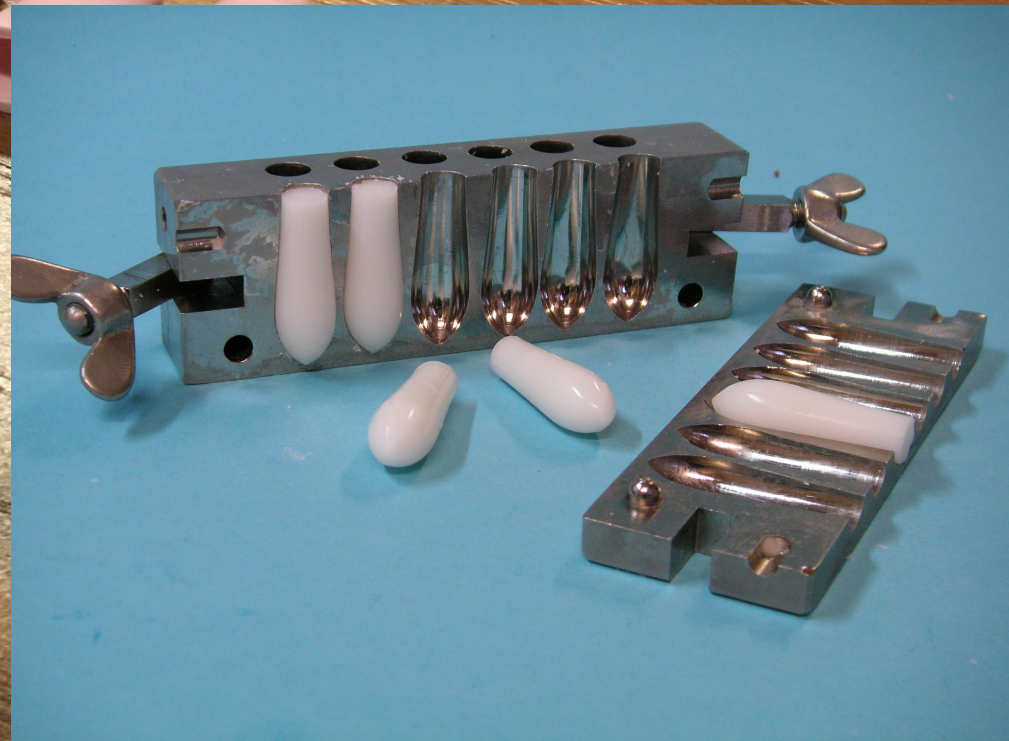
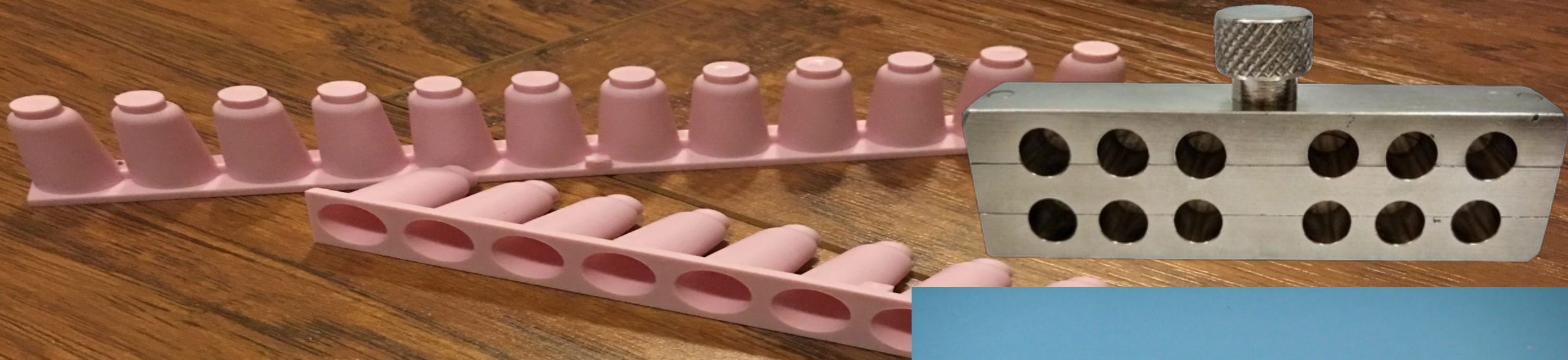




