# SUPPOSITORY

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## SUPPOSITORY

- It is solid dosage form meant to be inserted into Body cavity like rectum , urethra, vagina, where they melt or soften to release the drugs and produce their local or systemic effect.
- It is comes under semi solid preparation because it is prepared by melting all ingredients (bases and other additives along with active ingredient).
- All types of suppositories are melt at normal body temperature after introducing in body cavity and produce their effect.

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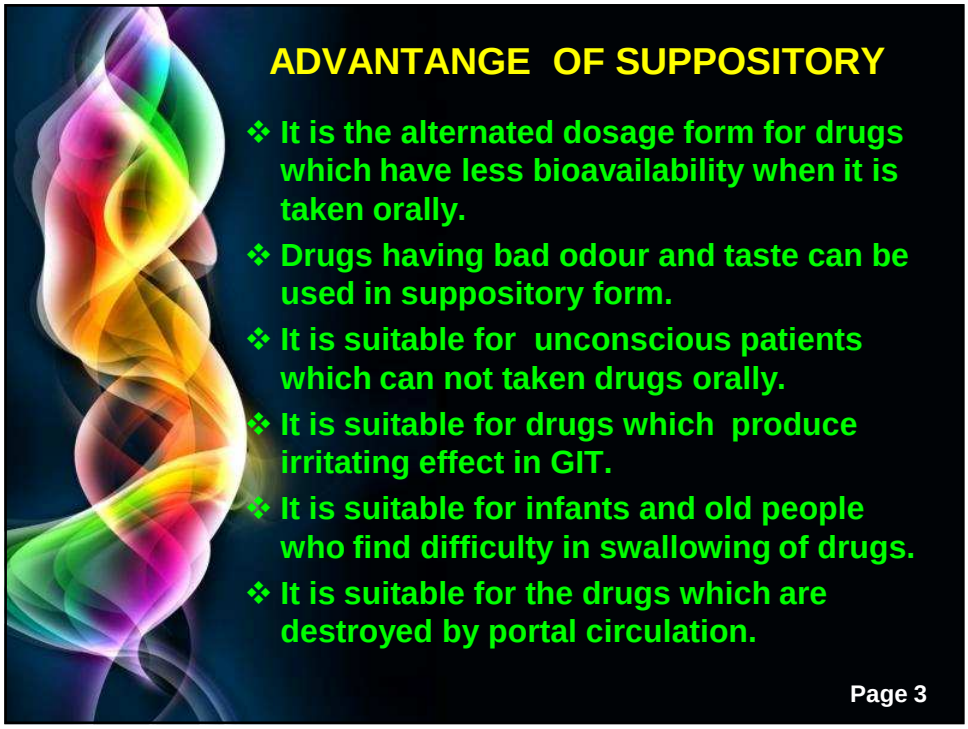
ADVANTANGE OF SUPPOSITORY
❖ It is the alternated dosage form for drugs which have less bioavailability when it is taken orally.
❖ Drugs having bad odour and taste can be used in suppository form.
❖ It is suitable for unconscious patients which can not taken drugs orally.
❖ It is suitable for drugs which produce irritating effect in GIT.
❖ It is suitable for infants and old people who find difficulty in swallowing of drugs.
❖ It is suitable for the drugs which are destroyed by portal circulation.
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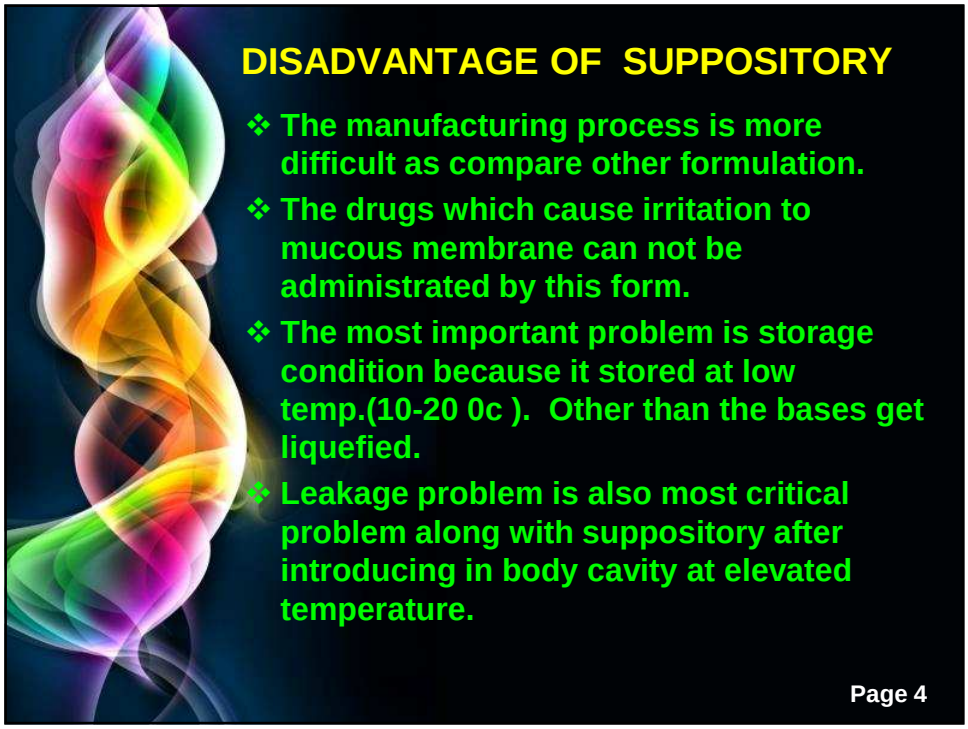
DISADVANTAGE OF SUPPOSITORY
❖ The manufacturing process is more difficult as compare other formulation.
❖ The drugs which cause irritation to mucous membrane can not be administrated by this form.
❖ The most important problem is storage condition because it stored at low temp.(10-20 0c ). Other than the bases get liquefied.
❖ Leakage problem is also most critical problem along with suppository after introducing in body cavity at elevated temperature.
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## TYPES OF SUPPOSITORY

