

SUPPOSITORIES and INSERTS

DR

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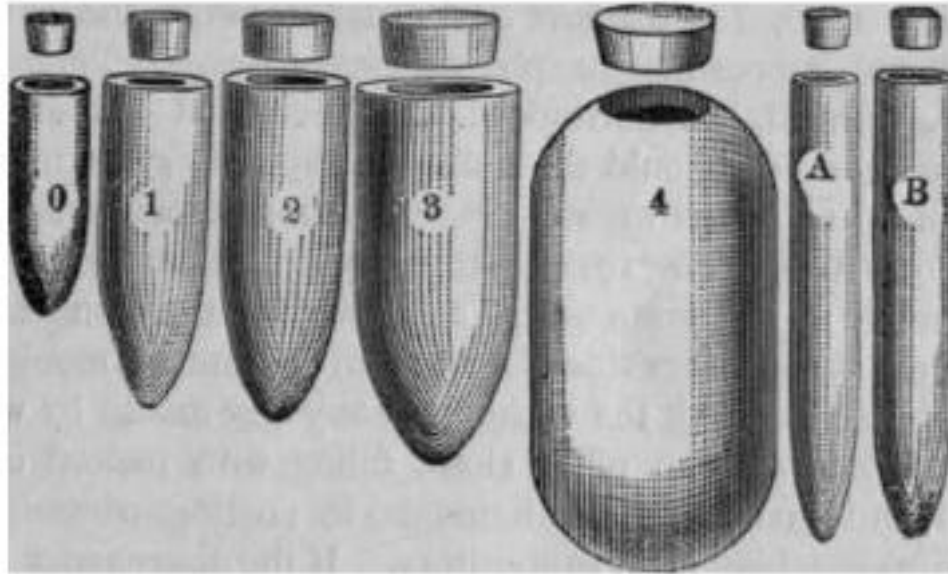
SUPPOSITORIES

Solid dosage forms intended for insertion into the body orifices where it; melt , soften dissolve and exert localized or systemic effects

- Suppositories are commonly used rectally and vaginally and occasionally urethrally.
- They have various shapes and weights , related to the intended orifice.



Shape and size of suppositories



SUPPOSITORIES & PESSARIES

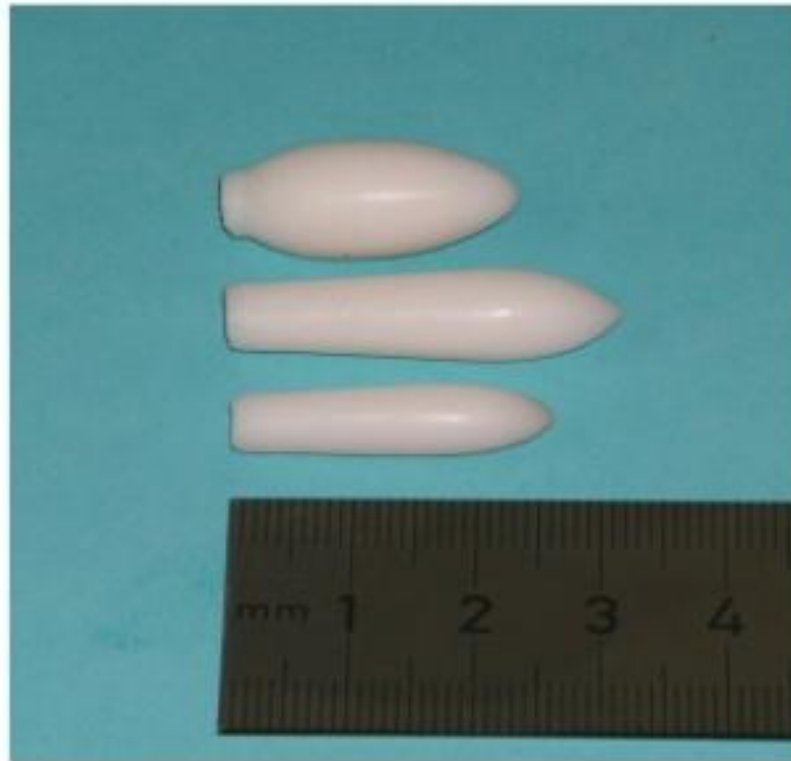
ADVANTAGES:

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

DISADVANTAGES OF SUPPOSITORIES:

- The problem of patient acceptability.
- Suppositories are not suitable for patients suffering from diarrhea.
- 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.
- Incomplete absorption may be obtained because suppository usually promotes evacuation of the bowel.

