Semisolids

Mr. Pankaj U. Valvi

Definition:

“Semisolid pharmaceutical system comprise a body of product, which when applied to skin or accessible mucous membranes tends to alleviate or treat a pathological condition or other protection against harmful environment.”

Ointments

Definition:

“Ointments are semisolid preparations for application to the skin or mucosa. The ointment bases are almost always anhydrous and generally contains one or more medicaments in suspension or solution.”
**Uses:**
1. Emollient
2. Application for active ingredients to the skin
3. Occlusive

**Characteristics of an Ideal Ointment:**
1. It should be chemically and physically stable.
2. It should be smooth and free from grittiness.
3. It should melt or soften at body temperature and be easily applied.
4. The base should be non-irritant and should have no therapeutic action.
5. The medicament should be finely divided and uniformly distributed throughout the base.

**Classification of Ointments:**

**A.** Ointments classified according to their therapeutic properties based on penetration are as follows:

a) Epidermic,
b) Endodermic,
c) Diadermic
(a) 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 act as protectives, antiseptics and parasiticides.

(b) 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.

B. According to therapeutic uses the ointments are classified as follows:

(i) Acne treatment: resorcinol, sulfur.
(ii) Antibiotics: Used to kill microorganisms. e.g. bacitracin, chlortetracycline, neomycin.
(iii) Antieczematosus: Used to stop oozing and exudation from vesicles on the skin. e.g. hydrocortisone, coal tar, ichthamol, salicylic acid.
(iv) Antifungal: Used to inhibit or kill the fungi. e.g. benzoic acid, salicylic acid, nystatin, clotrimazole, etc.
(v) Anti-inflammatory: Used to relieve inflammatory, allergic and pruritic conditions of the skin. e.g. betamethasone valerate
(vi) Antipruritic: Used to relieve itching. e.g. benzocaine, coal tar.
(vii) Antiseptic: Used to stop sepsis. e.g. ammoniated mercury
(vii) Astringent: Reduces the secretion of glands or discharge from skin surface. e.g. calamine, zinc oxide.

(c) Diadermic Ointments:
- These ointments are intended to release the medicaments that pass through the skin and produce systemic effects.

(ix) Counter irritant: These are applied locally to irritate the intact skin, thus reducing or relieving another irritation or deep seated pain. e.g. capsicum oleoresin, iodine (lodox), methyl salicylate.
(x) Dandruff treatment: e.g. salicylic acid and cetrimide (cetyl trimethyl ammonium bromide)
(xi) Emollient: Used to soften the skin (for example in the dry season). e.g. soft paraffin
(xii) Keratolytic: Used to remove or soften the horny layer of the skin. e.g. resorcinol, salicylic acid and sulfur.
(xii) Keratoplastic: Tends to increase the thickness of horny layer e.g. coal tar.
(xiii) Parasiticide: These ointments destroy or inhibit living infestations such as lice and ticks. e.g. benzyl benzoate, sulfur etc.
(xiv) Protective: Protects the skin from moisture, air, sun rays or other substances such as soaps or chemicals. e.g. calamine, zinc oxide, petrolatum.
Ointment Bases:

- The ointment base is that substance or part of an ointment preparation which serves as carrier or vehicle for the medicament.
- An ideal ointment base should be inert, stable, smooth, compatible with the skin, non-irritating and should release the incorporated medicaments readily.

Classification of Ointment Bases:

1. Oleaginous bases
2. Absorption bases
3. Water-miscible bases
4. Water soluble bases

1. Oleaginous Bases

- These bases consists of oils and fats. The most important are the Hydrocarbons i.e. petrolatum, paraffins and mineral oils.
- The animal fat includes lard.
- The combination of these materials can produce a product of desired melting point and viscosity.

