

Suppositories and Inserts

Chapter 12

Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems,
9th Edition

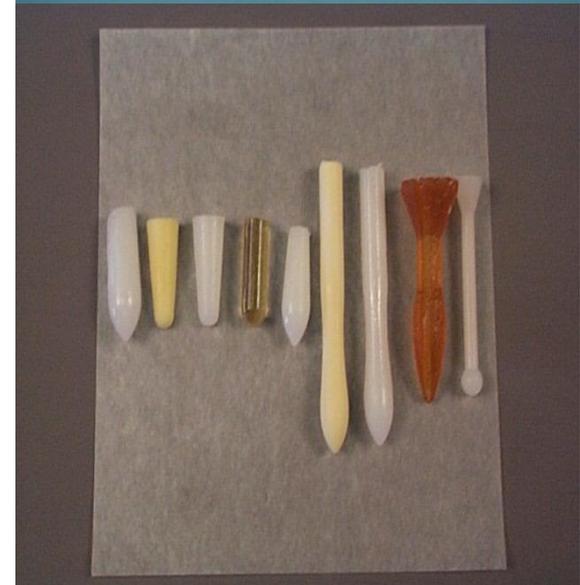
SUPPOSITORIES

- **Suppositories are solid dosage forms intended for insertion into body orifices where they melt, soften, or dissolve and exert local or systemic effects.**
- **The derivation of the word suppository is from the Latin supponere, meaning “to place under,” as derived from sub (under) and ponere (to place).**
- **Thus, suppositories are meant both linguistically and therapeutically to be placed under the body, as into the rectum**
- **Suppositories are commonly used rectally and vaginally and occasionally urethrally**
- **They are used to deliver both systemically and locally acting medications**

SUPPOSITORIES

SHAPES

- Suppositories have various shapes and weights.
- The shape and size of a suppository must be such that it can be easily inserted into the intended orifice without causing undue distension, and once inserted, it must be retained for the appropriate period.
- Rectal suppositories are inserted with the fingers, but certain vaginal suppositories, particularly the inserts, or tablets prepared by compression, may be inserted high in the tract with the aid of an appliance.



Rectal suppositories

- Rectal suppositories are usually about 32 mm (1.5 in.) long, are cylindrical, and have one or both ends tapered. Some rectal suppositories are shaped like a bullet, a torpedo, or the little finger.
- Depending on the density of the base and the medicaments in the suppository, the weight may vary.
- Adult rectal suppositories weigh about 2 g when cocoa butter (theobroma oil) is employed as the 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.



Vaginal suppositories

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



Urethral suppositories

- Urethral suppositories, also 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, although this may vary. When cocoa butter is employed as the base, these suppositories 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
- Urethral suppositories may be
- antibacterial or
- a local anesthetic preparative for a urethral examination.



Fate of the suppository

- **Once inserted, the suppository base melts, softens, or dissolves, distributing its medicaments to the tissues of the region.**
- **These medicaments may be intended for retention within the cavity for local effects, or they may be intended to be absorbed for systemic effects.**
- **They may exhibit the effect immediately or sustain the release of the drug such as 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.**

Local rectal suppositories

- Rectal suppositories intended for local action are most frequently used to relieve

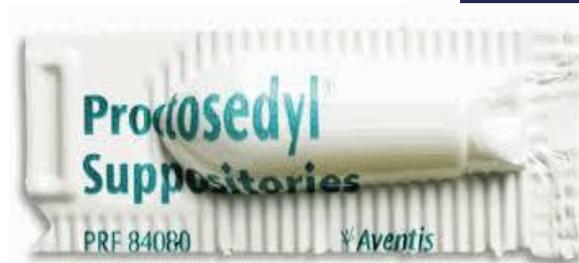
1- constipation

A popular laxative, glycerin suppositories promote laxation by local irritation of the mucous membranes, probably by the dehydrating effect of the glycerin on those membranes.



2- the pain, irritation, itching, and inflammation associated with hemorrhoids or other anoctal conditions.

Anti-hemorrhoidal suppositories frequently contain a number of components, including local anesthetics, vasoconstrictors, astringents, analgesics, soothing emollients, and protective agents.



Local vaginal suppositories

- Vaginal suppositories or inserts intended for local effects are employed mainly as
 1. contraceptives, the drugs used are nonoxynol-9
 2. antiseptics in feminine hygiene, trichomonacides to combat vaginitis caused by *Trichomonas vaginalis*
 3. specific agents to combat an invading pathogen. Most commonly, antifungals to treat *Candida* (*Monilia*) *albicans*, and anti-infectives/antibiotics directed at other microorganisms



Bayer

Canesten® 1

Broad-spectrum antimycotic with fungicidal and trichomonacidal action
Vaginal tablet for the 1-day treatment.

