

# SUPPOSITORIES and INSERTS



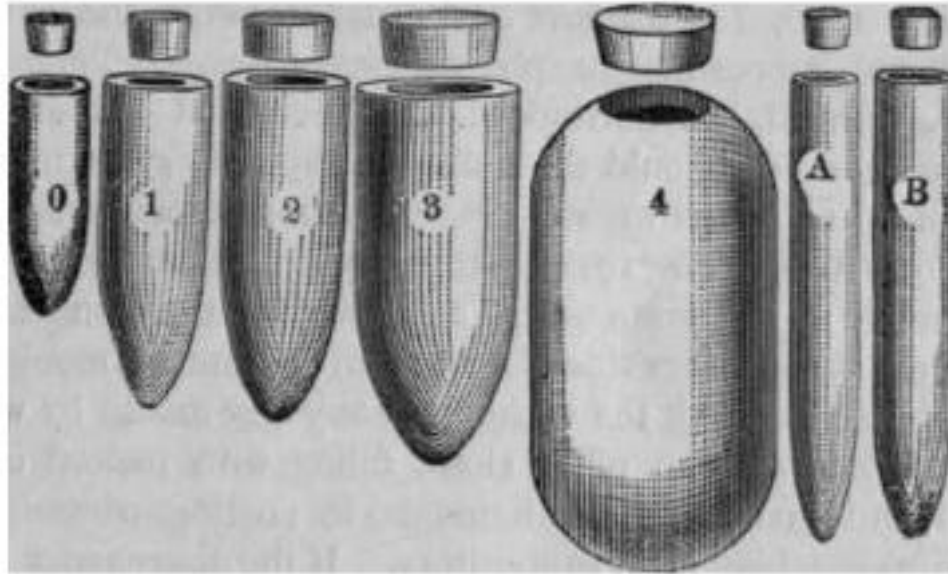
# SUPPOSITORIES

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

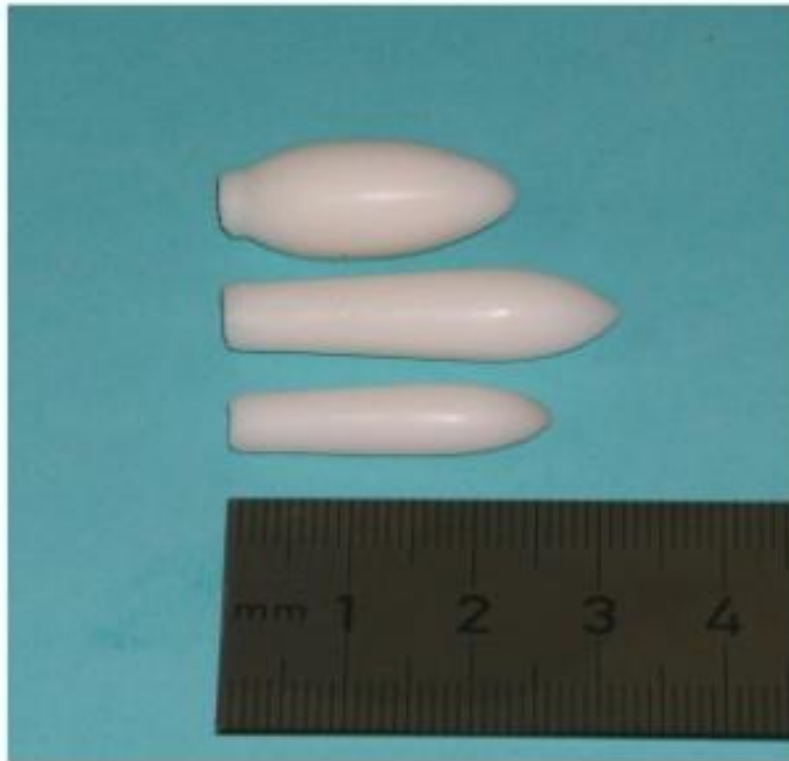
## **ADVANTAGES:**

- \_ 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 pencillike shape.
- Intended for both local and systemic actions

# Vaginal suppositories

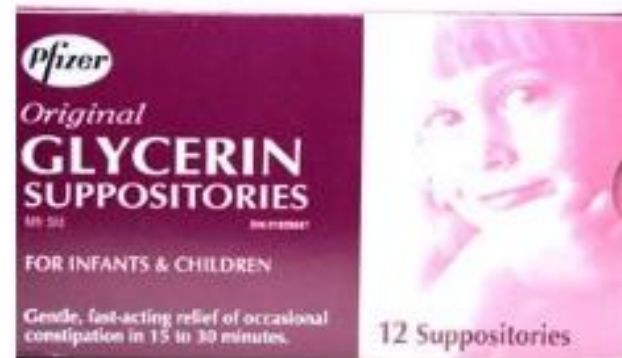
- Called *pessaries*, are usually globular, oviform, or cone-shaped and weigh about 5 g when cocoa butter is the base.
- Depending on the base and the manufacturer's product, the weights of vaginal suppositories may vary widely.



