

Cocoa Butter (Theobroma Oil)
It is obtained from the seed of theobroma cocoa

It is triglycerides containing oleopalmitostearin and oleodistearin.

It is yellowish white, solid brittle fat

It has smell and tastes like chocolate

It has butter like consistency

It melts between $30-35^{\circ}\text{C}$.

Iodine value - 34 to 38

Acid value - less than 4

Advantages

- 1) Solid at even high Room Temperature but melts quickly at Body temperature
- 2) It is very stable
- 3) Chemically inert
- 4) Plasticised by trituration.
- 5) It is innocuous bland & non-reactive
- 6) Miscible with many ingredients.

Disadvantages

- 1) Due to oily nature hinders; absorption of medicinal substances into circulation.
- 2) Melts immediately in body cavity which obscures local effect
- 3) It can rancidity.
- 4) Melts in warm weather.
- 5) Adherence to mould.
- 6) Deterioration during storage due to oxidation.

- 7) Poor water absorbing capacity.
- 8) leakage of melted Base
- 9) Cocoa Butter exhibits polymorphism, each has different melting points.

- α -form - 24°C
- β' -form - 28 to 31°C
- β -form - 34°C to 35°C
- γ -form - 18°C

- β' changes slowly into stable β form.

b) Synthetic Triglycerides:-

- It is prepared from either synthetic (or) natural origin.
- Vegetable oils are modified by esterification and hydrogenation.
- These materials have no tendency of polymorphism.

eg:- Witepsols.

- Advantage:- Resistant to oxidation, No need of lubrication, produces cation of mould, colourless, odourless & elegant supposition.

2) Water-soluble / Water miscible:-

The most important water soluble bases are glycerinated gelatin & polyethylene glycol polymers. used for making pessaries also.

a) Crelato gelatin

U.S.P	B.P	Formula
20%	14	Gelatin
70%	70	Glycerin
10%	16	Water

these don't melt at body temperature, but rather dissolve in secretions of the body cavity & gives sustained action.

quite suitable for a wide variety of medicaments.

often used for local application of antibacterial agents to vagina it ~~absorbs~~ and urethra

Glycerin is hygroscopic it absorbs water from atmosphere and also support for bacterial growth so packaged in air tight container & suitable preservatives should be included.

These are unsuitable for substances that combine with protein.

eg:- Tannic acid & merbromin.

b) Soap Glycerin

• In this soap replaced with gelatin sodium stearate & incorporate 95% glycerin.

• Soap is generally produced in situation by interaction of stearic acid & sodium carbonate.

→ suppositories must be wrapped in waxed paper or tin foil.

• Disadvantage is very hygroscopic.

Glycerin → 90gm

Sodium carbonate → 4.5gm

Stearic acid → 7.5gms

c) Polylethylene glycols polymers:-

Also known as Carbowax or macrogols.

• It exists as liquid when molecular weight ranges from

200-600 + wax like solid when mol. wt above 1000.

- Macrogols are incompatible with phenols.

eg:- PEG 1000, PEG 4000, PEG 6000

Advantages: Chemically stable, these provides prolonged action because they do not melt in the body cavity.

3) Water-dispersible (or) Hydrophilic but dissolves slowly for long time.

- Cocoa Butter can be modified into oil-in-water (o/w) (or) water-in-oil (w/o) emulsion type suppository bases by the incorporation of suitable emulgents (or) surfactants.

- The w/o type base can be formed by the addition of 2% cholesterol (or) 5 to 10% wool fat to cocoa butter.

- While o/w emulsion base formed by incorporation of following emulgents.

→ 5% glyceryl monostearate

→ Lanette wax

→ 2-3% cetyl alcohol

→ 2% decithin.

Preparation of Suppositories

(A) Suppository moulds:-

- Moulds are of various kinds, the most common being brass nickels, Iron (or) other alloys.
- Rectal moulds usually hold 12 to 24 gm of melted Theobroma oil per dozen (12) (weighing each about 1 to 2 gm).
- While vaginal moulds hold two four times these quantities (24 to 96 gm).

Glass tubing with an inner diameter of 3 to 5 mm is suitable for urethral suppositories.

Standardisation of moulds:-

Capacity & displacement value. It is as per tablet triturate mould. Here instead of dactose use of Theobroma oil as a reference.

Lubrication of Mould:-

To prevent sticking of suppository to mould. The best lubricant is one which is immiscible with base.

The lubricant must be different in nature from suppository base.

For oily base: Theobroma oil use follows

Soft soap - 10 gm

Glycerin - 10 gm

Alcohol (90%) - 50 ml

For aqueous base: gelatin glycerin use any oil.