### (A) RECTAL SUPPOSITORY-

- It is inserted in the rectal .
- The weight of suppository used in children is about 1g and in adult about 2g.
- The shape of suppository used in rectal is torpedo shape. The length is about 3 cm.

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### (B) URETHRAL SUPPOSITORY

- The weight of this type suppository is about 2g and 60-75 mm long in Females.
- Those intended for males weigh 4 gm each and are 100-150 mm long.
- It is available in pencil shape.

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## (C) VAGINAL SUPPOSITORY

- It is in oviform shape.
- It is about 3-5g in weight.
- It is contains the drugs which are used in treatment of the infections of female genitourinary tract and meant for contraception.
- It is contains the combination of polyethylene glycol of different molecular weights as suppository bases.

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## (D) NASAL SUPPOSITORY

- These suppository are meant for introduction into nasal cavity.
- It is about 1g in weight.
- The glycero- gelatin is used as suppository bases.

## (E) EAR CONE

- It is also known as AURINARIES.
- These are meant for introduction into the ear.
- It is cylindrical in shape.
- It is about 1g in weight.

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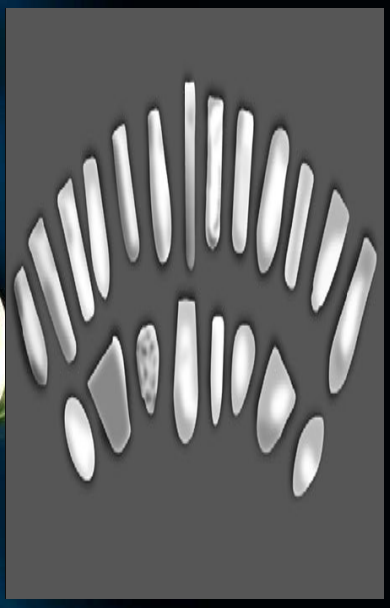
## VARIOUS SHAPES OF SUPPOSITORY



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## FORMULATION OF SUPPOSITORIES

### (A) SUPPOSITORIES BASES-

**IDEAL PROPERTIES OF SUPPOSITRIES BASES-**

The following properties should be required for bases---

- Bases should be exist in solid form at room temperature.
- It should not irritate and produced inflamed sensation in body cavity.
- It should be stable during storage condition , No change in colour, shape , odour.
- It should retain hardness and shape during manufacturing and handling.

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## IDEAL PROPERTIES OF SUPPOSITRY BASES

- It should not reacts with drugs and additives
- It should have good emulsifying and wetting property.
- It should have acid value less than 0.2 or zero.
- It should have iodine value less than 7.
- It should have sponification no. range between200-245.

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## (1) HYDROPHILIC BASES

### (A) WATER DISPERSIBLE BASES-

- These are the mixture of non ionic surfactants which are chemically related to polyethylene glycol.
- These are used alone or in combination with other type of bases.
- Cellulose derivatives like methylcellulose, sod.carboxymethyl cellulose are also comes under this class.

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## Advantages

- They are suitable for both water soluble and oil soluble drugs.
- They do not support the growth of microbes in the preparation.
- They can be stored at elevated temperature.

**Disadvantages-**

- This types of bases are interact with few drugs and alter the bioavailability of these drugs.

