

CHAPTER 8-9

-Vaginal Administration of drugs. Characteristics of Vaginal membrane. Vaginal disorders. Dosage forms. Factors influencing vaginal absorption.

- The Ear Administration of drugs. Pharmaceutical forms. Factors affecting the drugs absorption.

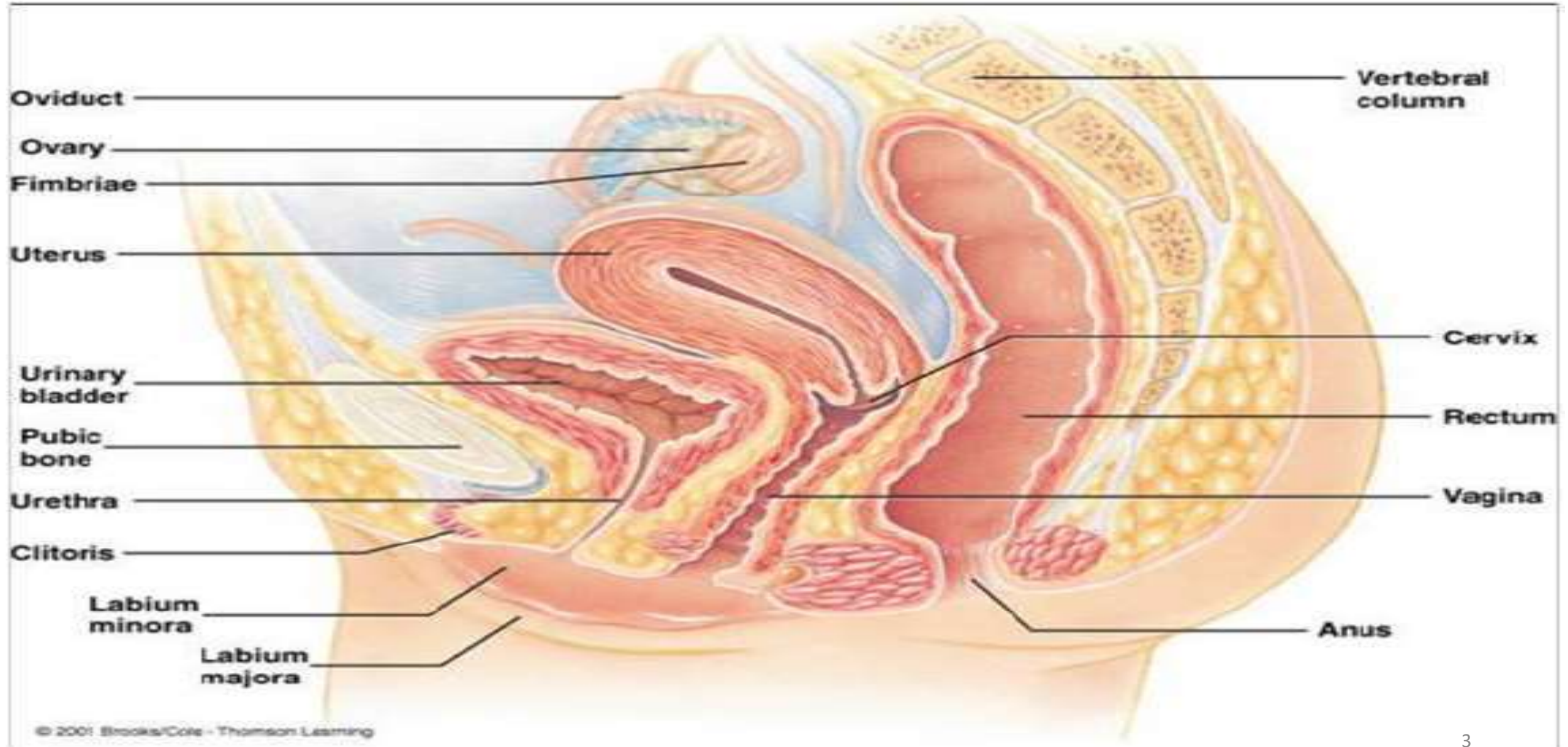
□ The vaginal cavity acts as a favorable site for drug administration.