(a) Petrolatum (Soft paraffin):

- This is a purified mixture of semi-solid hydrocarbons obtained from petroleum or heavy lubricating oil.
- Yellow soft paraffin (Petrolatum; Petroleum jelly)
  - This a purified mixture of semisolid hydrocarbons obtained from petroleum. It may contain suitable stabilizers like, antioxidants e.g. \( \alpha \)-tocopherol (Vitamin E), butylated hydroxy toluene (BHT) etc.
  - Melting range : 38 to 56°C.
- White soft paraffin (White petroleum jelly, White petrolatum)
  - This a purified mixture of semisolid hydrocarbons obtained from petroleum, and wholly or partially decolorized by percolating the yellow soft paraffin through freshly burned bone black or adsorptive clays.
  - Melting range : 38 to 56°C.
  - Use: The white form is used when the medicament is colourless, white or a pastel shade. This base is used in:
    - Dithranol ointment B.P.
    - Ammoniated Mercury and Coal tar ointment B.P.C.
    - Zinc ointment B.P.C.
(b) Hard paraffin (Paraffin):
- This is a mixture of solid hydrocarbons obtained from petroleum.
- It is colourless or white, odorless, translucent, wax-like substance.
- It solidifies between 50 and 57°C and is used to stiffen ointment bases.

(c) Liquid paraffin
(Liquid petrolatum; White mineral oil)
- It is a mixture of liquid, hydrocarbons obtained from petroleum. It is transparent, colourless, odourless, viscous liquid.
- On long storage it may oxidize to produce peroxides and therefore, it may contain tocopherol or BHT as antioxidants.
- It is used along with hard paraffin and soft paraffin to get a desired consistency of the ointment.
- Tubes for eye, rectal and nasal ointments have nozzles with narrow orifices through which it is easy to expel very viscous ointments without the risk of bursting the tube.
- To facilitate the extrusion up to 25% of the base may be replaced by liquid paraffins.

Advantages of Hydrocarbons Bases:
1. They are not absorbed by the skin. They remain on the surface as an occlusive layer that restricts the loss of moisture hence, keeps the skin soft.
2. They are sticky hence ensures prolonged contact between skin and medicament.
3. They are almost inert. They consist largely of saturated hydrocarbons, therefore, very few incompatibilities and little tendency of rancidity are there.
4. They can withstand heat sterilization, hence, sterile ophthalmic ointments can be prepared with it.
5. They are readily available and cheap.

Disadvantages of Hydrocarbon Bases:
1. It may lead to water logging followed by maceration of the skin if applied for a prolonged period.
2. It retains body heat, which may produce an uncomfortable feeling of warmth.
3. They are immiscible with water; as a result rubbing onto the surface and removal after treatment both are difficult.
4. They are sticky, hence makes application unpleasant and leads to contamination of clothes.
5. Water absorption capacity is very low, hence, these bases are poor in absorbing exudate from moist lesions.
2. Absorption Bases:

- The term absorption base is used to denote the water absorbing or emulsifying property of these bases and not to describe their action on the skin.
- These bases (sometimes called emulsifiable ointment bases) are generally anhydrous substances which have the property of absorbing (emulsifying) considerable quantity of water yet retaining its ointment-like consistency.
- Preparations of this type do not contain water as a component of their basic formula but if water is incorporated a W/O emulsion results.

(b) Hydrous Wool Fat (Lanolin):
- It is a mixture of 70% w/w wool fat and 30% w/w purified water. It is a w/o emulsion. Aqueous liquids can be emulsified with it.
- It is used alone as an emollient.
- Example:- Hydrous Wool Fat Ointment B.P.C., Calamine Coal Tar Ointment.

(c) Wool Alcohol:
- It is the emulsifying fraction of wool fat. Wool alcohol 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.

(A) Wool Fat (Anhydrous Lanolin):
- It is the purified anhydrous fat like substance obtained from the wool of sheep.
- It is practically insoluble in water but can absorb water up to 50% of its own weight. Therefore it is used in ointments the proportion of water or aqueous liquids to be incorporated in hydrocarbon base is too large.
- Due to its sticky nature it is not used alone but is used along with other bases in the preparation of a number of ointments.
- e.g. Simple ointment B.P. contains 5% and the B.P. eye ointment base contains 10% woolfat.