Suppositories Dosage Forms

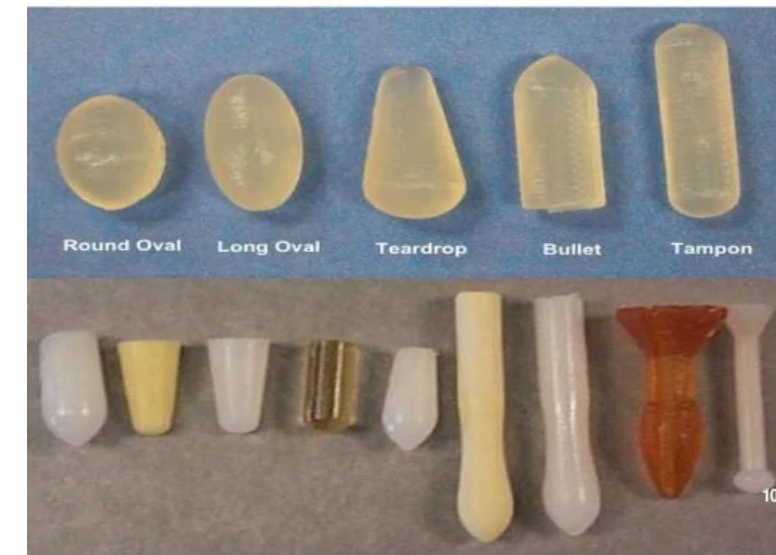
Mohammed Albarki, BSP Pharm, PhD.



Suppository

- Dosage forms are designed for application into the body orifices. They usually **melt /soften /dissolve** at **body temperature**.
- Suppository comes from a Latin word meaning “to place under”.
- 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:

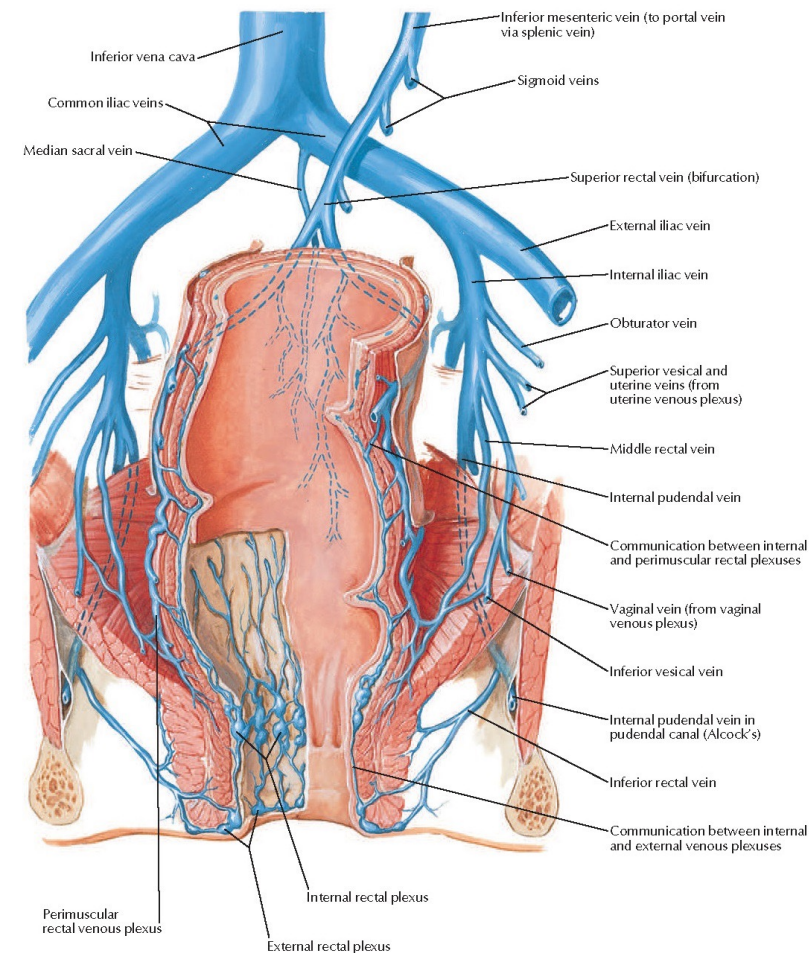
1. **Partially** bypass first-pass hepatic metabolism (**superior** hemorrhoidal vein transports drug to the liver, the **middle and inferior** hemorrhoidal veins bypass the liver). More than 50-70 % of drugs bypass portal circulation.