RECTAL SUPPOSITORIES



Rectal Suppositories

- Rectal Suppositories About 32 mm (1.5 inches) in length, cylindrical, one or both ends tapered and some are bullet shaped. Depending on the density of the base and the medicaments in the suppository, the weight may vary
- Adult rectal suppositories weigh about 2 grams when cocoa butter (theobroma oil) is used as a base.
- Rectal suppositories for use by infants and children are about half the weight and size of the adult suppositories and assume a more pencil-like shape.
- Intended for both local and systemic actions

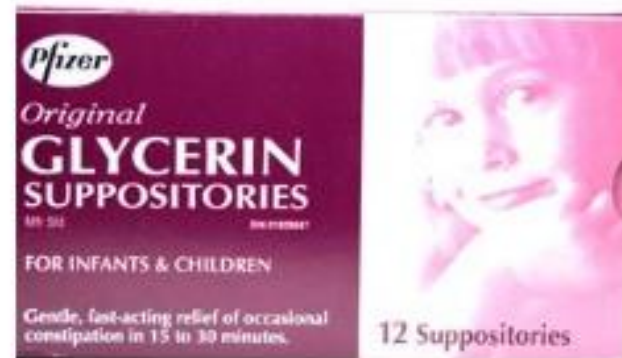
Vaginal suppositories

- Called *pessaries*, are usually globular, oviform, or cone-shaped and weigh about 5 g when cocoa butter is the base.
- Depending on the base and the manufacturer's product, the weights of vaginal suppositories may vary widely.

Urethral suppositories

- called *bougies*, are slender, pencil-shaped suppositories intended for insertion into the male or female urethra.
- Male urethral suppositories may be 3 to 6 mm in diameter and approximately 140 mm long, cocoa butter is employed as the base, weigh about 4 g.
- Female urethral suppositories are about half the length and weight of the male urethral suppository, being about 70 mm long and weighing about 2 g when made of cocoa butter.

RECTAL SUPPOSITORIES



RECTAL SUPPOSITORIES FOR LOCAL EFFECT

- Used to relieve constipation, as laxative.

Examples:

- Dulcolax (Bisacodyl) suppositories
- Glycerin suppositories , promote laxation by local irritation of the mucous membranes, due to the dehydrating effect of the glycerin on those membranes
- Used to relieve pain, irritation, itching, and inflammation associated with hemorrhoids and other anorectal conditions

Examples: Hydrocortisone suppositories

Mesalamine suppositories

Antihemorrhoidal suppositories

- frequently contain a number of components, including :
 - Local anesthetics,
 - vasoconstrictors,
 - astringents,
 - analgesics,
 - soothing emollients, and
 - protective agents.

RECTAL SUPPOSITORIES FOR SYSTEMIC ACTIONS

- For systemic effects, the mucous membranes of
- the rectum and vagina permit the absorption of
- many soluble drugs. Although the rectum is used
- frequently as the site for the systemic absorption
- of drugs, the vagina is not as frequently used for
- this purpose.

