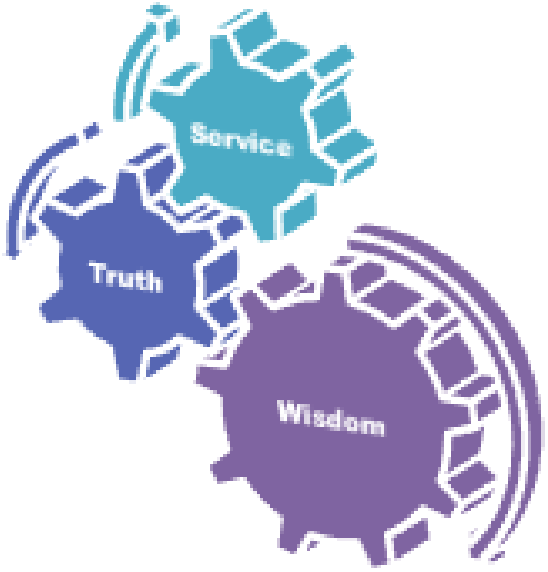
IN THE NAME OF ALLAH

THE MOST BENEFICIENT
THE MOST MERCIFUL

MOTTO AND VISION



- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

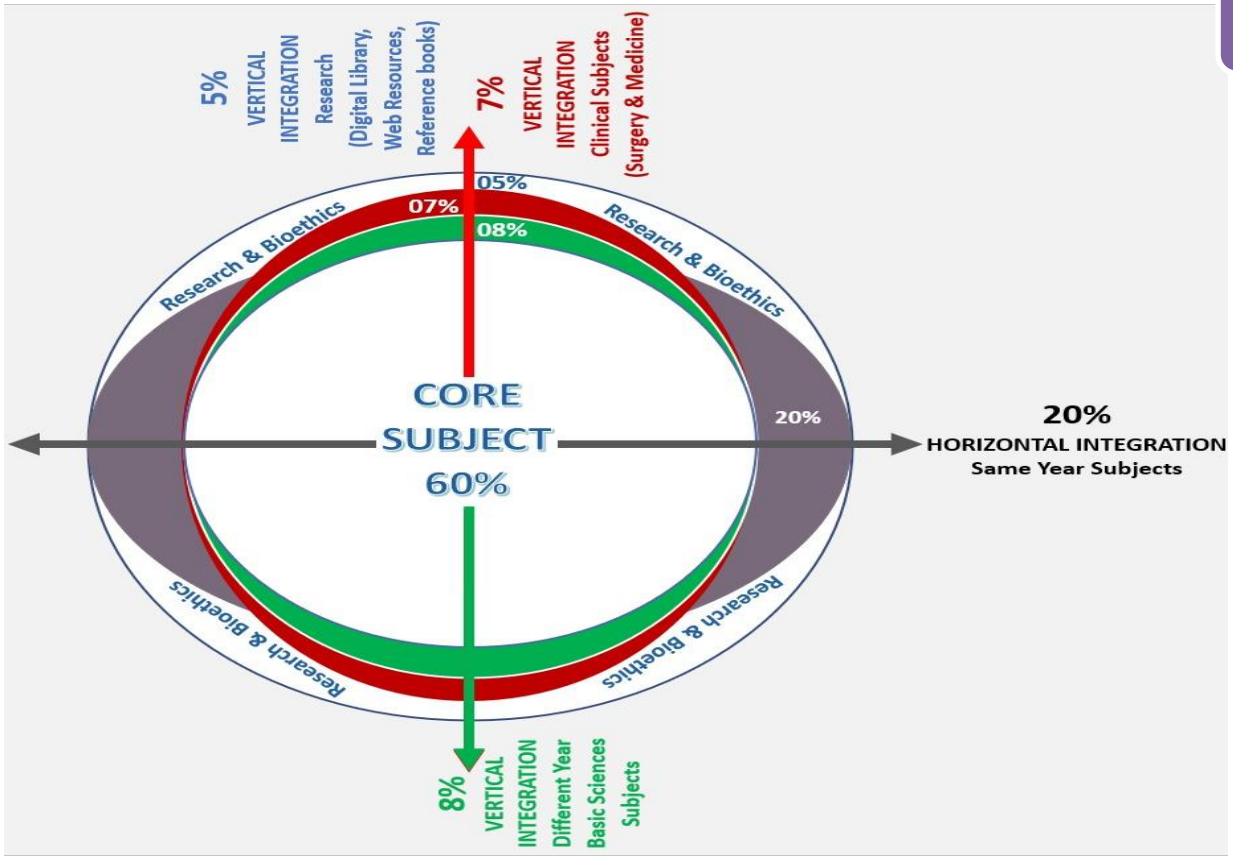
FOUNDATION MODULE

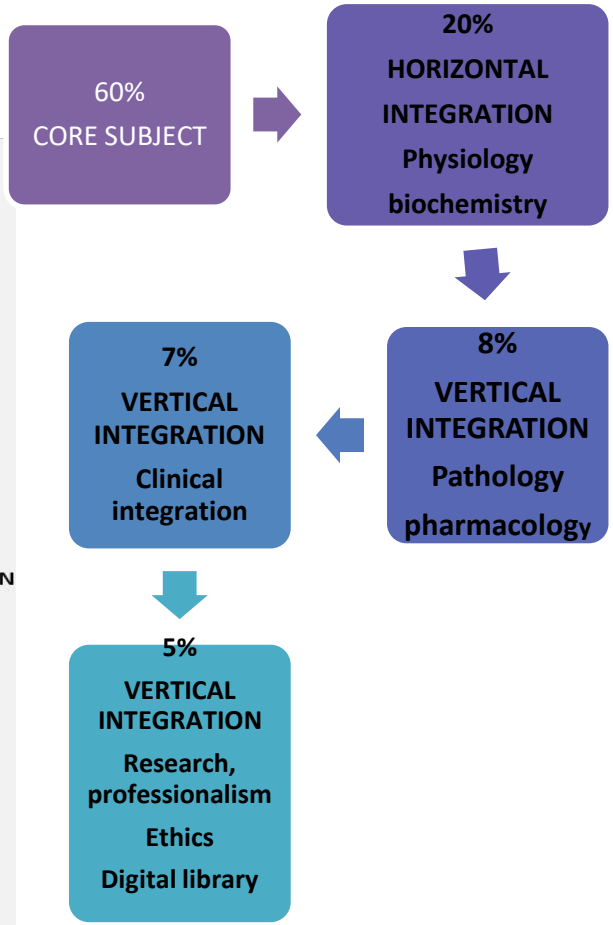
ABSORPTION OF DRUGS AND FACTORS AFFECTING ABSORPTION OF DRUGS

Sources:

- **Bertram G. katzung Basic & Clinical Pharmacology 16th Edition**
- **Goodman and Gilman's The Pharmacological Basis of Therapeutics 13th edition.**

PROFESSOR UMAR MODEL OF INTEGRATED LECTURE

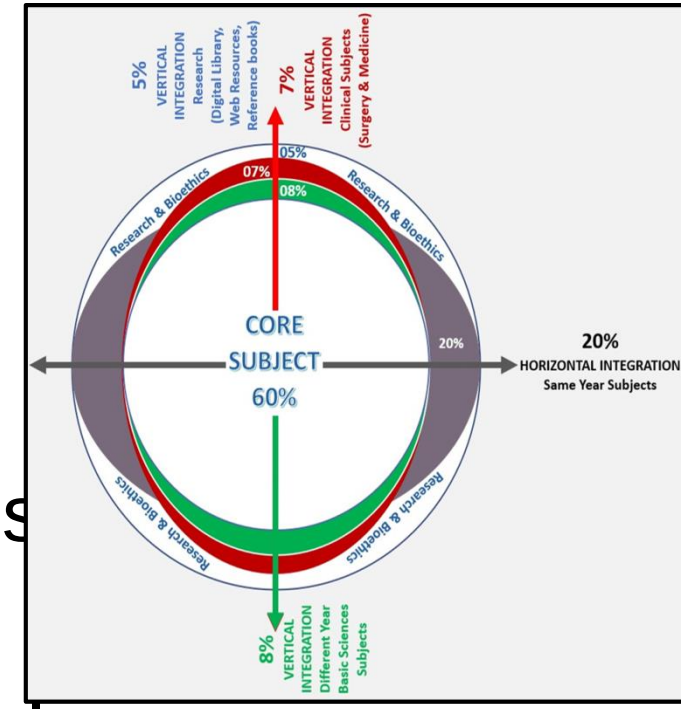




Sequence Of Lecture

- Core Subject
- Spiral Integration
- Horizontal Integration
- Vertical integration
- EOLA(End of lecture assess
- Digital Library References

(Research, Bioethics, Artificial Intelligence)



Learning Objectives

- Define pharmacokinetic processes
- Recall physiology of transport across biological membranes
- Explain factors affecting absorption of drugs
- Comprehend the concept of ion trapping and its clinical use

Pharmacokinetics

- What the body does to the drug
- Quantitative study of the drug movement in, through and out of the body
- Determine ?