(d) Beeswax:
- It is purified wax, obtained from honey comb of bees.
- It contains small amount of cholesterol. It is of two types: (a) yellow beeswax and (b) white beeswax.
- Use:-
  - Beeswax is used as a stiffening agent in ointment preparations.
- Examples:- Paraffin ointment B.P.C. contains beeswax.
(e) **Cholesterol:**
- It is widely distributed in animal organisms.
- Wool fat is also used as a source of cholesterol.
- **Use:** It is used to increase the water absorbing power of an ointment base.
- **Example:** Hydrophilic petroleum U.S.P. contains:
  - Cholesterol 3%
  - Stearyl alcohol 3%
  - White beeswax 8%
  - White soft paraffin 86%

3. **Water Miscible Bases:**
- They are miscible with an excess of water. Ointments made from water-miscible bases are easily removed after use.
- There are three official anhydrous water-miscible ointment bases:
  - Emulsifying ointment B.P. – contains anionic emulsifier.
  - Cetrimide emulsifying ointment B.P. – contains cationic emulsifier
  - Cetomacrogol emulsifying ointment B.P. – contains non-ionic emulsifier
- **Uses:** they are used to prepare o/w creams and are easily removable ointment bases
  - e.g. Compound Benzoic Acid Ointment (Whitfield’s Ointment) – used as antifungal ointment.

**Advantages of Absorption Bases:**
1. They are less occlusive nevertheless, are good emollient.
2. They assist oil soluble medicaments to penetrate the skin.
3. They are easier to spread.
4. They are compatible with majority of the medicaments.
5. They are relatively heat stable.
6. The base may be used in their anhydrous form or in emulsified form.
7. They can absorb a large quantity of water or aqueous substances.

**Disadvantages:** Inspite of their hydrophilic nature, absorption bases are difficult to wash.

**Advantages of water miscible bases:**
1. Readily miscible with the exudates from lesions.
2. Reduced interference with normal skin function.
3. Good contact with the skin, because of their surfactant content.
4. High cosmetic acceptability, hence there is less likelihood of the patients discontinuing treatment.
5. Easy removal from the hair.
4. Water Soluble Bases:

- Water soluble bases contain only the water soluble ingredients and not the fats or other greasy substances, hence, they are known as grease-less bases.

- Water soluble bases consists of water soluble ingredients such as polyethylene glycol polymers (PEG) which are popularly known as “carbowaxes” and commercially known as “macrogols”.

- They are a range of compounds with the general formula: \( \text{CH}_2\text{OH} \cdot (\text{CH}_2\text{OCH}_2)_n \text{CH}_2\text{OH} \)

- The PEGs are mixtures of polycondensation products of ethylene and water and they are described by numbers representing their average molecular weights.

Advantages of PEGs as ointment base:

1. They are water soluble; hence, very easily can be removed from the skin and readily miscible with tissue exudates.
2. Helps in good absorption by the skin.
3. Good solvent properties. Some water-soluble dermatological drugs, such as salicylic acid, sulfonamides, sulfur etc. are soluble in this bases.
5. They do not hydrolyze, rancidify or support microbial growth.
6. Compatibility with many dermatological medicaments.

Disadvantages:

1. Limited uptake of water. Macrogols dissolve when the proportion of water reaches about 5%.
2. Reduction in activity of certain antibacterial agents, e.g. phenols, hydroxybenzoates and quaternary compounds.
3. Solvent action on polyethylene and bakelite containers and closures.

- Certain other substances which are used as water soluble ointment bases include tragacanth, gelatin, pectin, silica gel, sodium alginate, cellulose derivatives, etc.
Preparation of Ointments:

A well-made ointment is —
- (a) Uniform throughout
- (b) Free from grittiness

Two mixing techniques are frequently used in making ointments:
1. **Fusion**, in which ingredients are melted together and stirred to ensure homogeneity.
2. **Trituration**, in which finely-subdivided insoluble medicaments are evenly distributed by grinding with a small amount of the base or one of its ingredients followed by dilution with gradually increasing amounts of the base.

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1. **Ointments Prepared by Fusion Method:**

- When an ointment base contain a number of solid ingredients such as white beeswax, cetyl alcohol, stearyl alcohol, stearic acid, hard paraffin, etc. as components of the base, it is required to melted them. The melting can be done in two methods:

  **Method-I**
  - The components are melted in the decreasing order of their melting point i.e. the higher m.p. substance should be melted first, the substances with next melting point and so on. The medicament is added slowly in the melted ingredients and stirred thoroughly until the mass cools down and homogeneous product is formed.