- Avoidance of first pass effect.
- Large permeation area.
- Rich vascularization and
- Relatively low enzymatic activity.

□ The vaginal cavity has a potential for:

- Non-invasive.
- Controlled transmucosal delivery of both local and systemic therapeutically active compounds.

Anatomy & Physiology of Vagina



❑ **Anatomy and Physiology of Vagina.**

- The vagina in the adult premenopausal female is approximately 7-8 cm in length and 2 cm wide, shrinking in the postmenopausal female to approximately 4.5-6 cm in length and 1-1.5 cm in width.
- Normal pH of the vagina in premenopausal women ranges from 4 to 5, and rises to almost 7 in the post-menopausal female.
- The vagina is characterized by an **exceptional elasticity** and the surface area of the vagina is increased by numerous folds by **microridges** covering the epithelium cell surface.
- The vaginal wall consists of three layers:
 - ❑ The epithelial layer.
 - ❑ The muscular coat.
 - ❑ The tunica adventia.

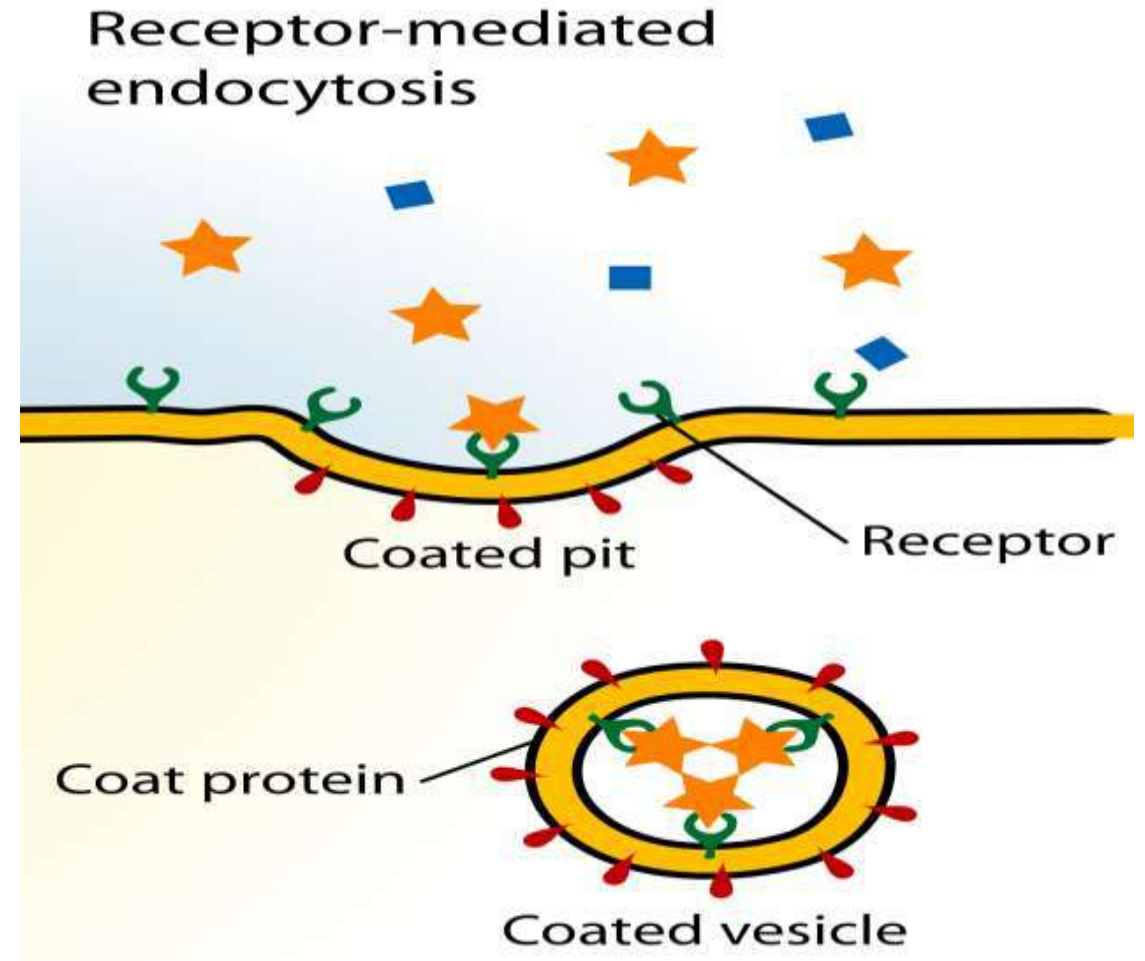
- The vagina has an **excellent elasticity** because of the presence of **smooth elastic fibers** in the muscular coat.
- Loose connective tissue of tunica adventia further increases the elasticity of this organ.
- The network of blood vessels that supply blood to the vagina include a plexus of arteries extending from the internal iliac artery, uterine, middle rectal and internal pudendal arteries.
- Drugs absorbed from the vagina does not undergo first-pass metabolism because blood leaving the vagina enters the peripheral circulation via a rich venous plexus, which empties primarily into the internal iliac veins.
- The vaginal epithelium has a **high activity of enzymes** that could potentially affect short- and long-term stability of intra-vaginal delivery systems and devices.