RECTAL SUPPOSITORIES FOR SYSTEMIC ACTIONS

Examples of drugs administered rectally in the form of suppositories for their systemic effects include :

- (a) relief of nausea and vomiting - ondansetron suppositories.
- (b) tranquilizer prochlorperazine and chlorpromazine suppositories
- (c) Opioid analgesia - oxycodone HCl suppositories
- (d) NSAID (for migraine)- ergotamine tartrate
- (e) analgesic and antipyretic- opiate (paracetamol) suppository
- (f) theophylline as a smooth muscle relaxant in treating asthma,

PHYSICOCHEMICAL FACTORS OF THE DRUG AND SUPPOSITORY BASE

- The relative solubility of the drug in lipid and in water .
- The particle size of a dispersed drug.
- Physicochemical factors of the base include its ability to melt, soften, or dissolve at body temperature, its ability to release the drug substance, and its hydrophilic or hydrophobic character

Particle Size

- To prevent undue sedimentation during or after preparation, the particle size should be limited (the use of particles smaller than approximately 150 μm is recommended)
- the smaller the particle, the greater the surface area, the more readily the dissolution of the particle and the greater the chance for rapid absorption. Therefore drugs with low water solubility should be dispersed as small, preferably micronized, particles.

Amount of drug.

- An additional complicating factor is the amount (proportion) of drug present in a suppository.
- If the number of particles increases, this would also increase the rate of agglomerate formation.
- This will depend on the particle size and on the presence of additives.

Additives

For several widely varying reasons, formulators of suppositories make use of additives to improve their product.

The dispensing aspects include formulations for specific drugs which affect the melting point of the suppository; it may become depressed (by a soluble liquid compound) or increased (by a high amount of soluble high melting active compound).

Nature of the Base

- The base must be capable of melting, softening, or dissolving to release its drug for absorption.
- The base should not irritate the mucous membranes of the rectum, avoid colonic response and prompt a bowel movement, eliminating the prospect of complete drug release and absorption.
- No chemical and/or physical interactions between the medicinal agent and the suppository base, which may affect the stability and/or bioavailability of the drug.
- Long-acting or slow-release suppositories are also prepared. Morphine sulfate in slow-release suppositories is prepared by compounding pharmacists. The base includes a material such as alginic acid, which will prolong the release of the drug over several hours .

Polyethylene glycols base (Macrogols)

- Polymers of ethylene oxide and water prepared to various chain lengths, molecular weights, and physical states
- PEGs Hardness increases with an increase in the molecular weight.
- Various combinations of these polyethylene glycols may be combined by fusion, using two or more of the various types to achieve a suppository base of the desired consistency and characteristics.

• 300	-15°C -18°C	• 3350	54°C -58°C
• 400	4°C -8°C	• 4600	57°C -61°C
• 600	20°C -25°C	• 6000	56°C -63°C
• 1000	37°C -40°C	• 8000	60°C -63°C
• 1450	43°C -46°C		

- Polyethylene glycol suppositories do not melt at body temperature but rather dissolve slowly in the body's fluids. Therefore, the base need not be formulated to melt at body temperature.
- Thus, suppositories from mixtures prepared having melting points considerably higher than body temperature to permits a slower release of the medication from the base , and permits convenient storage of these suppositories without need for refrigeration .
- Polyethylene glycol suppositories that do not contain at least 20% water should be dipped in water just before use to avoid irritation of the mucous membranes after insertion.

- The most commonly used base for vaginal suppositories consists of combinations of the various molecular weight polyethylene glycols.
- To this base is frequently added surfactants and preservative agents, commonly the parabens.
- Many vaginal suppositories and other types of vaginal dosage forms are buffered to an acid pH usually about 4.5, consistent with the normal vagina. This acidity discourages pathogenic organisms and provides a favorable environment for eventual recolonization by the acid- producing bacilli normally found in the vagina.

