

# SUPPOSITORIES

# Defination

- “Suppositories are solid dosage forms intended for insertion in to body cavities or orifices (Rectum, Vagina & Urethra) where they melt or dissolved & exert localized or systemic effect.”

# Advantages

It avoid first pass effect.

Melt at body temperature.

It gives localized and systemic action.

It can be given to unconscious patient.

It is easy to use for pediatric and geriatric patients.

Useful to produce local effect.

Useful for rapid and direct effect in rectum.

Useful to promote evacuation of bowel

Convenient for those drug causes GIT irritation , vomiting etc.

# Disadvantages

Irritant drug cant administered

Embarrassment to patients

Need to store at low temp.

Cant easily prepared

Cost-expensive.

fluid content of the rectum is much less than that of the small intestine; this may effect dissolution rate, etc.

Some drug may be degraded by the microbial flora present in the rectum.

# Types of Suppositories

- 1. Rectal suppositories.**
- 2. Vaginal suppositories.**
- 3. Urethral suppositories.**
- 4. Nasal suppositories.**
- 5. Ear cones.**



# Newer Concept of Suppositories

- Tablet Suppositories
- Layered Suppositories
- Coated Suppositories
- Capsule Suppositories

# Tablet suppositories

- This type of tablets prepared by compression like tablets.
- Such type of suppositories used for rectal & vaginal purposes.
- Pessaries tablet suppositories are present in almond like shape.
- Rectal tablets covered with thin layers of materials such as polyethylene glycol for protecting.

# Layered Suppositories

- In that type of suppositories are contains different drugs in different layers.
- So that, incompatibility drugs can be separated from each other.
- Similarly drugs having different melting points can be incorporated to control the absorption rate.



# Coated Suppositories

- In that type of suppositories contains polyethylene glycol, cetyl alcohol etc.
- Those materials controls their disintegration rate, to impart lubricant properties & to provide protection action during storage.

# Capsule Suppositories

- Soft gelatin capsules of different shapes & size are prepared in that type of suppositories.
- In that type of capsule suppositories are filled with liquids, semisolids or solids.
- These type of capsules are increasing in popularity.

# Suppository Bases

- Suppository bases play an important role in maintaining their shape, solidity & also play an important role when inserted into the body cavity.
- There are a large number of bases used but theobroma oil, glycerogelatin base & polyethylene glycol fulfill the above mentioned requirements.

# Ideal Properties of Bases

- It must retain the shape and size.
- It should melt at body temperature.
- It should be non-irritant.
- It should shrink sufficiently to remove from mould.
- It should not interfere in release or absorption of drug.
- It should permit incorporation of drug.
- It should be compatible with variety of drugs.
- It should be physically stable on storage.
- It should not be soften or harden on storage.

# TYPES OF SUPPOSITORY BASES

- **Oily Bases or Oleaginous bases**
- **Water Soluble & Water miscible bases**  
**Or**  
**Hydrophilic bases**
- **Emulsifying/Synthetic bases**

# Oily Bases or Oleaginous bases

- Cocoa butter or Theobroma Oil
- Emulsified cocoa butter.
- Hydrogenated oils.

# Cocoa butter or Theobroma Oil

- Cocoa butter is fat obtained from the roasted seed of *Theobroma cocoa*.
  - At room temperature it is a yellowish, white solid having a faint, agreeable chocolate like odour.
  - Chemically, it is a triglyceride (combination of glycerin and one or different fatty acids) primarily of oleopalmitostearin and oleodistearine.
  - It melts at 30 - 35°C



## Advantages

- Melting just below the body temperature.
- Maintaining its solidity at usual room temperatures.
- Readily liquefy on heating and solidify on cooling.

## Disadvantages

- Rancidity.
- Stick to mould.
- Leakage from body cavity.
- Costly.
- Immiscibility with body fluid.
- Chloral hydrate or lactic acid liquefy it.



# Emulsified cocoa butter or Emulsified Theobroma Oil

- Emulsified theobroma oil may be used as a base when large quantities of aqueous solutions are to be incorporated.
- 5% glyceryl monostearate, 10% lanette wax, 2-3% cetyl alcohol & 4% bees wax is recommended for emulsified theobroma oil.

# Hydrogenated Oils

- Hydrogenated oils are used as a substitute of theobroma oil.
- E.g. Hydrogenated edible oil, coconut oil, hydrogenated pea oil, stearic acids, palm kernel oil etc.

## □ Advantages

- Overheating does not affect the solidifying point.
- They are resistant to oxidation.
- Lubrication of the mould is not required.
- Their emulsifying & water absorbing capacity are good.

