**PERCUTANEOUS DOSAGE FORMS!**

- **Liquid reservoir**: readily diffuses; but the rate controlling step is not the membrane itself, it's the stratum corneum
- **Solid reservoir**: equal distribution of oil/water; polar & nonpolar; e.g. nitroglycerin
- **Adhesive**: like bandaids! The drug is imbedded into the adhesive
- **Drugs that work**: alkaloids, bases, and neutral compounds (none acidic, very few in practice)

**OINTMENTS**
- Greasy, oily, not water soluble
- Hydrocarbon based (hence the oiliness)
- Composed of petrolatum, sometimes high melting waxes (e.g. cetyl alcohol) with mineral oil
- Plastibase = polyethylene + mineral oil
- Prevents TEWL by forming an occlusive covering over skin prevent $H_2O$ evaporation
- w/o emulsions: absorption base: Aquaphor (has emulsifiers)

**CREAMS**
- Water soluble/washable, leaves a thin film
- o/w emulsions
- To $\uparrow$ viscosity, add more oil or higher mp oil (e.g. cetyl alcohol)
- To $\downarrow$ viscosity, add mineral oil (linament)
- Vanishing cream = stearic acid

**COUNSELING POINTS**

*Percutaneous*:
- Shower first!
- If using with topical steroids, it will cause vasoconstriction and decrease the absorption of the drug in the patch
- Take off the old patch before putting on the new patch

*Suppositories*:
Evacuate bowel first, clear up the junk!

**STRATUM CORNEUM**
- Barrier layer
- Comprised primarily of keratin
- 10 um in thickness
- Dead
- Use keratolytics to remove s. corneum

**VIA BLE EPIDERMIS**
- Living tissue
- Includes s. germinativum
- 100 um in thickness

**DERMIS**
- Primarily collagen, reticulin, and elastin
- Flexible due to elastin
- Semi-gel matrix of mucopolysaccharide ground substance
- Contains network of nerves, microcirculation, and lymphatic circulation, so important for drug distribution to body

**EUTECTIC MIXTURE**
Mixture of chemical compounds that forms a single chemical composition but has a lower melting point than any one of its constituents. For example, Lidocaine/prilocaine is a eutectic mixture of equal quantities. Separately, lidocaine and prilocaine are solid bases. When mixed together in equal quantities by weight, however, they form a eutectic mixture — that is, the melting point of the mixture is lower than the melting points of the individual components. This allows higher concentrations of anaesthetic to be formulated into the preparation and maintained during application. Eutectic mixtures of drugs or mixtures of agents have a tendency to liquefy when admixed.
### Three Types of Suppositories

1. **Rectal**
   - Mostly for hemorrhoidal remedies
   - Good for patients with nausea and vomiting
   - May contain legend drugs
   - Most common type of suppository
   - Form: Mostly for hemorrhoidal remedies
   - Use: Rectal, pH and content vary with age, menstrual cycle, location w/in vagina matters
   - Vehicle: Cocoa butter: immiscible, high mp
   - Uses: PEG (water soluble), absorption is erratic
   - Site pH: Affects disintegration, dissolution, and drug partitioning into rectal fluid vs. tissues
   - Drug pKa: Henderh-Halselbalch! Don’t want ionized drug

2. **Vaginal**
   - Tear drop shaped (globular/oviform)
   - Weighs 4 to 5 grams
   - Similar to troches
   - Absorption is erratic
   - Polyethylene Glycols (PEGs)
   - Water soluble
   - Does not depend on body temp to melt
   - Cannot hand roll
   - To make: fusion → molding
   - Heat above mp to ↓fissuring caused by crystallization, will contract when cool

3. **Urethral**
   - Also called “bougies” or “inserts”
   - Shorter for women (50mm, 2g), longer for men (125mm, 4g)
   - Purpose: to get some of the drug into the bladder to treat infections

### Factors Affecting Absorption

<table>
<thead>
<tr>
<th></th>
<th>Rectal</th>
<th>Vaginal</th>
<th>Urethral</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physio</strong></td>
<td>↓Fluid ↓buffering, neutral pH, mucous/lipoidal epithelium</td>
<td>↓Fluid (&lt;rectum), pH and content varies with age, menstrual cycle, location w/in vagina matters</td>
<td>Small diameter, variable in length, least amount of fluid</td>
</tr>
<tr>
<td><strong>Vehicle</strong></td>
<td>Cocoa butter: immiscible, high mp</td>
<td>Use PEG (water soluble), absorption is erratic</td>
<td>Use PEG (water soluble), absorption is even more erratic than in vagina</td>
</tr>
<tr>
<td><strong>Site pH</strong></td>
<td>Affects disintegration, dissolution, and drug partitioning into rectal fluid vs. tissues</td>
<td>Very variable</td>
<td>Affects disintegration, dissolution, and drug partitioning</td>
</tr>
<tr>
<td><strong>Drug pKa</strong></td>
<td>Henderh-Halselbalch! Don’t want ionized drug</td>
<td></td>
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<tr>
<td><strong>Lipid Solubility</strong></td>
<td>Henderson-Halselbalch! Don’t want ionized drug</td>
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</tbody>
</table>

 Absorption is by non-ionic passive diffusion (just like the percutaneous dosage forms)

### Cocoa Butter
- Theobroma oil, natural triglyceride (very greasy, 40% unsaturated fatty acids)
- Immiscible with body fluids, melts at body temperature, ↓absorption overall
- Don’t overheat! Will denature proteins (β crystalline form) and won’t solidify when cooled
- ↑viscosity and to help solidify: add higher mp waxes

### Polyethylene Glycols (PEGs)
- Water soluble
- Doesn’t depend on body temp to melt
- Cannot hand roll
- To make: fusion → molding
- Heat above melt to ↓fissuring caused by crystallization, will contract when cool

### Glycerinated Gelatin
- Mostly for vaginal use (sometimes rectally as laxative, ↑conc. of gelatin so it’s firmer)
- Glycerin = plasticizer (or in the case of rectal use, as the laxative at higher concentrations)
- Cannot hand roll, need a mold to make
- Needs preservatives (e.g. methyl paraben, propyl paraben)

### Methods of Preparation:
- Hand rolled
- Compression molding
- Fusion: Trial method
- Fusion: Double pour method