# 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- paracetamol ( paracetamol ) suppository
- (f) theophylline as a smooth muscle relaxant in treating asthma,

# VAGINAL SUPPOSITORIES



# VAGINAL SUPPOSITORIES OR INSERTS FOR LOCAL EFFECT

- Are employed principally to :
  - To combat infections in the female genitourinary tract,
  - To restore the vaginal mucosa to its normal state, and
  - For contraception.
- Among the anti-infective agents in commercial vaginal preparations are nystatin, clotrimazole, butoconazole nitrate, terconazole, and miconazole (antifungals) and triple sulfas, sulfanilamide, povidone iodine, clindamycin phosphate, metronidazole, and oxytetracycline (antibacterials).
- Nonoxynol-9, a spermicide, is employed for vaginal contraception .
- Estrogenic substances such as dienestrol are found in vaginal preparations to restore the vaginal mucosa to its normal state.



# VAGINAL SUPPOSITORIES

**TABLE 12.2 EXAMPLES OF VAGINAL SUPPOSITORIES AND TABLETS**

PRODUCT (MANUFACTURER)	ACTIVE CONSTITUENTS	CATEGORY AND COMMENTS
Cleocin suppositories (Pfizer)	Clindamycin phosphate 100 mg	Bacterial vaginosis
Monistat 7 suppositories (Personal products)	Miconazole nitrate 100 mg	Antifungal for local vulvovaginal Candidiasis (moniliasis)
Mycelex-G vaginal tablets (Bayer)	Clotrimazole 500 mg	Vulvovaginal yeast ( <i>Candida</i> ) infections
Semicid vaginal contraceptive inserts (Whitehall-Robins)	Nonoxynol-9 100 mg	Nonsystemic reversible birth control
Encare contraceptive inserts (Blairex)	Nonoxynol-9 100 mg	Nonsystemic reversible birth control

# Urethral suppositories

Urethral suppositories may be antibacterial or a local anesthetic preparative for a urethral examination

## **Alprostadil Urethral Microsuppository (MUSE)**

- **A single-use medicated transurethral system for the delivery of the drug, Alprostadil to the male urethra.**
- **Indicated for the treatment of erectile dysfunction (ED)**



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# Factors affecting the absorption of drugs from rectal suppositories

## ▪ **Physiologic factors**

- Colonic content
- Circulation route
- pH and Lack of buffering capacity of the rectal fluids

## ▪ **Physicochemical factors**

- Lipid-water solubility
- Particle size
- Nature of the base
- Amount of drug
- Additives

- Absorption of drug from the rectum is primarily by passive diffusion
- In general, the rate and extent of drug absorption is lower than the oral route, mainly due to the small surface area for absorption.

# PHYSIOLOGIC FACTORS

- Colonic contents, A drug will obviously have greater opportunity to make contact with the absorbing surface of the rectum and colon in an empty rectum.
- circulation route, The lower and middle rectal (inferior and middle haemorrhoidal) veins drain into the inferior vena cava, hence this blood goes directly to the heart and into the general circulation.

In contrast, the upper rectal (superior haemorrhoidal) vein drains into the portal vein and therefore this blood passes through the liver before reaching the heart.

# PHYSIOLOGIC FACTORS

## Rectal fluids:

- The total volume of mucus is estimated at approximately 3 mL, spread over a total surface area of approximately 300 cm<sup>2</sup>.
- The pH of the mucous layer is reported as approximately 7.5 (i.e. close to neutral) in adults, and slightly alkaline in most children.
- Furthermore, there seems to be little buffering capacity.

**For Systemic drug effect, absorption is greater in a rectum that is void /empty.**

**Diarrhea, Fecal matter**

**Tumor growth**

**Tissue dehydration**

**Slow down rectal  
drug absorption**



- The suppository base has a marked influence on the release of active constituents.
- While cocoa butter melts rapidly at body temperature, because of its immiscibility with fluids, it fails to release fat-soluble drugs readily.
- For systemic drug action using a cocoa butter base, it is preferable to incorporate the ionized (salt) form rather than the un-ionized (base) form of a drug to maximize bioavailability. Although un-ionized drugs more readily partition out of water-miscible bases such as glycerinated gelatin and polyethylene glycol, the bases themselves tend to dissolve slowly and thus retard release of the drug.

# **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

# Lipid–Water Solubility

- The lipid–water partition coefficient of a drug is an important consideration in the selection of the suppository base and in anticipating drug release from that base.
- A lipophilic drug that is distributed in a fatty suppository base in low concentration has less tendency to escape to the surrounding aqueous fluids than a hydrophilic substance in a fatty base.
- Water soluble bases—for example, polyethylene glycols—that dissolve in the anorectal fluids release for absorption water-soluble and oil-soluble drugs. Naturally, the more drug a base contains, the more drug will be available for absorption. However, if the concentration of a drug in the intestinal lumen is above a particular amount, which varies with the drug, the rate of absorption is not changed by a further increase in the concentration of the drug.

