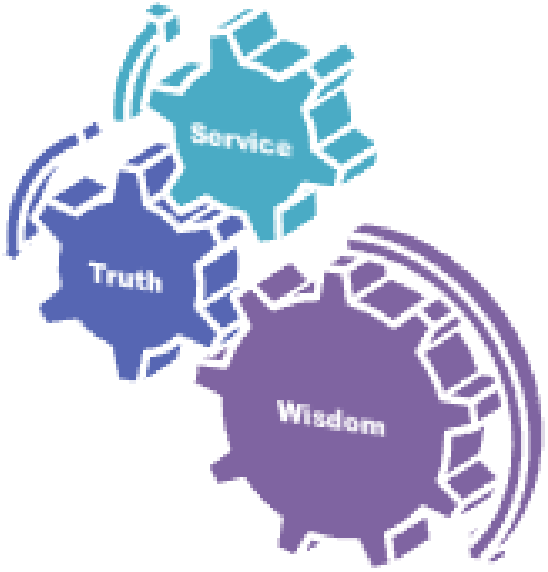
IN THE NAME OF ALLAH

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 15th Edition**
- **Goodman and Gilman's The Pharmacological Basis of Therapeutics 13th edition.**

Prof. Umar's Model of Teaching Strategy

- **Self Directed Learning** **Assessment Program**

- **Objectives** :To cultivate critical thinking, analytical reasoning, and problem-solving competencies.
- To instill a culture of self-directed learning, fostering lifelong learning habits and autonomy.
- **How to Assess?**
- Ten randomly selected students will be evaluated within the **first 10 minutes of the lecture** through 10 multiple-choice questions (MCQs) based on the PowerPoint presentation shared on Students Official WhatsApp group, one day before the teaching session.
- The number of MCQs from the components of the lecture will follow the guidelines outlined in the **Prof. Umar model of Integrated Lecture**.

Component of LGIS	Core Knowledge	Horizontal Integration	Vertical Integration	Spiral Integration
No of MCQs	6-7	1-2	1	1

1. A 30-year-old woman is prescribed sublingual nitroglycerin for angina. Which of the following best explains why this route is preferred over oral administration?

A. It prevents first-pass metabolism

B. It increases bioavailability by reducing gastric degradation

C. It has a faster onset due to increased lipid solubility

D. It undergoes active transport in the intestines

E. It provides a sustained release of the drug

CORE KNOWLEDGE

SDL ASSESSMENT PROGRAM

2. A patient is prescribed an enteric-coated aspirin tablet. What is the most important reason for this formulation?

A. To increase solubility in the stomach

B. To enhance dissolution in acidic pH

C. To prevent gastric irritation

D. To increase hepatic metabolism

E. To allow absorption in the duodenum

3. A physician prescribes a prodrug that requires metabolic activation in the liver. How does this influence the drug's absorption and efficacy?

A. The drug has no effect until metabolized

B. The drug has reduced absorption in the intestines

C. The drug undergoes enterohepatic circulation

D. The drug is excreted unchanged in urine

E. The drug must be administered intravenously

4. A 25-year-old woman takes an antibiotic that undergoes active transport in the intestines. Co-administration of another drug inhibits the transporter, leading to treatment failure. What is the most likely mechanism behind this interaction?

A. Increased gastric acid secretion

B. Increased hepatic metabolism

C. Decreased drug absorption due to transporter inhibition

D. Increased first-pass metabolism

E. Enhanced renal clearance

CORE KNOWLEDGE

SDL ASSESSMENT PROGRAM

5. A 45-year-old male with chronic diarrhea is started on an extended-release formulation of a painkiller. After a week, he reports no pain relief. What is the most likely reason for treatment failure?

A. Increased first-pass metabolism

B. Increased gastric acid secretion

C. Decreased drug dissolution time

D. Reduced transit time through the intestine

E. Drug accumulation in the liver

6. A newborn is prescribed an oral antibiotic. Compared to adults, which of the following physiological differences in neonates will most likely reduce drug absorption?

A. Increased gastric acid secretion

B. Decreased gastric emptying time

C. Increased bile salt secretion

D. Increased intestinal enzyme activity

E. Increased P-glycoprotein activity

7. A 30-year-old man is prescribed a highly lipophilic drug for a chronic condition. Which of the following anatomical factors will most significantly enhance its absorption in the small intestine?

A. Increased intestinal motility
B. High density of villi and microvilli
C. Increased mucous secretion
D. Presence of tight junctions
E. High pH in the duodenum

8. A 45-year-old male with chronic diarrhea is started on an extended-release formulation of a painkiller. After a week, he reports no pain relief. What is the most likely reason for treatment failure?

A. Increased first-pass metabolism
B. Increased gastric acid secretion
C. Decreased drug dissolution time
D. Reduced transit time through the intestine
E. Drug accumulation in the liver