## ➤ Disadvantages

- On rapid cooling they become brittle.
- When melted they are more fluid than theobroma oil & result in greater sedimentation of the added substance.

# Water Soluble & Water miscible bases Or Hydrophilic bases

- Glycero-gelatin base.
- Soap-glycerin base.
- Polyethylene glycol.

# Glycero –Gelatin Bases



➤ It is a mixture of glycerin and water which is made stiff by the addition of gelatin.

This base is used to prepare all type of suppositories but mainly used to prepare pessaries.

## **Properties:**

- it is colourless, transparent, translucent in nature.
- It is soft to touch.
- It melts at 30 - 35°C.
- used for vaginal suppositories.



## Advantages

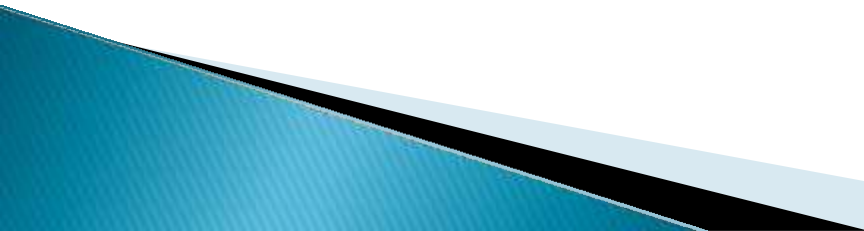
- It melt at body temperature.*
- It mix with bodyfluid.*
- Not rancid.*
- It can be used to prepare suppositories using boric acid, chloral hydrate bromides, iodides, iodoform opium etc.*

## Disadvantages:

- Difficult to prepare and handle.*
- Chance of bacterial growth.*
- Hygroscopic in nature. (become hard on drying and soft in cont with moisture)*
- Laxative in action.*
- Incompatible with tannic acid, ferric chloride etc.*



## ***Soap glycerin suppositories:***

- *In this base the gelatin is replaced with either curd soap or sodium stearate which makes the base sufficiently hard to prepare good quality of suppositories.*
  - *The main disadvantage of this base is that they are very hygroscopic in nature.*
  - *Therefore the suppositories prepared with this base must be protected from atmosphere and wrapped in waxed paper .*
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# Polyethylene Glycols/ Macrogols

- These are commonly known as carbowaxes & Polyglycols.
- These are available in solid, liquid or semi-solid state depending on molecular weight.
- Those polymers having the molecular weight betw. 200 to 1000 are liquids & those having M.W higher than 1000 are wax like solids.
- They are chemically stable & physiologically inert substances & do not allow the bacterial or mold growth to take place.



# Advantages:

- They are chemically stable.
- Inert, Non-irritant.
- Do not allow bacterial growth.
- Physical properties changes according to molecular weight.
- Provide prolonged action.
- Do not stick to mould.
- Suppositories are clean and smooth in appearance.

# Emulsifying / Synthetic bases

- Witepsol
- Massa estarinum
- Massuppol.

# Advantage of Emulsifying bases

- They solidify rapidly.
- They are non-irritant.
- The lubrication of mould is not required.
- Overheating does not affect the physical properties of the base.
- They can absorb fairly large amount of water or aqueous liquids.
- The white, odourless, clean and attractive suppositories are produced.
- They are less liable to get rancid.

# Disadvantage of Emulsifying bases

- They should not be cooled rapidly in a refrigerator because they become brittle.
- They are not very viscous on melting, so the medicaments incorporated with the base settle down rapidly.

# Witepsol

- They consist of triglycerides of saturated vegetable fatty acid with varying percentage of partial esters.
- A small amount of beeswax is added for use in hot climate.
- It should not be cooled rapidly as it become brittle and fracture.
- Lubrication is required.

# Massa Estarinum

- It is a mixture of mono, di and triglycerides of saturated fatty acids.
- It is a white, brittle, almost odourless and tasteless solid.
- It has a m.p. 33.5 to 35.5<sup>0</sup>C.
- They are available in various grades but grade Bis commonly used in dispensing.