□ Absorption mechanisms

- **Transcellular** via concentration dependent diffusion through the cells,
- **Paracellular** mediated by tight junctions.
- **Vesicular** or receptor mediated transport.

• Absorption of drugs from vaginal delivery systems occurs in two **main steps**:

1. Drug dissolution in vaginal lumen.
2. And membrane penetration.



❑ **Applications of Vaginal Drug Delivery System**

- ❖ This route of drug administration is useful for vaginal immunization.
- ❖ Multi-cycle administration of vaginal contraceptive rings.
- ❖ Effective route for the treatment of HIV infection.
- ❖ Effective route for the treatment of local fungal infection.
- ❖ Effective for the delivery of hormones.

❑ **Advantages of vaginal drug delivery system**

- This route is the most preferred and targeted goal of new drugs and dosage forms, vaginal administration can be used as an alternative route in certain cases of therapeutic importance:

1. In cases of nausea and vomiting, the act of taking medication **orally** may induce emesis so that the drug is vomited before it is absorbed.

2. **Irritation to the stomach** and small intestine associated with certain drugs can be avoided.

3. **Hepatic first pass elimination** of high clearance drugs may be avoided partially.

4. Contact with digestive fluid is avoided, thereby **preventing enzymatic degradation of some drugs.**

5. Drug delivery can be **stopped** by removing the dosage form e.g. Vaginal rings.

6. Drugs, which traditionally are only given **parental**, may be administered vaginally either as such or in combination with absorption-promoting additives.
7. Rapid drug absorption and **quick onset** of action can be achieved.
8. Convenient for the patients, especially for those on **long-term therapy**, when compared with parenteral medication.
9. The vaginal **bioavailability** of smaller drug molecules is **good**.
10. The bioavailability of larger drug molecules can be improved by means of absorption enhancers or other approach.
11. **Self-medication** is possible.

❑ **Limitations of Vaginal Drug Delivery Systems**

1. Some of the drugs are sensitive at the vaginal pH.
2. Local irritation of some drugs.
3. Influence of sexual intercourses.
4. Gender specificity.
5. Personal hygiene.

