

PREPARATION OF OINTMENTS

A well-made ointment is –

- (a) *Uniform throughout* i.e. it contains no lumps of separated high melting point ingredients of the base, there is no tendency for liquid constituents to separate and insoluble powders are evenly dispersed.
- (b) *Free from grittiness*, i.e. insoluble powders are finely subdivided and large lumps of particles are absent. Methods of preparation must satisfy this criteria.

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.

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.

Advantages:

This will avoid over-heating of substances having low melting point.

Method-II

All the components are taken in subdivided state and melted together.

Advantages:

The maximum temperature reached is lower than Method-I, and less time was taken possibly due to the solvent action of the lower melting point substances on the rest of the ingredients.

Cautions:

- (i) Melting time is shortened by grating waxy components (i.e. beeswax, wool alcohols, hard-paraffin, higher fatty alcohols and emulsifying waxes) by stirring during melting and by lowering the dish as far as possible into the water bath so that the maximum surface area is heated.
- (ii) The surface of some ingredients discolors due to oxidation e.g. wool fats and wool alcohols and this discolored layers should be removed before use.
- (iii) After melting, the ingredients should be stirred until the ointment is cool, taking care not to cause localized cooling, e.g. by using a cold spatula or stirrer, placing the dish on a cold surface (e.g. a plastic bench top) or transferring to a cold container before the ointment has fully set. If these precautions are ignored, hard lumps may separate.
- (iv) Vigorous-stirring, after the ointment has begun to thicken, causes excessive aeration and should be avoided.
- (v) Because of their greasy nature, many constituents of ointment bases pickup dirt during storage, which can be seen after melting. This is removed from the melt by allowing it to sediment and decanting the supernatant, or by passage through muslin supported by a warm strainer. In both instances the clarified liquid is collected in another hot basin.
- (vi) If the product is granular after cooling, due to separation of high m.p. constituents, it should be remelted, using the minimum of heat, and again stirred and cooled.

Example:

(i) **Simple ointment B.P. contains**

Wool fat	50g
Hard paraffin	50g
Cetostearyl alcohol	50g
White soft paraffin	850g

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.

(ii) **Paraffin ointment base**

Type of preparation: Hydrocarbon ointment base

(iii) **Wool alcohols ointment B.P.**

Type of preparation: Absorption base

(iv) **Emulsifying ointment B.P.**

Type of preparation: Water-miscible ointment base.

(v) **Macrogol ointment B.P.C**

Type of preparation: Water soluble ointment base

Formula: Macrogol 4000
Liquid Macrogol 300

Method: Macrogol 4000 is melted and previously warmed liquid macrogol 300 is added. Stirred until cool.

2. OINTMENT PREPARED BY TRITURATION

This method is applicable in the base or a liquid present in small amount.

- (i) Solids are finely powdered are passed through a sieve (# 250, # 180, #125).
- (ii) 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.
- (iii) 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.

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.

(ii) Salicylic acid sulphur ointment B.P.C.

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, 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 $KI.I_2$, $KI.2I_2$, $KI.3I_2$ etc.

These solutions may be incorporated in absorption-type ointment bases.

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.

- (i) Due to improper storage the water dries up and the iodine crystals irritate the skin, hence glycerol was some times added to dissolve the iodine-potassium iodide complex instead of water.

Example: Strong Iodine Ointment B. Vet.C.

Iodine
Woolfat
Yellow soft paraffin
Potassium iodide
Water

Procedure:

- (i) KI is dissolved in water. I_2 is dissolved in it.
- (ii) Woolfat and yellow soft paraffin are melted together over water bath. Melted mass is cooled to about $40^{\circ}C$.

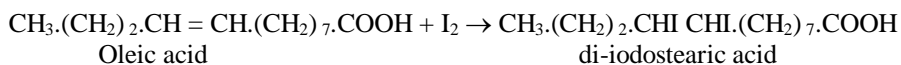
(iii) I₂ solution is added to the melted mass in small quantities at a time with continuous stirring until a uniform mass is obtained.

(iv) It is cooled to room temperature and packed.

Use: - Ringworm in cattle.

(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, e.g.



