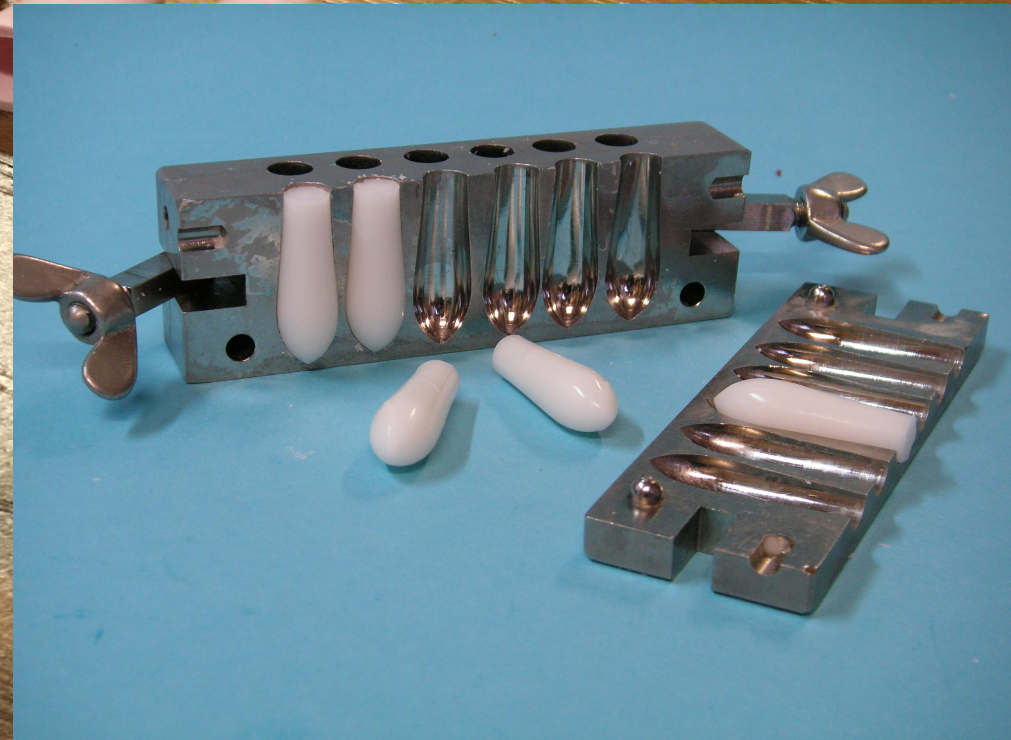
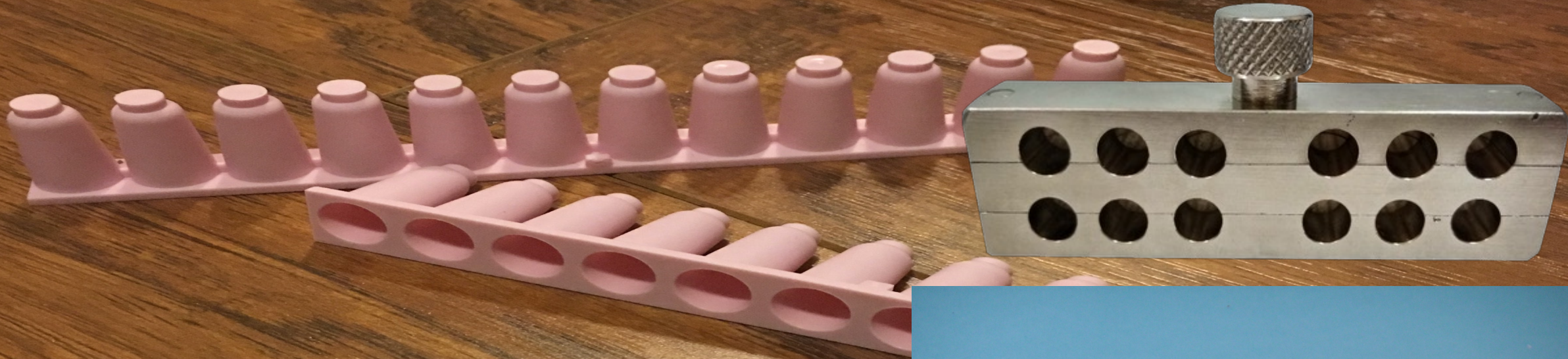