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**Example:**

Simple ointment B.P. contains

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wool fat</td>
<td>50g</td>
</tr>
<tr>
<td>Hard paraffin</td>
<td>50g</td>
</tr>
<tr>
<td>Cetostearyl alcohol</td>
<td>50g</td>
</tr>
<tr>
<td>White soft paraffin</td>
<td>850g</td>
</tr>
</tbody>
</table>

**Type of preparation:** Absorption ointment base

**Procedure:**
- Hard paraffin and cetostearyl alcohol on water-bath. Wool fat and white soft paraffin are mixed and stirred until all the ingredients are melted.
- If required decanted or strained and stirred until cold and packed in suitable container.
2. **Ointment Prepared by Trituration**:

- This method is applicable in the base or a liquid present in small amount.
- Solids are finely powdered are passed through a sieve (#250, #180, #125).
- The powder is taken on an ointment-slab and triturated with a small amount of the base. A steel spatula with long, broad blade is used. To this additional quantities of the base are incorporated and triturated until the medicament is mixed with the base.
- Finally liquid ingredients are incorporated. To avoid loss from splashing, a small volume of liquid is poured into a depression in the ointment an thoroughly incorporated before more is added in the same way. Splashing is more easily controlled in a mortar than on a tile.

3. **Ointment Preparation by Chemical Reaction**:

- Chemical reactions were involved in the preparation of several famous ointments of the past, e.g. Strong Mercuric Nitrate Ointment, both of the 1959 B.P.C.

(a) **Ointment containing free iodine**:

- Iodine is only slightly soluble in most fats and oils but readily soluble.
- Iodine is readily soluble in concentrated solution of potassium iodide due to the formation of molecular complexes KI.I₂, K₂I₂, K₃I₂ etc.
- These solutions may be incorporated in absorption-type ointment bases.

Example:

(i) **Whitfield ointment**

(Compound benzoic acid ointment B.P.C.)

- **Formula:**
  - Benzoic acid, in fine powder 6gm
  - Salicylic acid, in fine powder 3gm
  - Emulsifying ointment 91gm

- **Method:**
  - Benzoic acid and salicylic acid are sieved through No. 180 sieves. They are mixed on the tile with small amount of base and levigated until smooth and dilute gradually.

 e.g. **Strong Iodine Ointment B. Vet.C** (British Veterinary Pharmacopoeia) is used to treat ringworm in cattle.

- It contains free iodine.

- At one time this type of ointments were used as counter-irritants in the treatment of human rheumatic diseases but they were not popular because:
  - They stain the skin a deep red color.
  - Due to improper storage the water dries up and the iodine crystals irritate the skin, hence glycerol was some times to dissolve the iodine-potassium iodide complex instead of water.
Example:

**Strong Iodine Ointment B. Vet.C.**
- Iodine
- Woolfat
- Yellow soft paraffin
- Potassium iodide (KI)
- Water

**Procedure:**
1. KI is dissolved in water. I₂ is dissolved in it.
2. Woolfat and yellow soft paraffin are melted together over water bath. Melted mass is cooled to about 40°C.
3. I₂ solution is added to the melted mass in small quantities at a time with continuous stirring until a uniform mass is obtained.
4. It is cooled to room temperature and packed.

**Use:** Ringworm in cattle.

Method:

1. Iodine is finely powdered in a glass mortar and required amount is added to the oil in a glass-stoppered conical flask and stirred well.
2. The oil is heated at 50°C in a water-bath and stirred continually. Heating is continued until the brown color is changed to greenish-black; this may take several hours.
3. From 0.1g of the preparation the amount of iodine is determined by B.P.C. method and the amount of soft paraffin base is calculated to give the product the required strength.
4. Soft paraffin is warmed to 40°C. The iodized oil is added and mixed well. No more heat is applied because this causes deposition of a resinous substance.
5. The preparation is packed in a warm, wide-mouthed, amber color, glass bottle. It is allowed to cool without further stirring.

