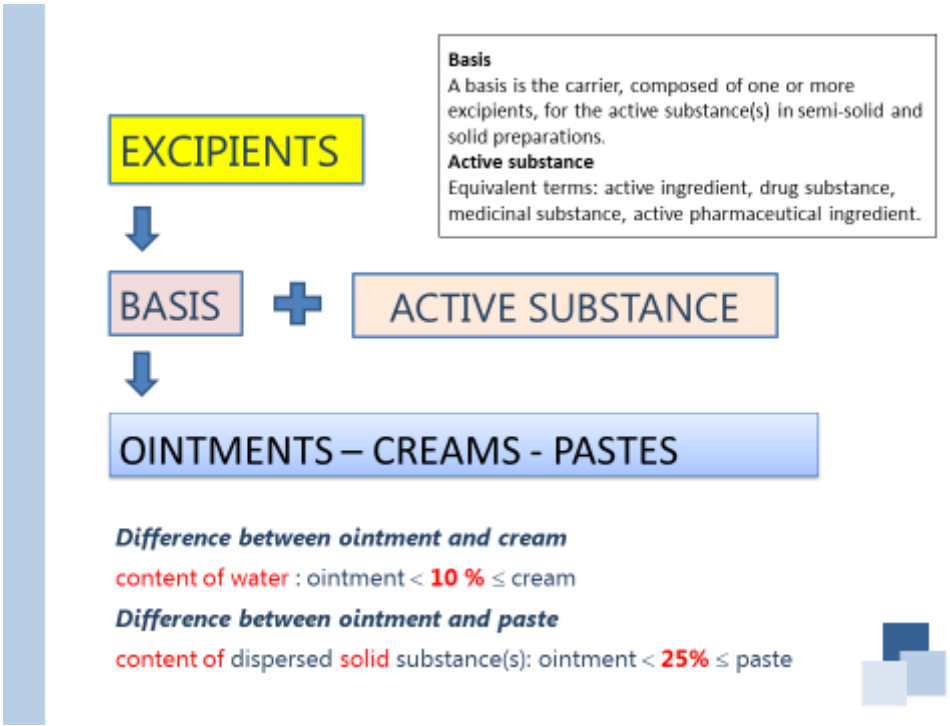
SEMISOLID DOSAGE FORMS - ointments, creams, pastes

Semi-solid preparations for cutaneous application are intended for local or transdermal delivery of active substances, or for their emollient or protective action. They are of homogeneous appearance. They consist of a simple or compound basis in which, usually, 1 or more active substances are dissolved or dispersed. According to its composition, the basis may influence the activity of the preparation.

Ph.Eur. introduces monograph on *Semi-solid preparations for cutaneous application*. Where appropriate, additional requirements specific to semi-solid preparations intended to be applied to particular surfaces or mucous membranes may be found in other general monographs, for example *Ear preparations*, *Nasal preparations*, *Rectal preparations*, *Eye preparations and Vaginal preparations*.



OINTMENTS

An ointment consist of a single-phase basis in which solids or liquids may be dispersed.

Hydrophobic ointments can absorb only small amounts of water.

Water-emulsifying ointments can absorb larger amounts of water and thereby produce W/O or O/W emulsions after homogenisation, depending on the nature of the emulsifiers.

Hydrophilic ointments are preparations having bases that are miscible with water.

CREAMS

A cream is a multiphase preparation consisting of a lipophilic phase and an aqueous phase.

Lipophilic creams have as the continuous phase the lipophilic phase (semisolid emulsions W/O). They usually contain water-in-oil emulsifying agents. Unlike emulsion ointments creams contain more water. By convention, the limit is set at more than 10%.

Hydrophilic creams have as the continuous phase the aqueous phase (semisolid emulsions O/W). They contain oil-in-water emulsifying agents.

PASTES

A paste is semisolid preparation containing large proportions of solids finely dispersed in the basis. By convention, the limit is set at more than 25 %. Pastes can be used to treat infections by making use of their high osmotic effect, or as very thick material to prevent irritant drugs spreading over the skin surface.