Physiological Factors

changes in the thickness of epithelium layer

cyclic changes

changes in the hormones level

volume of vaginal fluid

alteration of vaginal pH

Sexual arousal

Physicochemical Factors

Lipophilicity

Ionization

Molecular weight

Surface charge

Chemical nature

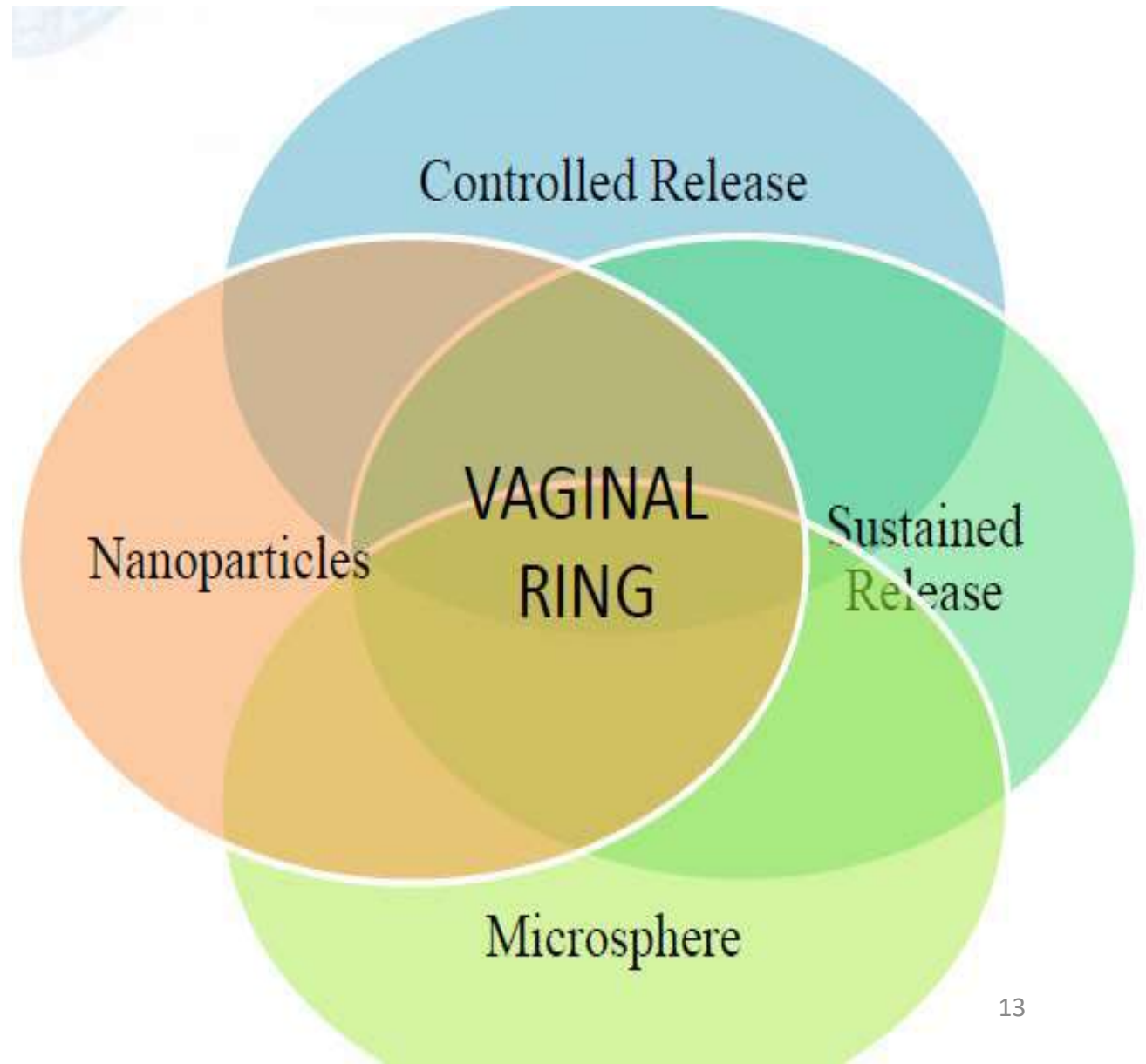
❖ **Improvement of vaginal absorption:**

1. Using of penetration enhancers → PEG.
2. Using of mucoadhesive polymers (increasing contact time between the dosage form and the vaginal membrane) → Carbopol.
3. Increasing vaginal blood flow → raising conc. Gradient across the vaginal mucosa.