Suppositories Dosage Forms

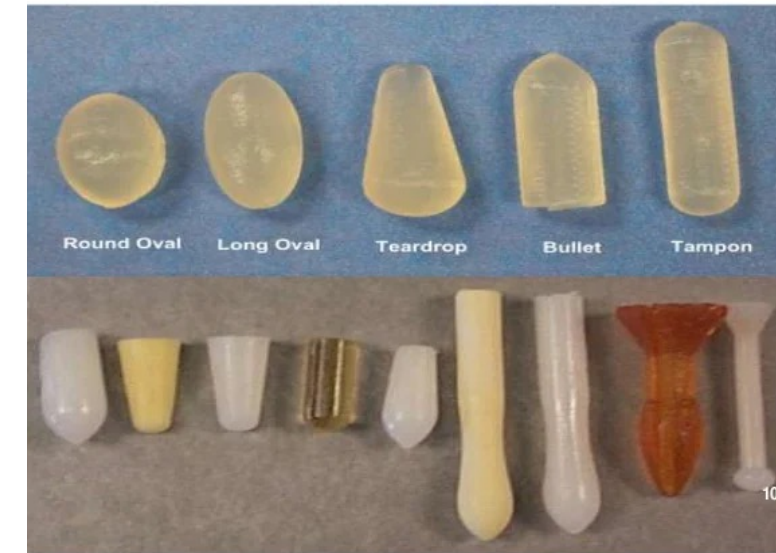
Mohammed Albarki, PhD.



Suppository

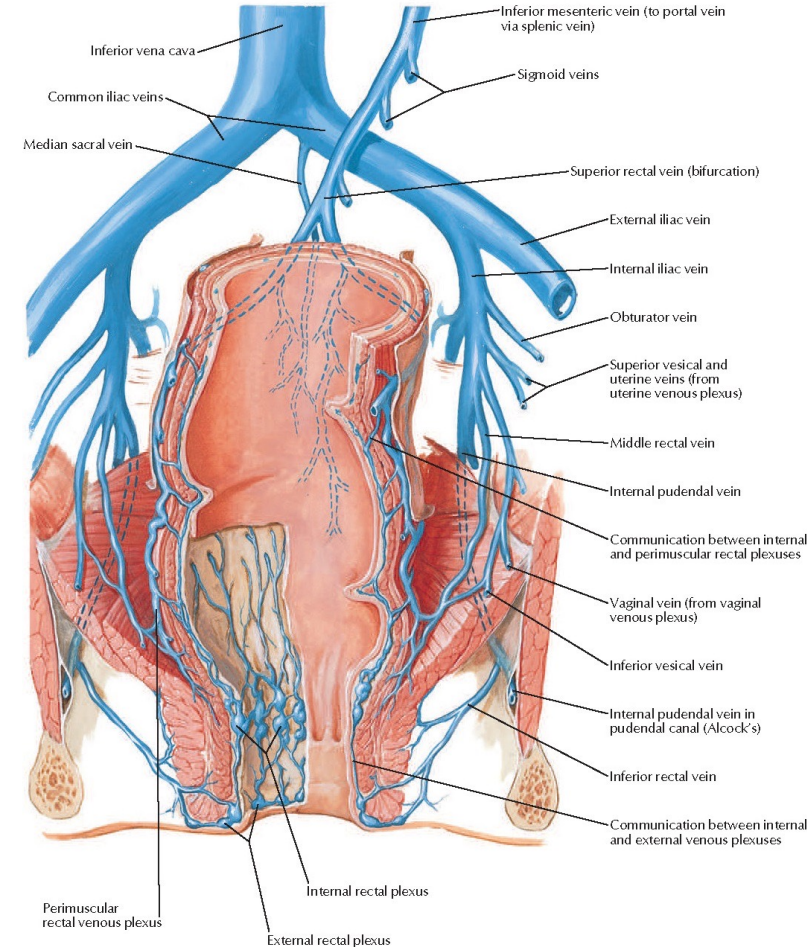
- Dosage forms are designed for application into the body orifices. They usually **melt /soften /dissolve** at **body temperature**.
- Manufactured in a variety of shapes to meet treatment requirements such as drug properties, patient age, drug release requirements, and routes of administration.
- Rectal Suppositories: weigh about ~ 2 g for adult suppositories and ~ 1g for infants and usually tapered ends to resemble a torpedo.
- Vaginal Suppositories (Pessaries) ~ 5 g and usually molded in oviform shape
- Urethral Suppositories (Bougies) weigh about 4 g and pencil shape

