Suppositories

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Suppositories:

- "Suppositories are **solid dosage forms** intended for **insertion** into body orifices where they **melt, soften, or dissolve and exert localized or systemic effects**."
- A suppositories is a drug delivery system that is inserted into the rectum (rectal suppository), vagina (vaginal suppository) or urethra (urethral suppository), where it dissolves or melts.
- The alternative term for delivery of medicine via such routes is **pharmaceutical pessary**.

- **Dosage form characteristics:**

a. **Rectal suppositories** for adults weigh 2 gm and are **torpedo shape**.

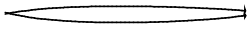
- Children's suppositories weigh about 1 gm.

b. **Vaginal suppositories or Pessaries** weigh about 3-5gm and are molded in **globular or oviform shape or compressed on a tablet press into conical shapes.**

Pear Cone Rod

c. **Urethral suppositories** called bougies are **pencil shape**. Those intended for males weigh 4 gm each and are 100-150 mm long.

- Those for females are 2 gm each and 60-75 mm in length.



d. **Nasal suppositories:** called nasal bougies or buginaria meant for introduction in to nasal cavity.

- They are prepared with glycerogelatin base.
- They weigh about 1 gm and length 9-10 cm.

e. **Ear cones:**

- They meant for introduction into ear.
- Rarely used
- Theobroma oil is used as base.
- Prepared in urethral bougies mould and cut according to size.

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Advantages:

1. Can exert **local effect** on rectal mucosa.
2. Used to **promote evacuation of bowel**.
3. Avoid any **gastrointestinal irritation**.
4. Can be used in **unconscious patients** (e.g. during fitting).
5. Can be used for systemic absorption of drugs and **avoid first-pass metabolism.**
6. Babies or old people **who cannot swallow oral** medication.
7. **Post operative people** who cannot be administered oral medication.
8. People suffering from **severe nausea or vomiting.**

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Disadvantages:

1. The problem of **patient acceptability.**
2. Suppositories are **not suitable** for patients suffering from **diarrhea**.
3. In some cases the **total amount** of the drug must be given will be either **too irritating or in greater amount** than reasonably can be placed into suppository.
4. **Incomplete absorption** may be obtained because suppository usually promotes evacuation of the bowel.

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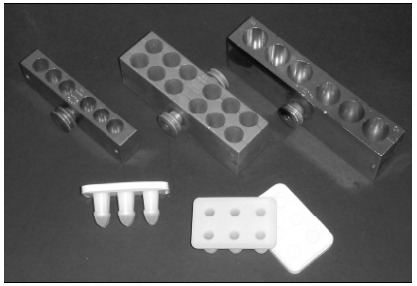

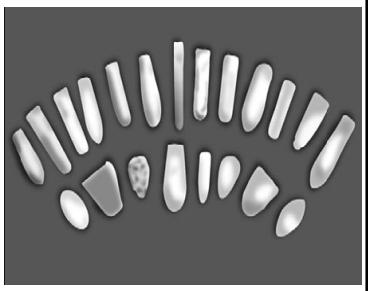

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SUPPOSITORIES:

British Pharmacopoeia (BP) definition:

"Suppositories are solid, single-dose preparations. The shape, volume and consistency of suppositories are suitable for rectal administration."

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- Pessaries are a type of suppository intended for vaginal use.
- The larger size moulds are usually used in the preparation of pessaries such as 4 g and 8 g moulds.
- Pessaries are used almost exclusively for local medication, the exception being prostaglandin pessaries that do exert a systemic effect.

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- **Pessaries**
- Common ingredients for inclusion in pessaries for local action include:
  - Antiseptics
  - Contraceptive agents
  - Local anaesthetics
  - Various therapeutic agents to treat trichomonal, bacterial and monilial infections.

