ABSORPTION

University of Pécs

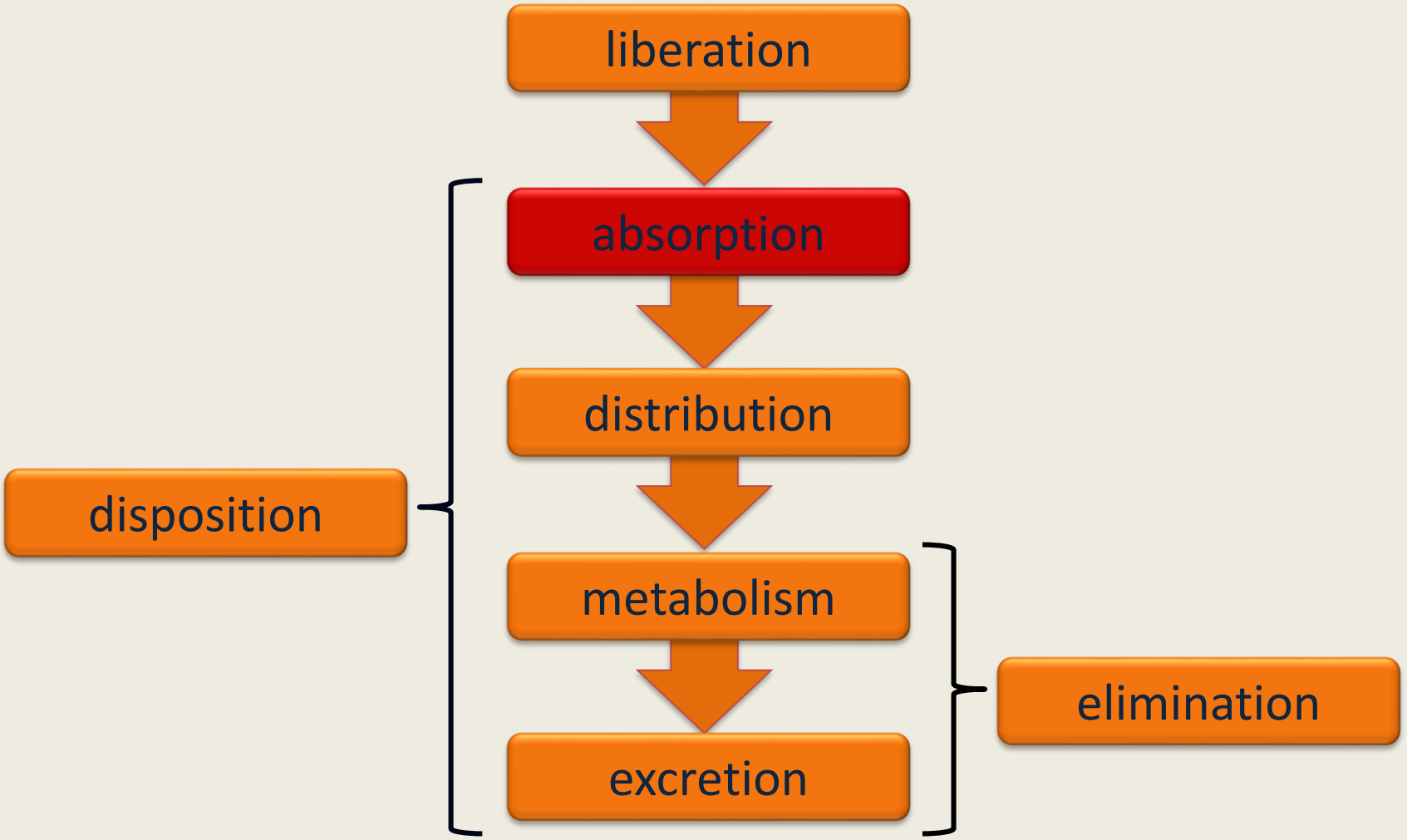
Institute of Pharmaceutical Technology and Biopharmacy

Absorption

Definition

Absorption is the movement of the API into the systemic circulation.

ADME → LADME


liberation
absorption
distribution
metabolism
excretion
disposition
elimination

Transport processes

Intercellular and intracellular processes

API can be absorbed by

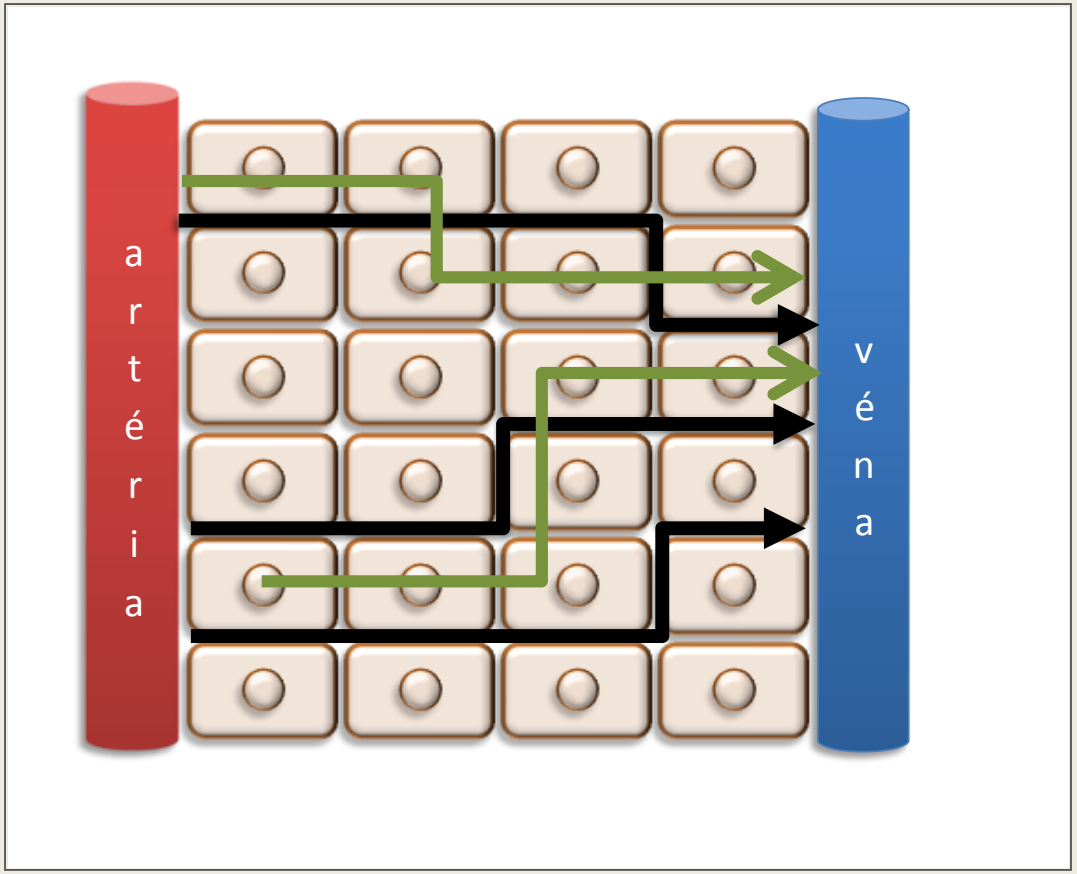
1. transcellular transport – across the cells

2. paracellular transport – through the gaps between the cells

Paracellular / transcellular transport

transcellular

paracellular



Transcellular/paracellular transport

Transcellular transport	transport without carrier molecule - passive diffusion - ionpair transport carrier-mediated transport - facilitated diffusion, - active transport endocytosis (phagocytosis, pinocytosis) exocytosis
Paracellular transport	filtration through pores

Paracellular transport

- Filtration through pores

It is determined by:
•Difference in pressure between the areas divided by the membrane
•Size of molecules
•Pore size