Pharmacokinetic Processes

- Absorption
- Distribution
- Metabolism
- Excretion

ADME

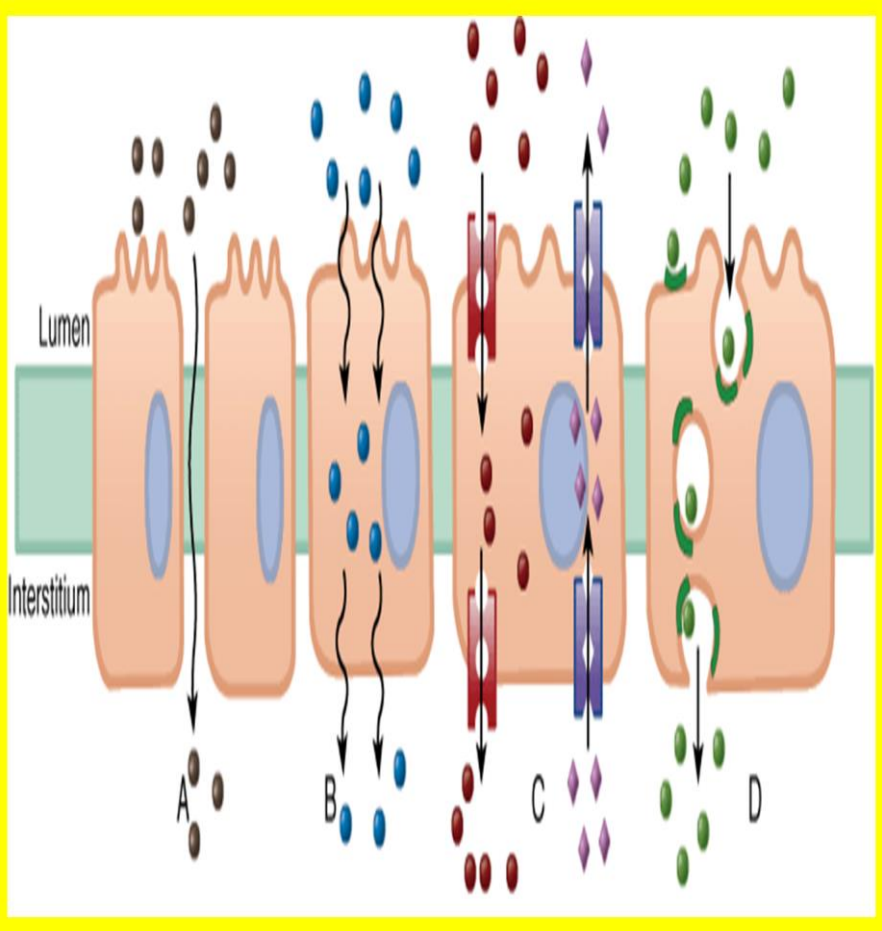
ABSORPTION OF DRUGS

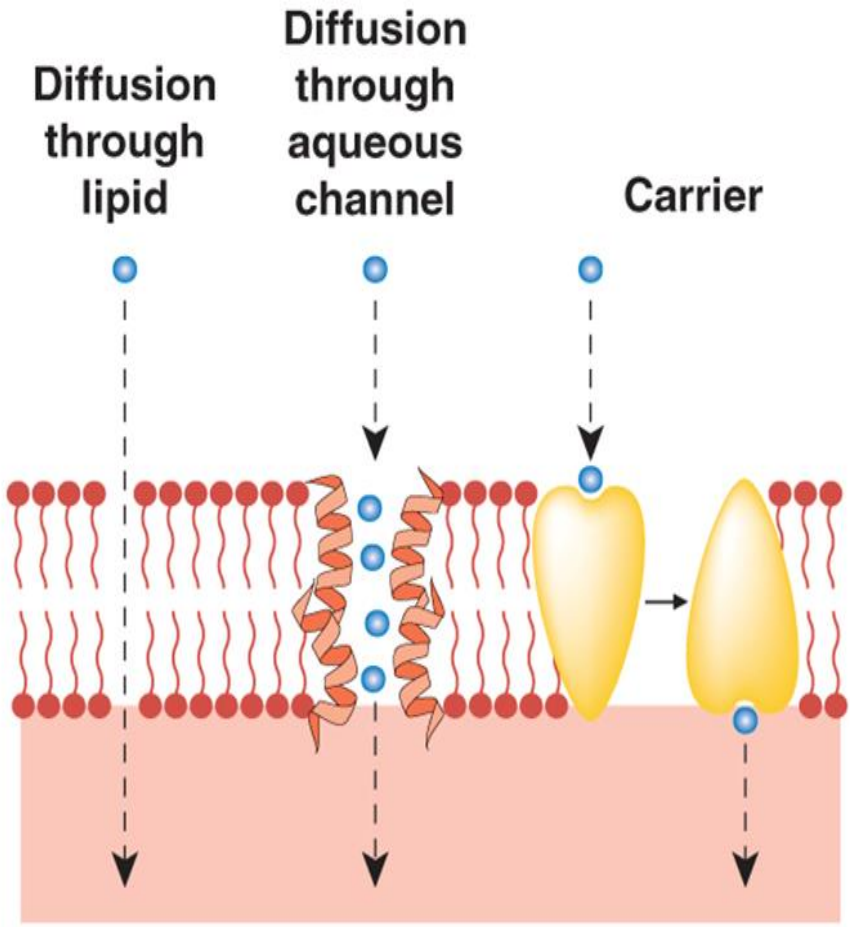
- Absorption is the movement of drug from its site of administration into the circulation.
- The rate of absorption affects the onset , duration and intensity of drug action.