SHAPE OF SUPPOSITORIES



Advantages

1. Treatment of **local** conditions in the area of administration such as hemorrhoids.
- When intended for **systemic** application:
 1. **Partially** bypass first-pass hepatic metabolism (**superior** hemorrhoidal vein transports drug to the liver, the **middle and inferior** hemorrhoidal veins bypass the liver). More than 50-70 % of drugs bypass portal circulation.
 2. Avoid **degradation** of the drug in the stomach
 3. Useful for patients with **nausea or vomiting**
 4. Avoid issues of **taste**.
 5. Useful for administration to patients with **trouble swallowing** (geriatric, infants, terminally ill)



Disadvantages

1. Not preferred by **patients**
2. **Small fluid volume** available in the colon for dissolution of the base and release of the drug
3. **Small area** for absorption compared to oral administration.
4. **Variable** retention times due to expulsion can lead to variable absorption.
5. Not suitable for patients with **Diarrhea**.

Ideal Suppository Base

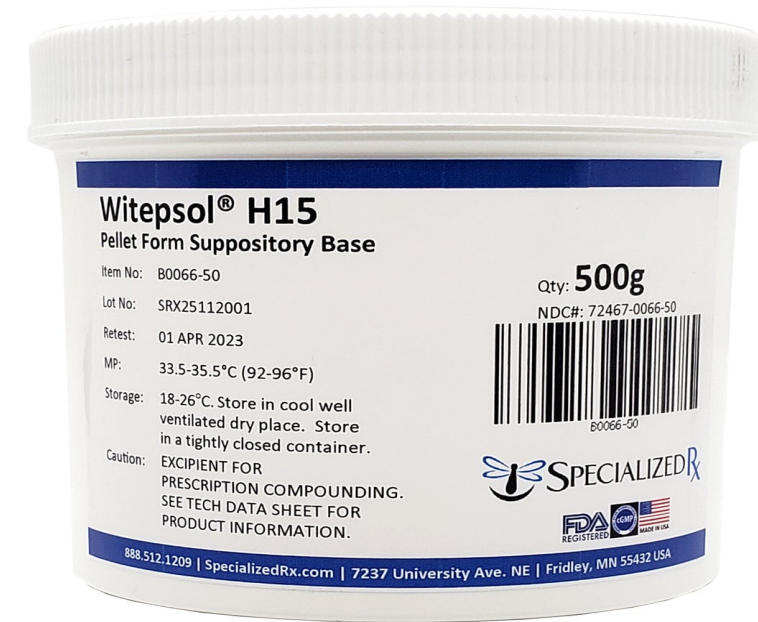
1. Completely **non-toxic** and should not irritate the surrounding tissues.
2. **Inert** material.
3. Melt and/or **dissolve at physiological temperature** (~36°C).
4. **Compatible** with a wide variety of drugs.
5. Has **no metastable** form.
6. **Shrink slightly upon** cooling to easily remove from the mold.
7. **Has wetting and emulsifying properties.** Because of the limited amount of fluid in the rectal area so is needed to enhance drug release and dissolution.
8. Allows a **good amount of water** to be added to the base.
9. **Stable** on storage (no change in color, odor, or drug release pattern)
10. **Fits all suppositories** manufacturing techniques.