Example: Non-staining Iodine Ointment B.P.C. 1968

Iodine
Arachis Oil
Yellow Soft Paraffin

Method:

- (a) 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.
- (b) 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.
- (c) 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.
- (d) 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.
- (e) The preparation is packed in a warm, wide-mouthed, amber color, glass bottle. It is allowed to cool without further stirring.

4. PREPARATION OF OINTMENTS BY EMULSIFICATION

An emulsion system contains an oil phase, an aqueous phase and an emulsifying agent.

For o/w emulsion systems the following emulsifying agents are used:

- (i) water soluble soap
- (ii) cetyl alcohol
- (iii) glyceryl monostearate
- (iv) combination of emulsifiers: triethanolamine stearate + cetyl alcohol
- (v) non-ionic emulsifiers: glyceryl monostearate, glyceryl monooleate, propylene glycol stearate

For w/o emulsion creams the following emulsifiers are used:

- (i) polyvalent ions e.g. *magnesium, calcium and aluminium* are used.
- (ii) combination of emulsifiers: *beeswax + divalent calcium ion*

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

Example:

Cold cream:

Procedure:

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

N.B. The aqueous phase is heated otherwise high melting point fats and waxes will immediately solidify on addition of cold aqueous solution.

MANUFACTURE OF OINTMENTS / CREAMS IN INDUSTRIAL SCALE

1. Preparation of oil and aqueous phase

Oils + Fats
 ↓ *Equipment: Steam jacketed kettle*
 Melted and mixed
 ↓
 Strained through several layers of cheese cloths to remove foreign matter

Water soluble ingredients + Purified water
 ↓ *Equipment: Mechanical stirrer*
 Dissolved
 ↓
 Filtered
 ↓
 Heated to the melting point of oil phase

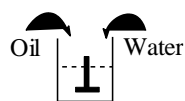
- Cakes, flakes or powdered waxes are directly weighed in a physical balance.
- Semisolid petrolatum is melted in the container supplied by an immersion heater, the liquid petrolatum is then transferred by a *metering pump* through *metal reinforced inert plastic hoses and insulated pipes*.

2. Mixing of oil and water phases

Mixing temperature is 70–72°C for proper mixing.

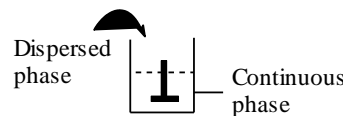
Three methods of mixing are there:

(A) Simultaneous blending



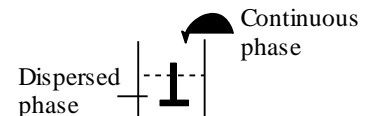
- For continuous or large batch operation
- *Equipments*
 Proportioning pump
 Continuous mixer

(B) Addition of disperse phase to continuous phase



- For an emulsion having low volume of dispersed phase.
- *Equipment:*
 Simple metering pump

(C) Addition of continuous phase to disperse phase



- For an emulsion formed by phase inversion method.
- *Equipment:*
 Simple metering pump.

- Batch sizes are on weight basis. For weighing a *hydraulic load cell* is fitted under one of the leg of the mixing kettle.

3. Cooling the semisolid

Cooling should be slow to prevent crystallization of high m.p. waxes. Perfumes are added at 43 to 45°C.

Equipments: Kettle fitted with heating / cooling arrangements, agitator and sweep blades (for scrapping the wall).

Cooled to 43 to 45°C
 ↓ *Kettle with agitator and sweep blades*
 Addition of perfume
 ↓
 Addition of drug powder
 ↓
 Dispersed or dissolved

4. Homogenization

Creams or ointments
 ↓ *Equipment: Low-shear gear pump and roller mill / colloid mill / valve type homogenizer*
 Homogenization

5. Storage of semisolids

Stored before packaging. In the mean time Q.C. report comes. Stored in a tight-fitting stainless steel (SS#316) container.

6. Transfer of materials for packaging

Equipment: Ointment filling machine

Washing of the equipments with high-pressure (up to 1000psi), low-volume pumps and hot water and detergents should be done.

To sterilize the equipments, containers, pumps and other accessories are flushed with chlorinated water or formalin – followed by rinsing them with bacteria free water.