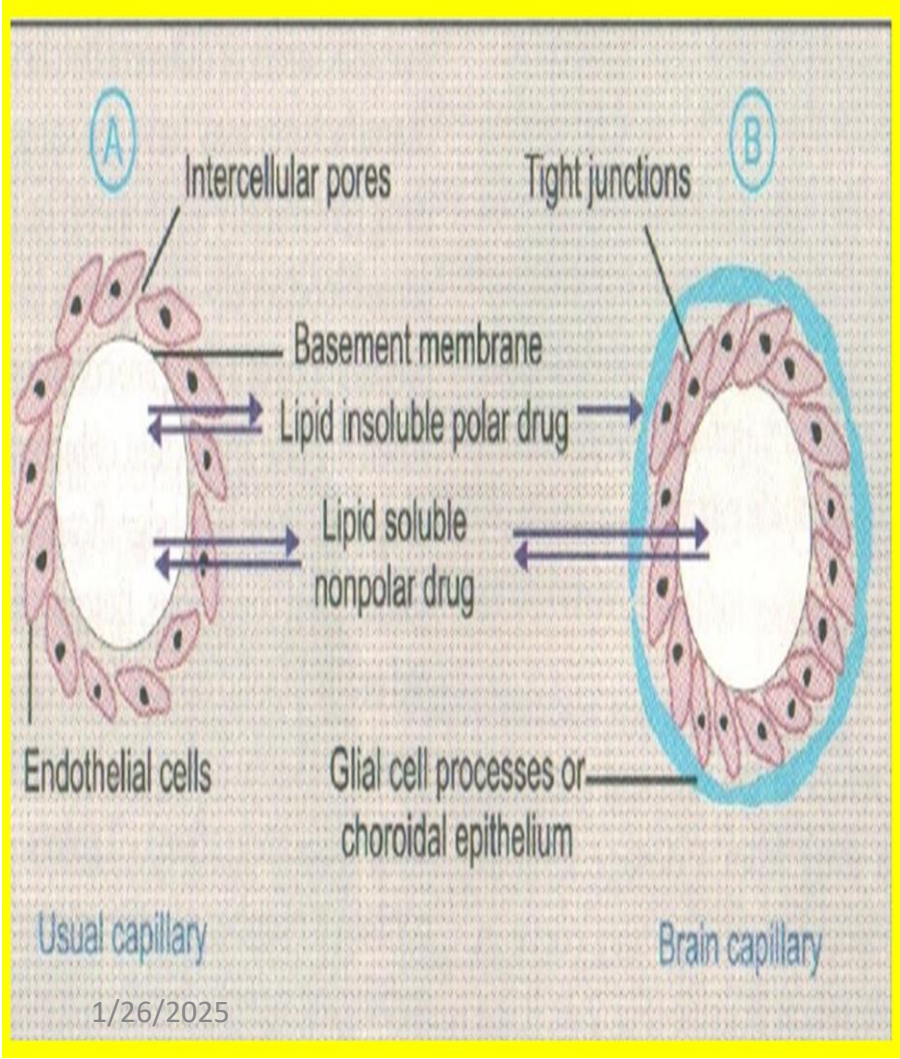
Permeation

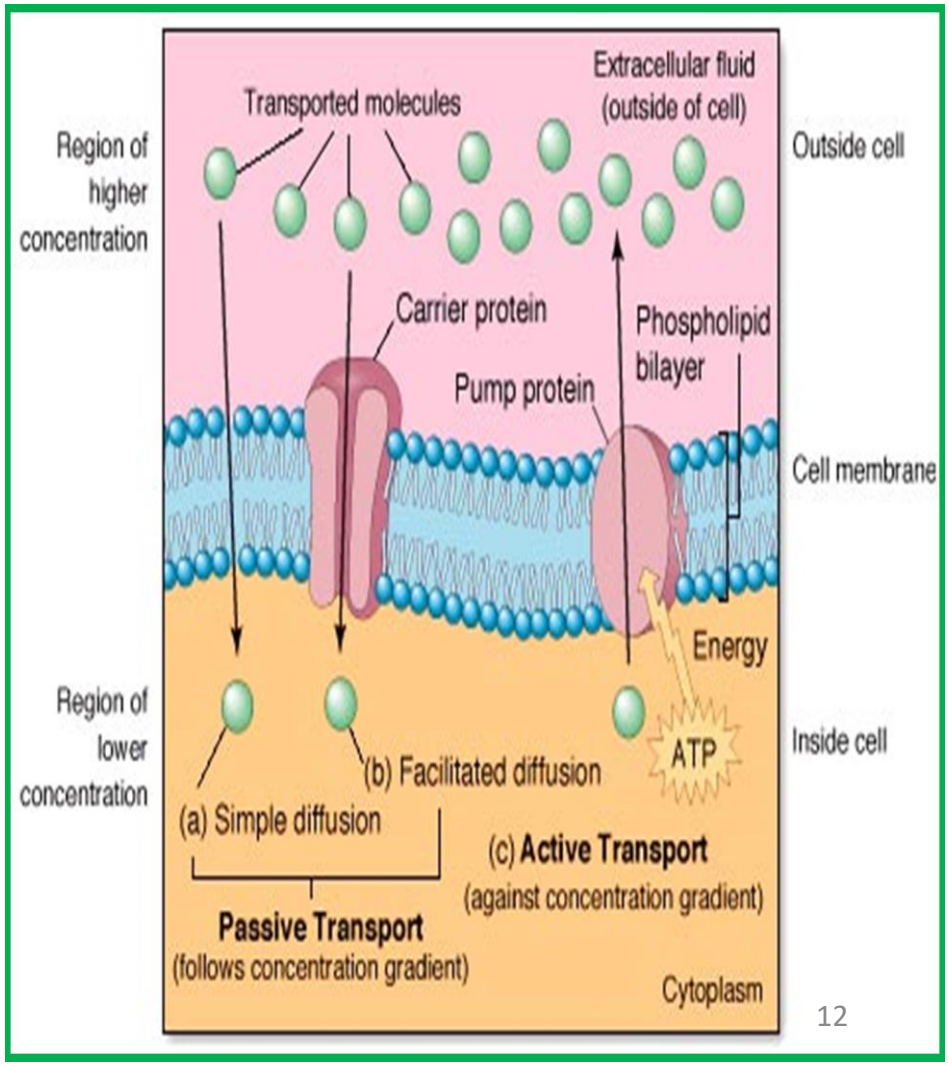
- **Aqueous diffusion**
  - Filtration
  - Bulk flow
- **Lipid diffusion**
- **Special carriers**
  - Facilitated diffusion
  - Active transport
  - Primary active transport
  - Secondary active transport
- **Endocytosis & exocytosis**