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## EXAMPLES

- Polyoxyethylene sorbitan fatty acid ester(TWEENS)
- Polyoxyethelene stearates(MYRIS)
- Sorbitan fatty acid esters(SPANS)
- Combination of Tween 61(60%) and Tween 60(40%)
- Combination of Tween 61 (85%) and glyceryl monostearate (15%)

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## (B) WATER SOLUBLE BASES

**(1) GLYCERO-GELATIN-**

- This occurs as a gels
- It is a mixture of gelatin, glycerol, and water.
- According to BP the composition of the bases –

  GELATIN- 14% w/w

  GLYCEROL– 70% w/w

  WATER– QS

- For gets a stiff mass , the quantity of gelatin should be increased to 32.5% and reduced the glycerol to 40%.

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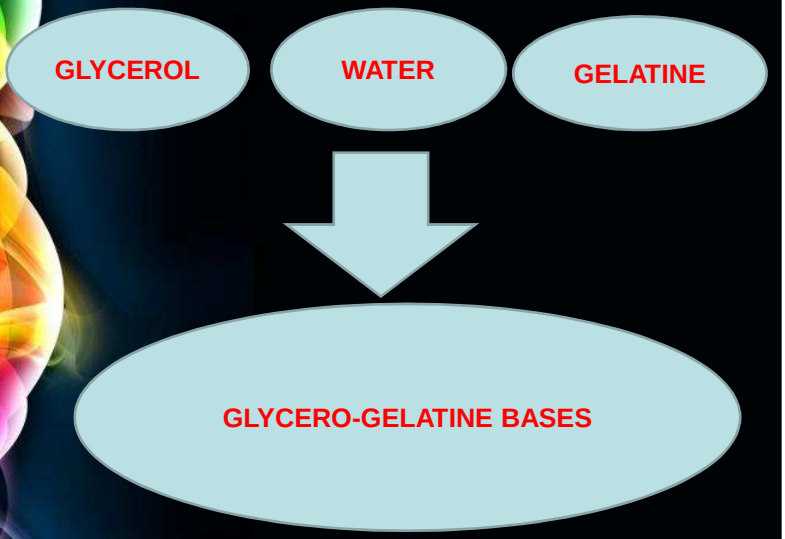
## PREPARATION OF GLYCERO-GELATINE BASES

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## ADVANTAGES

- Suppository prepared by glycero-gelatin bases are strong and translucent unlike cocoa butter suppositories.
- This base is disperse slowly in the body cavity fluids and provides prolonged release and action of drugs.

## DISADVANTAGES-

- It absorbs moisture and promotes microbial growth , so this reason preservatives are used .

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## DISADVANTAGES

- The bases are show incompatibility with protiens prescipitants due to the gelatin
- It causes dehydration and irritation of rectal mucosa
- It exerts undesirable laxative action.
- It requires special storage condition at about 10-15 0c.
- Handling and manufacturing of these type of suppository are difficult.

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## (2) POLY ETHYLENE GLYCOL(POLYGLYCOL)

- It is also called as PASTONALS (GERMANY).
- CARBOWAXES(U.S)
- They are long chain polymers of ethylene oxide.
- They occur in liquid and solids.
- Liquids have mol.weight about 200-600.
- Solid have mol.weight about more than 1000.
- They are also called as macrogols.
- They are the mixture of two or more grades of macrogols used as suppository bases.

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## EXAMPLES

- PEG 4000- 33 parts
  PEG 6000- 47 parts
  PURIFIED WATER- 20 parts

- FOR HARD SUPPOSITORY
  PEG 1000- 75 parts
  PEG 4000- 25 parts

- FOR SOFT SUPPOSITORY
  PEG 1000- 96 parts
  PEG 4000- 4 parts

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## ADVANTAGES

- This base is thermostable.
- It does not get degraded or hydrolysed.
- It does not support microbial growth.
- It dose not move out from body cavity after introducing.
- It has good water absorbing capacity.
- It is chemically stable.

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## DISADVANTAGES

- It is susceptible to rancidification,so it should be stored in dry place away from light.
- It melt easily in warm weather,so it should stored in cool place in warm season.
- Large quantities of water can not be incorporated into the bases.So emulsifier such as tween 61 (6-10%) are useful to increase the absorption of water.
- The physical characteristics of the bases are change from batch to batch.
- Some times leakage may be occur after introducing in body cavity.

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## (2) LIPOPHILIC BASES

### (a) COCOA BUTTER

- It is natural triglyceride.
- Among all fatty acid about 40% are unsaturated fatty acid .
- It can exist in more than one crystalline form or exhibits polymorphism.
- At room temperature ,it is yellowish-white with a paints,chocolate like odour.
- It consists of a mixture of ester of oleic acid,palmatic acid,stearic acid and other fatty acid with glycerol.

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## ADVANTAGES

- It is liquified readily on warming and sets rapidly on cooling.
- It has emollient effect which is useful to relieve inflammation.
- It shows good release of water soluble drugs.
- It does not cause irritation in mucous membrane.

