# Semisolid dosage form

LEC 3

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# Raw material

## D) Fatty acids and alcohols

1. **Stearic acid** is used in water-removable creams as an emulsifier By:

- ❖ Developing consistency in the cream.by addition of certain amount of potassium hydroxide or triethanolamine to react with about 8 to 20% of the stearic acid. The unreacted fatty acid increases the consistency of the cream.
- ❖ developing a sheen or luster upon aging (give a matt effect on the skin), owing to the formation of stearic acid crystals.
- ➢ Creams formed with sodium stearate are much firmer in consistency.

**2. Stearyl alcohol and cetyl alcohol (palmityl alcohol)** are used in creams as auxiliary emulsifiers and emollients. In sufficient quantity, stearyl alcohol produces a firm cream that may be softened with cetyl alcohol.

## E) Emulsifiers

The water-soluble soaps were among the first emulsifiers used for semisolid o/w emulsions, The viscosity of the cream or ointment prevents coalescence of the emulsified phases and helps to stabilize the emulsion.

**Additional substances added to achieve stability:**

1) cetyl alcohol and glyceryl monostearate tend to stabilize the o/w emulsion by formation of interfacial film around the dispersed phase globules thereby making the emulsified preparation more rigid.

2) Polyvalent ions, such as magnesium, calcium, and aluminum, tend to stabilize w/o emulsions by cross-linking with the polar groups of the fatty materials.

3)Mixed emulsifier system(The combination of a surface active agent with an oil-soluble auxiliary).

- **Anionic surfactant**

**oil-in-water mixed emulsifier**

**Prepared from combination of** Triethanolamine stearate soap with cetyl alcohol.

**water-in-oil mixed emulsifier**

**prepared from combination** of beeswax and divalent calcium ions.

Maximum stability of an emulsion occurs when a complex interfacial film is formed.

**Note:** increasing $Ca^{2+}$ ions as an auxiliary emulsifier. made soft w/o base while decreasing mineral oil content made firmer bases.

- **Cationic surfactant** used for emulsion when drugs required acid pH (like quaternary ammonium comds. –cetyl triethyl ammonium chloride [cetrimide]- in combination with cetyl alcohol) to achieve stability for emulsion.

- **Non-ionic surfactant** (employed for both O/W or W/O emulsion) since they are compatible with many drugs

*Formula #3*
*Tripelennamine Hydrochloride Cream**

| | %(w/w) |
|---|---|
| *Oil Phase* | |
| Cetyl alcohol | 5.0 |
| Glyceryl monostearate | 15.0 |
| Sorbitan monooleate | 0.3 |
| Polysorbate 80, USP | 0.3 |
| *Aqueous Phase* | |
| Tripelennamine HCl | 2.0 |
| Methylcellulose 100 cps | 1.0 |
| Purified water, q.s. ad | 100.0 |
| Preservative | q.s. |

Tween 80 used together with sorbitan to form o/w or w/o emulsion

Non-ionic surfactants

**4) The clay, magnesium aluminum silicate**, has been used as a thickener, suspending agent, and o/w emulsion stabilizer because of the colloidal structure of its aqueous dispersions.

It also contributes to the stability of w/o emulsions when used with suitable emulsifiers, probably owing to its thickening action on the internal phase whereby it inhibits coalescence. The magnesium aluminum silicate may migrate to the interfacial area, resulting in a stronger film.