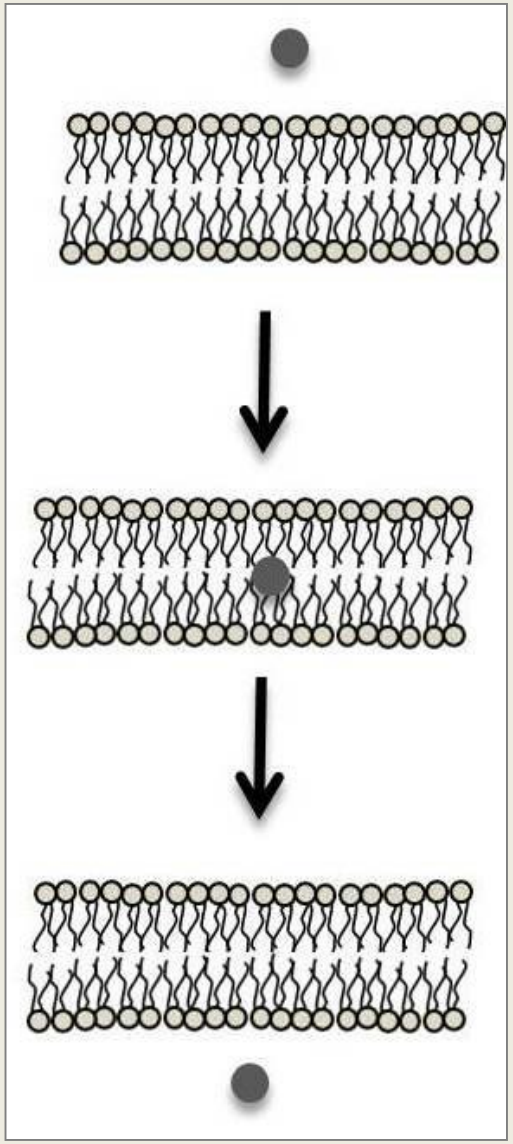
Substances: Ca ion, sugar, aminoacids, proteins

Passisve diffusion

The most frequent type of transport of APIs.

Apolar, non-ionised APIs can cross the membrane according to the concentration gradient.

This type of transport lasts until the equilibrium in concentration, it does not need energy.



Ionisation

Degree of ionisation of molecules is calculated by the Henderson-Hasselbalch equation. Using this formula the ratio of ionised and non-ionised amount of molecules can be determined which highly depends on the pH of environment.

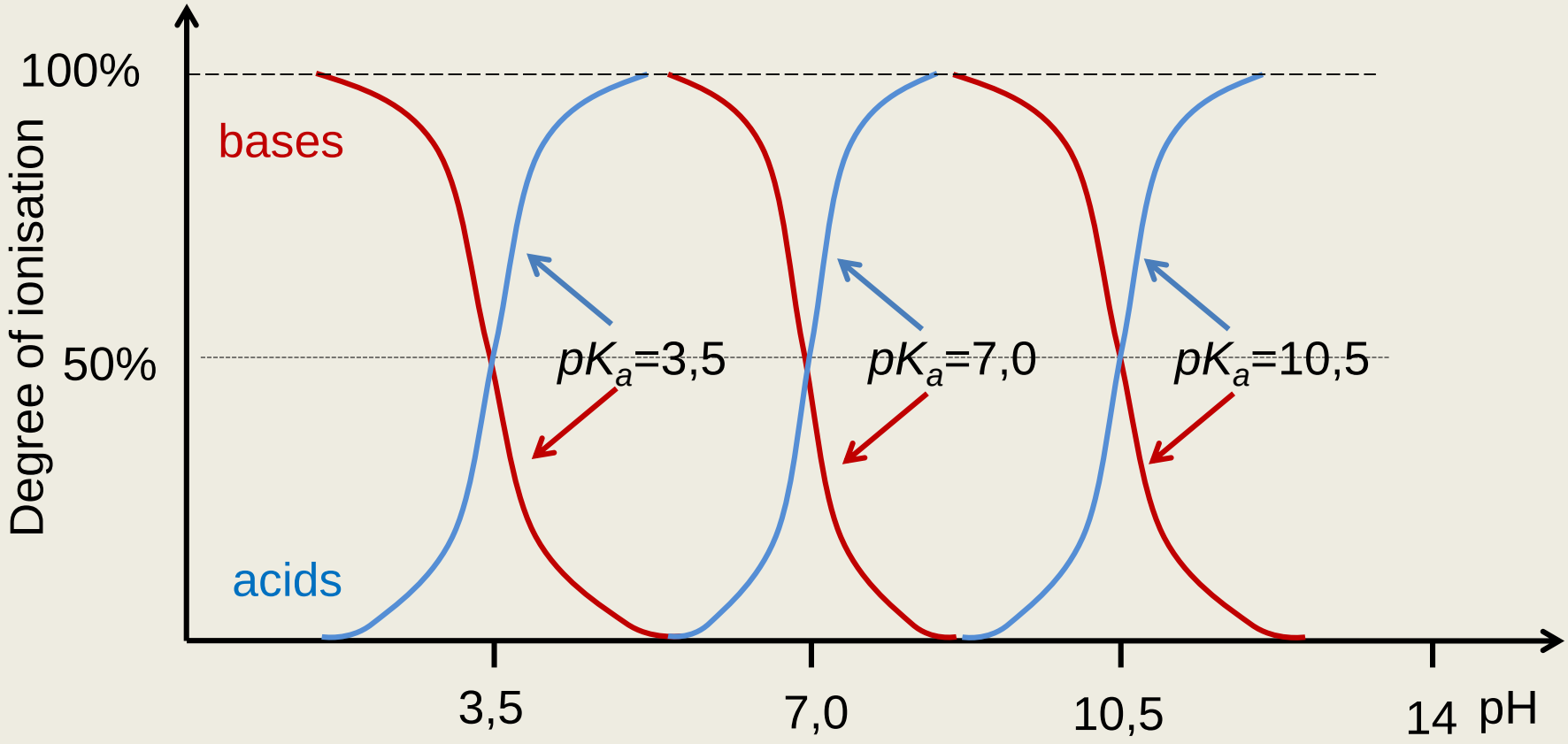
In case of weak bases:

$$pH - pK_a = \lg \frac{C_{non-ionised}}{C_{ionised}}$$

In case of weak acids:

$$pH - pK_a = \lg \frac{C_{ionised}}{C_{non-ionised}}$$

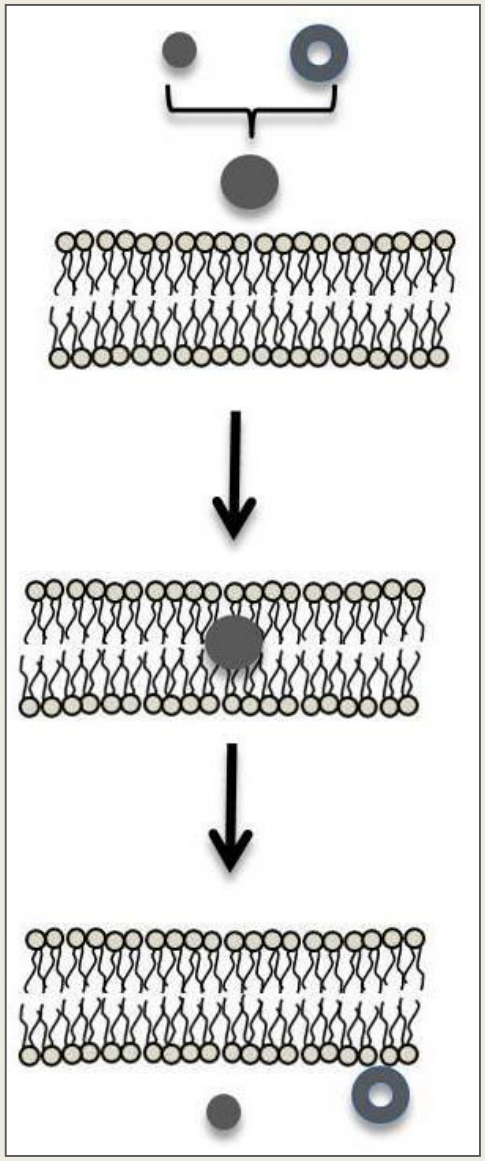
Ionisation


100%
50%
Degree of ionisation
bases
acids
pK_a=3,5
pK_a=7,0
pK_a=10,5
3,5
7,0
10,5
14
pH

Ion-pair transport

Ion-pair transport facilitates the passive diffusion of ionised molecules with low lipid-water partition coefficient.