1 vaginal tablet of 0.5g with applicator

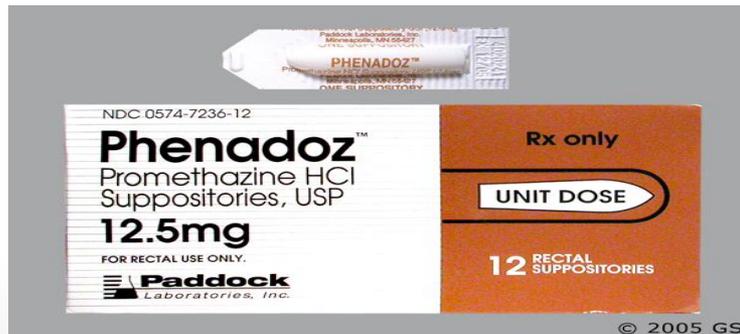
Prescription only.
Insert into the vagina as directed by your doctor.
Do not store at temperatures above 30°C.

Systemic effect of rectal suppositories

- 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.**
- Among the advantages over oral therapy of the rectal route for systemic effects are these:
 - (a) Drugs destroyed or inactivated by the pH or enzymatic activity of the stomach or intestines need not be exposed to these destructive environment
 - (b) Drugs irritating to the stomach may be given without causing such irritation.
 - (c) Drugs destroyed by portal circulation may bypass the liver after rectal absorption (drugs enter the portal circulation after oral administration and absorption).
 - (d) The route is convenient for administration of drugs to patients who are unable or unwilling to swallow medication.
 - (e) It is an effective route in the treatment of patients with vomiting.

Examples of drugs administered rectally for systemic effect

- (a) prochlorperazine and chlorpromazine for the relief of nausea and vomiting and as a tranquilizer;
- (b) oxymorphone HCl for opioid analgesia;
- (c) ergotamine tartrate for the relief of migraine syndrome;
- (d) indomethacin, a nonsteroidal anti-inflammatory analgesic and antipyretic; and
- (e) ondansetron for the relief of nausea and vomiting



SOME FACTORS OF DRUG ABSORPTION FROM RECTAL SUPPOSITORIES

- **The dose of a drug administered rectally may be greater than or less than the dose of the same drug given orally, depending on such factors as**
- **the physicochemical nature of the drug and**
- **its ability to traverse the physiologic barriers to absorption,**
- **and the nature of the suppository vehicle and its capacity to release the drug and make it available for absorption.**

Rectal absorption

- The factors that affect rectal absorption of a drug may be divided into two main groups:
 - (a) physiologic factors and
 - (b) physicochemical factors of the drug and the base