Types of Suppositories Bases: Fatty Bases

- **Cocoa Butter** (Theobroma Oil).
- **Advantages:**
 1. Smells like chocolate and has a melting point of $\sim 35^{\circ}\text{C}$
 2. **Widely** used base in manufacturing suppositories.
 3. Inert, non-toxic, and melts at body temperature.
- **Disadvantages:**
 1. Can melt in warm temperatures.
 2. Can become **rancid** when aging (have a bad smell and taste). So needs to be stored **in a cool, dry place** and protected from light.
 3. Can exist in different '**polymorphic forms**' which can turn into a polymorph that has **a lower** melting temperature or can affect the drug release rate. This can happen by **rapidly** cooling the melted base.
 4. Preparation requires care to ensure that 'low melting' forms are not produced.
 5. **Poor emulsification** capability so **no** large quantities of water can be added

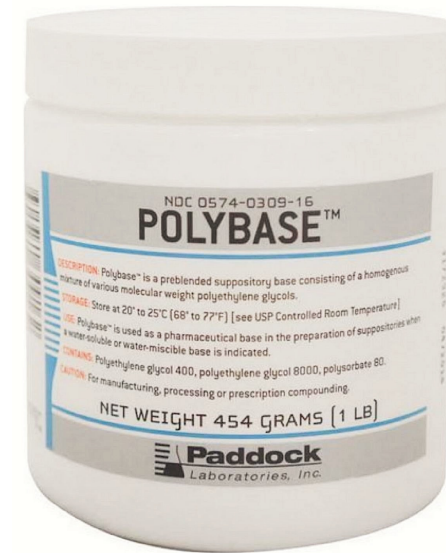
Cocoa Butter Substitute

- Hydrogenated vegetable oil bases :
- semisynthetic bases which are modified to allow for controlling properties like melting point, brittleness, and solubility.
- Drug release is facilitated by the **melting** of the base upon administration.
- Examples: Witepsol®,
- Drugs **dissolved** in the fatty base would **partition** into the surrounding aqueous fluids and then be available for absorption
- Drug particles **dispersed** in the fatty base would be released from the molten matrix, dissolve in the surrounding aqueous fluids, and be available at the site of absorption



Hydrophilic Bases: The Polyethylene Glycol Bases

- **Mixtures** of polyethylene glycols (PEG) of different molecular weights to obtain the right consistency and properties. So these bases can be **designed** for immediate or slow release of active ingredients.
- If the base mixture doesn't contain water → , **possible irritation** to the rectal mucosa can happen. This irritation or “sting” is caused because water is **drawn** from the rectal mucosa since this base type has some water solubility.
- → To **eliminate** this irritation, the suppository should be **dipped in water** before insertion.
- Drug release is facilitated by the **dissolution of the base (not melting)** and hence can be influenced by the volume of liquid present in the rectum.
- Example: Polybase® contains water-soluble ingredients polyethylene glycol and polysorbate (surfactant).