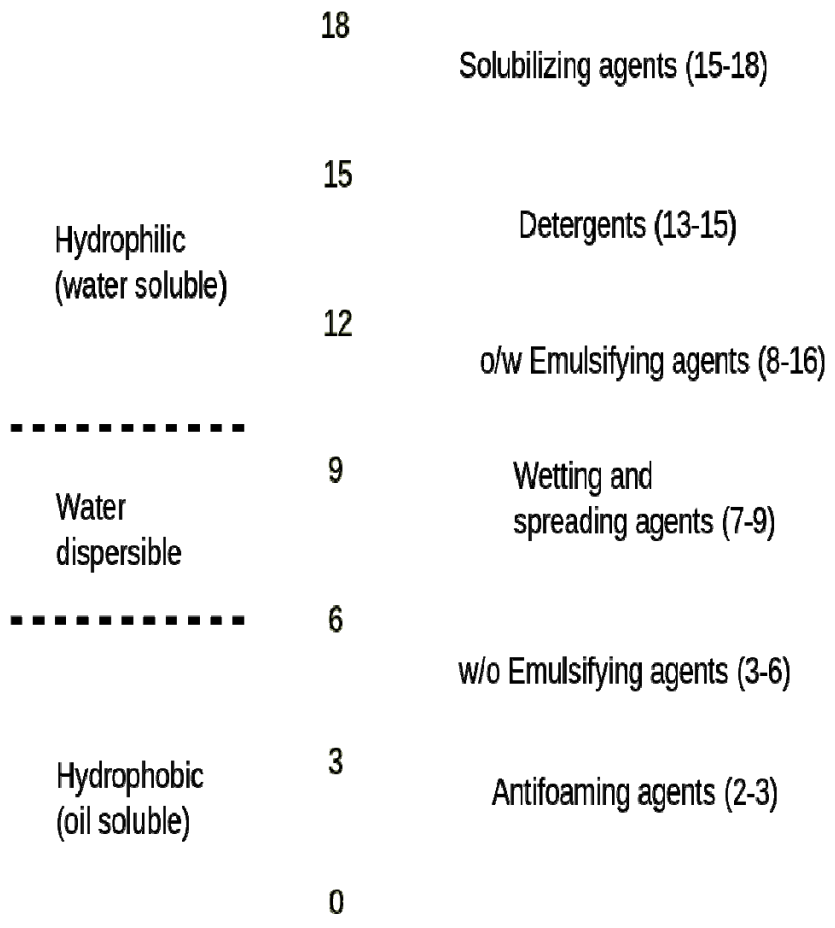
| | *Formula #2* | *%(w/w)* |
|---|---|---|
| *A* | Magnesium aluminum silicate (MAS)* | 2.0 |
| | Purified water | 37.0 |
| *B* | Mineral oil, light | 20.0 |
| | Petrolatum | 9.0 |
| | Isopropyl myristate | 5.0 |
| | Lantrol (lanolin oil)† | 3.0 |
| | 70% sorbitol solution | 20.0 |
| | Arlacel 186 (glyceryl oleate and propylene glycol)‡ | 1.0 |
| | Polysorbate 80 | 1.0 |
| | Preservative | q.s. |

**5) Recently, a series of emulsifiers have been marketed that contain chemically bonded lactic acid with fatty acids.**

Uses: to produce an emollient feel to the skin, and to serve as oil-in-water or water-ill-oil emulsifiers. They claimed to be mild and nonirritating to the skin and eyes.

| *Types of Fatty Acid* | *Calculated HLB* |
|---|---|
| 1. Stearic | 6.5 |
| 2. Stearic/Palmitic | 8.3 |
| 3. Lauric/Myristic | 14.4 |
| 4. Capric/Lauric | 11.3 |
| 5. Isostearic | 5.9 |

Items 3 and 4 are detergent. Item 4 shows good bacteriostatic properties, owing to the presence of the moderately short chain capric acid



**6) The Promulgens:** are a series of nonionic emulsifiers composed of a mixture of fatty alcohols and their ethoxylates.
Two types available, D and G, they are differ in melting point and in consistency of the emulsions that they form.
**The emulsions formed with type D are usually thicker in consistency therefore** type D tends to form creams while type G tends to form liquid emulsions. It is suggested that they be used in combination to achieve a desired viscosity level
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| | *Promulgen D* | *Promulgen G* |
|---|---|---|
| CTFA adopted name— | Cetearyl alcohol and Ceteareth-20 | Stearyl alcohol and Ceteareth-20 |
| Chemical description— | Cetearyl alcohol and ethoxylated cetearyl alcohol | Stearyl alcohol and ethoxylated cetearyl alcohol |
| Melting point— | 47 to 55°C | 55 to 63°C |

| Formula #4 | %(w/w) |
|---|---|
| *A Oil Phase* | |
| Cetearyl alcohol | 5.0 |
| Silicone oil, 200 fluid | 1.0 |
| Isopropyl myristate | 2.0 |
| Sodium stearoyl-2-lactylate | 2.0 |
| *B Aqueous Phase* | |
| Propylene glycol | 5.0 |
| Sodium citrate | 0.2 |
| Preservative | q.s. |
| Purified water, q.s. ad | 100 |