**Preparation of Ointments: CONTD...**

**Preparation of Ointments by Emulsification:**

- An emulsion system contain an oil phase, an aqueous phase and an emulsifying agent.
- For o/w emulsion systems the following emulsifying agents are used:
  1. Water soluble soap
  2. Cetyl alcohol
  3. Glyceryl monostearate
  4. Combination of emulsifiers: triethanolamine stearate and cetyl alcohol
  5. Non-ionic emulsifiers: glyceryl monostearate, glyceryl monooleate, propylene glycol stearate
- For w/o emulsion creams the following emulsifiers are used:
  1. Polyvalent ions e.g. Magnesium, Calcium and Aluminium are used.
  2. Combination of emulsifiers: beeswax + divalent calcium ion

**Preparation of Ointments CONTD...**

**(B) Ointment Containing Combined Iodine:**

- Fixed oils and many vegetable and animal fats absorb iodine which combines with the double bonds of the unsaturated constituents

**Example:**

**Non-staining Iodine Ointment B.P.C. 1968**
- Di-Iodostearic Acid
- Iodine
- Arachis Oil
- Yellow Soft Paraffin

**Preparation of Ointments CONTD...**

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The viscosity of this type of creams prevent coalescence of the emulsified phases and helps in stabilizing the emulsion.

**Example:**

**Cold cream:**

**Procedure:**
1. Water immiscible components e.g. oils, fats, waxes are melted together over water bath (70°C).
2. Aqueous solution of all heat stable, water soluble components are heated (70°C).
3. Aqueous solution is slowly added to the melted bases with continuous stirring until the product cools down and a semi-solid mass is obtained.

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**Definition:**

- Viscous semisolid emulsion with opaque appearance as:
- Contrasted with translucent ointments
- Consistency depends on whether the cream is W/O or O/W

<table>
<thead>
<tr>
<th>W/O Creams</th>
<th>O/W Creams</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contains lipophilic emulsifying agent</td>
<td>Contains O/W emulsifying agent</td>
</tr>
<tr>
<td>Used as emollient or as cleansing agent</td>
<td>O/W creams are elegant drug delivery system</td>
</tr>
</tbody>
</table>
- Pastes generally contain a large amount (50%) of finely powdered solids. So they are often stiffer than ointments.
- When applied to the skin, pastes adhere well, forming a thick coating that protects and soothes inflamed and raw surfaces, minimizing damage caused by scratching in itchy conditions such as chronic eczema.
- Because of the powder content, pastes are porous; hence, perspiration can escape. Since the powders absorb exudate, pastes with hydrocarbon base are less macerating than ointments with a similar base.

### Bases of Pastes:

#### 1. Hydrocarbon Base:
- Soft paraffin and liquid paraffin are commonly used bases for the preparation of pastes.

<table>
<thead>
<tr>
<th>Name of the preparation</th>
<th>Active ingredients</th>
<th>Base</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound Zinc Paste B.P.</td>
<td>Zinc oxide</td>
<td>Soft paraffin</td>
<td>Eczema, psoriasis</td>
</tr>
<tr>
<td>Compound Zinc &amp; Salicylic acid Paste B.P. (Lassar’s Paste)</td>
<td>Zinc oxide &amp; Salicylic acid</td>
<td>Soft paraffin</td>
<td>Eczema, psoriasis</td>
</tr>
<tr>
<td>Coal tar paste</td>
<td>Coal tar</td>
<td>Soft paraffin</td>
<td>Eczema, psoriasis</td>
</tr>
<tr>
<td>Dithranol paste compound</td>
<td>Dithranol</td>
<td>Soft paraffin</td>
<td>Ringworm or psoriasis</td>
</tr>
<tr>
<td>Aluminium paste B.P.C.</td>
<td>Aluminium oxide</td>
<td>Liquid paraffin</td>
<td>Protective</td>
</tr>
</tbody>
</table>

#### 2. Water Miscible Base:
- They are less greasy than ointments but since their efficacy depends on maintaining a thick surface layer, they are far from attractive cosmetically.
- Most of the pastes are unsuitable for treating scalp conditions because they are difficult to remove from the hair.

<table>
<thead>
<tr>
<th>Name of the preparation</th>
<th>Base</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resorcinol &amp; sulfur Paste B.P.C.</td>
<td>Emulsifying ointment</td>
<td>Dandruff, and are easily removable from the hair.</td>
</tr>
<tr>
<td>Zinc &amp; Coal tar Paste</td>
<td>Emulsifying wax</td>
<td>Eczema</td>
</tr>
<tr>
<td>Magnesium sulfate paste B.P.C. (Morison’s paste)</td>
<td>Magnesium sulfate - 45%</td>
<td>Used to treat boils, because of their powerful osmotic effect of the salt and the glycerol.</td>
</tr>
<tr>
<td>Titanium dioxide paste B.P.C.</td>
<td>Suspension of TiO₂, ZnO, light kaolin and red Fe₂O₃ in glycerol + water.</td>
<td>Absorbs exudates from weeping skin conditions.</td>
</tr>
</tbody>
</table>
### 2. Water Soluble Base:

Water soluble bases are prepared from mixtures of high and low molecular weight polyethylene glycols (or macrogols).