GENERAL CLASSES OF OINTMENT BASES

1. *Oleaginous Ointment Bases*
   - made of hydrophobic excipients
   - contain no water phase
   - contain no emulsifiers
2. *Emulsifying Ointment Bases*
   - made of hydrophobic excipients
   - contain no water phase
   - contain emulsifiers
     a) *W/O Emulsifying Ointment Bases*
     b) *O/W Emulsifying Ointment Bases*
3. Water-miscible Ointment Bases
   - made of hydrophilic excipients (Macrogols, hydrogels)

GOOD DISPENSING PRACTICE RULES

Semisolids are commonly made using a stainless-steel bowl (a basin) and a pestle, which are tarred together. The components of preparation are weighed depending on their consistency. A lab spoon is used for manipulation with solid materials, spatula is used for semisolid excipients, and liquids are poured carefully from a bottle.

MIXING BY FUSION

The compounding includes the blending together of oily materials, some of which are solids at room temperature. This is achieved by the process called "mixing by fusion". It involves melting the ingredients together. The process is carried out on a thermostatically controlled hot-water bath. It should be noted that a high temperature is not required to prevent degradation of oil materials; 60-80°C is generally adequate. The infra-red lamp is possible to use for melting of the heat-stable excipients.

Excipients are melted according to decreasing melting point. Melting (fusion) begins with the highest melting point excipient. Each excipient should be melted at the lowest possible temperature as the mixture progressively cools. The waxy solid should be grind prior to weighing and should be added to the tared basin and heated (melted) first. Excipients of semisolid consistency are then added, which soften spontaneously from the heated basin or a heating continues. When all the ingredients are melted, the basin is removed from water bath (infra-red lamp) and **gently stir until cold** to prevent lumps forming. Lumps formation could happen because the higher melting point ingredients in the system may precipitate out. Mixing should be gentle to avoid air bubbles.

SUSPENSION OINTMENTS

For suspension ointments, usually hydrophobic base without emulsifiers can be used.

Insoluble solids (APIs) are incorporated into bases using the technique called "**mixing by trituration**". Powders are placed into basin and incorporated using "**doubling-up**" as it is worked in. At each step, it is necessary to add the powder in the same volume of liquid excipient (= levigation) or part of the molten base. When only soft material is used, a partial melting is enough because the more effective mixing is possible wherever material is more viscous. Thus, a blend of the ointment bases should be melted to be softened.

Levigation is the process when solid particles are mixed with somewhat viscous to improve ease of wetting of the solid. Often the ointment formulation contains an ingredient that can be

used as levigation agent (oils and/or mineral oils for hydrophobic bases; glycerine for hydrophilic, polysorbate as a surfactant). The melted ointment base can also be used.

Because a smooth, non-gritty preparation is desired, any solids incorporated into an ointment should be **in the finest state possible**. Therefore, the careful grinding (= reducing particle size) of powder material in a ceramic (porcelain) rough mortar is necessary (e.g. boric acid powder rather than boric acid crystals).

Certain crystalline ingredients such as urea and camphor are difficult to levigate to a fine powder and should be dissolved in a suitable solvent before incorporation into the ointment base. Water-miscible solvents include water, alcohol, isopropyl-alcohol, glycerine, propylene glycol, and macrogol. Lipophilic solvents include mineral oil, fixed oils (castor oil, cottonseed oil, olive oil).

EMULSION OINTMENTS

For emulsion ointments, usually hydrophobic base containing an emulsifier (= **emulsifying ointment base**) is used. If the content of water phase is larger it should also be added by **trituration** (= step by step in ratio 1:1). The blend of ointment bases should be **completely melted** to the form a liquid phase. Water phase is prepared separately and usually heated within the few degrees the same (± 5°C) temperature as the ointment bases. If the cold-water phase is added solid ointment bases might congeal again leading to lumps. After addition of water, continual stirring until cold follows. A rapid cooling is not recommended. It will cause the separation of high melting point material, and excessive aeration as a result of vigorous stirring can also produce a granular product.

To improve water absorption capacity, **surfactant agent** is necessary. Emulsifying ointment bases and/or surfactants are used. Drugs may, if they are stable, be dissolved in the appropriate phase before emulsification, or may be added by trituration when cold. The addition of water may influence stability of preparation as some drugs undergo hydrolysis. Also, **preservatives** are needed. Flavours and perfumes are available either as oils (aetheroleum) or as alcoholic concentrates. They are usually added to cold preparation when finishing compounding.