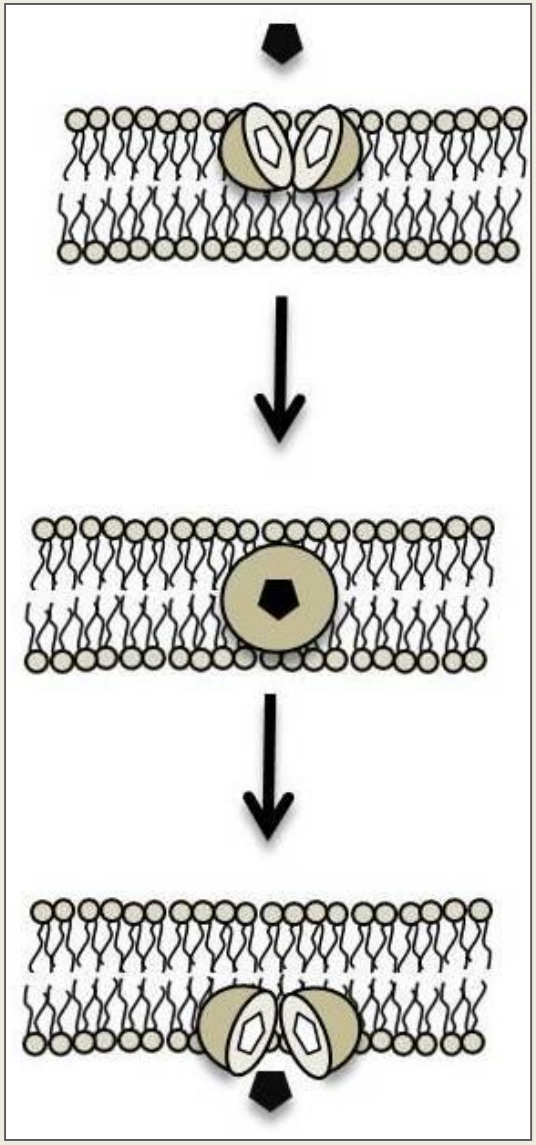
Lipophobic molecules make ion-pair complex with the GI tract's mucous or other molecules with opposite charge thus making an apolar, shielded complex which is able to cross the membrane by passive diffusion.



Facilitated transport

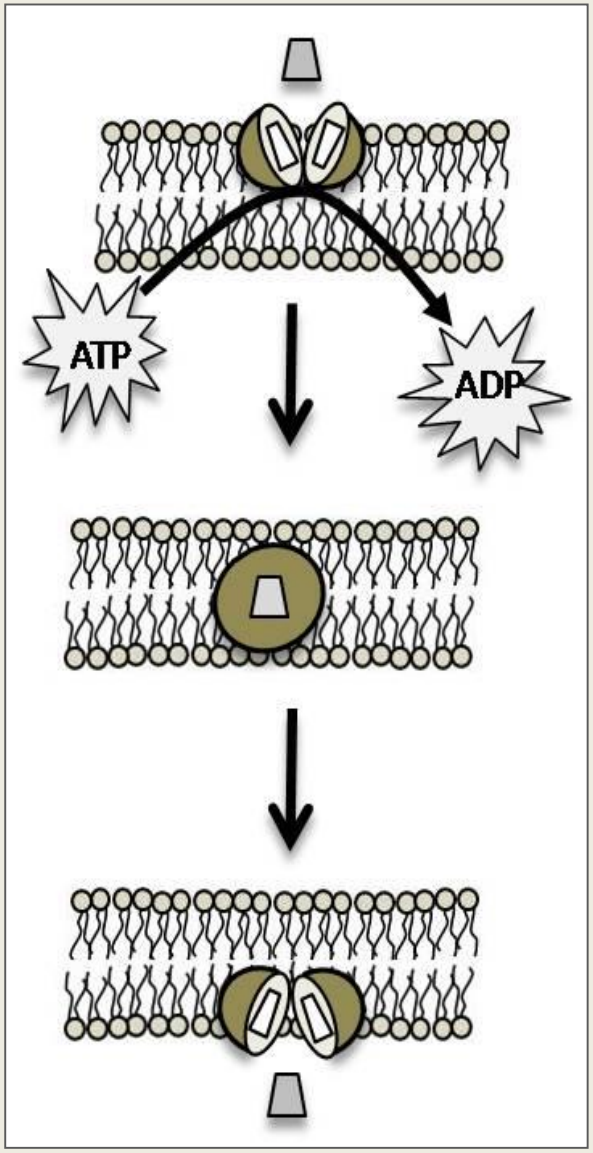
Mostly applicable at small, polar molecules.

Carrier molecule eases the crossing through the membrane by making a complex with the API. The transport mechanism is determined by the concentration gradient. It does not need energy, but it can be saturated.



Active transport

In this case the molecule can cross the membrane against the concentration gradient. This transport needs energy, which is provided by the ATP.



Endocytosis and exocytosis

Endocytosis – the cell absorbs molecules by engulfing them. Bigger particles (>500nm) are absorbed by phagocytosis, smaller particles are absorbed by pinocytosis.

Exocytisis is the opposite process to endocytosis.

DDS

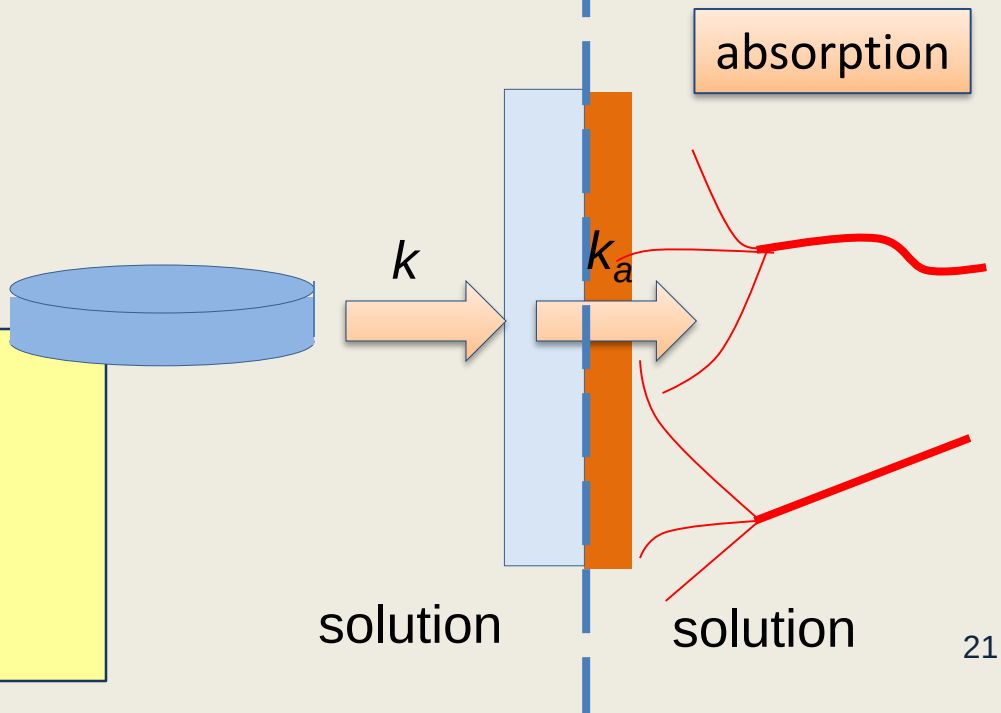
DDS

Absorption can be controlled by the liberation by making it the rate controlling step.