<table>
<thead>
<tr>
<th>Name of the preparation</th>
<th>Base</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Triamcinolone Dental paste B.P.C.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Method of Preparation:

- **Type of preparation:** Paste with semi-solid base prepared by fusion and trituration.

**Procedure:**

- Zinc oxide and starch powder are passed through No. 180 sieve.
- Soft paraffin is melted on a water bath.
- The required amount of powder is taken in a warm mortar, triturated with little melted base until smooth. Gradually rest of the base is added and mixed until cold.

**Preparation 2:**

**Name:** Zinc and Coal tar Paste B.P.C.

**Formula:** Zinc oxide, finely sifted
- Coal tar
- Emulsifying wax
- Starch
- Yellow soft paraffin.

- **Type of preparation:** Paste with semi-solid base prepared by fusion.
**Procedure:**

**Method-I**
- Emulsifying wax is melted in a tared dish (70°C).
- The coal tar is weighed in the dish. Stirred to mix.
- Soft paraffin is melted in a separate dish (70°C) and about half is added to the tar-wax mixture; stirred well. Remainder is added; stirred again until homogeneous.
- Allowed to cool at about (30°C) and zinc oxide (previously passed through 180 mesh) and starch, in small amount with constant stirring. Stirred until cold.

**Method-II**
- Wax and paraffin melted together, mixed well and stirred until just setting. Powders are mixed on a slightly warm tile and the tar is incorporated. This method eliminates the risk of over heating.

**Definition:**
- “Gels are semisolid system in which liquid phase is constrained with a 3-D polymeric matrix having a high degree of physical or chemical cross linking.”
- Gels are aqueous colloidal system of hydrated forms of insoluble medicaments.
- “Jellies are transparent or translucent, non-greasy, semisolid preparation generally applied externally.”
- They are used for medication, lubrication and some miscellaneous applications.

**Gel Composition**
- Gelling agent
- Water
- Cosolvents
- Preservatives
- Stabilizers

**Kinds of Gels**
- Hydrogels
  - Silica, bentonite, pectin, sodium alginate, methylcellulose, alumina
- Organic Gels
  - Contain an organic liquid (e.g., Plastibase)
- Carbomer Gels
  - Aqueous dispersion neutralized with sodium hydroxide or triethanolamine
- Methylcellulose Gels
- Starch Glycerite
- Aluminum Hydroxide Gel

**Gelation**
- As a hot, colloidal dispersion of gelatin cools, the gelatin macromolecules lose kinetic energy.
- With a reduction of kinetic energy or thermal agitation.
- Gelatin, agar, pectin, Irish moss, pectin, tragacanth form gels by this mechanism.
Types of Gels:

A. Controlled Release Gels:

- Drug delivery to nasal or ocular mucosa for either local or systemic action suffers from many obstacles. Gel formulations with suitable rheological and mucoadhesive properties increase the contact time at the site of absorption.
- However, drug release from the gel must be sustained if benefits are to be gained from the prolonged contact time.
- These gels were formed in simulated tear fluid at concentrations of polymer as low as 0.1%, and it was shown that sodium was the most important gel-promoting ion in vivo.

B. Organogels:

- Sorbitan monostearate, a hydrophobic nonionic surfactant, and numbers of organic solvents such as hexadecane, isopropyl myristate, and a range of vegetable oils are present. Gelation is achieved by dissolving/dispersing the organogelator in hot solvent to produce an organic solution/dispersion, which, on cooling sets to the gel state.
- Such organogels are affected by the presence of additives such as the hydrophilic surfactant, polysorbate 20, which improves gel stability and alters the gel microstructure from a network of individual tubules to star-shaped "clusters" of tubules in the liquid continuous phase.