PREPARATION OF SUPPOSITORIES

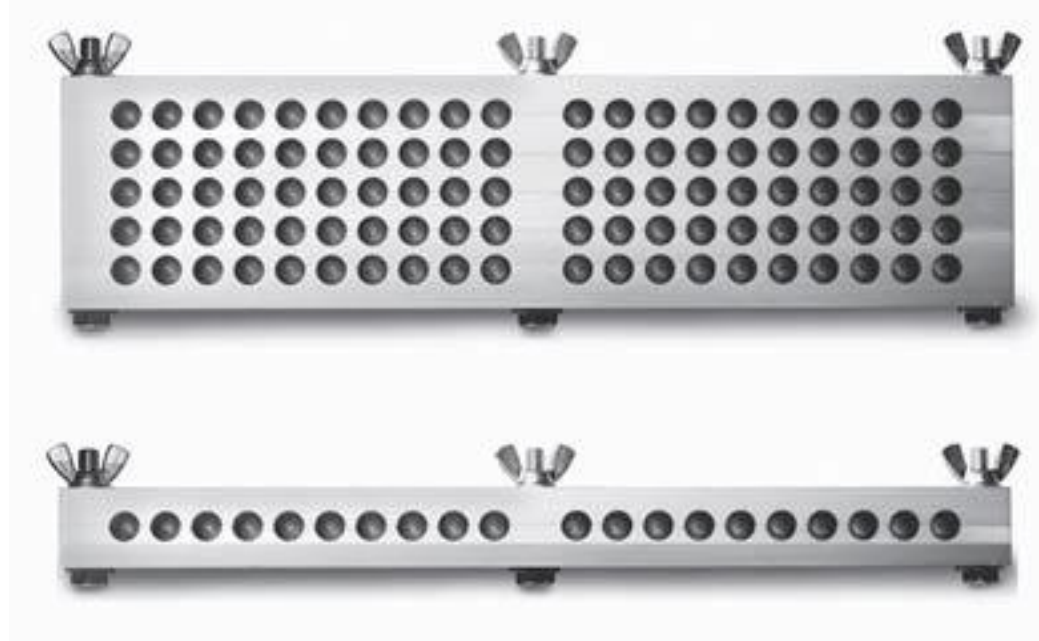
- Suppositories are prepared by three methods:
 - *(a) molding* from a melt,
 - *(b) compression*
 - *(c) hand rolling* and *shaping*.
- The method most frequently employed both on a small scale and on an industrial scale is molding.

PREPARATION BY MOLDING

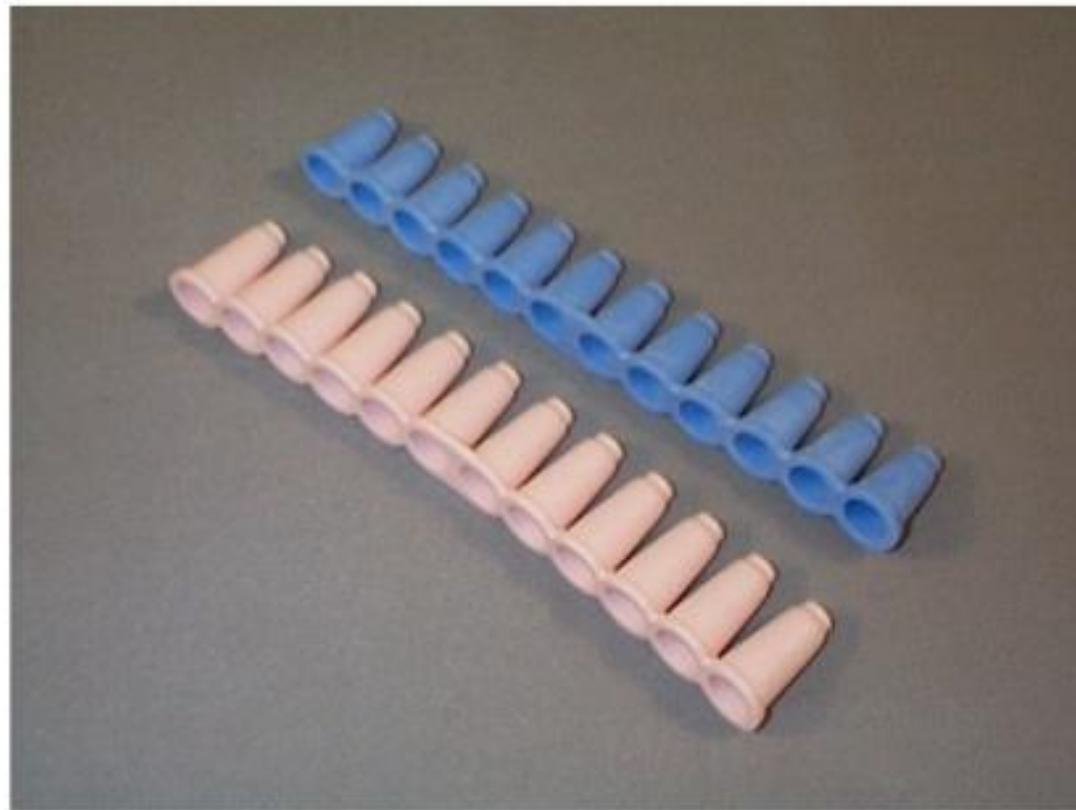
- The steps in molding include
 - (a) melting the base,
 - (b) incorporating any required medicaments,
 - (c) pouring the melt into molds,
 - (d) allowing the melt to cool and congeal into suppositories,
 - (e) removing the formed suppositories from the mold.
- Cocoa butter, glycerinated gelatin, polyethylene glycol, and most other bases are suitable for preparation by molding.