Speed of drug release

liberation

absorption



If $k > k_a$ then resultant rate = k_a

If $k = k_a$ then resultant rate = k_a

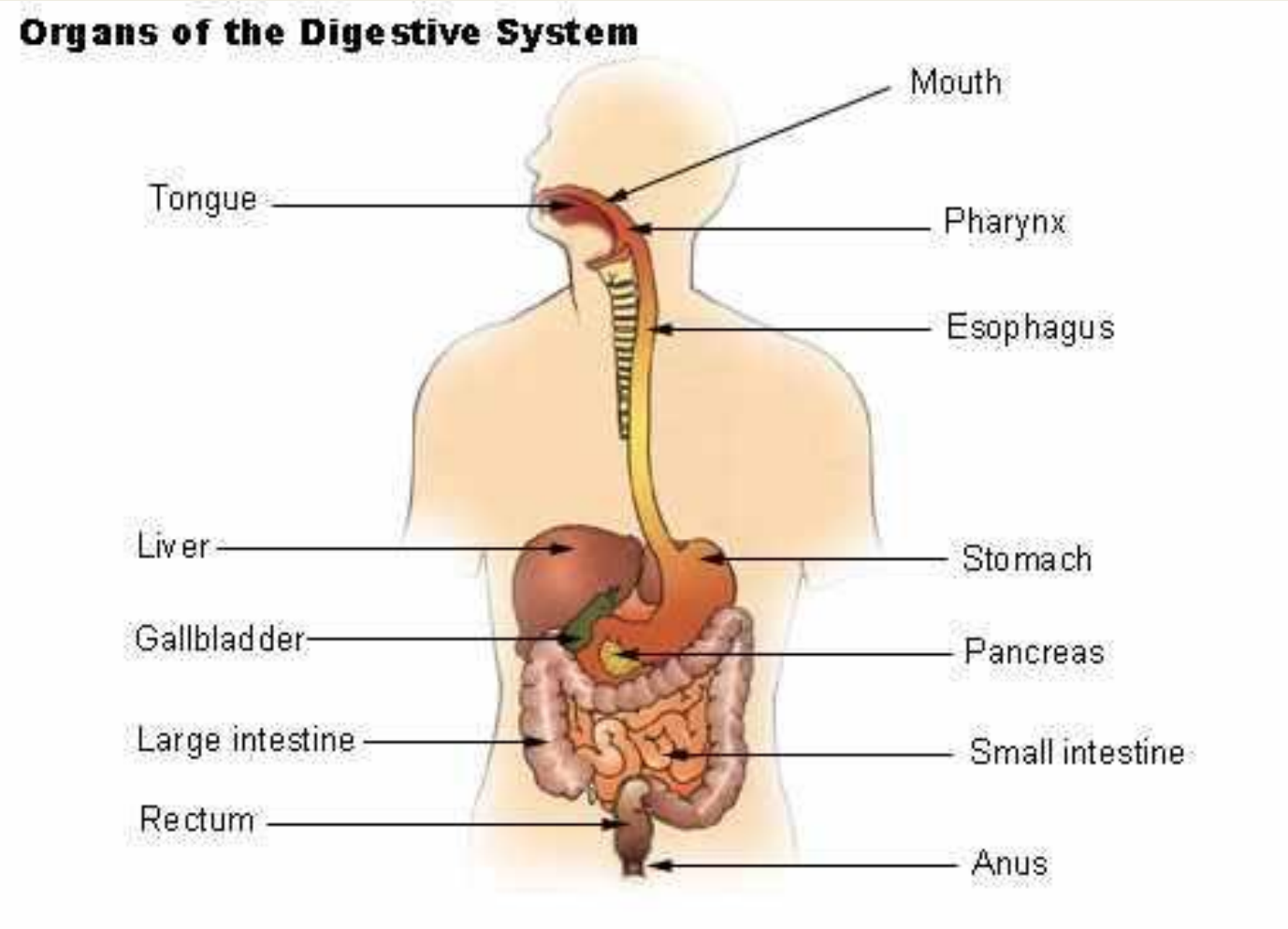
If $k < k_a$ then resultant rate = k

Routes of administration

Rate and speed of absorption is determined by the absorption surface (absorption window), wich depends on the route of administration.

Absorption through the GI tract

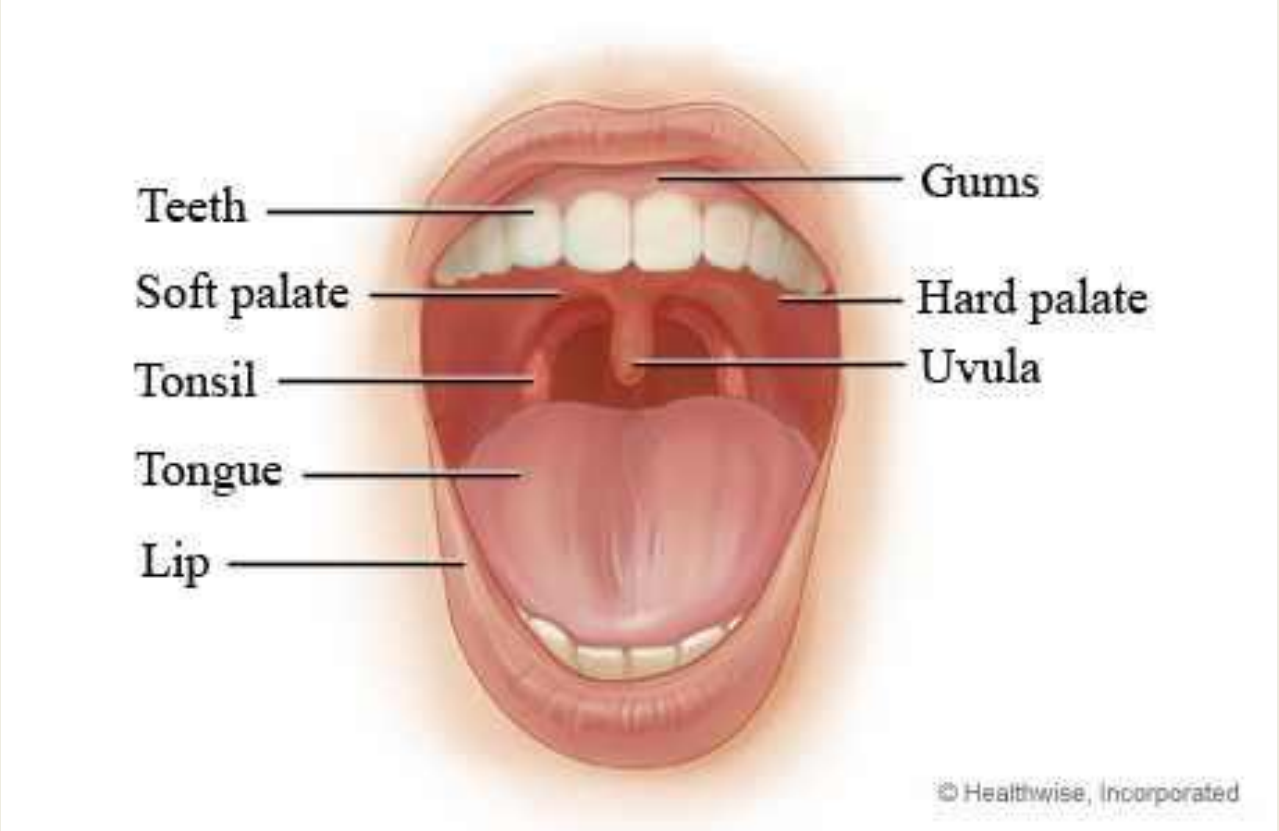
GI tract

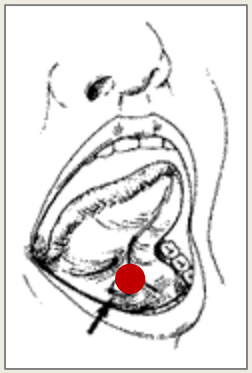

Organs of the Digestive System
Mouth
Tongue
Pharynx
Esophagus
Liver
Stomach
Gallbladder
Pancreas
Large intestine
Small intestine
Rectum
Anus

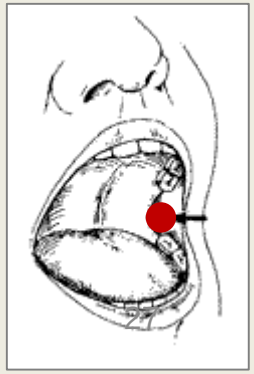
Characteristics of the GI tract

- huge absorption surface
- specific organs with specific tissue
- retention time
- specific pH environment
- specific enzymatic system