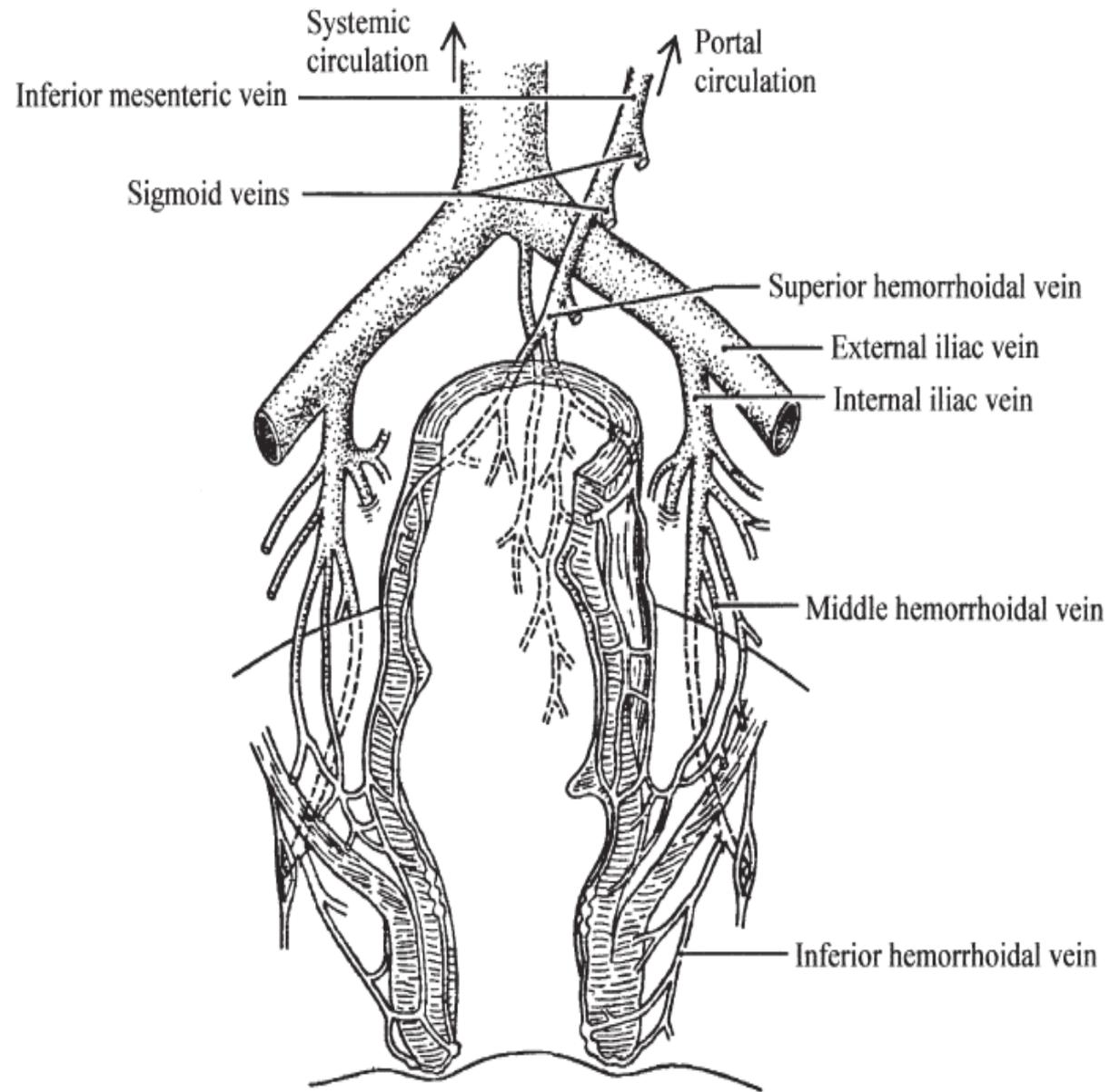


Figure 10. Anatomy of colonic and hemorrhoidal veins.

PHYSIOLOGIC FACTORS

- The human rectum is approximately 15 to 20 cm long.
- When empty of fecal material, the rectum contains only 2 to 3 mL of inert mucous fluid. (low volume of fluid available)
- In the resting state, the rectum is not motile; there are no villi or microvilli on the rectal mucosa .
- However, there is abundant vascularization of the submucosal region of the rectum wall with blood and lymphatic vessels.
- Among the physiologic factors that affect drug absorption from the rectum are the colonic contents,
- and the pH and lack of buffering capacity of the rectal fluids.

Colonic Content

- When systemic effects are desired, greater absorption may be expected from a rectum that **is void than from one that is distended with fecal matter.**
- A drug will obviously have greater opportunity to make contact with the absorbing surface of the rectum and colon in an **empty rectum.**
- Therefore, when **deemed desirable**, an **evacuant enema may be administered and allowed to act before the administration of a suppository of a drug to be absorbed.**
- Other conditions, such as **diarrhea, colonic obstruction** due to tumorous growths, and **tissue dehydration** can all **influence the rate and degree of drug absorption from the rectum**

Circulation Route

- Drugs absorbed **rectally**, unlike those absorbed after oral administration, **bypass the portal circulation during their first pass into the general circulation**, thereby enabling drugs otherwise destroyed in the liver to exert systemic effects.
- The lower hemorrhoidal veins surrounding the colon receive the absorbed drug and initiate its circulation throughout the body, bypassing the liver.
- **Lymphatic circulation also assists in the absorption of rectally administered drugs**

pH and Lack of Buffering Capacity of the Rectal Fluids

- Because rectal fluids are essentially neutral in pH (7) and have **no effective buffer capacity**, the form in which the drug is administered **will not generally be chemically changed by the environment**.
- 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.**

PHYSICOCHEMICAL FACTORS OF THE DRUG AND SUPPOSITORY BASE

- Physicochemical factors of **the drug** include such properties as:
 1. the **relative solubility** of the drug in lipid and in water and
 2. the **particle size of a dispersed drug**, and surface properties
 3. **Amount** of drug
 4. **pKa of the drug**
- Physicochemical factors of **the base** include:
 1. its ability to melt, soften, or dissolve at body temperature,
 2. its ability to release the drug substance, and
 3. its hydrophilic or hydrophobic character (composition of the base)
 4. Rheological properties

Thank You