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Ideal Suppository Base:

1. It should **melt at rectal temperature (36^0) or dissolve or disperse in body fluid.**
2. **Release** medicaments easily.
3. Shape should **remain intact while handling.**
4. **Non-toxic and non-irritant** to sensitive and inflammed mucous membrane.
5. It should be **stable on storage** i.e. it does not change color, odor, or drug release pattern.
6. **Compatible** with broad variety of drug and adjuvants.
7. It **should shrink** so that it comes out easily from the mould without the use of any lubricants.

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*For **fatty bases** the following additional specifications are required:*

1. "Acid value" is below 0.2
2. "Saponification value" ranges from 200 to 245
3. "Iodine value" is less than 7
4. The interval point and solidification point is small.

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Suppository Bases:

Classification of suppository bases

1. ***Fatty bases:*** They melt at body temperature.
2. ***Water-soluble or water miscible base:*** They dissolve or disperse in rectal secretions.
3. ***Emulsifying bases:*** They emulsifies small amount of aqueous solution of drug.

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1. Fatty Bases:

Designed to melt at body temperature.

Example: Theobroma oil (Cocoa butter), Synthetic fats.

A) Theobroma oil (Cocoa butter):

- It is a **yellowish-white solid** with an odour of **chocolate** and is a **mixture of glyceryl esters of different unsaturated fatty acids.**
- **Advantages:**

1. A melting range of 30-36°C (solid at room temperature but melts in the body).
2. Readily melted on warming, rapid setting on cooling.
3. Miscible with many ingredients.
4. Non-irritating.

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- **Disadvantages:**

1. **Polymorphism**:

- When melted and cooled it solidifies in different crystalline forms, depending on the temperature of melting, rate of cooling and the size of the mass.
- **If melted at not more than 36°C and slowly cooled it forms stable beta crystals with normal melting point.**
- **If over-heated then cooled it produce unstable gamma crystals which melt at about 15°C or alpha crystals melting at 20°C.**

- Cocoa butter must be slowly melted over a warm water bath to avoid the formation of the unstable crystalline form.

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2. **Adherence to mould:** Because **theobroma oil does not contract enough on cooling** to loosen the suppositories in the mould, sticking may occur, particularly if the mould is worn. This is prevented by lubricating the mould before use.
3. **Softening point too low for hot climates:** To raise the softening point, whit beeswax may be added to theobroma oil suppositories intended for use in tropical and subtropical countries.
4. **Melting point reduced by soluble ingredients:** Substances, such as chloral hydrate, that dissolve in theobroma oil, may lower its melting point to such an extent that the suppositories are too soft for use. To restore the melting point, a controlled amount of white beeswax may be added.

5. **Slow deterioration during storage:** This is due to oxidation of the unsaturated glycerides.
6. **Poor water absorbing capacity:** This fault can be improved by the addition of emulsifying agents.
7. **Leakage from the body:** Sometimes melted base escapes from the rectum or vagina. This is most troublesome with pessaries because of their larger size, and therefore, these are rarely made with theobroma oil.
8. **Relatively high cost**

B) Synthetic Hard Fat:

As a **substitute of theobroma oil**, a number of hydrogenated oils.

e.g. hydrogenated edible oil, arachis oil, coconut oil, palm kernel oil, stearic and a mixture of oleic and stearic acids are recommended.

Advantages:

1. Their solidifying points are **unaffected by overheating**.
2. They have **good resistance to oxidation** because their unsaturated fatty acids have been reduced.
3. Their **emulsifying and water absorbing capacities** are good.
4. **No mould lubricant is required** because they contract significantly on cooling.
5. They produce **colorless, odourless and elegant suppositories.**

Disadvantages:

1. They **should not be cooled in refrigerator** because they become brittle if cooled quickly.
2. They are **more fluid than theobroma oil** when melted and at this stage sedimentation

2. Water Soluble & Water Miscible Bases:

A) Glycero-Gelatin Base:

- This is a **mixture of glycerol and water made into a stiff jelly by adding gelatin.**
- It is used for the preparation of jellies, suppositories and pessaries. The stiffness of the mass depends upon the proportion of gelatin used which is adjusted according to its use.
- Depending upon the compatibility of the drugs used a suitable type of gelatin is selected for the purpose. Two types of gelatins are used as suppository base.
  - **Type-A or Pharmagel-A**
  - **Type-B or Pharmagel-B**

Disadvantages:

Glycerogelatin base suppositories are **less commonly used than the fatty base** suppositories because:

1. Glycerol has **laxative action.**
2. They are **more difficult to prepare and handle.**
3. They are **hygroscope**, hence must be carefully stored.
4. **Gelatin is incompatible with drugs those precipitate with the protein** e.g. tannic acid, ferric chloride, gallic acid, etc.

B) Soap-Glycerin Suppositories:

- In this case **gelatin and curd soap or sodium stearate** which makes the glycerin sufficiently hard for suppositories and a **large quantity of glycerin up to 95%** of the mass can be incorporated.
- Further the soap helps in the evacuation of glycerin.
- The **soap glycerin suppositories** have the disadvantage that they are **very hygroscopic**, therefore they must be protected from atmosphere and **wrapped in waxed paper or tin foil.**

C) Polyethylene glycol bases/Macrogol bases (Carbowaxes):

- Depending on their **molecular weight** they are available in different physical forms.
- Examples of Macrogol bases:

	I	II	III	IV
Macrogol 400	-	-	20	-
Macrogol 1000	-	-	-	75
Macrogol 1540	-	33	33	-
Macrogol 4000	33	-	-	25
Macrogol 6000	47	47	47	-
Water	20	20	-	-

- By choosing a **suitable combination** a suppository base with the desired characteristics can be prepared.
- **Advantages:**

1. The **mixtures** generally have a **melting point above 42^{0}C,** hence, does **not require cool storage** and they are satisfactory for use in hot climate.
2. Because of the **high melting point** they **do not melt** in the body cavity, rather they gradually dissolve and disperse, **releasing the drug slowly.**
3. They **do not stick to the wall of the mould** since they contract significantly on cooling.

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3. Emulsifying Bases:

- These are **synthetic bases** and a number of proprietary bases of very good quality are available, few of which are described below:

A) Witepsol: They consist of **triglycerides of saturated vegetable acids** (chain length C12 to C18) with varying proportions of partial esters.

B) Massa Esterium: This is another range of bases, consisting of a **mixture of di-, tri- and mono- glycerides of saturated fatty acids** with chain lengths of C11 to C17.

C) Massuppol: It consists of **glyceryl esters mainly of lauric acid, to which a small amount of glyceryl monostearate** has been added to improve its water absorbing capacity.

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Advantages of these bases over cocoa butter:

1. Over heating does not alter the physical characteristics.
2. They do not stick to the mould. They do not require previous lubrication of the mould
3. They solidify rapidly.
4. They are less liable to get rancid.
5. They can absorb fairly large amount of aqueous liquids.

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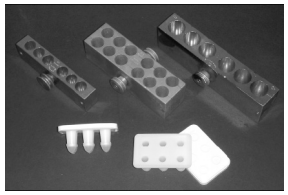
Manufacturing of Suppositories:

Moulds:

- The suppository and pessary moulds are made of metals and have four, six or twelve cavities.
- By removing a screw, they can be opened longitudinally for lubrication, extraction of the suppositories and cleaning.



- The nominal capacities of the common moulds are 1g, 2g, 4g and 8g.

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- ***Displacement value:***

  The volume of a suppository from a particular mould is uniform but its weight will differ with the density of the base.

- ***Definition :***

  It is the **quantity of the drug that displaces one part of the base.** e.g. Zinc oxide, D = 5.