Mouth

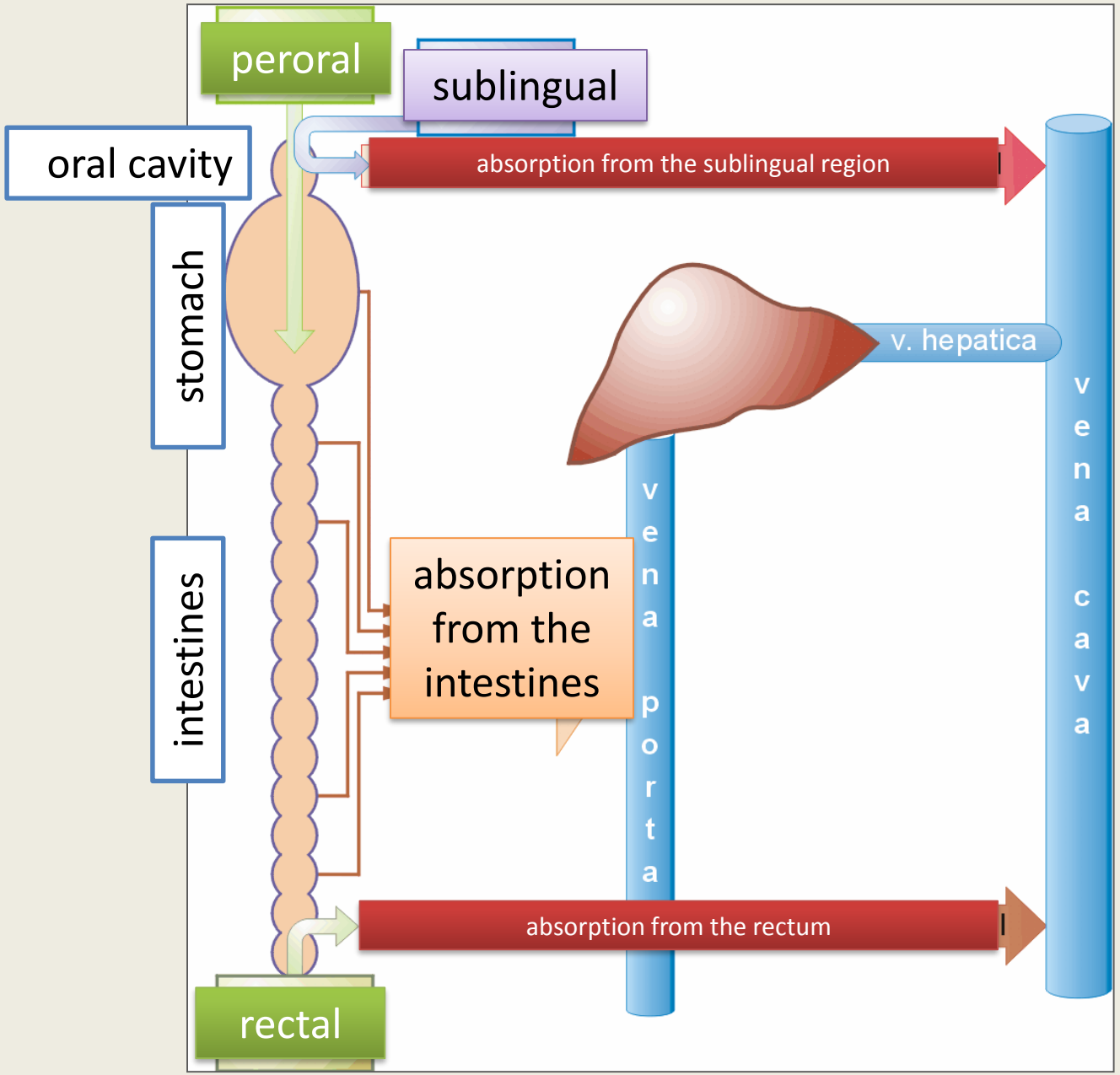

Teeth
Gums
Soft palate
Hard palate
Tonsil
Uvula
Tongue
Lip
© Healthwise, Incorporated





Absorption

GI tract



nitroglycerol

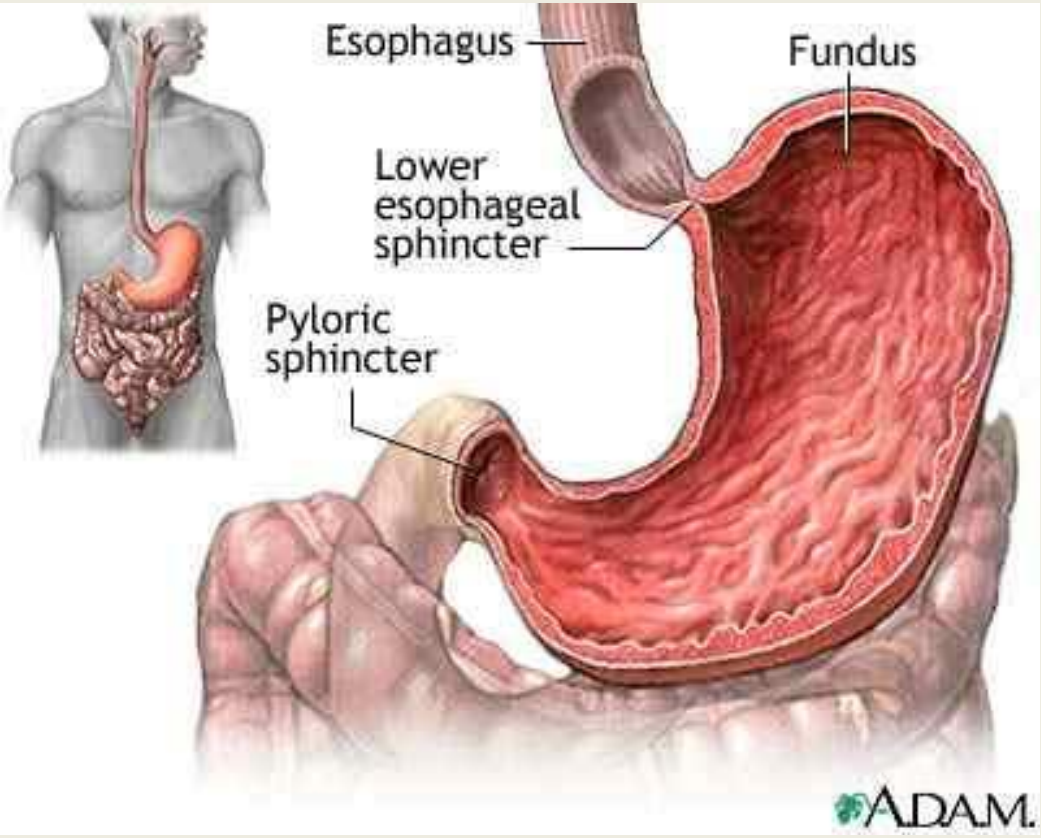
nifedipin

captopril

Absorption from the sublingual region

Advantage	*Disadvantage*
•*Quick absorption*	•*May be irritative*
•*No first-pass effect*	•*Unpleasant taste*
•*Increased patient complience*	•*Cannot be administered to unconscious patients*

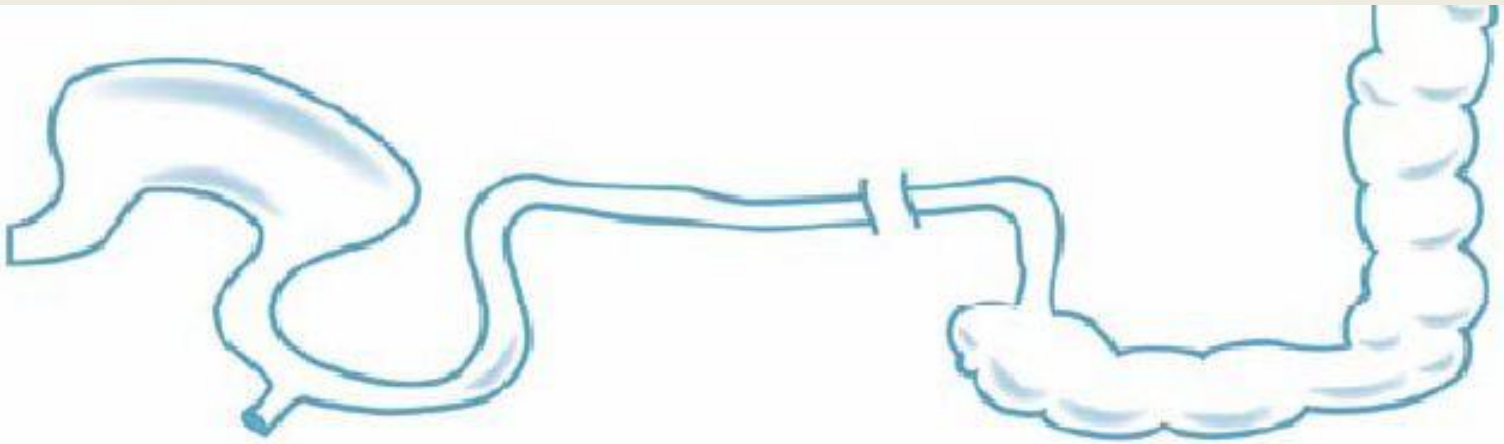
Stomach



organ	length (m)	surface (m^2)	pH	retention time	micro-organizms
stomach gaster	0.2	0.2	1.0-2.5	1-5 hrs	~10^2