Since there are no ester linkages, these emulsifiers are not subject to hydrolysis. In addition, they are compatible with anionic surfactants of the sodium lauryl sulfate type or with cationic such as quaternary ammonium compounds

# Polyols(Humectants)

Glycerine, propylene glycol, sorbitol 70%, and the lower molecular weight polyethylene glycols are used as humectants in creams.

**The choice of a humectant is based not only on its rate of moisture exchange, but also on its effect on the texture and viscosity of the preparation.**

**Benefits:**

1. These materials prevent the cream from drying out .
2. prevent the formation of a crust when the cream is packaged in a jar.
3. They also improve the consistency and rub-out qualities of the cream when it is applied to the skin, permitting the cream to be spread without rolling.

❖ Increasing the humectant content tends to cause **tackiness**.

Sorbitol 70% is more hygroscopic than glycerine and is used at a lower concentration.

Propylene glycol and the polyethylene glycols occasionally are used in combination with glycerine, since their ability to absorb moisture is less than that of glycerine.

# Insoluble Powders

Insoluble drugs must be uniformly dispersed throughout the vehicle to ensure homogeneity of the product and avoid grittiness.

- Milling to a finely divided state provides more surface area for contact with the dermal site and increases the rate of dissolution of poorly soluble substances.
- Some powders do not disperse uniformly (aggregate in the base) may be due to the electrically charged surface condition of the particles after milling. **(P.S.< 5M)**

- Particles less than 74 microns in size, equivalent to the mesh openings in a 200-mesh sieve in the U.S. Standard Sieve series, are impalpable to most people

- Many drug substances used in topical preparations (e.g., prednisolone; fluorocortisone acetate) exist in several polymorphic states.(Compounds that exist in different crystalline forms at room temperature possess varying amounts of free energy or thermodynamic activity).The physiologic activity and availability of a drug substance often ate directly related to its thermodynamic activity.

- the choice of the proper crystalline form for use in the semisolid is vitally important

- Following its incorporation into the semisolid, the maintenance of the selected polymorphic form in the semisolid is of equal concern

- The components of the vehicle and the method of preparation of the semisolid dosage form affect the stability of the polymorphic form.