# massuppol

- *It consists of glyceryl esters.*
- *Small amount of glyceryl monostearate has been added to improve its water absorbing capacity.*

# Method of preparation

***Hand rolling method***

***Hot process or fusion method***

***Cold compression method***



# Hand Rolling

- ❑ *It is the oldest and simplest method of suppository preparation and may be used when only a few suppositories are to be prepared in a cocoa butter base.*
- ❑ *It has the advantage of avoiding the necessity of heating the cocoa butter.*
- ❑ *A plastic-like mass is prepared by triturating grated cocoa butter and active ingredients in a mortar.*



- ❑ *The mass is formed into a ball in the palm of the hands, then rolled into a uniform cylinder with a large spatula or small flat board on a pill tile.*
- ❑ *The cylinder is then cut into the appropriate number of pieces which are rolled on one end to produce a conical shape.*
- ❑ *Effective hand rolling requires considerable practice and skill.*
- ❑ *Now a days this method is not used.*

# Fusion Method

- *Melting the suppository base*
- *Dispersing or dissolving the drug in the melted base.*
- *The mixture is removed from the heat and poured into a suppository mold.*
- *Allowing the melt to congeal*
- *Removing the formed suppositories from the mold.*
- *The fusion method can be used with all types of suppositories and must be used with most of them.*
- *Small scale molds are capable of producing 6 or 12 suppositories in a single operation.*
- *Industrial molds produce hundreds of suppositories from a single molding.*

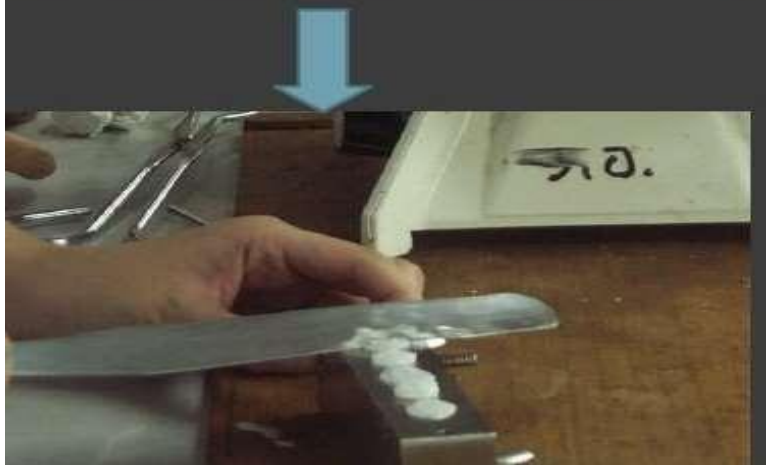
# ***Method of preparation***

- *Thoroughly clean and lubricate the mould with a suitable lubricant.*
- *Keep the mould on ice in the inverted position to cool and drain an excess of the lubricant.*
- *The lubrication of the mould is not required in case the emulsifying base or synthetic base is used.*
- *Heat the china dish over a water bath.*
- *To this add the required quantity of cocoa butter or any other base after taking into account the displacement value of the medicament.*
- *Allowance is made for unavoidable wastage during preparation by calculating for two extra suppositories.*
- *Remove the china dish from the water bath, when two third of the base melts and stir thoroughly until whole of the mass melts.this process prevents overheating of base.*

- *Place the weighed quantity of powdered medicament to be incorporated with the suppository base on an ointment tile.*
- *Pour about half of the melted base over it and mix it thoroughly with a spatula.*
- *Transfer the mixed mass to the china dish and mix thoroughly so that a homogenous mass is formed.*
- *Warm the china dish over a water bath for a few seconds with constant stirring, so that mass becomes pourable.*
- *Pour the melted mass into the cavities of the suppository mould, kept over the ice.*
- *Fill each cavity to overflowing, in order to prevent the formation of hollows in the tops of the finished suppositories because cocoa butter contracts on cooling and hollows are formed at the top of the suppositories.*
- *The precautions must be taken while pouring the mass into the cavities. It must be continuously stirred to ensure even distribution of the medicament in all the suppositories.*

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- *Remove the excess mass with the help of sharp knife or blade when the mass is properly set.*
- *Keep the mould over ice or in cool place for 10 -15 min.*
- *Open the mould and remove the suppositories.*
- *Wipe off the suppository lightly with a clean cloth or filter paper*
- *Wrap the individual suppository in a wax paper.*