SPIRAL-INTEGRATION


Lumen
Interstitium
A
B
C
D


Diffusion through lipid
Diffusion through aqueous channel
Carrier


A
Intercellular pores
Tight junctions
B
Basement membrane
Lipid insoluble polar drug
Lipid soluble
nonpolar drug
Endothelial cells
Glial cell processes or
choroidal epithelium
Usual capillary
Brain capillary


Transported molecules
Extracellular fluid
(outside of cell)
Region of
higher
concentration
Outside cell
Carrier protein
Phospholipid
bilayer
Pump protein
Cell membrane
Energy
Region of
lower
concentration
ATP
Inside cell
(b) Facilitated diffusion
(a) Simple diffusion
(c) Active Transport
(against concentration gradient)
Passive Transport
(follows concentration gradient)
Cytoplasm

Factors Affecting Diffusion

1. Concentration Gradient Across Membrane:

- Fick's law of diffusion

- Flux (molecules/unit time) =

$$(C1\text{-}C2) \times \frac{\text{Area} \times \text{Permeability coefficient}}{\text{Thickness}}$$

Factors Affecting Diffusion

CONT--

2. Molecular/ Particle Size

3. Membrane Surface Area

4. Lipid :Aqueous Partitian Coefficient

CONT--

4. Ionization of Drugs

- Most of the drugs are either weak acids or weak bases. Therefore they are part ionized and part unionized. The ionized portion is charged , which attracts water molecules , thus forming large complexes. These complexes cannot cross the membranes because they are less lipid soluble. This is why the ionized part of the drug cannot cross the membrane.
- **Drugs are better absorbed in unionized form.**

Acidic drugs

CONT--

- AH ⟷ A- + H+ (eq 1)
- Acidic drugs on dissociation give anion and proton.

Basic drugs

- B + H+ ⟷ BH+ (eq 2)
- Basic drugs on combining with a proton become a cation.
- The existence of drugs as neutral or charged particles **depends on the pH.**

CONT--

$$C_8H_7O_2COOH \rightleftharpoons C_8H_7O_2COO^- + H^+$$

Neutral aspirin	Aspirin anion	Proton

Ionized/Unionized
Protonated/Un protonated

$$C_{12}H_{11}ClN_3NH_3^+ \rightleftharpoons C_{12}H_{11}ClN_3NH_2 + H^+$$

Pyrimethamine cation	Neutral pyrimethamine	Proton

Factors Affecting Diffusion

- Henderson-Hasselbalch equation

$$\log \frac{(\text{Protonated})}{(\text{Unprotonated})} = pK_a - pH$$

- Weak Acids
- Weak bases

Factors Affecting Diffusion

- **<u>The lower the pH relative to the pKa, the greater will be the fraction of drug in the protonated form</u>**
- **<u>For Acidic Drugs</u>**
  - pKa – pH = log [AH / A-]
  - If pH is lower than pKa, AH will be more
- **<u>For basic drugs</u>**
  - pKa – pH = log [BH+ / B]
  - If pH is lower than pKa, BH+ will be more

$$\log \frac{(\text{Protonated})}{(\text{Unprotonated})} = pK_a - pH$$

Drugs in intestines

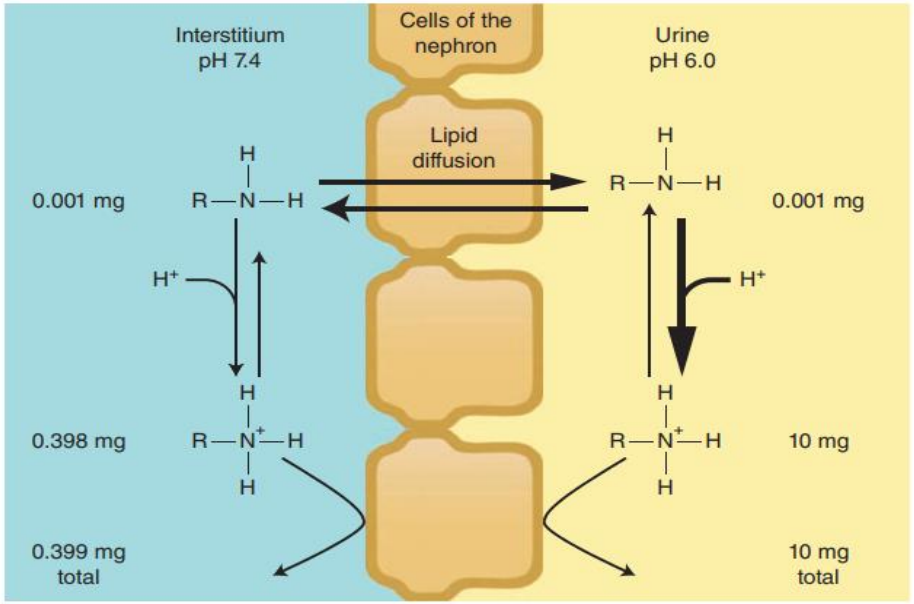
- For acidic drugs A- is more , so the drugs are present in ionized form in the intestines , thus are less absorbed.
- For basic drugs , B is more , thus are present in unionized form in the intestines and are absorbed in a much greater quantity.
- **In short , we can say that acidic drugs are better absorbed in the acidic medium while basic drugs are better absorbed in the basic medium.**