pH values

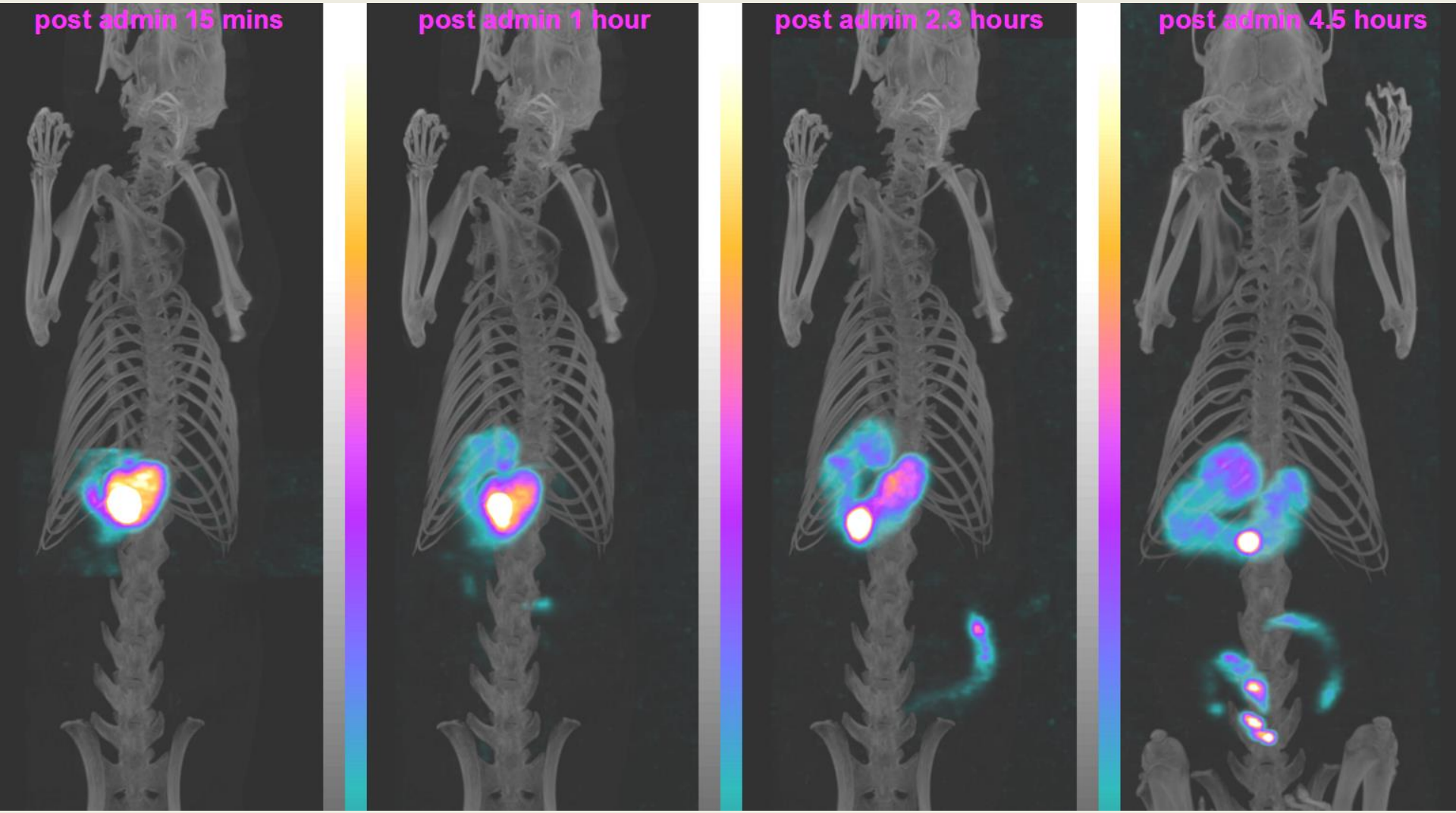
GI tract



	Stomach	Jejunum	Ileum	Colon	
pH	1.4-2.1	4.4-6.6	6.8-8.6	5-8	fasting
	3-7	5.2-6.2	6.8-8.0	5-8	fed

FDDS – floating drug delivery system (Gastroretentive systems)

Gallium-76 isotope marked floating tablets



Preformulation studies and optimization of sodium alginate based floating drug delivery system for eradication of *Helicobacter pylori*

Péter Diós[a,], Sándor Nagy[a], Szilárd Pál[a], Tivadar Pernecker[a], Béla Kocsis[b], Ferenc Budán[c, d], Ildikó Horváth[c], Krisztián Szigeti[c], Kata Bölcskei[e], Domokos Máthé[c], Attila Dévay[a]

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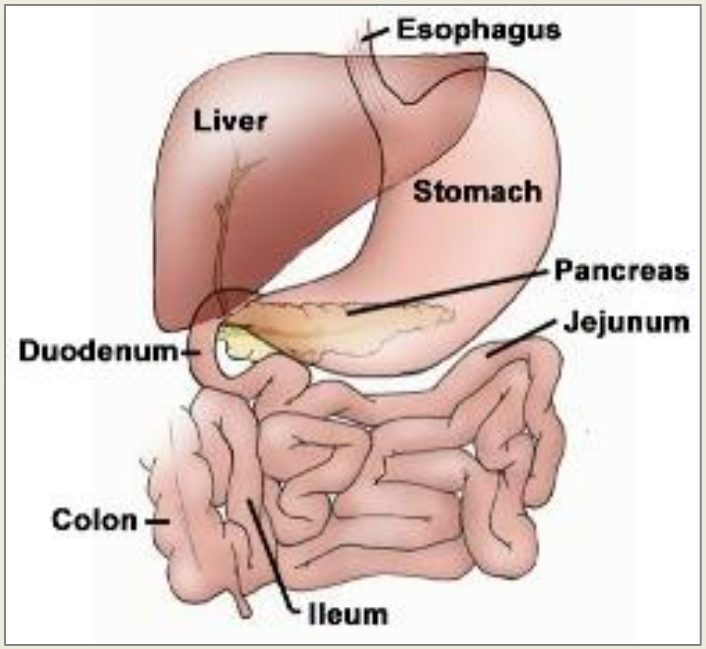
Absorption from intestines (bowel)

- **Excellent blood and lymphatic circulation**
- **pH increases (3-7)**
- **Mostly weak bases can absorb from intestines**
- **The absorption mostly ends at the upper part of the jejunum**
- **Passive diffusion is the most important type of transport which is determined by the dissociation constant and the environment's pH**