- When a drug has a high vehicle-to-water partition coefficient, it is likely to be in solution to an appreciable extent (or completely) in the suppository.
- This generally means that the tendency to leave the dosage form will be low and thus the release rate into the rectal fluid will be slow. This is obviously unfavorable for rapid absorption.
- On the other hand, some lipid solubility is required for penetration through the rectal membranes

Table 42.2 Drug solubility and suppository formulation

Solubility in		Choice of base
Fat	Water	
Low	High	Fatty base (rule 1)
High	Low	Aqueous base (rule 2)
Low	Low	Indeterminate

# Particle Size

- To prevent undue sedimentation during or after preparation, the particle size should be limited (the use of particles smaller than approximately 150  $\mu\text{m}$  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.

# Particle Size

- One should be aware of the increased tendency of these small particles to agglomerate due to strongly increased van der Waals forces as particle size is reduced.

# 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 be irritates the mucous membranes of the rectum, avoiding 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 .

# **SUPPOSITORY BASES**

- (a) fatty or oleaginous bases.
- (a) water-soluble or water-miscible bases.
- (a) miscellaneous bases, generally combinations of Lipophilic and hydrophilic substances.

# fatty or oleaginous bases.

- Cocoa butter
- Hydrogenated fatty acids of vegetable oils ,i.e. such as palm kernel oil and cottonseed oil
- Fat based compounds containing compounds of glycerin with the higher–molecular-weight fatty acids, such as glyceryl monostearate and glyceryl monopalmitate
- many commercial products employ varied combinations of these types of materials to achieve the desired hardness under conditions of shipment and storage and the desired quality of submitting to the temperature of the body to release their medicaments

# Fatty or Oleaginous Bases

## Cocoa Butter, NF,

- Fat obtained from the roasted seed of *Theobroma cacao*.
- Yellowish-white solid having a faint, agreeable chocolate-like odor.
- Chemically, it is a triglyceride (combination of glycerin and one or different fatty acids).
- melts at 30°C to 36°C (86°F to 97°F), it is an ideal base, melting just below body temperature and yet maintaining its solidity at usual room temperatures.



- Disadvantages of Cocoa butter:
  1. Exhibits *polymorphism*, because of its triglyceride content.
  2. Substances such as phenol and chloral hydrate have a tendency to lower the melting point of cocoa butter.
  3. High price
  4. Insufficient contraction during cooling
  5. Chemical instability

The fatty vehicles in use nowadays are almost exclusively semi- or fully synthetic.

Theobroma oil (also known as cocoa butter) a very commonly used base – is no longer used because of its many disadvantages

- in practice The fatty vehicles in use nowadays are almost exclusively semi- or fully synthetic.

- Commercial examples include: Cotmar, Dehydag, Fattibase, Suppocire and Witepsol. These are mixtures of natural or synthetic vegetable oils, consisting of mixed triglycerides of C12-C18 saturated fatty acids, waxes and fatty alcohols.

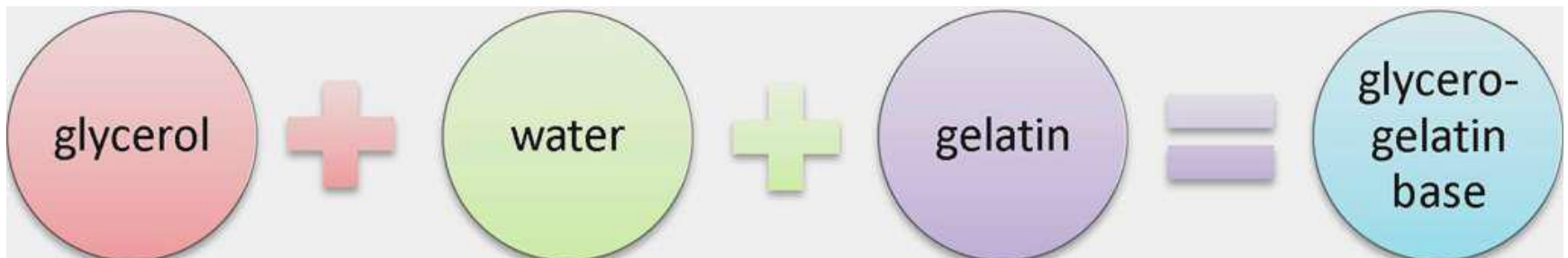


# Water-Soluble and Water-Miscible Bases



- Hydrophilic water-soluble (or miscible) vehicles are much less frequently used
- They comprise the classic glycerinated gelatin (glycerol-gelatin) and polyethylene glycol (macrogol)bases..
- Glycerinated gelatin suppositories may be prepared by dissolving granular gelatin (20%) in glycerin (70%) and adding water or a solution or suspension of the medication (10%).
- A glycerinated gelatin base is most frequently used in preparation of vaginal suppositories, with which prolonged local action of the medicinal agent is usually desired.
- The glycerinated gelatin base is slower to soften and mix with the physiologic fluids than is cocoa butter and therefore provides a slower release.