❖ **Classification of Mucoadhesive vaginal drug delivery systems:**

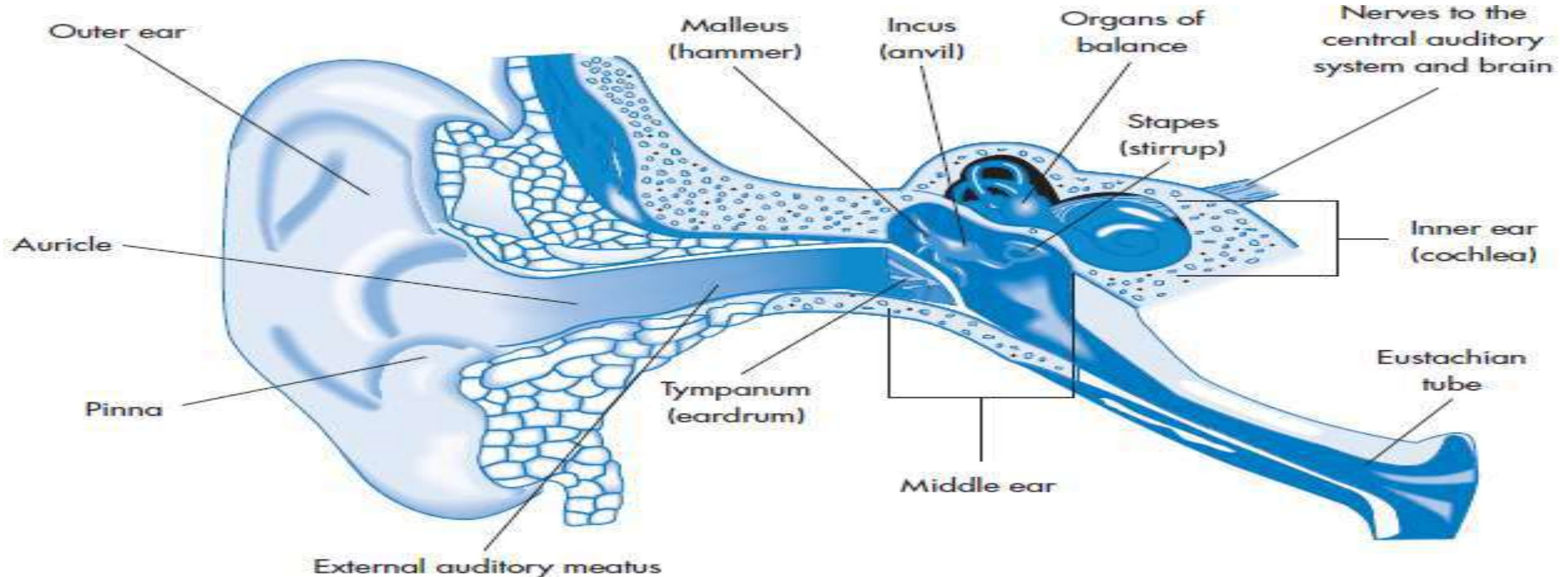
1. Mucoadhesive Gels .
2. Mucoadhesive Tablets.
3. Mucoadhesive Films.
4. Emulsion type mucoadhesive systems.
5. Pessaries or Suppositories.
6. Bioadhesive Vaginal Foams.

Novel Formulations



The ear (the aural route)

- Medications are administered to the ear only for local treatment.
- Drops and other vehicles administered to the ear will occupy the external auditory meatus, which is separated from the middle ear by the tympanic membrane.



- The sebaceous and apocrine glands of the mucosa secrete an oily fluid that, when mixed with exfoliated cells of the stratum corneum, forms the cerumen or wax composed of, inter alia, fats, fatty acids, protein, pigment, glycoprotein and water.
- The acidic environment of the ear skin surface (around pH 6) → a defense against invading microorganisms. Various ceruminolytic agents achieve their action by partially dissolving the wax.
- Several commercial ear drops contain surfactants such as poloxamers or sodium dioctyl sulfosuccinate (docusate sodium) to assist in the process.
- In otitis media, infection of the Eustachian tube is involved; antibiotic treatment is indicated along with oral analgesics.

- Active agents for local use:
 - ✓ Antibiotic – infections.
 - ✓ Antifungal agents → Nystatin
 - ✓ Anti-inflammatory.
 - ✓ Antiseptics.
 - ✓ Cleansing solutions.
 - ✓ Wax softeners.