Small intestine

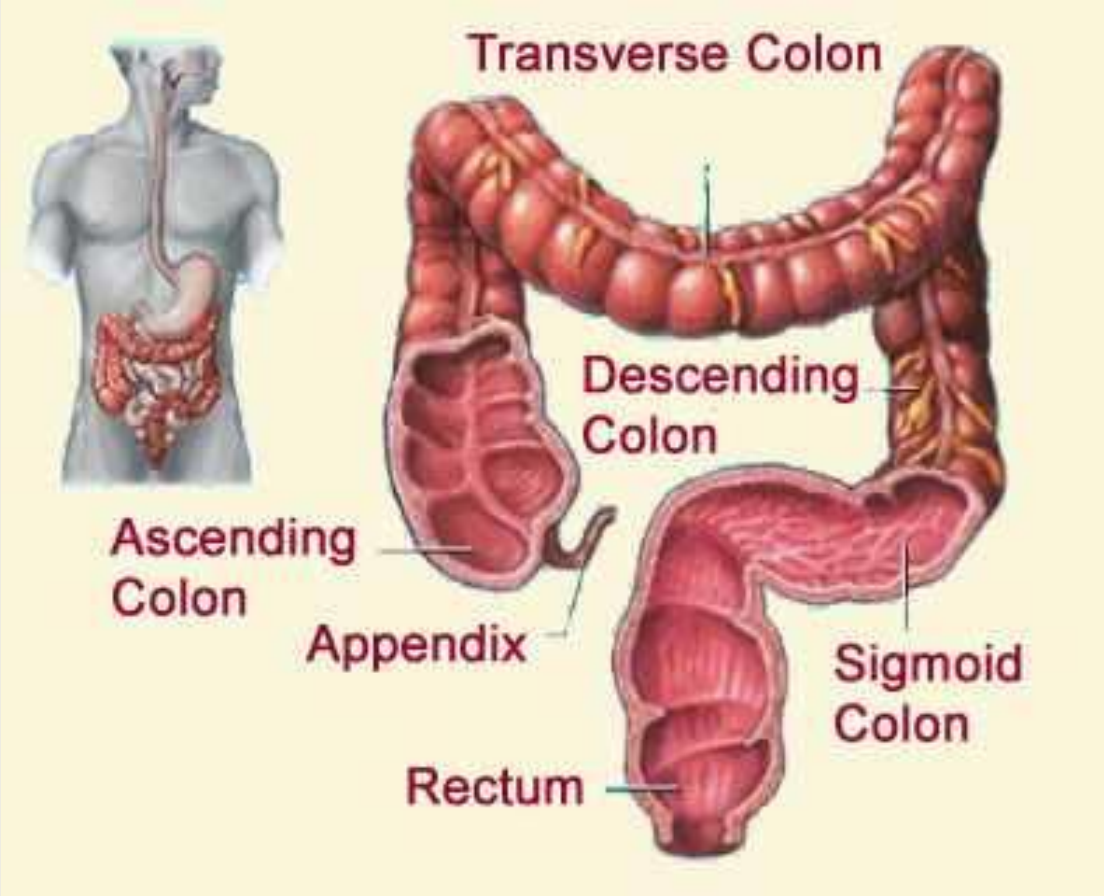


organ	length (m)	surface (m^2)	pH	retention time	micro-organizms
duodenum	0.3	0.02	5-6.5	>5 min	~10^2
jejunum	3	100	6.9	1-2 hrs	~10^2
ileum	4	100	7.6	2-3 hrs	~10^7

Absorption from the small intestine

- **Absorption occurs here in almost all cases**
- **Its surface is only 1 m^2, but actually it is huge because of the microvilli (100 m^2)**
- **Duration of passage can influence the absorption (diarrhea, constipation)**
- **Short transit time decreases, long transit increases the absorption.**

Large intestine

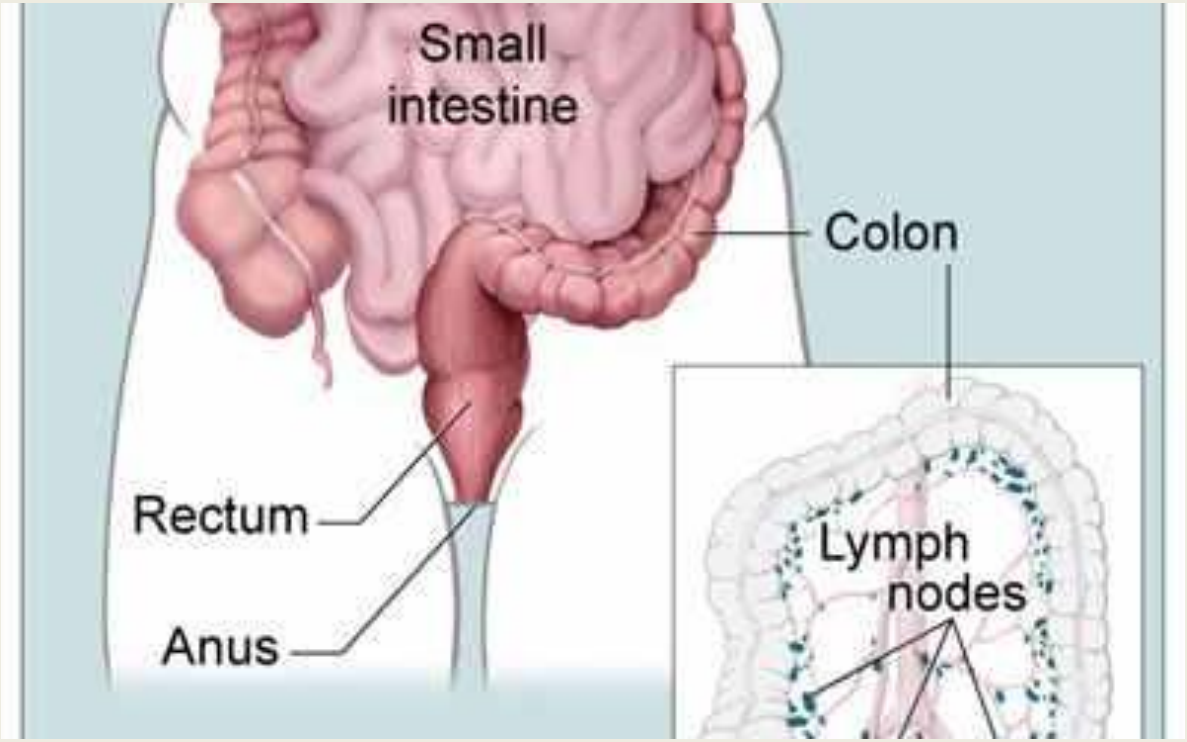


organ	length (m)	surface (m^2)	pH	retention time	micro-organizms
Large intestine cecum, colon	1.5	3	5.5-7.8	15-48 hrs	~10^{11}

Absorption from the large intestine

- **Absorption occurs in a negligible quantity**
- **It has its own bacterial flora, which can be utilized to achieve a local therpy of the colon**

Rectum



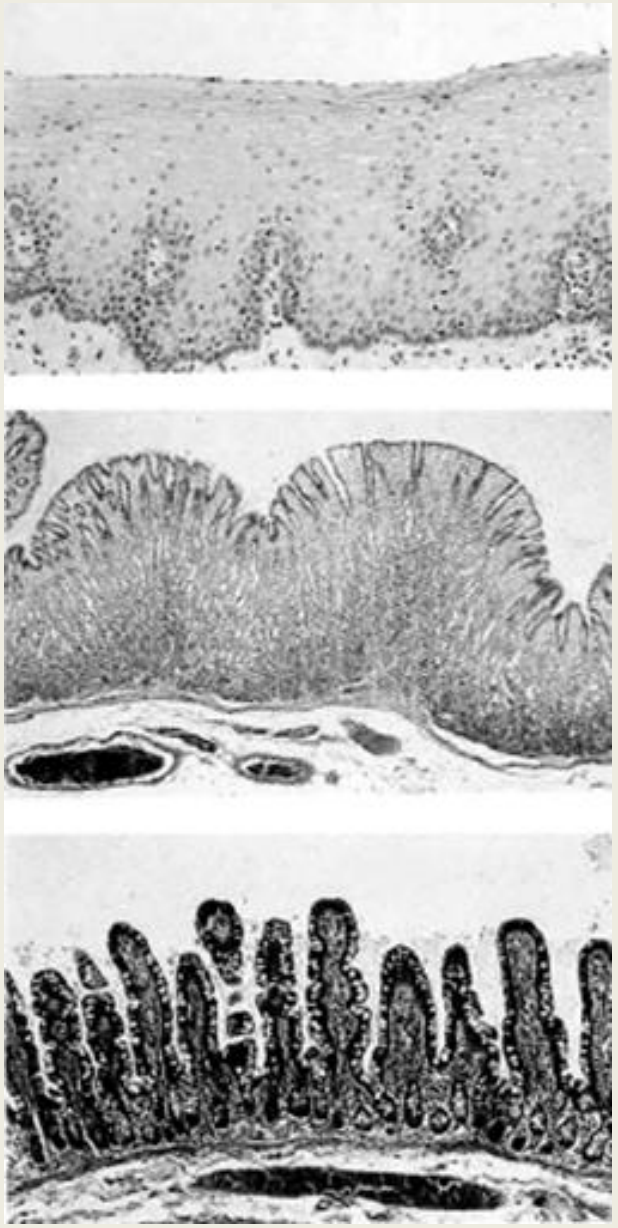
organ	length (m)	surface (m^2)	pH	retention time	micro-organizms
rectum	0,15-0,18	0,03	7,3-7,7	10-30 perc	~10^{10}

Absorption from the rectum

- **Quick absorption**
- **No first-pass-effect**
- **In case of unconscious people and children**
- **In case substances that irritate stomach or intestines**
- **Suppository, enema**