Suppository Molds

- Molds in common use today are made from stainless steel, aluminum, brass, or plastic.
- reusable and disposable Commercially available molds available for preparation of rectal, vaginal, and urethral suppositories, can produce individual or large numbers of suppositories of various shapes and sizes.



RUBBER / LATEX SUPPOSITORY MOLDS



Lubrication of the Mold

- Depending on the formulation, suppository molds may require lubrication before the melt is poured to facilitate clean and easy removal of the molded suppositories.
- Lubrication is seldom necessary when the base is cocoa butter or polyethylene glycol.
- Lubrication is usually necessary with glycerinated gelatin.
- A thin coating of mineral oil applied with the finger to the molding surfaces usually suffices.



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Determination of the Amount of Base Required

- Knowing the amount of drug substances provided in each suppository subtracted from the total volume of the mold will give the volume of base required.
- if considerable quantities of other substances are to be used, The total volume of these materials is subtracted from the volume of the mold, and the appropriate amount of base is added.

- Because the bases are solid at room temperature, the volume of base may be converted to weight from the density of the material.

Example,

- if 12 mL of cocoa butter is required to fill a suppository mold and if the medicaments in the formula have a collective volume of 2.8 mL, 9.2 mL of cocoa butter will be required. By multiplying 9.2 mL times the density of cocoa butter, 0.86 g/ mL, it may be calculated that 7.9 g of cocoa butter will be required.

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The most used method of calculating the quantity of base that the active medication will occupy and the quantities of ingredients required

Preparing and Pouring the Melt

- Using the least possible heat over a water bath, the weighed suppository base material is melted on porcelain casserole .
- Medicinal substances are incorporated into a portion of the melted base by mixing on a glass or porcelain tile with a spatula.
- After incorporation, this material is stirred into the remaining base, which has been allowed to cool almost to its congealing point.
- Any volatile materials or heat-labile substances should be incorporated at this point with thorough stirring.

Preparing and Pouring the Melt

- The melt is poured carefully and continuously into each cavity of the mold, which has been previously equilibrated to room temperature.
- If any undissolved or suspended materials in the mixture are denser than the base, so that they have a tendency to settle, constant stirring, even during pouring, is required,
- The mold is usually placed in the refrigerator , after harding , the mold is removed from the refrigerator and allowed to come to room temperature. Then the sections of the mold are separated, and the suppositories are dislodged, with pressure being exerted principally on their ends and only if needed on the tips.
- Generally, little or no pressure is required, and the suppositories simply fall out of the mold when it is opened.

Packing and storage of suppositories

- Cocoa butter base
 - Individually wrapped
 - Keep refrigerated
- Glycerinated gelatine based suppositories
 - Packed in tightly closed container
 - Store at controlled room temperature (20° C to 25 ° C
- PEG based suppositories
 - Stored at usual room temperature
 - No refrigeration required

BLISTER PACKAGING FOR SUPPOSITORIES