- ***Calculation of displacement value***

  Formula for calculation of the amount of base required in each mould

$$\text{Amt. of base required for each suppository (gm)} = \text{Capacity of each mould (gm)} - \frac{\text{Dose of drug (gm)}}{\text{Displacement value of drug}}$$

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Preparation of Suppositories:

1. Hand molding [Cold Hand Shaping]:

1. **Drug** is triturated in a mortar into **fine powder.**
2. **Cocoa butter** is grated into small particles.
3. Drug is **mixed with small portion** of cocoa butter in a mortar.
4. **One drop fixed vegetable oil** is added to give **plasticity** to the mass.
5. **Remainder of the cocoa butter is added** by geometric dilution (i.e. by adding the same amount of base as is already in the mortar), triturated with pressure.
6. **Heat generated by trituration results in a plastic mass**, which is cohesive and ready to roll.

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6. **The mass** is scrapped from the mortar with a spatula and **rolled into a ball.**
7. An **ointment tile** is taken, **dusted lightly with starch** powder, ball is placed on it, **rolled with a flat faced spatula to form a cylinder**. The cylinder is **cut into desired number of pieces** with a sharp blade.
8. **One end** of a suppository is **held firmly with a finger** and the other end is tapered with the spatula to give the **shape of suppository**.

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2. Compression Molding:

1. In this case an instrument known as ***compression mould*** is used.
2. **Drug is powdered and mixed with grated cocoa butter.**
3. The mixture is filled into a chilled cylinder.
4. The **mixture is pressed** within the **cylinder by a piston** until a pressure is felt.
5. Then the suppositories are **expelled from the cylinder.**

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3. Pour molding (Fusion method):

This is the main method of preparing suppositories.

1. **Drug is powdered** in a mortar.
2. Carefully **grated cocoa butter** is taken into a beaker and **heated in a water bath**. When 2/3rd portion is **melted** the beaker is taken out of the heat source.
3. The rest of the mass is melted by stirring with a glass rod. [If cocoa butter is heated to clear liquid then unstable α, and γ-crystals will form and the suppositories will remain in melted state at room temperature].
4. **Drug is added** into the beaker and stirred thoroughly to mix with the **"creamy" base**. The "creamy" melted base is then **poured into previously lubricated mould.**

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5. The mould is **allowed to congeal**, then placed in the **refrigerator for 30 minutes to harden** (forms stable β-crystal after 24 hours of refrigeration).
6. Mould is taken out from the refrigerator and surface is trimmed off. The mould is opened and the suppositories are expelled out of the mould by gentle pressure with the finger.

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4. Automatic Molding Machine:

- Two types of molding machines are available: **(a) rotary molding machine and (b) straight-line molding machine**

Manufacturing cycles in rotary molding machine:

1. Prepared mass is filled in a into a filling hopper where it is continuously mixed and maintained at constant temperature.
2. The suppository molds are lubricated by brushing or spraying lubricant solution.
3. The molten mass is filled in the molds to a slight excess.
4. The mass is *cooled* to solidify and the excess material is *scrapped off* and collected for re-use.

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5. In the ejecting section the mold is opened and the suppositories are pushed out by steel rods.
6. The mold is closed, and then moved to the first step of the cycle.
7. The output of a typical rotary machine ranges from 3500 to 6000 suppositories an hour.

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Packaging and Storage:

- Suppositories are usually packed in tin or aluminium, 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.



Question Bank:

2 Marks

1. Classify suppository bases.
2. Give any four merits (advantages) of suppositories.
3. Define suppository. Give merits & demerits.
4. Define suppository. Give any four ideal properties of suppository bases.

5 Marks

1. Short note- Methods of compounding of suppositories.**

10 Marks

1. Define and classify suppositories. Classify suppositories bases. Explain in detail method of compounding and add note on suppository bases.*

The End

SUCCESSFUL PEOPLE NEVER WORRY ABOUT WHAT OTHERS ARE DOING.

KUSHANDWIZDOM