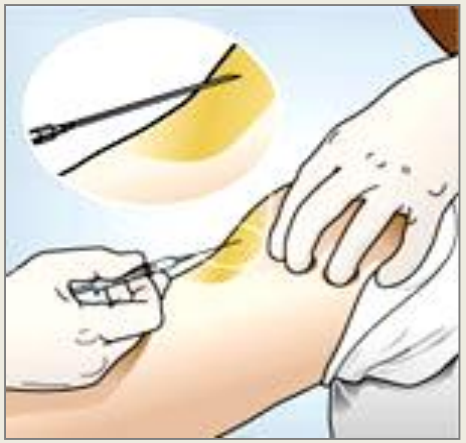
Absorption surfaces

1. Mouth
2. Stomach
3. Small intestine

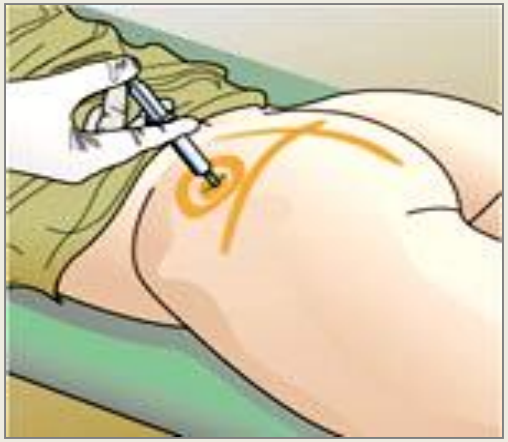


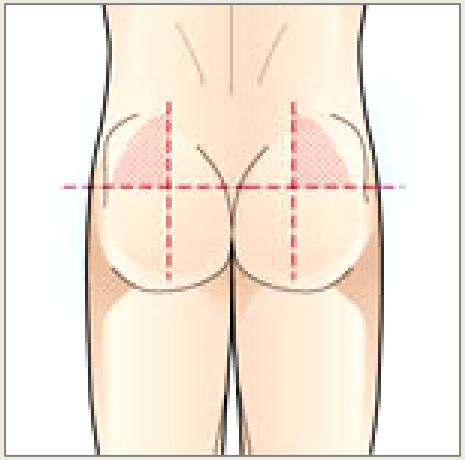
Parenteral absorption

Subcutaneous route



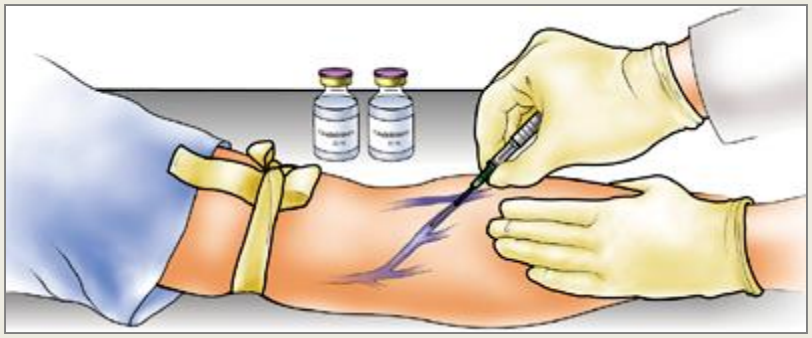
Intramuscular route

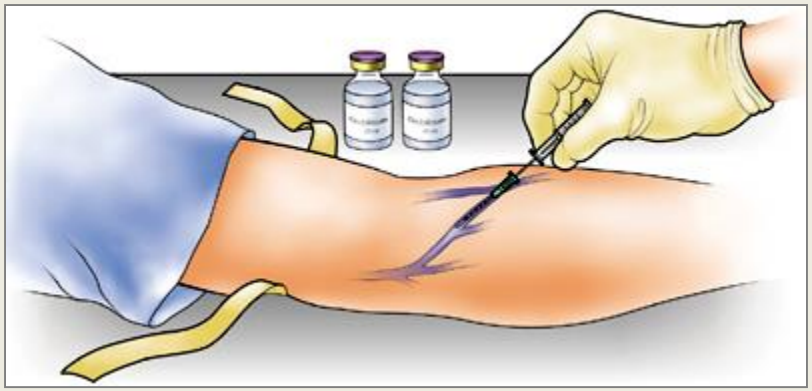




~~Absorption~~

Intravenous route

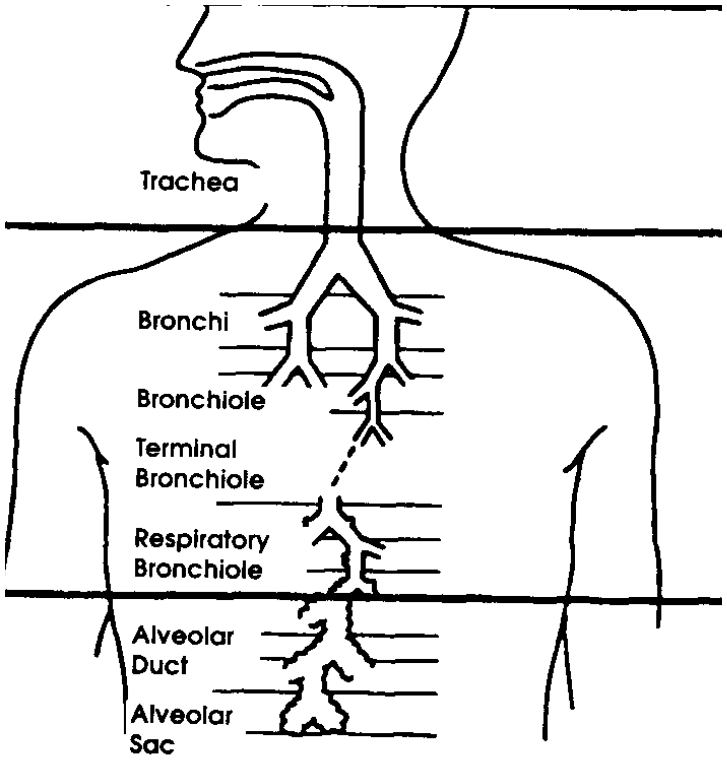




Parenteral absorption

- **Respiratory system**

  - nasopharingeal
  - tracheobronchial
  - pulmonary region



Absorption from the respiratory system

- Characteristics
  - Alveolar region
    - huge surface (150 m^2)
    - 1-2 cell thickness – thin layer of cells

Absorption through the respiratory system

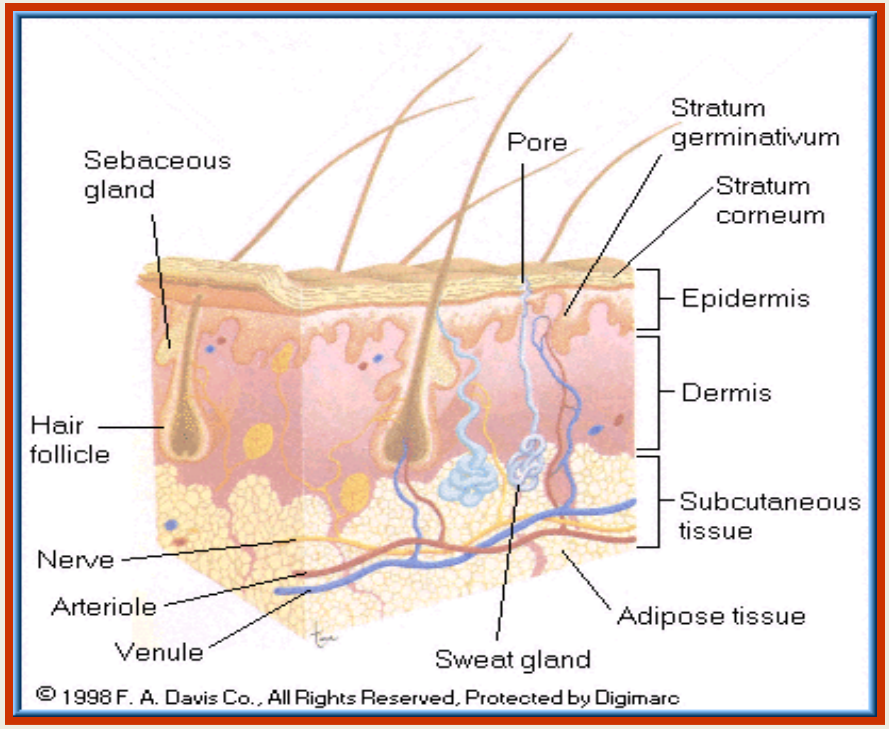
- Effect of size on the settling of particles
  - **Nasopharingeal** **5-30 µm**
  - **Tracheobronchial** **1-5µm**
  - **Pulmonary** **1-2 µm**

Absorption through the respiratory system

- **Absorption is determined by:**
  - **Ventillation**
  - **Concentration gradient**
  - **Alveolar surface**
  - **Alveolar capillaries' blood circulation**
- **Used in:**
  - **Inhalational anaesthesy (ether, halothane)**

Absorption through the skin

- **Structure of the skin**
  - Epidermis
  - Dermis
  - Subcutaneous tissue



Thank you for your attention!