Ion trapping

- Most of the drugs are reabsorbed from the kidneys. Acidic drugs are better reabsorbed from acidic urine. This is an important fact , which can be manipulated to get desired results , as is the case of poisoning with acidic drugs. If we make the urine alkaline (by administering sodium bicarbonate) , decreased reabsorption of acidic drugs take place , a phenomenon known as **ion trapping.**

Cont--

- In case of poisoning with basic drug , urine can be made more acidic (by administering ammonium chloride) , by virtue of which the basic drug becomes ionized and is not reabsorbed , with the result that more of it excreted out.



Factors Affecting Absorption

- Related to Drugs
  - Lipid water solubility coefficient
  - Molecular/Particle size
  - Degree of ionization
  - Physical form
  - Chemical nature
  - Dosage form
  - Formulation
  - Moisture, Adjuvant
  - Concentration

Factors Affecting Absorption

- Related to Body
  - Area of absorptive surface
  - Vascularity
  - pH
  - Presence of other substances
  - GI motility
  - Functional integrity of absorptive surface
  - Diseases…….

HORIZONTAL INTEGRATION …PATHOLOGY

Factors Affecting Absorption

- Methods for Delaying Absorption
- 1. Vasoconstrictors
- 2. Formulation

- Methods for Enhancing Absorption
- 1. Formulation
- 2. Massage

EOLA(End Of Lecture Assessment)

- A 78-year-old woman is brought to the hospital because of suspected aspirin overdose. She has taken aspirin for joint pain for many years without incident, but during the past year, she has exhibited many signs of cognitive decline. Her caregiver finds her confused, hyperventilating, and vomiting. The caregiver finds an empty bottle of aspirin tablets and calls 911. In the emergency department, samples of venous and arterial blood are obtained while the airway, breathing, and circulation are evaluated. An intravenous (IV) drip is started, and gastrointestinal decontamination is begun. After blood gas results are reported, sodium bicarbonate is administered via the IV. What is the purpose of the sodium bicarbonate?

EOLA(End Of Lecture Assessment)

- Aspirin overdose commonly causes a mixed respiratory alkalosis and metabolic acidosis. Because aspirin is a weak acid, serum acidosis favors entry of the drug into tissues (increasing toxicity), and urinary acidosis favors reabsorption of excreted drug back into the blood (prolonging the effects of the overdose). Sodium bicarbonate, a weak base,is an important component of the management of aspirin overdose. It causes alkalosis, reducing entry into tissues, and increases the pH of the urine, enhancing renal clearance of the drug.

- **Research, Bioethics, Artificial Intelligence**

Digital Library/Further Reading

- Shinde, A.A., Velhal, A.B., Jadhav, P.D. and Redasani, V.K., 2022. Improvement of Topical Absorption of Drug. Asian Journal of Research in Pharmaceutical Science, 12(4).
- Farjadian, F., Ghasemi, A., Gohari, O., Roointan, A., Karimi, M. and Hamblin, M.R., 2019. Nanopharmaceuticals and nanomedicines currently on the market: challenges and opportunities. Nanomedicine, 14(1), pp.93-126.
- Chou, W.C. and Lin, Z., 2023. Machine learning and artificial intelligence in physiologically based pharmacokinetic modeling. *Toxicological Sciences*, *191*(1), pp.1-14.