C. Extended Release Gels:

- It is a controlled release technology consists of an agglomerated, hydrophilic complex that, when compressed, forms a controlled-release matrix. It consisting of xanthan and locust bean gums (two polysaccharides) combined with dextrose surrounds a drug core. In the presence of water, interactions between the matrix components form a tight gel while the inner core remains unwetted.
- The drug is encapsulated in the pores of the gel, and as the matrix travels through the patient’s digestive system, the tablet swells and begins to erode. This erosion allows the drug to “back-diffuse” out through the gel-matrix at a controlled rate until the matrix erodes and a majority of the drug is released. The fundamental component controlling the rate of release lies in the properties of the gel matrix.

D. Amphiphilic Gels:

- Amphiphilic gels can be prepared by mixing the solid gelator like sorbitan monostearate or sorbitan monopalmitate and the liquid phase like liquid sorbitan esters or polysorbate and heating them at 60°C to form a clear isotropic sol phase, and cooling the sol phase to form an opaque semisolid at room temperature.
- Amphiphilic gel microstructures consisted mainly of clusters of tubules of gelator molecules that had aggregated upon cooling of the sol phase, forming a 3D network throughout the continuous phase. The gels demonstrated thermoreversibility. Gelation temperature and viscosity increased with increasing gelator concentration, indicating a more robust gel network.
E. Hydrophilic Gels:
- Hydrophilic gels are composed of the internal phase made of a polymer producing a coherent threedimensional net-like structure, which fixes the liquid vehicle as the external phase. Intermolecular forces bind the molecules of the solvent to a polymeric net, thus decreasing the mobility of these molecules and producing a structured system with increased viscosity.

F. Non Aqueous Gels:
- Ethylcellulose was successfully formulated as a nonaqueous gel with propylene glycol dicaprylate/dicaprate. The novel nonaqueous gel exhibited rheological profiles corresponding to a physically cross-linked three-dimensional gel network, with suitable mechanical characteristics for use as a vehicle for topical drug delivery.
- The gel matrices exhibited prominent viscoelastic behavior, yield stress and thixotropy. Rheological and mechanical properties showed significant upward trends with increased polymeric chain length and polymer concentrations. Good linear correlations were obtained between rheological and mechanical properties.

Types of Jellies:

Medicated Jellies:
- Water soluble drugs like local anesthetics, spermicides and antiseptics are suitable for incorporation in the jellies.
- They are easy to apply and evaporation of the water content produces a pleasant cooling effect.
- The medicinal film usually adheres well and gives protection but is easily removed by washing when the treatment is complete.
- Example:
  - Ephedrine sulfate jelly used to arrest bleeding from nose.
  - Pramoxine HCl, a local anaesthetic relieves discomfort of pruritis and haemorrhoids.
  - Phenylmercuric nitrate as spermicidal contraceptive.

Lubricant Jelly:
- Catheters, items of eletrodiagnostic equipment, such as cystoscopes, and rubber gloves or finger stalls used for rectal and other examinations require lubrication before use.
- The lubricants must be sterile for articles inserted into sterile regions of the body, such as urinary bladder.
- For painful investigations a local anaesthetic may be included as in Lignocaine Gel B.P.C.
Miscellaneous uses:
The following are more specialized jellies

(a) **Patch testing**
- Here the jelly is the vehicle for allergens applied to the skin to detect sensitivity. Several allergens may be applied on one person. The viscosity of the jelly and it leaves on drying help to keep the particles separate.

(b) **Electrocardiography**
- To reduce electrical resistance between the patient's skin and electrodes of the cardiograph, an electrode jelly may be applied. This contains NaCl to provide good conductivity and often pumice powder which, when applied onto the skin, removes part of the horny layer of the epidermis, the main layer of electrical resistance.

**Definition:**
- “Poultice are paste-like preparations used externally to reduce inflammation because they retain heat well. After heating, the preparation is spread thickly on a dressing and applied, as hot as the patient can bear it, to the affected area.”