- Glycerinated gelatin–based suppositories have a tendency to absorb moisture as a result of the hygroscopic nature of glycerin, they must be protected from atmospheric moisture , the suppository may have a dehydrating effect and irritate the tissues upon insertion.
- water in the formula for the suppositories minimizes this action; however, if necessary, the suppositories may be moistened with water prior to insertion to reduce the initial tendency of the base to draw water from the mucous membranes and irritate the tissues.



- For urethral suppositories, the gelatin constitutes
- about 60% of the weight of the formula, the glycerin about 20%, and the medicated aqueous portion about 20%. Urethral suppositories of glycerinated gelatin are much more easily inserted than those with a cocoa butter base owing to the brittleness of cocoa butter and its rapid softening at body temperature.

# 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.

Table 42.1 Compositions of PEG bases with different physical characteristics

	Base A	Base B
PEG 1000	95%	75%
PEG 4000	5%	25%
Properties	Low melting temperature, immediate drug release	Higher melting temperature, sustained drug release

# **counseling points a pharmacist should share with the patient prescribed a drug in a suppository drug delivery system**

- If the polyethylene glycol suppository formulation does not contain at least 20% water, dipping it into water just prior to insertion prevents moisture from being drawn from rectal tissues and decreases irritation.
- The shape of the suppository determines how it will be inserted. Bullet-shaped rectal suppositories should be inserted pointed end first.
- Most suppositories are dispensed in paper, foil, or plastic wrappings, and the patient must be instructed to remove the wrapping completely before 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.



- The polyethylene glycol–based vaginal suppositories are water miscible and are generally sufficiently firm for the patient to handle and insert without great difficulty. However, to make the task easier, many manufacturers provide plastic insertion devices that are used to hold the suppository or tablet for proper placement within the vagina .



- As noted earlier, pharmacists frequently are called on to prepare progesterone vaginal suppositories.
- Micronized progesterone powder is used in a base of polyethylene glycol, although in some formulas cocoa butter is employed.
- The suppositories are prepared by adding the progesterone to a melt of the base and molding. Some representative formulas:

Rx	
Progesterone, micronized powder	q.s.
Polyethylene glycol 400	60%
Polyethylene glycol 8000	40%

Rx	
Progesterone, micronized powder	q.s.
Polyethylene glycol 1000	75%
Polyethylene glycol 3350	25%

Rx	
Progesterone, micronized powder	q.s.
Cocoa butter	100%

- The amount of progesterone per suppository ranges from 25 to 600 mg.
- The suppositories are used in treating luteal phase defect, premenstrual syndrome, luteal phase spotting, and in preparation of the endometrium for implantation .

# Miscellaneous Bases

- Mixtures of oleaginous and water-soluble or water-miscible materials.
- These materials may be chemical or physical mixtures.
- Some are preformed emulsions, generally of the water-in-oil type, or they may be capable of dispersing in aqueous fluids.
- Example is polyoxyl 40 stearate, a surface-active agent that is employed in a number of commercial suppository bases.
- Mixtures of many fatty bases (including cocoa butter) with emulsifying agents capable of forming water-in-oil emulsions have been prepared.

The inclusion of viscosity-increasing additives (e.g. colloidal silicon oxide or aluminium monostearate, both at approximately 1–2%) will create a gel like system with, in general, a slower release rate of the drug

# PREPARATION OF SUPPOSITORIES

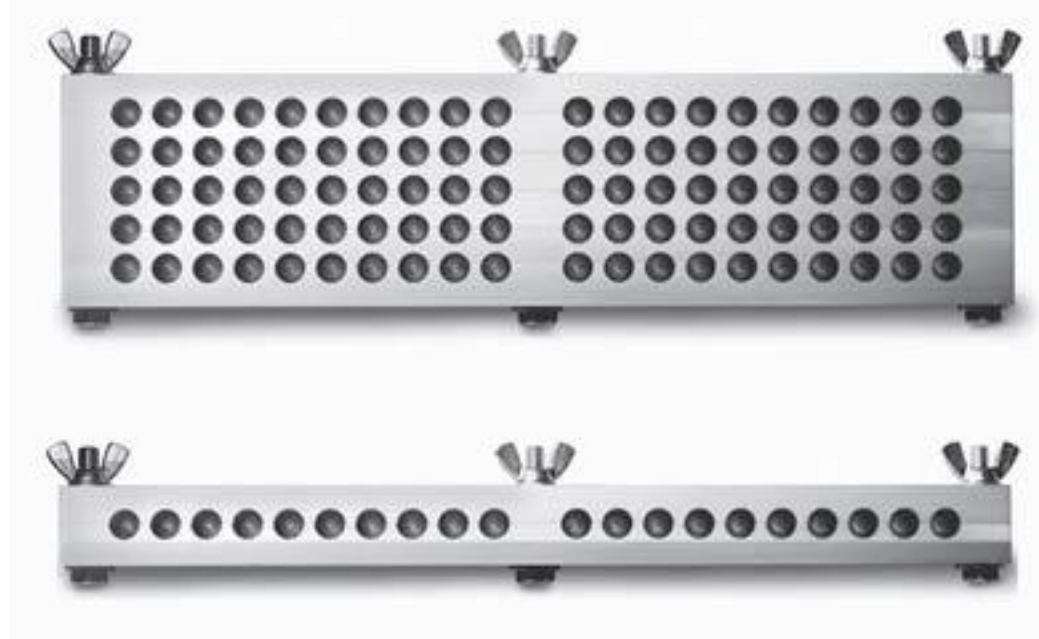
- Suppositories are prepared by three methods:
  - (a) *molding* from a melt,
  - (b) *compression*
  - (c) *hand rolling and shaping*.
- The method most frequently employed both on a small scale and on an industrial scale is molding.

