoroughly until the mass cools down and homogenous product is formed.

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. In case, this precaution is not observed, then upon mixing the two portions, the waxes or the solids will cool down quickly and get separated. This will prevent the uniform mixing of all the ingredients.

### Example 8.6 Prepare and dispense 100 g of cetrimide ointment. R Cetrimide 1 g Cetostearyl alcohol 10 g

White soft paraffin10 gLiquid paraffin29 gPurified water50 gMake an ointment.

Direction : To be applied on the affected area three or four times a day. Method : Melt cetostearyl alcohol and white soft paraffin. Add liquid paraffin and mix together. Dissolve cetrimide in purified water and warm it to the same temperature as that of the melted ingredients of ointment base. Add the warmed aqueous solution of cetrimide into the melted mixture. Stir, till it get solidified. Pack it in a suitable container, label and dispense. 3. Chemical reaction method : Certain chemical reactions are involved in the preparation of several ointments. For example, iodine ointment. Iodine may be present in free form or in combined form with the ointment base.

Ointments containing free iodine Iodine is only slightly soluble in most of the fats and vegetable oils. But it is readily soluble in concentrated potassium iodide solution in water, due to the formation of polyiodides (KI.I<sub>2</sub>, KI.2I<sub>2</sub>, KI.3I<sub>3</sub>). These polyiodides are readily soluble in water, alcohol and glycerin. While selecting a liquid to ensure proper distribution of a medicament, it is important that the liquid should be non-volatile, otherwise the distributed medicament may crystallise when the solvent evaporates. These solutions may be incorporated with the absorption-type ointment base. For example, strong iodine ointment which is used to treat ringworm infection in cattles.

Example 8.8 Prepare and dispe	nse 50.0 g of strong iodine ointment.
H	
Toume	2.0 g
Potassium iodide	2.0 g 2.0 g
Wool fat	2.0 g
Yellow soft paraffin	38.0 g
Water	6.0 ml
Make an ointment.	the is were in the first of the art that

Direction : To be applied on the affected area as directed.

*Method* : Dissolve the iodine in the presence of potassium iodide in water. Melt the wool fat, yellow soft paraffin together, cool to about 40°C and add iodine solution. Stir, until cold and stored in glass jar.

Ointments containing combined iodine The fixed oils and many fats obtained from vegetable and animal sources contain unsaturated constituents. The iodine combines with double bonds of the unsaturated constituents and thus free iodine is not available. For example,

 $CH_3(CH_2)_7 \cdot CH = CH - (CH_2)_7 \cdot COOH + I_2 \longrightarrow$ 

Oleic acid

CH<sub>3</sub>·(CH<sub>2</sub>)<sub>7</sub>·CHI.CHI(CH<sub>2</sub>)<sub>7</sub>·COOH Di-iodo stearic acid an air being entrapped in the on

4. Emulsification method : In this method, the fats, oils and  $w_{axes}$ 4. Emulsification method . In a temperature of 70°C. The  $aque_{OUS}$  are melted together on a water bath at a temperature of 70°C. The  $aque_{OUS}$ are melted together on a water bath at a soluble components is also heated solution of all of the heat stable water soluble components is also heated almost at the same temperature as that of the melted bases. 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.

It is very important to heat the aqueous liquid to almost the same temperature as that of the melted bases, otherwise high melting point fats and waxes will immediately get solidified when a cold aqueous solution is mixed with it and an ointment containing lumps will be formed.

An emulsifying agent is needed to make a stable emulsion, for a long time. Water soluble soaps are commonly used as emulsifier for semisolid o/w emulsions. Sometimes the emulsified ointments require a combination of emulsifiers. A combination of triethanolamine stearate soap and cetyl alcohol is used as an emulsifier in o/w emulsions and a combination of beeswax and divalent calcium ions is used as an emulsifier for w/o emulsions.

# PASTES

- Pastes are semi solid preparations intended for external application to the skin. These are generally 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 agent.

Bases used for Pastes:

- 1. Hydrocarbon bases
- 2. Water miscible bases
- 3. Water soluble bases

#### • HYDROCARBON BASES:-

Soft paraffins and liquid paraffins are commonly used for the preparation of pastes.

• WATER MISCIBLE BASES:-

Emulsifying ointment is used as a water miscible base for the preparation of pastes. Similarly glycerin is also used.

• 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.

# METHOD OF PRERPARATION

- Pastes are prepared by trituration and fusion method just like ointments.
- The trituration method is used only in those cases where the base is liquid or semi-solid.
- The fusion method is used when the base is semi-solid or solid in nature.

# **EXAMPLE OF HYDROCARBON BASE**

Example 8.11 Prepare and dispense 100 g of aluminium paste, compound B.P.C.