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## DISADVANTAGES

- It is susceptible to rancidification ,so it should be stored in dry place away from light.
- It gives soft suppository when formulated along with chloral hydrate , phenol, volatile oil, which have lower melting point.
- The physical property of the base is vary from batch to batch.
- It required extra lubricant during poring in holder.
- Some times leakage may be occur.

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## (B) ANTI OXIDANTS

- It is protect the drugs and bases from getting degraded due to oxidation.
- These are commonly used in all types of suppositories.

EXAMPLES-

- Ethyl or propyl gallate
- Ascorbic acid
- Butylated hydroxy anisole (BHA)
- Butylated hydroxy toluene (BHT)
- Hydroquinone
- Tocopherol

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## (C) EMULSIFYING AGENTS

- These are increase the water absorbing capacity of fatty bases.
- EXAMPLES
- Poly sorbates (TWEEN 61)
- Wool alcohol
- Wool fats

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## (D) HARDENING AGENTS

- These are involved in those formulation where the melting point of the bases is decrease by the drugs.
- These are the agents which are used to bring the melting point to normal.
- EXAMPLES
- Beeswax
- Macrogols at high molecular weight.

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## (E) PRESERVATIVES

- These are the agents which are used in prevent the growth of microbial in suppository which contains water soluble bases.
- EXAMPLES
- Chorocresol
- Methyl paraben
- Propyl paraben

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## (F) THICKENING AGENTS

- These are the agents which are used to increases the viscosity of molten bases and prevent sedimentation of suspended in solid bases.
- EXAMPLES
- Aluminium monostearate
- Colloidal silica
- Magnisium stearate
- Steary alcohol

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## (G) PLASTICIZERS

- These are the agent which are used to improved flexibility of suppositories.
- It is also used to make the less brittles to suppositories.

- EXAMPLES
- Castor oils
- Glycerine
- Glycol
- Tween 80
- Tween 85

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## METHODS OF PREPARATION OF SUPPOSITORIES

MOLDS USED IN PREPARATION OF SUPPOSITORIES-

- Molds used in preparation of suppositories are the metals devised with different shape.
- It is consists of two or more parts which are joined with a screw.
- In side the molds the cavities are made up of aluminium , brass, stainless steel , plastics.
- Molds have different capacities like 1,2,4,8gm.

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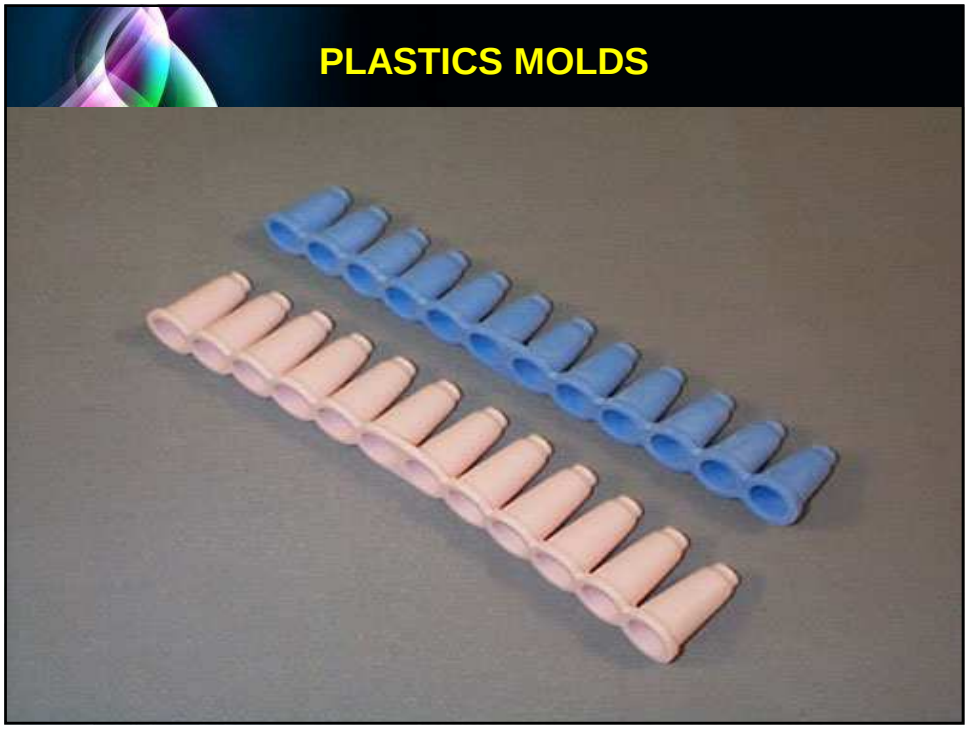
PLASTICS MOLDS

## CALIBRATION OF THE MOLDS

- The first step is to prepare molded suppositories from base material alone.
- The suppository's combined and average weight is recorded.
- To determine the volume of the mold, the suppositories are melted in a calibrated beaker, and the volume of the melt is determined.