# 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.

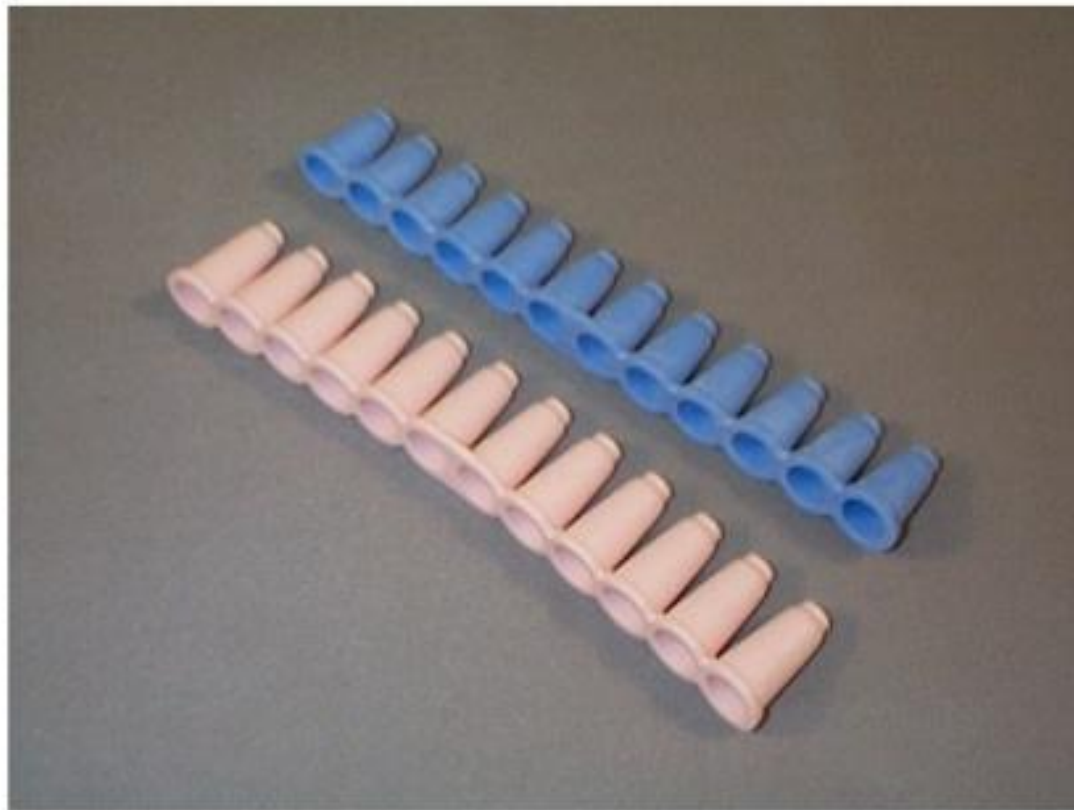
# Suppository Molds

- 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.