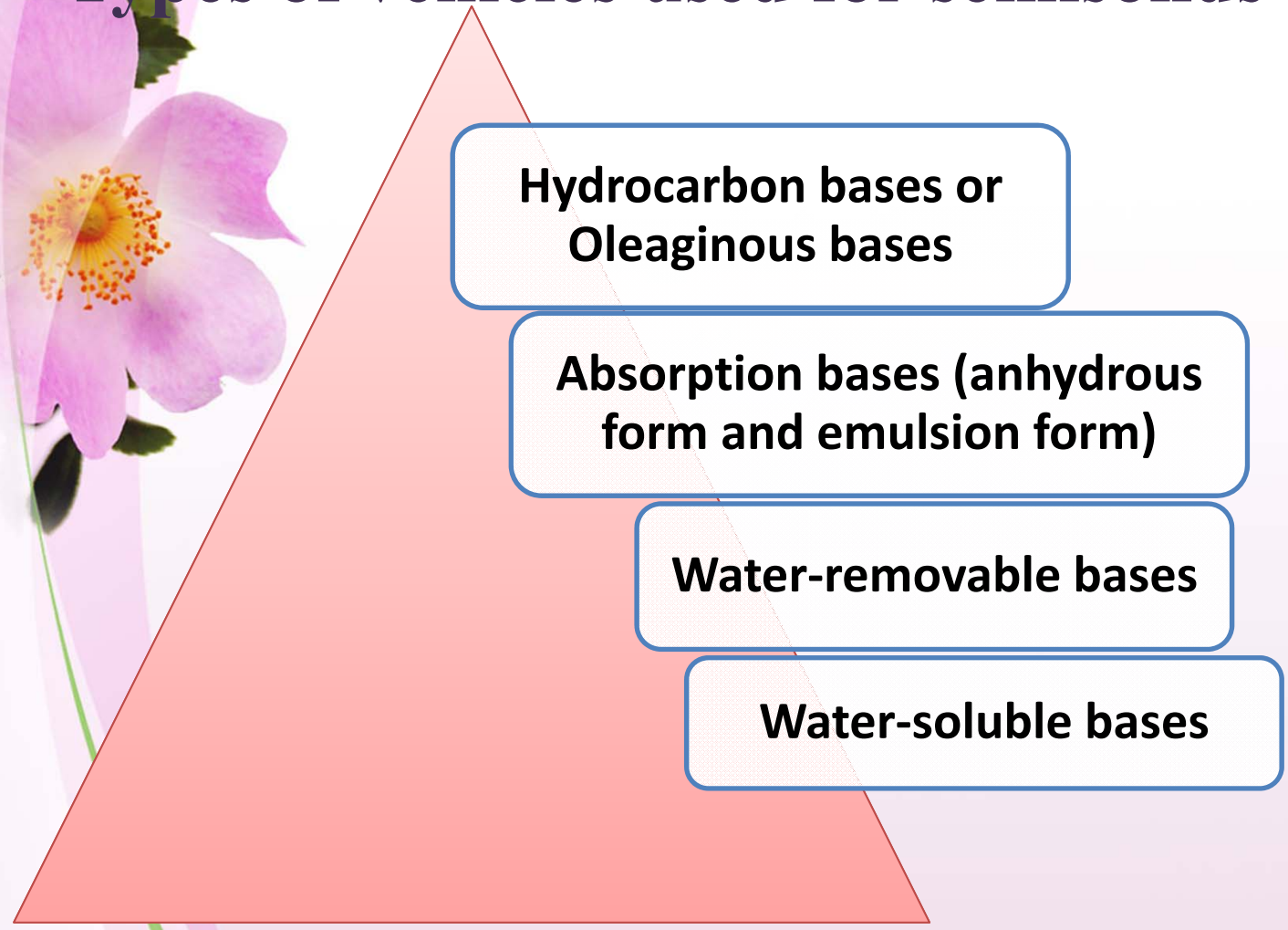
# Type of vehicles

The vehicle used for a pharmaceutical differs from that used for a cosmetic why?

because with a cosmetic, penetration into the skin is not desired. Penetration or protection is desired in a pharmaceutical semisolid, and its cosmetic effect or appearance on the skin is less important. A well formulated pharmaceutical semisolid should be both therapeutically effective and cosmetically appealing, with the major effort in the medical direction.

the choice of the semisolid vehicle depend on the **solubility** and **stability of the drug in the base**, as well as the **nature of the skin lesion**

# Types of vehicles used for semisolids are:



# 1. Hydrocarbon Bases

Petrolatum and white ointment, which is petrolatum with 5% beeswax, are typical of this class of lipophilic vehicles. The most commonly used raw material in ointment vehicles is petrolatum because of

1)its consistency,

2)its bland and neutral characteristics.

3)its ability to spread easily on the skin.

4) used as occlusive coverings to inhibit the normal evaporation of moisture from the skin.

Disadvantages

1. These bases are difficult to wash off the skin
2. A thin film of petrolatum produces a sensation of warmth on the skin because the insensible moisture does not evaporate.
3. Very little water can be incorporated into these greasy bases without the addition of other substances

# 2. Absorption Bases

The absorption bases are formed by the addition of substances miscible with hydrocarbons like:

1. Substances possessing polar groupings, such as the sulfate, sulfonate, carboxyl, hydroxyl.
2. Substances possessing an ether linkage. Lanolin, cholesterol and other sterols.
3. Substances possessing partial esters of polyhydric alcohols (e.g., sorbitan monosterate or monooleate)

May be added to make the hydrocarbon bases "absorption bases,“

- These bases do not absorb water on contact, but with sufficient agitation, they do absorb aqueous solutions and can be considered water /oil emulsions.