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## LUBRICANTS USED IN MOLDS

- Cocoa butter and glycero-gelatine bases are required lubrication of molds.
- This is prevent sticking of bases to the wall of molds cavity.
- It is also useful in easy removal of suppositories from the molds.
- The lubricants are form a film between the wall of mold cavity and base of suppositories so it prevent adhering of bases to the molds.
- The nature of lubricants should be different from nature of bases.

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## EXAMPLES

(1) FOR COCOA BUTTER BASES

ALCOHOL(90%)- 50ml
GLYCEROL - 10ml
SOFT SOAP - 10 gm

(2) LIQUID PARAFFIN

(3) ARACHIS OILS

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## MANUFACTURING OF SUPPOSITORIES

- Hand molding
- Automatics Machine Molding
- Compression Molding
- Heat Molding

1) HAND MOLDING-

- Hand molding is useful when we are preparing a small number of suppositories.
- It is suitable for thermo labile drugs.
- It is more economical methods.
- It is more time consuming and not uniformity process.

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## STEPS INVOLVED IN HAND MOLDING

- The drugs and other additives are made into a fine powder .
- It is incorporated into the suppository base by kneading with it or by trituration in a mortar.
- Then these masses are rolled into the shape of a cylindrical rod on the rolling tile in presence of lubricants to prevent the adherence of masses.
- Then cut the rods and made one end to pointed.

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DRUG+ADDITIVES → FINE POWDER

↓

MIXED IN BASES

↓

APPLY LUBRICANTS ON ROLLING TILE

↓

ABOVE MASSES ARE ROOLED IN CYLINDRICAL SHAPE

↓

CUT THE RODS

↓

PACKED

↓

STORED

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## (2) AUTOMATIC MACHINE MOLDING

- All the operations in pour molding are done by automatic machines.
- Using this machine, up to about 10,000 suppositories per hour can be produced.
- By this the rate of production of suppositories is more higher than hand molding.
- In this ,there are no chance of air entrapment and contamination of suppositories.
- In this ,if any mass deposited in mold is not removed during cleaning, so produce overweight suppositories with mold marks.

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There are two types of machines used they are following---

(a) Rotary Machine-

- The rate of production of suppositories are about 3500-6000/hr.
- This machine consists of a turn table in which metal molds are fitted.
- This table rotates sequentially, the mold gets filled with drug , additives, bases and cooled and ejects the suppositories.
- Before mass filled in mold ,the lubricant are apply in mold wall.
- The excess mass is removed by the scraping unit.
- The cooling system results the solidification of suppositories.

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- After the cooling the mold is moves towards ejection station , it consists of a stainless steel rod which push out the suppositories from molds.
- Then completed the ejection process , the empty molds are again moves towards the filling unit for further processes.
- STEPS INVOLVED IN PROCESS AS FOLLOWING

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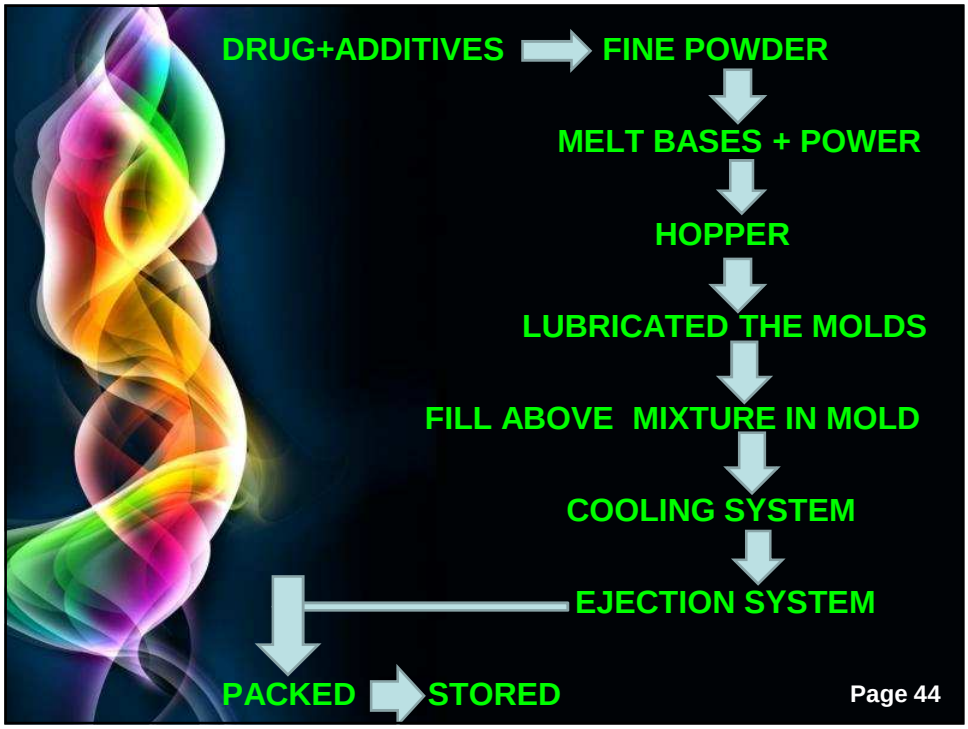