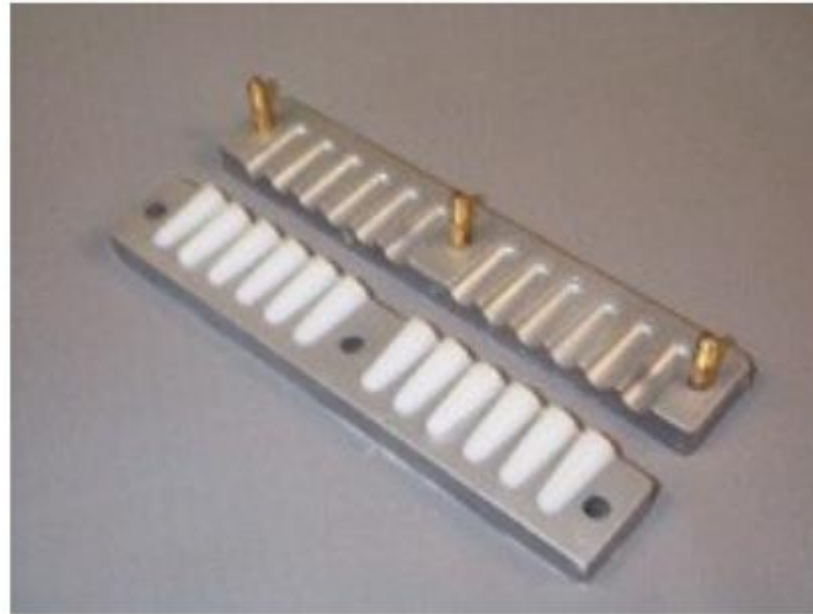


# **RUBBER / LATEX SUPPOSITORY MOLDS**



# 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.



lubrication before the melt is poured to facilitate clean and easy removal of the molded suppositories

# Calibration of the Mold

- Each individual mold is capable of holding a specific volume of material in each of its openings.
- Different bases prepared in the same mold will have different weight. Because of the difference in the densities of the materials, Similarly, any added medicinal agent alters the density of the base, and the weight of the resulting suppository differs from that of those prepared with base material alone.
- The pharmacist should calibrate each suppository mold for the usual base (generally cocoa butter and a polyethylene glycol base) so as to prepare medicated suppositories each having the proper quantity of medicaments.

# Calibration of the Mold

- in calibration of a mold is to prepare molded suppositories from base material alone. After removal from the mold, the suppositories are weighed and the total weight and average weight of each suppository are recorded (for the particular base used).
- To determine the volume of the mold, the suppositories are carefully melted in a calibrated beaker, and the volume of the melt is determined for the total number as well as for the average of one suppository.

# 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

# Density factors

- Ratio give the amount of base displaced by the active drug obtained by dividing the density of the active drug by the density of the base
- From table Aspirin density Factor 1.3  
Mean each 1.3g Aspirin displace 1 g of cocoa butter

Density factors for a selected number of ingredients are shown in Table .

**TABLE 1 DENSITY FACTORS FOR COCOA BUTTER SUPPOSITORIES**

Alum	1.7	Morphine HCl	1.6
Aminophylline	1.1	Opium	1.4
Aspirin	1.3	Paraffin	1.0
Barbital	1.2	Peruvian Balsam	1.1
Belladonna Extract	1.3	Phenobarbital	1.2
Benzoic Acid	1.5	Phenol	0.9
Bismuth Carbonate	4.5	Potassium Bromide	2.2
Bismuth Salicylate	4.5	Potassium Iodide	4.5
Bismuth Subgallate	2.7	Procaine	1.2
Bismuth Subnitrate	6.0	Quinine HCl	1.2
Boric Acid	1.5	Resorcinol	1.4
Castor Oil	1.0	Sodium bromide	2.3
Chloral Hydrate	1.3	Spermaceti	1.0
Cocaine HCl	1.3	Sulfathiazole	1.6
Digitalis Leaf	1.6	Tannic acid	1.6
Glycerin	1.6	White wax	1.0
Ichthammol	1.1	Witch hazel fluid extract	1.1
Iodoform	4.0	Zinc oxide	4.0
Menthol	0.7	Zinc sulfate	2.8

# OCCUPIED VOLUME METHOD

- 1. Determine the average weight per mold (blank) using the designated base.
- 2. Calculate Weight of base required for unmediated suppositories (mold capacity ).
- 3. find Density factor from table or Divide the density of the active drug by the density of the base to obtain a ratio( DF) .
- 4. Calculate the total amount of active ingredient required and Divide the total weight of active drug required for the total number of suppositories by the Density factor obtained in step 3. This will give the amount of base displaced by the active drug.
- 5. Subtract the amount obtained in step 4 from the total weight of the base of unmediated suppository to obtain the weight of base required for medicated one .

# EXAMPLE

Prepare 10 suppositories, each containing 200 mg of a drug with a density of 3.0. The base has a density of 0.9, and a prepared blank weighs 2.0 g. Using the determination of occupied volume method, prepare the requested suppositories.

- From step 1: The average weight per mold is 2.0 g.
- From step 2: The quantity required for 10 suppositories is  $2 \times 10 \text{ g} = 20 \text{ g}$ .
- From step 3: The quantity of active drug required is  $0.2 \times 10 \text{ g} = 2.0 \text{ g}$ .
- From step 4 : The Density Factor is  $3.0/0.9 = 3.3$ .
- From step 5: The amount of suppository base displaced by the active drug is  $2.0 \text{ g}/3.3 = 0.6 \text{ g}$ .
- From step 6: The weight of the base required is  $20 - 0.6 \text{ g} = 19.4 \text{ g}$ .
- The required weight of the base is 19.4 g, and the weight of the active drug is 2 g.