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

1. The anhydrous form(anhydrous lanolin and hydrophilic petrolatum) that are practically insoluble in water but can absorb water up to 50% of its own weight. to form w/o emulsions.
2. The emulsion form(Hydrous lanolin) was the prototype of the absorption bases for w/o emulsion because of its ability to permit the incorporation of additional quantities of aqueous solutions.

**Application** These vehicles have "emollient" properties and deposit an oily film upon the skin.

**anhydrous form**

*Formula #6*
*Hydrophilic Petrolatum (USP XX)*

| | g |
|---|---|
| Cholesterol | 30.0 |
| Stearyl alcohol | 30.0 |
| White wax | 80.0 |
| White petrolatum | 860.0 |
| | 1000.0 |

| Formulas | #8* % | #9† % |
|---|---|---|
| *Oil Phase* | | |
| Lanolin, anhydrous USP | 3.1 | 15.0 |
| Petrolatum, white, USP | 25.0 | — |
| Mineral oil, heavy | 25.0 | 8.0 |
| Beeswax (white wax, USP) | 10.0 | 7.0 |
| Sorbitan sesquioleate | 1.0 | — |
| Propylparaben | 0.05 | 0.05 |
| Amerchol CAB | — | 20.0 |
| *Aqueous Phase* | | |
| Sodium borate, USP | 0.7 | — |
| Polyethylene glycol 1500 | — | 5 |
| Methylparaben | 0.15 | 0.15 |
| Purified water | 35.0 | 49.8 |

Mineral oil is added to reduce the tackiness of the base.

*Formula #7*
*Lanolin Absorption Base*

| | % |
|---|---|
| Lanolin alcohols | 10 |
| Lanolin | 25 |
| Mineral oil, low viscosity | 30 |
| Purified water | 35 |

Non ionic water-in-oil emulsifiers, such as glyceryl monostearate, cholesterol, cetyl alcohol, and the sorbitan fatty acid derivatives, may be added for improved stability and water absorbing capacity.

**cold cream** type of emulsion frequently utilizes a borax-beeswax combination as the emulsifier, with mineral oil or a vegetable oil as the continuous phase. A protective oil film remains on the skin following the evaporation of the water. The slow evaporation of water gives the skin a cooling effect.

*Formula #10*
*Cold Cream*[29]

| | | % |
|---|---|---|
| A | Purified water | 34.60 |
| | Borax | 1.00 |
| | Methylparaben | 0.25 |
| B | Light mineral oil | 50.00 |
| | Synthetic beeswax flakes | 13.00 |
| | Glyceryl monostearate, pure | 1.00 |
| | Propylparaben | 0.15 |

- The maximum amount of water that can be added to 100 g of such a base at a given temperature is known as the water number. To determine the water number, the base is stirred continuously as the water is being added. Distilled or deionized water should be used. The end point is reached when no more water can be "absorbed“ into the base, as evidenced by droplets of water remaining in the container, it was found that the water-absorbing capacity of the base increased as the HLB number (hydrophilic lipophilic number) of the surfactant decreased.

**TABLE 18-1.** *Determination of Water Numbers Using 10-g Samples*

| *Surfactant* | *HLB* | *Grams Water Absorbed* | | *Water Number* |
|---|---|---|---|---|
| | | *Sample 1* | *Sample 2* | |
| (Control: White petrolatum) | | 0.40 | 0.40 | 4.0 |
| Sorbitan monolaurate | 8.6 | 5.21 | 5.41 | 53.1 |
| Sorbitan monopalmitate | 6.7 | 8.20 | 8.52 | 83.6 |
| Sorbitan monostearate | 4.7 | 10.59 | 10.17 | 103.8 |
| Sorbitan monooleate | 4.3 | 24.75 | 25.25 | 250.0 |
| Sorbitan sesquioleate | 3.7 | 29.84 | 31.04 | 304.4 |
| Sorbitan trioleate | 1.8 | 41.95 | 40.31 | 411.3 |


Thank
You!