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## (b) LINEAR MACHINE

- It is similar to rotary machine.
- Except the rate of production is more higher than rotary machine about 10000/hr.
- All steps involved is similar to rotary machine.
- There is no chance of air entrapment and contamination of suppositories as similar to rotary machine.
- The rate of production is higher than rotary machine.

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## (3) COMPRESSION MOLDING

- CONSTRUCTION- The compression machine consists of a cylinder, piston , molds, and a metallic stop plate at the bottom.
- WORKING- When placed the mass in cylinder and apply the pressure .
- Then mass fulfill in mold move and s remove the suppositories and keep them in cool placed.
- After cooling release them from compression machine and packed .

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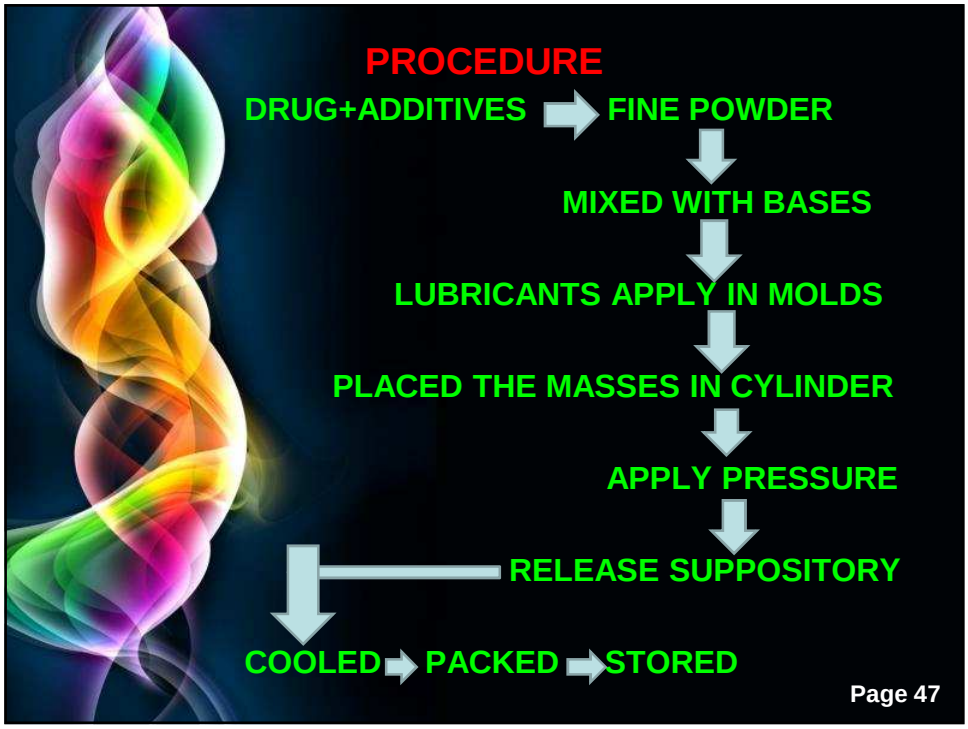
PROCEDURE
DRUG+ADDITIVES
FINE POWDER
MIXED WITH BASES
LUBRICANTS APPLY IN MOLDS
PLACED THE MASSES IN CYLINDER
APPLY PRESSURE
RELEASE SUPPOSITORY
COOLED
PACKED
STORED
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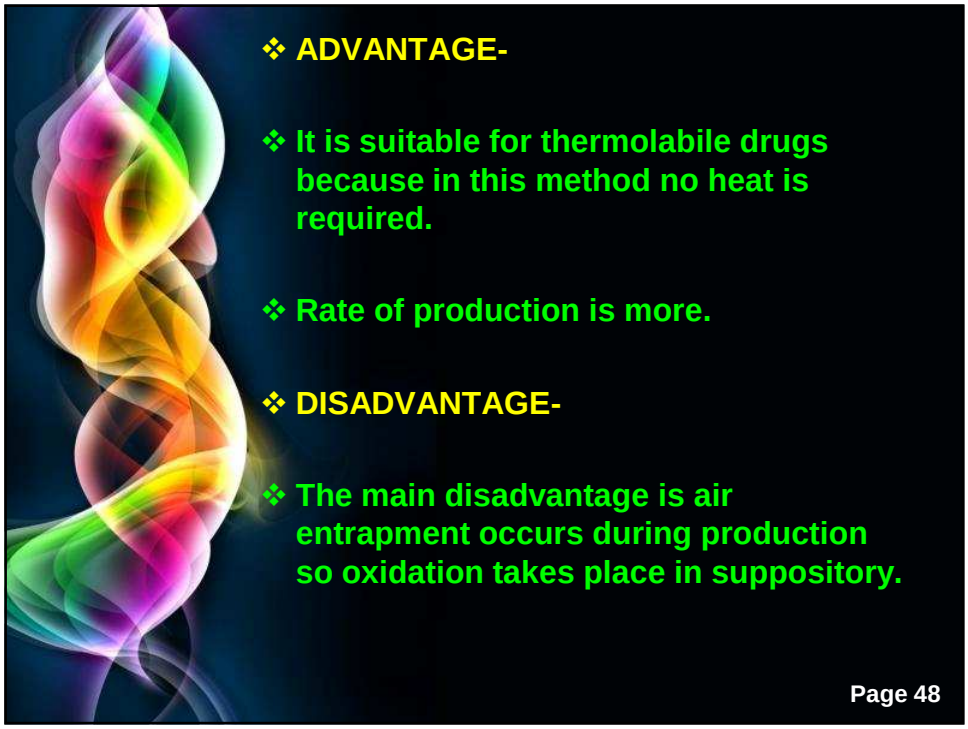
❖ ADVANTAGE-
❖ It is suitable for thermolabile drugs because in this method no heat is required.
❖ Rate of production is more.
❖ DISADVANTAGE-
❖ The main disadvantage is air entrapment occurs during production so oxidation takes place in suppository.
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## (4) HEAT MOLDING