**Uses:**
- Glycerol, because of its hygroscopic nature, is believed to draw infected materials from the tissues when the poultice is used for boils and similar infections.
- Methyl Salicylate (An Antirheumatic Drug),
- Thymol (A Powerful Bactericide),
- Boric Acid (A Weak Antimicrobial Agent),
- and Peppermint Oil (which contributes to the smell) are used for different purposes.
Plasters

Definition:

- “Plasters are solid or semisolid masses adhere to the skin when spread upon cotton felt line or muslin as backing material and they are mainly used to:
  - Afford protection and mechanical support
  - Furnish an occlusive and macerating action
  - Bring medication into close contact with the surface of the skin

Plasters are applied to the skin to provide prolonged contact at the site.

Unmedicated plasters provide protection or medicated support at the site of application.

Adhesive tape used to be official under the little adhesive plaster, the use of this material being well known.

Medicated plasters provide effects at the site of application.

They may be cut to size to conform to the surface to be covered.

Formulation of Semisolids
Ingredients used in preparation of semi solid dosage form:

- Active pharmaceutical ingredients
- Bases
- Preservatives
- Humectants
- Anti oxidants
- Emulsifier
- Gelling agent
- Buffers

Bases:

- It is one of the most important ingredient used in the formulation of semi solid dosage form.
- Ointments and suppository base do not merely acts as the carrier of the medicaments, but they also control the extent of absorption of medicaments incorporated with them.
- They should be:
  - Compatible with skin pH and drug
  - Inert, non irritating and non sensitizing
  - Good solvent and/or emulsifying agent
  - Emollient, protective, non greasy and easily removable
  - Release medicaments easily at the site of administration
  - Pharmaceutical elegant and possess good stability.

Classification of Bases:

- Water soluble base
- Emulsion base
- Absorption base
- Oleaginous base

Preservatives:

- Some bases, although, resist microbial attack but because of their high water content, it require an anti microbial preservative.
- Commonly used preservative include:
  - Methyl hydroxy benzoate
  - Propyl hydroxy benzoate
  - Chorocresol
  - Benzoic acid
  - Phenyl Mercuric Nitrate
Antioxidants:

- Oxygen is highly reactive atom that is capable of becoming 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 functions.
- To prevent this an antioxidant are added.
- Example: Butylated Hydroxy Anisole (BHA), Butylated Hydroxy Toluene (BHT)

Humectants:

- A humectant is a hygroscopic substance. It is often a molecule with several hydrophilic groups, most often hydroxyl group.
- Humectants are used to:
  - Increase the solubility of active ingredients
  - To elevate its skin preparation
  - Elevate the hydration of the skin.

Gelling Agents:

- Gelling agent forms a gel dissolves in a liquid phase as a colloid mixture that forms a weakly cohesive internal structure.
- These are organic hydrocolloids or hydrophilic inorganic substances.
- Example: Tragacanth, Sodium Alginate, Pectin, Gelatin, Cellulose Derivatives.

Emulsifiers:

<table>
<thead>
<tr>
<th>Anionic</th>
<th>Cationic</th>
<th>Non ionic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Alkyl sulphates</td>
<td>• Quaternary ammonium compounds</td>
<td>• Polyoxyethylene</td>
</tr>
<tr>
<td>• Soaps</td>
<td>• Alkyl-aryl ethers</td>
<td>• Polyoxy ethylene</td>
</tr>
<tr>
<td>• Dodecyl benzene</td>
<td>• Polyoxy esthers</td>
<td>• Sorbitan esters</td>
</tr>
<tr>
<td>• Sulphonates</td>
<td>• Sorbitan fatty acid esters</td>
<td>• Glyceryl fatty acid esters</td>
</tr>
<tr>
<td>• Lactylates</td>
<td>• Phosphate esters</td>
<td></td>
</tr>
</tbody>
</table>
Buffers:

- Buffers are added to various purpose such as:
  - Compatibility with skin
  - Drug solubility
  - Drug Stability
  - Influence on ionization of drug

- Example: Sodium acetate, Sodium Citrate, Potassium meta phosphate

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Formulation of Semisolids: CONTD...

Question Bank:

2 Marks
1. Define: creams & plasters.
2. Define: poultices & jellies.*
3. Classify ointment bases.
4. Define ointment & gels

5 Marks
1. Write a note method of preparation of ointment.
2. Short note: Gels & jellies.
3. Write a note on fusion method of ointment compounding.
4. Short note: plasters

10 Marks
1. Define ointment. Classify ointment bases and explain various method of compounding ointments.**
2. Define ointment. Discuss method of compounding with example.