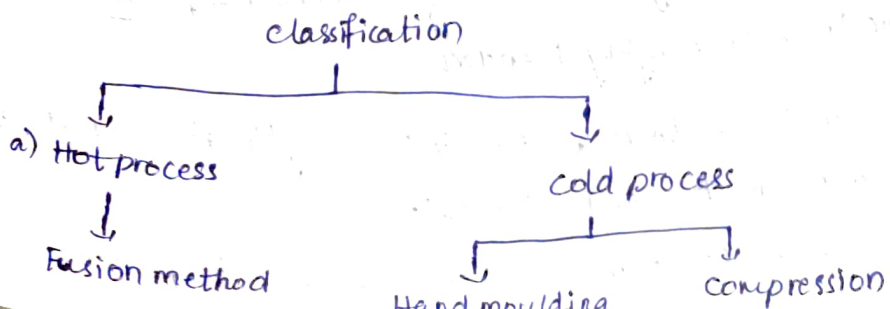
- Liquid paraffin

- Castor oil.

Mould must be lubricated before pouring the mass.

When adjusting powder is used starch is one of the choice.

Methods of Preparation



a) Fusion method

- 1) Standardise the mould (capacity) and calculate the base required as per displacement value of medicament.
 - 2) Take calculated amount of grated theobroma oil & is melted at $30-35^{\circ}\text{C}$ in porcelain dish on a water bath (or) steam bath.
 - 3) The powdered medicinal agents are weighed & are either emulsified (or) suspended in it.
 - 4) The mass is poured into cooled lubricated metal moulds.
 - 5) Keep the mould in refrigerated till the suppositories have hardened.
 - 6) After that trimmed off excess surface.
 - 7) Open the mould & eject the suppositories by slight pressure on the broad ends.
 - 8) Remove lubricant from the surface of suppositories by rolling ~~from~~ them on filter paper.
- This method can be used for large scale by machine.

B) Cold Process

1) Hand Moulding:-

- It is the simplest & oldest method.
- The base is first grated & then kneaded with medicaments by the use of a mortar & pestle till mass is plastic & thoroughly blended.
- The mass is then rolled into a cylindrical rod of a desired length and diameter.
- Starch (or) talacum powder is used to prevent the mass from adhesive.

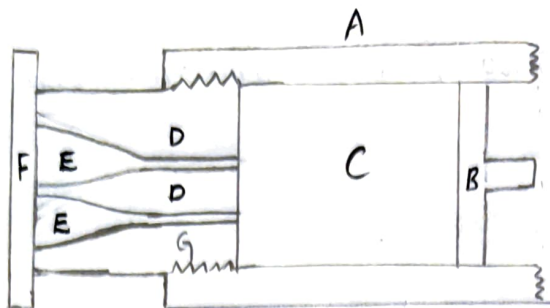
The rod is cut into portions and then ~~end~~ one end of each is pointed.

Advantages:-

- 1. Simple
- 2. No need of determinines of the capacity of the moulds.
- 3. Practical & economical for small numbers.

Compression:-

- A more uniform & pharmaceutically elegant suppository can be made by compressing the cold-grated mass into a desired shape.
- In this method mass is prepared by first mixing the powder medicament grated Theobroma oil. The mixture is then transferred into the cylinder of the machine & pressure is applied to force the material into the moulds.
- The machine is constructed so that a metal ram forces the material from the cylinder into the suppository mould, which is distal to the cylinder.
- When the wheel of machine is turned the mass is forced from the cylinder into the mould & against the movable end plate.
- When suppositories are formed the wheel is reversed to remove the pressure and end plate is lifted.
- A slight turn of wheel ejects the finished suppositories.



- The prepared mass 'C' is placed in a cylinder 'A' & forced through a narrow opening 'D' by means of a piston 'B' into a mould.
- The threads of mass passing into the mould 'G' are compressed until a homogeneous fused massed particle (or) substance is formed in E.
- For the removal of suppositories stop plate 'F' is removed, & suppositories are ejected by further pressure.

Advantages:-

- Useful for Insoluble solids as there is no risk of sedimentation.
- Useful for thermolabile drugs.

Dispensing (Packaging)

- Suppositories should be dispensed in cardboard boxes lined with impervious paper with special compartments so they do not come in contact with each other.
- If plain boxes are used suppositories should be wrapped in waxed paper.
- Glycerogelatin suppositories should be supplied in well closed glass (or) plastic containers.

Labelling

- store in a cool place
- not to be taken orally.

Evaluation:-

The following tests are included:-

A) Appearance:-

Cut longitudinally & examine the internal & external surfaces, they should be uniform.

B) Uniformity of Mix

It can be performed by chemical analysis

C) Uniformity of weight:-

20 suppositories are weighed singly and the average weight determined. No suppository must deviate from the average weight by more than 5%.

D) Disintegration:-

Three suppositories are tested and all must disintegrate within 30 minutes.