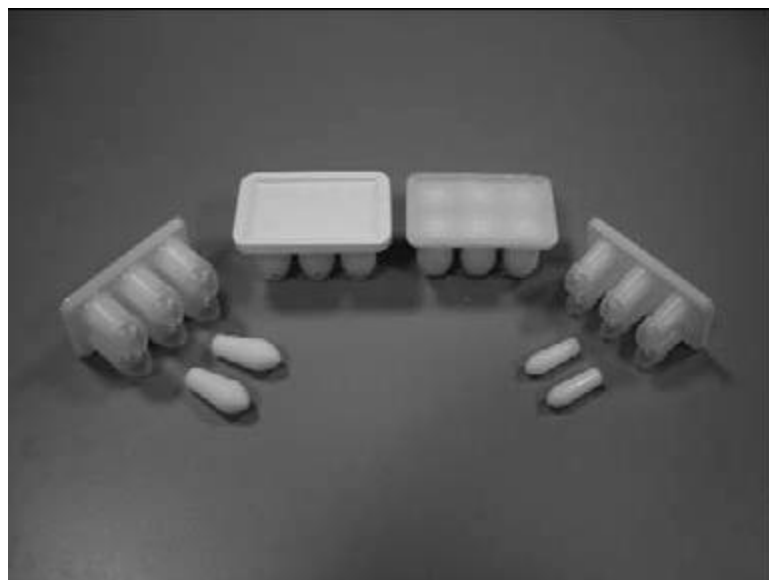
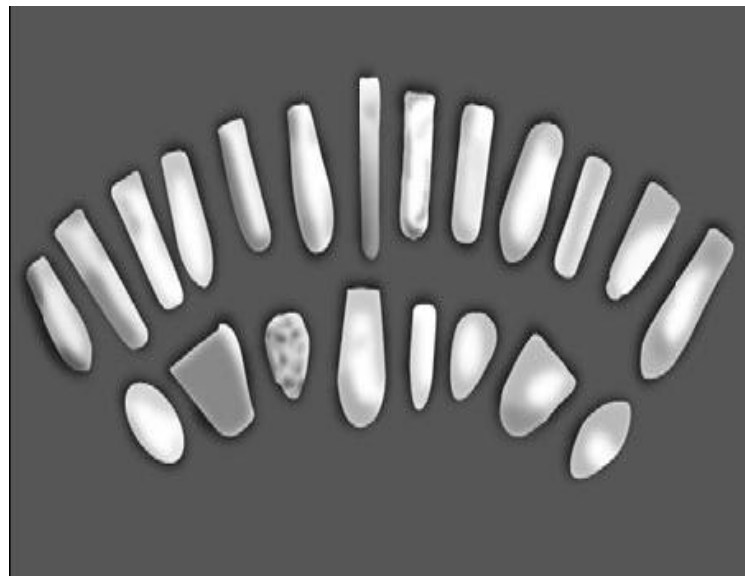
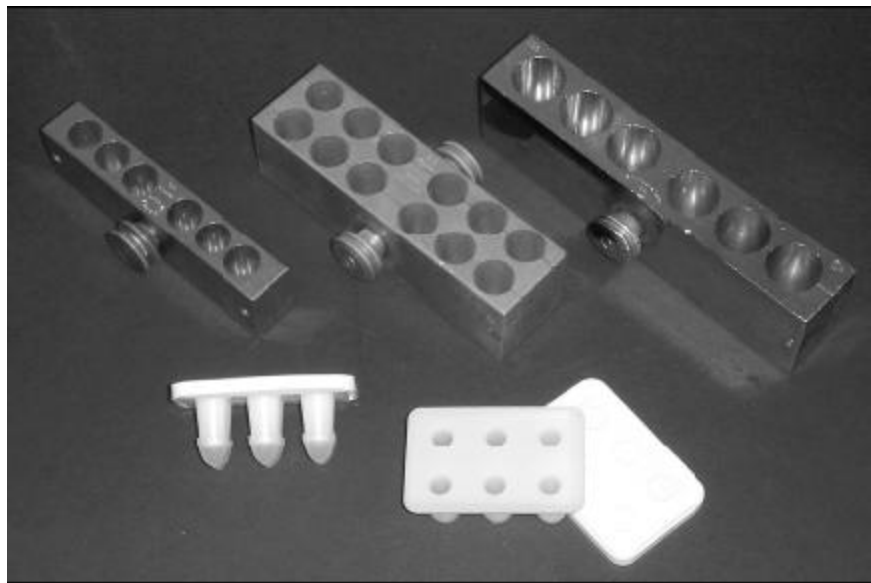
# Preparing and Pouring the Melt

- 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.