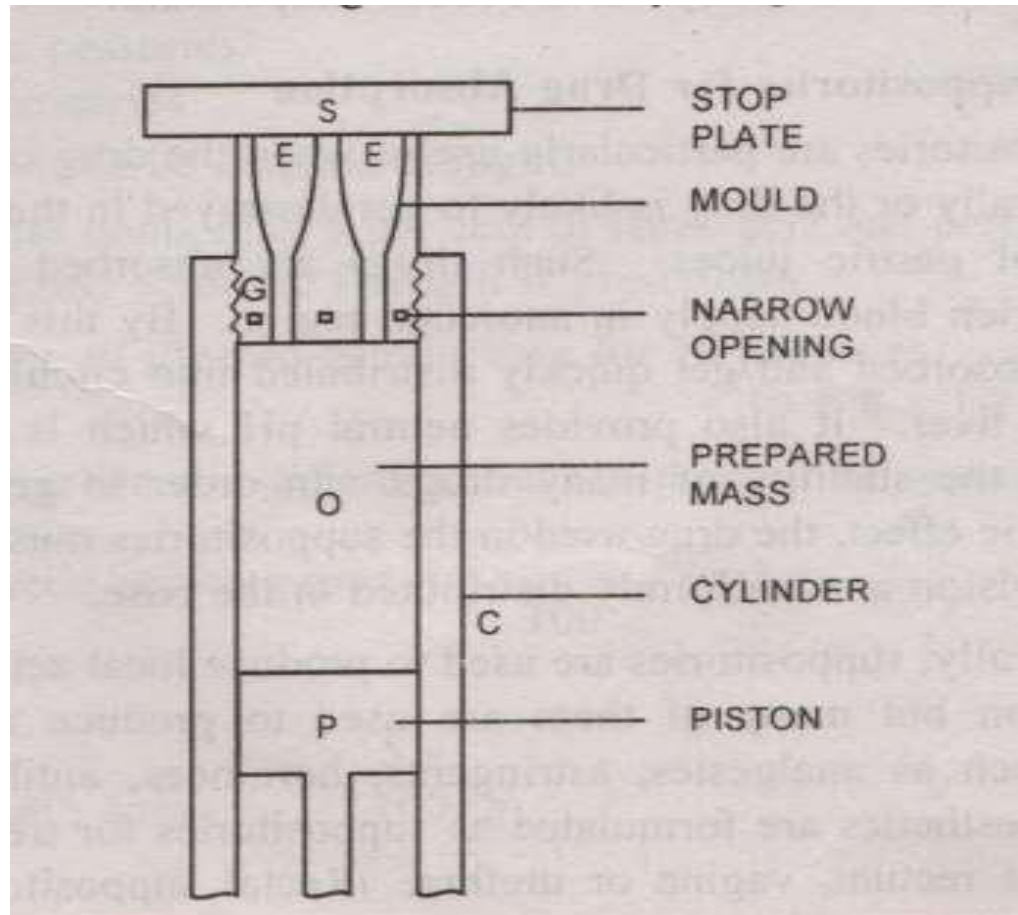
# Fusion Method



# Cold Compression moulding

- *The method is useful for thermolabile and insoluble drugs, because heating and stirring of the base is not required.*
- *Cocoa butter is grated.*
- *The ingredients are mixed with an equal quantity of grated cocoa butter.*
- *Add the remaining amount of grated cocoa butter.*
- *While calculating the amount of cocoa butter to be incorporated with the medicaments, allowances are made for unavoidable wastage during the preparation.*





- ❑ *The friction of the process causing the base to soften into a past-like consistency.*
- ❑ *On a small scale, a mortar and pestle may be used (preheated mortar facilitate softening of the base).*
- ❑ *On large scale, mechanically operated kneading mixers and a warmed mixing vessel may be applied.*
- ❑ *In the compression machine, the suppository mass is placed into a cylinder which is then closed.*
- ❑ *Pressure is applied from one end to release the mass from the other end into the suppository mold or die.*
- ❑ *When the die is filled with the mass, a movable end plate at the back of the die is removed and when additional pressure is applied to the mass in the cylinder, the formed suppositories are ejected.*
- ❑ *The end plate is returned, and the process is repeated until all of the suppository mass has been used.*

# Suppository mould

- *The suppository mould of various types and sizes are available .*
- *These moulds are generally made up of stainless steel, nickel copper alloy, brass, aluminium and plastic.*
- *The suppository mould can be opened longitudinally by removing the screw in the centre of the plates.*
- *The mould is opened at the time of cleaning, lubrication and removal of suppositories.*
- *The mould is cleaned by removing the plates and immersed in a hot water containing detergent.*
- *After washing with water the mould is dried thoroughly.*

### *Lubrication of mould:*

➤ *The lubrication of the mould is essential in case of cocoa butter or glycerogelatin base is used.*

*Cocoa butter –soft soap, glycerin, alcohol 90%*

*Glycerogelatin - liquid paraffin or arachis oil*

➤ *The lubricant should be applied with the help of brush or swab made of gauze.*

➤ *Excessive lubrication of the mould should be avoided.*

➤ *The excess of lubricant can be drained by closing the mould and put it in the inverted position on a white tile.*