R20.0 gAluminium powder20.0 gZinc oxide40.0 gLiquid paraffin40.0 gMake a paste.

Direction : Spread on white lint and apply to the affected area.
Method : Mix aluminium powder and zinc oxide in a mortar. Add
liquid paraffin with trituration thoroughly until smooth paste is obtained.
Transfer to a suitable container, label and dispense.

Lagos . Emulsifying ointment is used as a water

Differentiation between     Pastes	
1 They contain last	Ointments
1. They contain large amount of fine- ly powdered solids such as starch, zinc oxide, calcium carbonate etc.	<ol> <li>They contain medicaments which are generally dissolved/suspended/ emulsified in the base.</li> </ol>
2. They are very thick and stiff.	2. They are soft semisolid preparations.
3. They are less greasy.	3. They are more greasy.
4. They are generally applied with a spatula or spread on lint.	4. They are simply applied on the skin.
5. They form a protective coating to the area where it is applied.	5. They are used as protective or emollient for the skin.
. Paste contains a large amount of powder which is porous in nature, hence perspiration can escape.	6. They are used for the protection of lesions.
They are less macerating than ointments.	7. They are more macerating in action.

# 2-creams:

- **Creams** are homogeneous, semi-solid preparations consisting of **opaque emulsion**, contains lipophilic emulsifying agent . Their consistency depend on the type of emulsion, either water-in-oil (w/o) or oil-in – water (o/w), and on the nature of the solids in the internal phase. Creams are intended for the application to the skin or certain mucous membranes for:
- Protective
- Therapeutic
- prophylactic purposes (Intended to prevent disease)

# **Classification of creams**

- Creams containing microspheres
- (VIT. A CREAM ... 200-250 micron)
- Lamellar faced creams (Long lasting moisturising cream)
- (liquid paraffin in water emulsion)
- Cream containing liquid nanoparticles
- (a w/o cream )

# Preparation of creams

- Steps
- **Preparation of oil phase** :flack/powder ingredient are dispersed in mineral oil or silicone oil, heating may required for melting
- Hydration of aqueous phase: emulsifiers, stabilizer, thickener are dispersed in water, heating may required for hydrating
- Forming the emulsion: two phases are blended under vigorous agitation
- Dispersion of active ingredient

## 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. These are similar to mucilages because they may be prepared from gums, but they differ from mucilages in having jelly like consistency.

#### Types of Jellies

There are three types of jellies:-

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

1. Medicated jellies : These are chiefly used on mucous membrane and skin for their spermicidal, local anaesthetics, and antiseptic properties. These jellies contain sufficient water. After evaporation of water, jellies provide a local cooling effect and residual film gives protection. For example, ephedrine sulphate jelly is used as a vasoconstrictor to arrest the bleeding of nose. Jelly containing phenyl mercuric nitrate is used as spermicidal contraceptive.

2. Lubricating jellies : These jellies are used for lubrication of diagnostic equipment such as, surgical gloves, cystoscopes, fingerstalls, catheters, rectal thermometers etc. These jellies should be thin, transparent and water soluble. These jellies should be sterile because these are used as lubricants for articles to be inserted into sterile regions of the body such as urinary bladder etc.

3. Miscellaneous jellies : These jellies are meant for-

(a) **Patch testing :** These jellies are used as a vehicle for allergens which are applied on the skin to check the sensitivity. On drying, the residual film is formed which helps to keep the patches separate and avoid confusing results.

(b) **Electro-cardiography :** The jelly is applied on the electrode to reduce the electrical resistance between the patient's skin and the electrode. The jelly contains sodium chloride, pumice powder and glycerin. The sodium chloride is a good conductor of electricity where glycerin acts as humectant.

#### Formulation of Jellies

1. Gelling agents : These are usually organic hydrocolloids. Some inorganic hydrocolloids are also used as gelling agents. The following gelling agents are commonly used for the preparation of jellies:—

(i) **Tragacanth :** It is used for the preparation of lubricating, medicated and contraceptive jellies. The concentration of gum required for the preparation of jellies varies from 2 to 5%. The jelly prepared with tragacanth usually contains lumps which can be avoided by using a dispensing agent like alcohol, glycerin and volatile oil.

The tragacanth jellies are becoming less popular because of the following reasons:-

- (a) They cannot be stored for a long time.
- (b) They are prone to microbial growth.
- (c) They vary in viscosity because the gum is obtained from natural sources.
- (d) The residual film formed after the evaporation of jelly tends to flake.
- (e) They lose viscosity beyond pH range 4.5 to 7.0.