- A formula for glycerin suppositories is as follows:

Glycerin	91 g
Sodium stearate	9 g
Purified water	5 g
To make about	105 g

- In preparation of this suppository, the glycerin is heated in a suitable container to about 50°C Then the sodium stearate is dissolved with stirring in the hot glycerin, the purified water added, and the mixture immediately poured into the suppository previously heated mold.
- After cooling to solidification, the suppositories are removed. This formula will prepare about 50 adult suppositories.

- Glycerin, a hygroscopic material, contributes to the laxative effect of the suppository by drawing water from the intestine and from its irritant action on the mucous lining.
- The sodium stearate, a soap, is the solidifying agent and may also contribute to the laxative action.
- Because of the hygroscopic nature of glycerin, the suppositories attract moisture and should be maintained in tight containers, preferably at temperatures below 25°C (77°F).

# PREPARATION BY COMPRESSION

- Compression is especially suited for making suppositories that contain heat-labile medicinal substances or a great deal of substances that are insoluble in the base.
- In contrast to the molding method, compression permits no likelihood of insoluble matter settling during manufacture.
- The disadvantage to compression is that the special suppository machine is required and there is some limitation as to the shapes of suppositories that can be made.

# PREPARATION BY COMPRESSION

- In preparation for compression into the molds, the base and the other formulative ingredients are combined by thorough mixing,
- the friction of the process softening the base into a pastelike consistency. On a small scale, a mortar and pestle may be used. Heating the mortar in warm water (then drying it) greatly facilitates the softening of the base and the mixing.
- On a large scale, a similar process may be used, employing mechanical kneading mixers and a warm mixing vessel.
- Suppositories may be prepared by forcing the mixed mass of the base and the medicaments into special molds using suppository-making machines that apply pressure to the mass out of a cylinder into the mold .

# **HAND ROLLING METHOD**

- **The oldest and simplest method of suppository preparation.**
- **Method of choice 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 “trituration” grated cocoa butter and active ingredients in a mortar.**

# **HAND ROLLING METHOD**

**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.**

**counselling**



# **counseling points a pharmacist should share with the patient prescribed a drug in a suppository drug delivery system**

- Refrigerated suppositories should be allowed to warm to room temperature before insertion.
- The patient should be advised to rub cocoa butter suppositories gently with the fingers to melt the surface to provide lubrication for insertion.
- Glycerinated gelatin or polyethylene glycol suppositories should be moistened with water to enhance lubrication.
- The patient who is to use half of a suppository should be told to cut the suppository lengthwise with a clean razor blade.

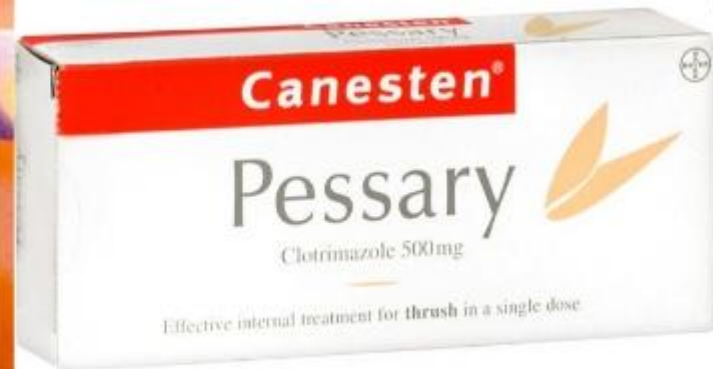
# **counseling points a pharmacist should share with the patient prescribed a drug in a suppository drug delivery system**

- If the polyethylene glycol suppository formulation does not contain at least 20% water, dipping it into water just prior to insertion prevents moisture from being drawn from rectal tissues and decreases irritation.
- The shape of the suppository determines how it will be inserted. Bullet-shaped rectal suppositories should be inserted pointed end first.
- Most suppositories are dispensed in paper, foil, or plastic wrappings, and the patient must be instructed to remove the wrapping completely before insertion.

## **counseling points a pharmacist should share with the patient prescribed a vaginal suppository**

- She should first be told to read the instructions with the product.
- The suppository should be inserted high into the vagina with the provided applicator.
- The patient should not discontinue therapy when the symptoms abate, and Patient should notify her physician if burning, irritation, or any signs of an allergic reaction occur.
- When vaginal inserts (i.e., compressed tablets) are prescribed, the pharmacist should instruct the woman to dip the tablet into water quickly before insertion.
- Because it is formulated from an oleaginous bases , it could be messy .

# VAGINAL INSERTS/ TABLETS



# VAGINAL INSERTS

- Vaginal tablets are more widely used than vaginal suppositories, because they are easier to manufacture, more stable, and less messy.
- They are usually ovoid, prepared by tablet compression and are accompanied in their packaging with a plastic inserter, a device for easy placement of the tablet within the vagina.
- Vaginal tablets contain the same types of anti-infective and hormonal substances as vaginal suppositories.
- The tablets are intended to disintegrate within the vagina, releasing their medication.
- Some vaginal inserts are capsules of gelatin containing medication to be released intra-vaginally.

# 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**