- In this process the bases are melted and the drugs , additives are mixed in bases.
- The following methods are involved in this process-

(a) Melting the bases
(b) Incorporation of the drugs and other additives
(c) Filling of mold
(d) Cooling and collection of suppositories

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- Incorporation of drug and additives-
- the drugs and additives are in solid form , they are converted in fine powder and mixed properly on a warm tile.
- Triturate the ingredient on warm tile with the sufficient water.
- These above liquid are mixed in melted bases in half amount after mixing , then added remaining liquid in bases.

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- **FILLING OF MOLDS-**
- First the lubricants are apply in molds.
- Then the above masses are introducing in molds.
- During introducing the masses in molds the stirring should be done to prevent the sedimentation of insoluble solids , if they present.
- Overfilling is required to prevent the depression in suppositories.

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- **COOLING AND COLLECTION OF SUPPOSITORIES**
- After the2-3 min . the mass just sets. Then remove the excess mass with warm spatula.
- Cool the suppositories for 10-15 min. in refrigerators.
- Then open the mold and collect the suppositories and packed.

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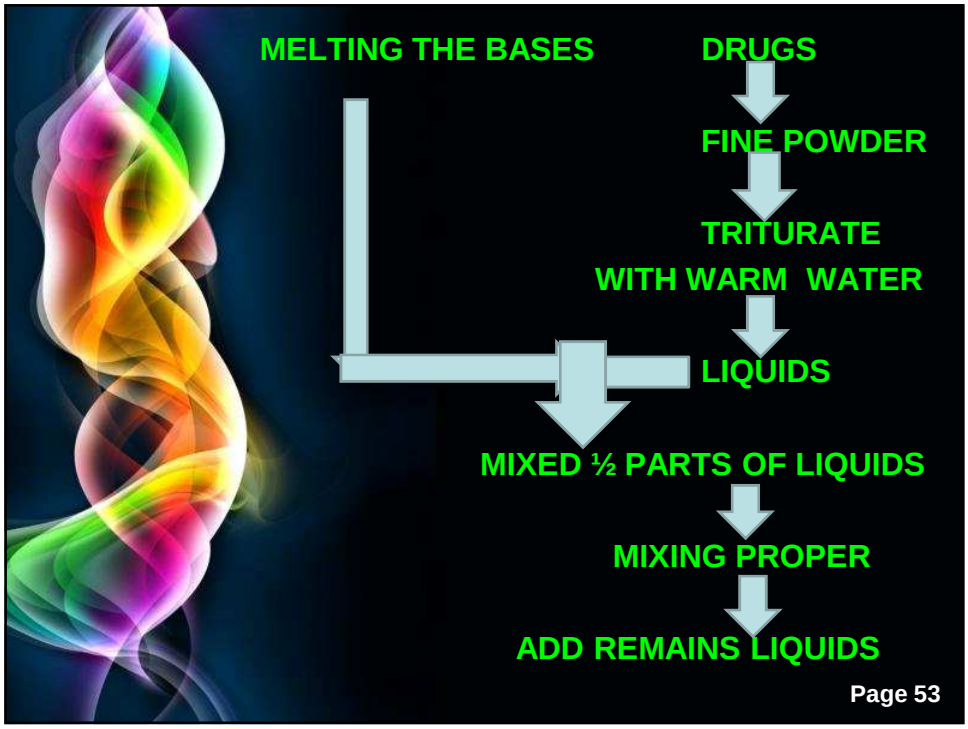
MELTING THE BASES
DRUGS
FINE POWDER
TRITURATE
WITH WARM WATER
LIQUIDS
MIXED ½ PARTS OF LIQUIDS
MIXING PROPER
ADD REMAINS LIQUIDS
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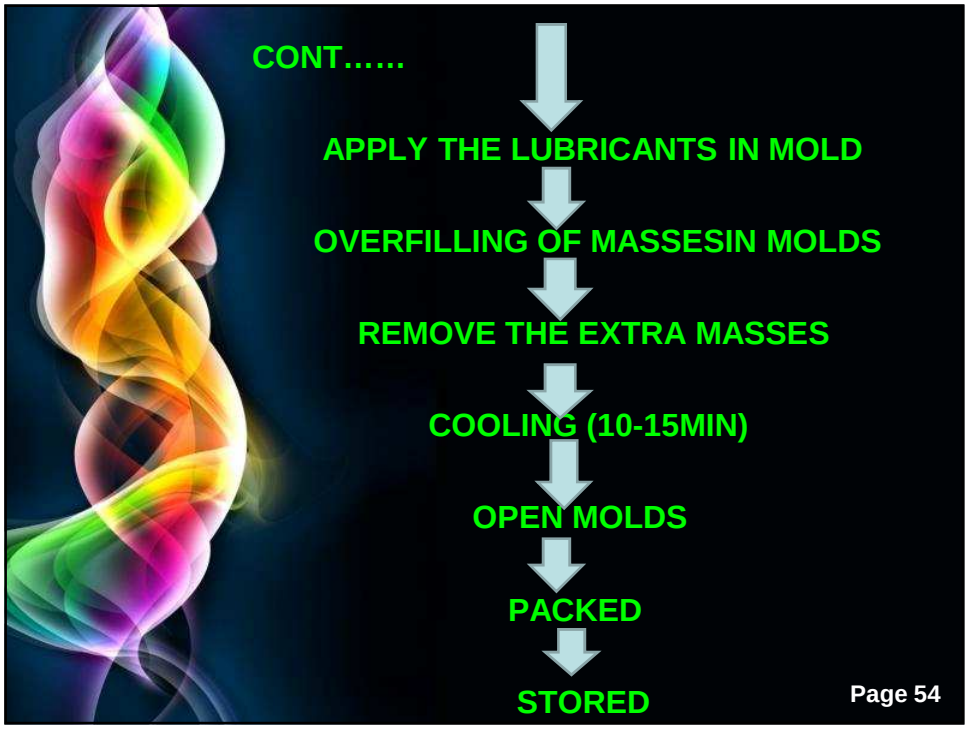