(ii) Sodium alginate : Sodium alginate jellies are used as lubricants (1.5-2%) and dermatological vehicles (5-10%). The viscosity of sodium alginate jelly can be increased by adding trace of soluble calcium salt. Sodium alginate has an advantage over tragacanth because it is available in several grades of standardised viscosity. Alcohol, glycerin and propylene glycol is included in certain formulations as dispersing agent.

(iii) Pectin : Pectin is a valuable gelling agent for acid products. Glycerin is used as a dispersing agent and humectant in dermatological jellies. Pectin jelly is prone to microbial growth, so a suitable preservative is needed to preserve it properly during its storage. Jelly prepared from pectin must be packed in well closed containers to prevent the loss of moisture by evaporation.

(iv) Starch : Starch mucilage prepared with water alone lead to bacterial growth, so a suitable preservative must be added. Starch in combination with other substances like gelatin and glycerin is commonly used for the preparation of jellies. The medicaments are mixed in cold jelly by trituration. Starch jellies should be freshly prepared and packed in well closed containers to prevent the loss of moisture by evaporation.

(v) Gelatin : Gelatin is soluble in hot water. A 2% gelatin solution in hot water form a jelly on cooling. Very stiff medicated jelly can be prepared by incorporating about 15% gelatin. Such jellies are melted before use and after cooling to desired temperature, are applied with a brush to the affected area of the skin. The area is covered with bandage and dressing may be left as such for several weeks.

2. Preparation of jellies : The pharmaceutical jellies are usually prepared by adding a thickening agent, such as tragacanth, carboxy methylcellulose etc. to an aqueous solution of drug. The mass is triturated in a mortar until a uniform product is obtained. The glass pestle and mortar is used in case of dark coloured drug. The whole gum should be preferred over the powdered gum to prepare the jelly because it produces a clear preparation of uniform consistency

## **Evaluations of ointment and creams:**

- 1. Drug content
- 2. Release rate of medicament from base
- 3. Penetration rate of medicament
- 4. Absorption of medicament into blood stream
- 5. Consistency of the preparation
- 6. Irritant effect

### 1. Drug content:--Minimum fill test

- Select any 10 filled containers
- Weigh the required amount of ointment
- Medicament is extracted in a suitable solvent
- Drug Content is determined by suitable analytical technique
- Results should be with in labeled quantity.

2. Release rate of medicament from base:--

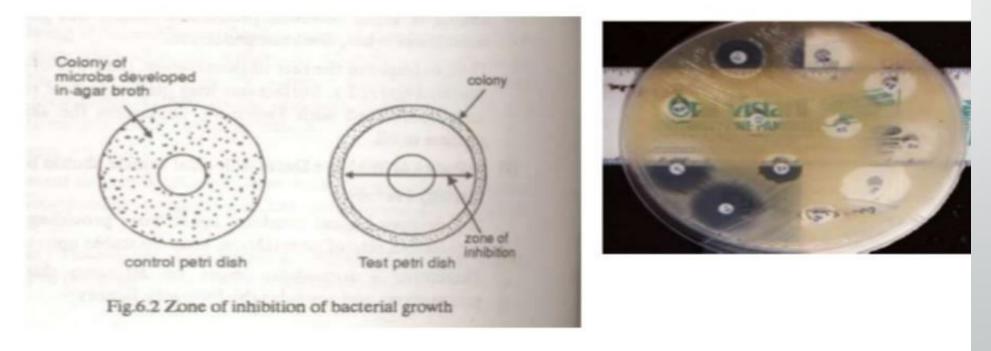
Two in vitro techniques are used

- 1. Agar cup plate method
- 2. Diffusion method



#### Agar cup Plate method

- Used to determine the release rate of antibacterial ointment
- Tested in agar medium seeded with staphylococus aures.
- Zone of inhibition of bacterial growth is measured around circular cups



#### Diffusion method:

Used to find the release rate of any type of medicament from the base

- A parchment membrane is tied at one end of glass tube
   Ointment is filled in the tube, properly spread on the membrane
   Tube is dipped in the distilled water maintained at 37±1°C
   Samples are withdrawn after a specified period of time.
   Samples are immediately replaced with fresh distilled water
   Analyzed for the drug content
- ➢Plot a graph between drug concentration and time