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**

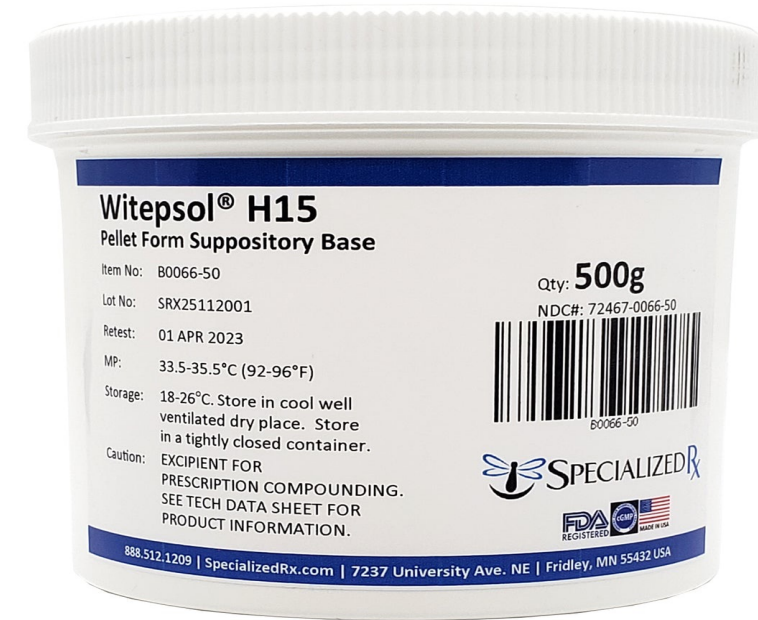


- **Cocoa Butter** (Theobroma Oil).
- **Advantages:**
 1. Smells like chocolate and has a melting point of **~35°C**
 2. **Widely** used base in manufacturing suppositories.
 3. Inert, non-toxic, and melts at body temperature.
- **Disadvantages:**
 1. Can melt in warm temperatures.
 2. Can become **rancid** 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**



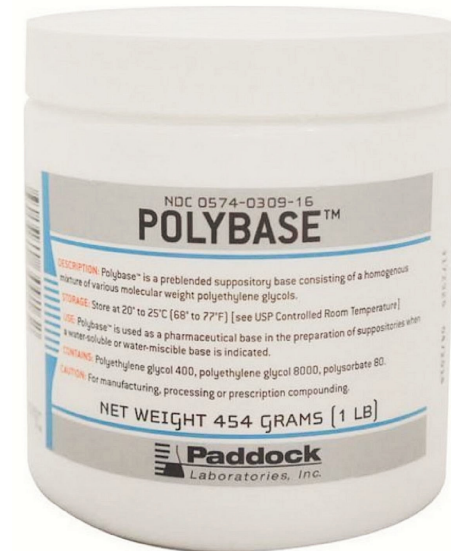
- **Hydrogenated** vegetable oil bases :
- **semisynthetic** bases which are modified to allow for controlling properties like melting point, brittleness, and solubility.
- Drug release is facilitated by the **melting** of the base upon administration.
- Examples: Witepsol® , Fattibase® , Supposire®
- 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 so that **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** prior to 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