# Calibration of the mould

- *Generally a standard mould of 1 gm capacity is used.*
- *The calibration of the mould is necessary because the size of the suppository from a particular mould remains the same, but the the weight varies.*
- *This is due to the reason, that the density of different bases and medicaments are different.*
- *So that the mould should be calibrated for individual base and medicament.*
- *This is done by preparing a set of suppositories using the base, weighing the suppositories and then find the avg,. Mean which will indicate the true capacity of mould.*

# Displacement value

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

# Determination of displacement value

- Prepare and weigh 6 suppositories containing theobroma oil = a gm
- Prepare and weigh 6 suppositories containing say 40% medicament = b gm
- Calculate the amount of theobroma oil present in medicated suppositories =  $60/100(b) = c$  gm
- Calculate the amount of medicament present in the medicated suppositories =  $40/100(b) = d$  gm
- Calculate the amount of theobroma oil displaced by d gm of medicament =  $(a-c)$  gm
- Displacement value of the medicament =  $d/a-c$

# Determination of displacement value

e.g. Determine the displacement value of a medicament in theobroma oil suppositories containing 40% medicament, prepared in 1 gm mould. The weight of 10 suppositories is 14.66 gm.

**Solution:**

1. Wt.of 10 suppo. Cont. theobroma oil alone prepared in 1 gm capacity mould =  $1 \times 10 = 10$  gm
2. Wt.of 10 suppo. Cont. 40% of medicament = 14.66 gm
3. Amt. of theobroma oil present =  $60/100 \times 14.66 = 8.79$  gm
4. Amt. of medicament present =  $40/100 \times 14.66 = 5.86$  gm
5. Amt. of theobroma oil displaced by 5.86 gm of medicament =  $10 - 8.79 = 1.20$  gm

So,

**Displacement value of medicament =  $5.86/1.20 = 5$  (Approx.)**



# Packaging and storage

- ❑ Suppositories are usually packed in tin or aluminum, paper or plastic.
- ❑ Poorly packed suppositories may give rise to staining, breakage or deformation by melting.
- ❑ Both cocoa butter and glycerinated gelatin suppositories stored preferably in a refrigerator.
- ❑ Polyethylene glycol suppositories stored at usual room temperature without the requirement of refrigeration.

# ***Evaluation of suppositories***

Suppositories are evaluated for following parameters.

## ***Appearance:***

- All the suppositories should be uniform in size and shape and should have elegant appearance.
- Suppositories are examined by visual inspection for cracks and pits on the surface.
- when cut longitudinally , the internal and external surface should be same.

## ***Physical strength:***

- The strength of suppositories is considered to assess their ability during normal handling.
- The apparatus used for this called as breaking test apparatus, which contains a double walled chamber in which water is pumped to maintain 37 oc temp. In between two walls of the chamber.
- The inner chamber contains a disc for holding the suppositories, to which a rod is attached.
- The other end of the rod contains a disc for holding the weights.

- When weights are added (upto 200gms) at one minute time interval until the suppository crumbles.
- All the weights used are added which gives the tensile strength.
- Tensile strength – max. Load that a material can support without fracture.
- Higher tensile strength indicate less will be tendency to fracture.

### ***Melting range:***

- it is also called as macro melting range test
- It is used to measure the time it takes to melt in body temp.
- It is the time taken by the entire suppository to melt in a constant temperature (37 oc) water bath.
- The test is conducted using the tablet disintegration test apparatus in which suppository is immersed in a constant water bath , finally the melting range is recorded.

### ***Solidification point:***

- It is the time taken to become solidify.

### ***Uniformity of weight:***

- Weigh twenty suppositories individually and determine their avg. Weight.
- Limit: not more than two individual weights should deviate from the avg. Weight and more than 5% and none deviates by more than 10%.

### ***Content uniformity:***

- This is carried out by performing assays for different suppositories.
- All suppositories should contain the same labelled quantity.
- Method:
  - Take 10 suppositories and determine the active ingredients of each of the ten suppositories by using a suitable analytical method.

Limit : if not more than one of the individual values thus obtained is outside the limit i.e. % of the average value and none of them outside the limit i.e. 25% of the average value.

### ***Softening time:***

➤ This test measures the time required for suppository to liquify under conditions that stimulate in vivo conditions , which also indicates the hardness of the base.

## **Dissolution test:**

- It is used for in vitro assessment of product efficacy.
- Used to determine the rate of drug release from the suppository.
- The rate of drug release from suppositories can be determined by using the same apparatus used for dissolution rate of compressed tablets i.e. apparatus 1,2, or 3.
- The test can be carried out by simple placement of the suppository in a beaker containing the dissolution medium.

# Thank You

[www.DuloMix.com](http://www.DuloMix.com)