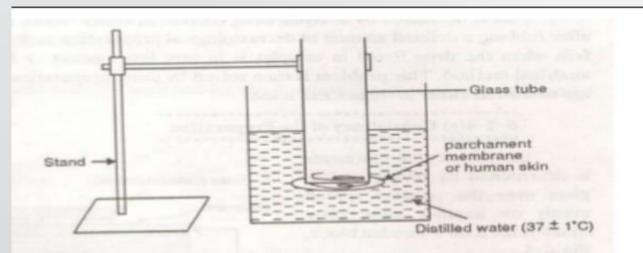
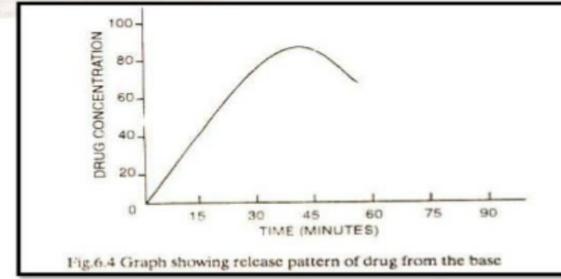


Fig.6.3 A apparatus designed to determine release rate of drug from the base by diffusion method



#### 3. Penetration rate of medicament:

Determined by rubbing weighed amount into defined areas for a fixed time

>Unabsorbed material is removed completely and weighed

Difference in weight provides total base penetrated

➢Rate is then calculated

4. Absorption of medicament into blood stream:

Diadermic ointments are tested by in-vivo method.

Determined by assaying drug content in either blood, urine, faeces or tissues after rubbing defined amount under standard conditions

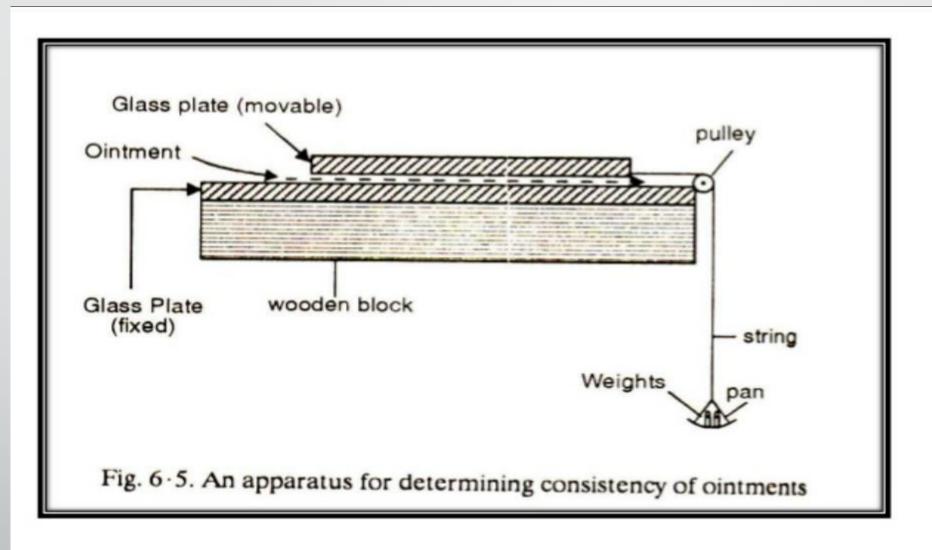
#### 5. Consistency of the preparation:

Determined by sliding a glass plate over the product by means of a pulley.

Product is spread evenly on another glass plate fixed on a wooden block

Weights are added to the pan so that sliding of the movable glass plate is obtained

Ointment which require more weights to allow the plate to slideover have high consistency or vice-versa



# **Skin Irritation Test**



- In general no ointment should possess irritant effect on the skin or mucous membranes the tests for irritancy can be carried out on the skin and eyes of rabbits or the skin of human beings.
- The irritant effect can also be judged to a certain extent by injecting the ointment into thigh muscles and under the abdominal skin of rats. Reaction are noted at intervals of 24,48,72 and 96 hours. Lesions on cornea, iris, conjunctiva are used for judging the irritancy to the eyes.

- Another Evaluation Parameters are:
- 1. Viscosity
- 2. Extrudability
- 3. Globule size
- **4.** pH
- 5. Spredability

## Viscosity :

• Viscosity can be measured using Brookfield viscometers is used for such formulations

## **Extrudability:**

• A simple method was adopted for determination of extrudability in terms of weight in grams required to extrude a 0.5cm ribbon of gel in 10 seconds from the collapsible tube.

### **Globule size :**

- This can be determined by microscopic study of the globules.
- Take a small quantity of formulation and dissolve it in a solvent. Take few droplets on slide and observed under microscope

## pH:

- The pH of semisolids were determined by digital pH meter.
- One gram of formulation was dissolved in 100ml of distilled water and stored at 4°C for two hours
- After 2 hours, take formulation and determine its pH

### **Spreadability:**

A modified apparatus consisting of two glass slides containing formulation in between with the lower slide fixed to a wooden plate and the upper one attached to a balance by a hook was used to determine spreadability