E) Fragility (Breaking test):-

It is used to ensure that the suppositories can be packaged & transported without breakage.

The apparatus used for the test consists of a double wall chamber. Water at 37°C is circulated in outer chamber & suppository contained in the dry inner chamber weight is applied on the suppository.

The weight at which the suppository collapses is the breaking point.

F) Melting Range Test (Macro melting Range Test):-

- It is applied to suppositories made with fatty bases.
- For hydrophilic suppositories melting point is replaced by solubility at body temperature

G) Liquification of (or) Softening Time test

H) Dissolution Testing

S) Emulsifying Bases

- These are synthetic bases & a number of proprietary synthetic bases are also available in market

a) Witepsol:-

- Consists of triglycerides of saturated vegetable acid with varying percentage of partial esters.
- A small amount of beeswax is added for use in hot climates. The suppositories prepared with witepsol bases should not be ~~could~~ cooled rapidly to prevent them from becoming brittle & fracture. The mould should be lubricated properly.

b) Massa estarinum:-

It is a mixture of mono, di & triglycerides of saturated fatty acids. This is also known as adeps solidus.

- It has Melting point of range - 33.5 to 35.5°C
Grade B is commonly used in dispensing.

Massuppol:-

It consists of glyceryl esters mainly of lauric acid to which small amount of glyceryl monostearate has been added to improve its water absorbing capacity.

Advantages over Theobroma oil

- 1) Solidify rapidly.
- 2) Non-irritant
- 3) Lubrication of mould is not required.
- 4) Absorb fairly large amount of water or aqueous liquids.
- 5) White, odourless, clean and attractive suppositories are produced.
- 6) They are less liable to get rancid.

Disadvantages

They should not be cooled rapidly in a refrigerator because they become brittle.

Displacement value:-

- The volume of suppository ~~form~~ from a particular mould is uniform but its weight will vary because of the densities of the medicaments usually differ from density of the base with which the mould was calibrated.
- To prepare the suppositories of uniform & accurate weight, allowance must be made for the change in density of the mass due to the added medicaments. For this purpose the displacement value of medicament is taken into consideration.

• Displacement value is defined as "The quantity of the drug which displaces one part of the base."

• It is calculated with reference to cocoa butter

Problems

$$D.V = \frac{d}{c} \quad \begin{matrix} \text{(gm of drug)} \\ \text{(Amr d} \\ \text{base} \\ \text{replace)} \end{matrix}$$

1) Calculate the displacement value of ZnO in Theobroma oil suppositories containing 10% ZnO & prepared in a 1gm mould. The weight of 8 suppositories is 11.74 grams

Sol: weight of suppositories containing = $1 \times 8 = 8\text{gm}$
Theobroma oil

weight of 8 suppositories containing 10% of ZnO
= 11.74 gm

Amount of Theobroma oil present in 8 suppositories

$$= \frac{60}{100} \times 11.74$$
$$= 7.044\text{ gm}$$

Amount of medicament in 8 suppositories

$$= \frac{10}{100} \times 11.74$$
$$= 4.696\text{ gm}$$

Amount of Theobroma oil displaced by 4.696 gm of medicament

$$= 8 - 7.044$$

$$= 0.956\text{ gm}$$

$$\text{Displacement value} = \frac{4.696}{0.956}$$

$$= 4.912$$

Prepare & dispense the Iodoform suppositories

Rx Iodoform - 0.9 gm

Cocoa butter sufficient quantity.

Send 8 suppositories of 2 gm each

Displacement value of Iodoform is 4.0

Always calculate for extra 2 suppositories

wt of cocoa butter for 10 suppositories

$$= 10 \times 2 \text{ gm}$$

$$= 20 \text{ gm.}$$

wt of Iodoform for 1 suppository = 0.9 gm

$$\text{Iodoform for 10 suppositories} = 10 \times 0.9$$
$$= 9 \text{ gm}$$

∴ The quantity of cocoa butter = Total amt of base - $\frac{\text{D.P.}}{\text{D.P.}}$

$$= 20 - \frac{9}{4}$$

$$= \frac{80-9}{4}$$

$$= \frac{71}{4}$$

$$= 17.75 \text{ gm.}$$

12 suppositories (2 gm size) of tannic acid each containing 300 mg of T.A

wt of cocoa butter for 12 sup = 12×2

$$= 4.2 \text{ gms} = 28 \text{ gms}$$

wt of tannic acid for 12 suppositories = 0.3 gms

$$12 \text{ supp} = 4.2 \text{ gms}$$

$$1 \text{ gm} \rightarrow 1000 \text{ mg}$$

$$? \rightarrow 300 \text{ mg}$$

$$\frac{300}{1000}$$

$$0.3 \text{ gms}$$