Hydrophilic Bases: Glycerin Suppositories

- Do **not melt** in body temperature, but rather **dissolve** in the secretions of the body cavity in which they are inserted.
- Solution time is regulated by the proportion of glycerin/gelatin/water.
- Can cause mucosal irritation due to the osmotic effect.
- **Mold growth** can happen in this type of suppositories so it should be stored in a cool place and often contain preservatives.
- Glycerinated Gelatin base **Example:**
 - Gelatin70 g
 - Glycerin20 g
 - Drug and Purified Water.....10 g.
 - Gel base, used for vaginal suppositories



Other Formulation Ingredients

- **Wetting agents:** Surfactants can be incorporated **to** facilitate the dispersion of the API in the base during the preparation and also **to** facilitate the dissolution of the drug upon administration.
- **Viscosity modifiers:** For example aluminum monostearate, cetylalcohol, and colloidal silica. These agents thicken the suppository base to the desired viscosity. They help to **keep the active ingredient suspended** till the product has cooled and set.
- **Drug Incorporation aids:** Drug incorporation into the suppository base can be facilitated with the use of appropriate oils or water.
- **Mechanical Strength:** PEG bases have a tendency to fracture. The use of adjuvants like polysorbates or propylene glycol can make them less brittle.
- **Chemical stabilizers and anti-microbial preservatives.**

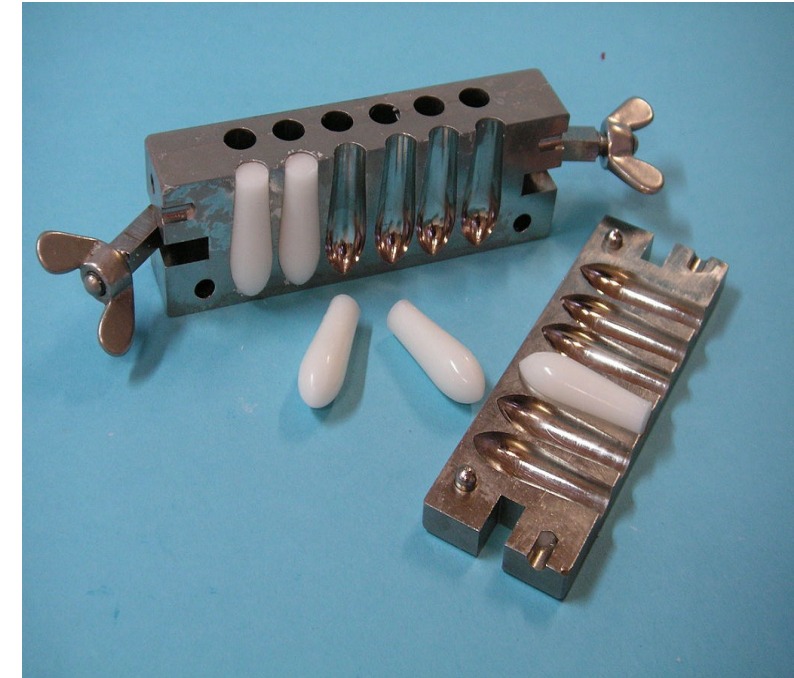
Suppositories Preparation: Hand Rolling

- Simplest and oldest method.
- A **cocoa butter** base can be used.
- **Procedure:**
 - The base is grated and mixed with the active ingredients.
 - The plastic mass is rolled into a cylinder and cut on a tile to yield the appropriate number of pieces.
 - The suppositories are then shaped by hand if required.
- Starch or talcum powder on the rolling surface and hands prevent the mass from adhering.
- No special calculations are required.
- The final product may **not** look very elegant.
- This method is for **small-scale** production



Suppositories Preparation: Pour Molding

- The **most commonly** used method both for small and large-scale production
- **Procedure:**
 - Melt the suppository base (preferably on water steam to avoid local overheating).
 - The drug is uniformly distributed in the base by dispersion or dissolution.
 - The molten mixture is poured into a mold of fixed volume (overfill to allow for contraction).
 - Allow to cool and congeal.
 - Trim off excess material on top of the mold.
 - Remove the final suppositories from the mold.



Evaluation of Suppositories

- General Appearance: color, check for absence of fissuring, sedimentation etc.
- Uniformity of the mix.
- Dissolution test.
- Content uniformity.
- Melting range test is performed to check physical stability
- Fragility test to make sure that supp can be packed and shipped with minimal breakage.