CONT……
APPLY THE LUBRICANTS IN MOLD
OVERFILLING OF MASSESIN MOLDS
REMOVE THE EXTRA MASSES
COOLING (10-15MIN)
OPEN MOLDS
PACKED
STORED
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## PACKING OF SUPPOSITORIES

**(1) DISPOSABLE MOLDS-**

These are meant for packing the suppositories.

These are made of plastics or aluminium foil.

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## (2) MODERN PACKING MACHINE

It is consist of roll of packing material which cut in the required size and rolled around each suppositories.

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- **STORAGE CONDITION**

❖ It is stored at 10-15 0c

❖ Used air tight container

❖ The suppositories with cocoa butter stored at < 30 0c.

❖ The suppositories with glycero-gelatin stored at < 35 0c.

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## EVALUATION OF SUPPOSITORIES

❖ Test of appearance(size , shape)

❖ Test of physical strength

❖ Test of dissolution rate

❖ Test of melting range

❖ Test of softening time

❖ Test of uniformity of drug content

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## STABILITY PROBLEMS OF SUPPOSITORIES

- BLOOMING-
- During storage , cocoa butter suppositories sometimes show deposition of white powder on the surface.
- This result in suppositories of disagreeable appearance.
- HARDENING-
- During storage , the suppositories made of fatty bases become hard.
- I is occurs due to crystallization of bases.
- This also effect the melting and rate of absorption of drugs.

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# THANKS

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