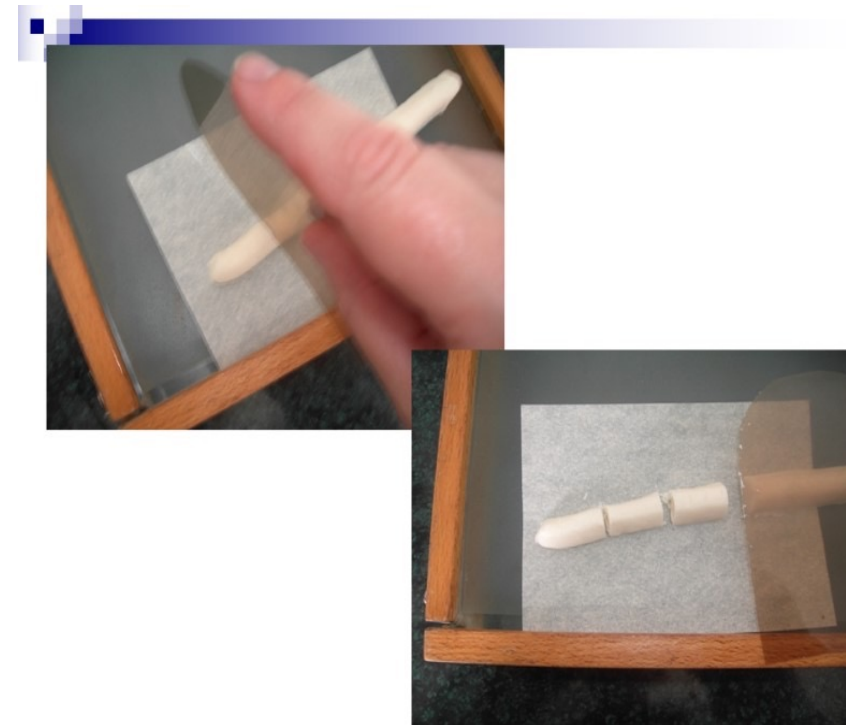


- **Wetting agents:** Surfactants can be incorporated **to** facilitate the dispersion of the API in the base during the preparation and also **to** facilitate the dissolution of the drug upon administration.
- **Viscosity modifiers:** For example aluminum monostearate, cetylalcohol, and colloidal silica. 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. 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**

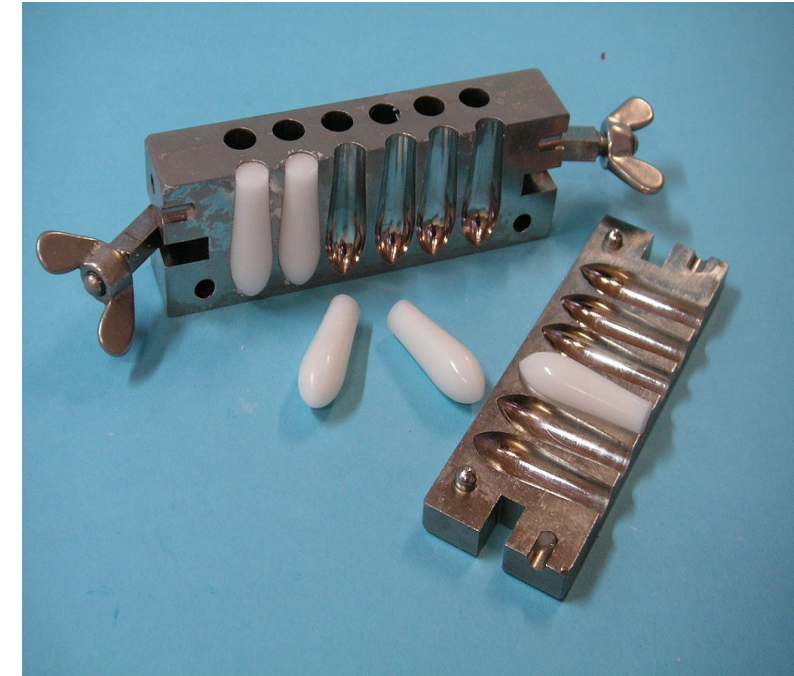


Suppositories Preparation: Pour Molding



- The most commonly used method both for small and large-scale production
- 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 (overflow 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.

- Caution while using heat-sensitive materials.
- Special molds are required.



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.