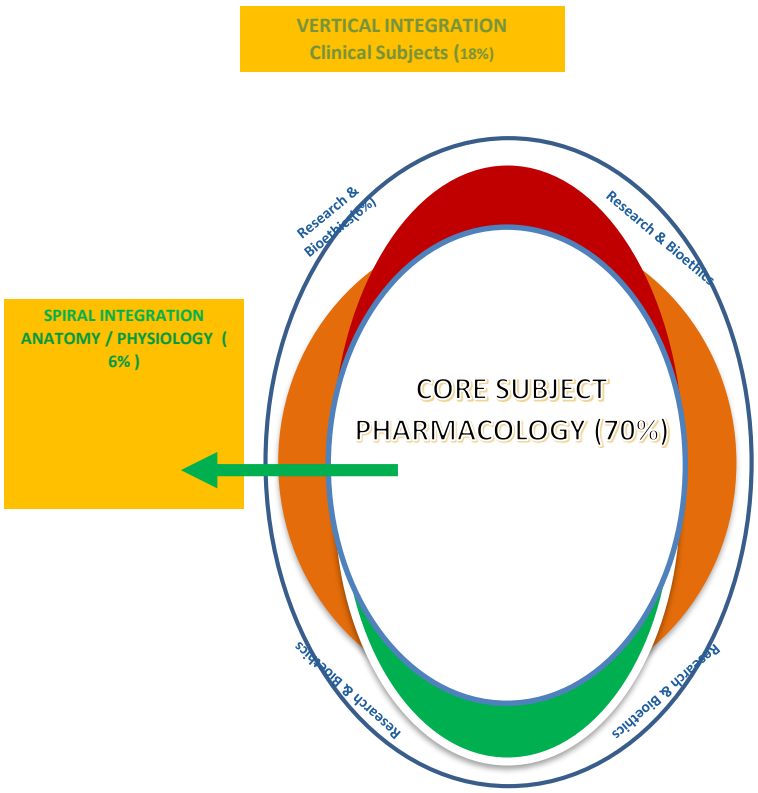
9. A 55-year-old male with celiac disease is started on oral iron supplements for anemia. However, his hemoglobin levels do not improve. What is the most likely explanation?

A. Reduced gastric acid secretion
B. Damage to duodenal mucosa
C. Enhanced first-pass metabolism
D. Increased renal clearance of iron
E. Increased hepatic metabolism of iron

10. A patient with Crohn's disease affecting the terminal ileum develops Vitamin B12 deficiency despite adequate dietary intake. What is the most likely reason for this deficiency?

A. Increased gut motility
B. Decreased gastric acid production
C. Loss of intrinsic factor secretion
D. Loss of site of absorption
E. Increased bile acid excretion

PROFESSOR UMAR'S CLINICALLY ORIENTED INTEGRATION MODEL FOR INTERACTIVE LECTURES



3RD Year Pharmacology LGIS (20 slides)		
Core Subject – 15 slides (75%)		
Vertical integration (Clinical Subjects)	•	1 slide (5%)
Spiral Integration (basic sciences subjects)	•	2 slideS (10%)
Spiral integration	•	2 slides (10%)

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 ?

CORE SUBJECT

PHARMACOKINETIC PROCESSES

- Absorption
- Distribution
- Metabolism
- Excretion

ADME

CORE SUBJECT

ABSORPTION OF DRUGS

- Absorption is the movement of drug from its site of administration into the circulation.

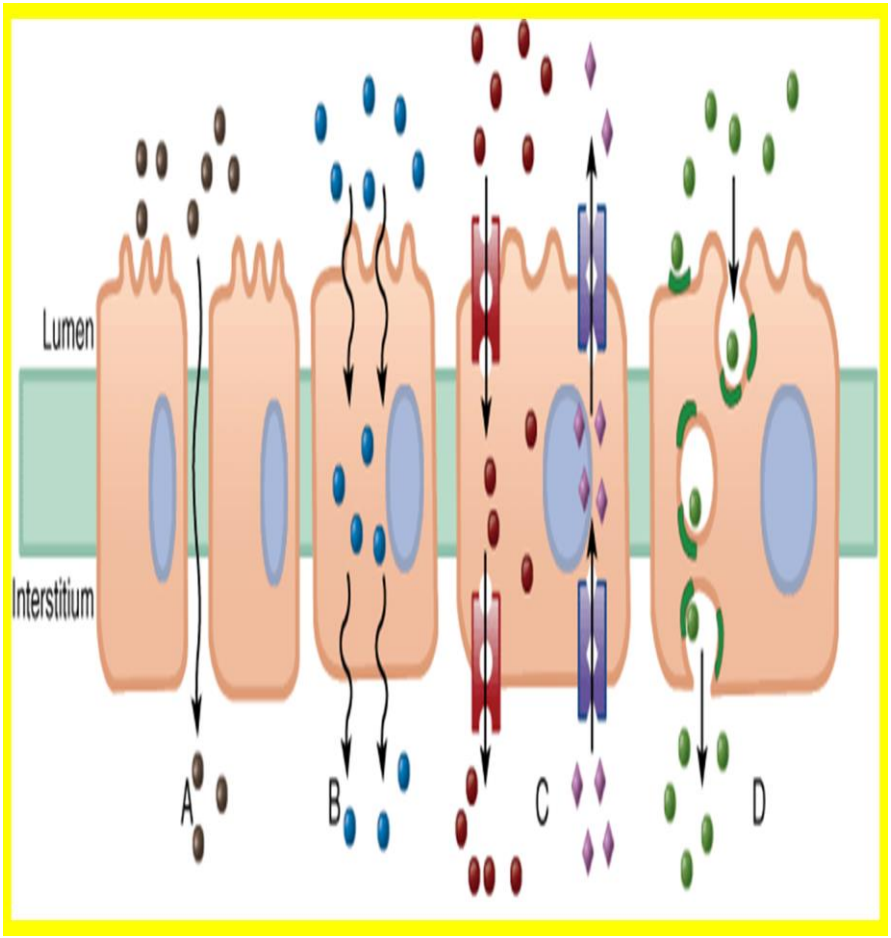
- The rate of absorption affects the onset , duration and intensity of drug action.

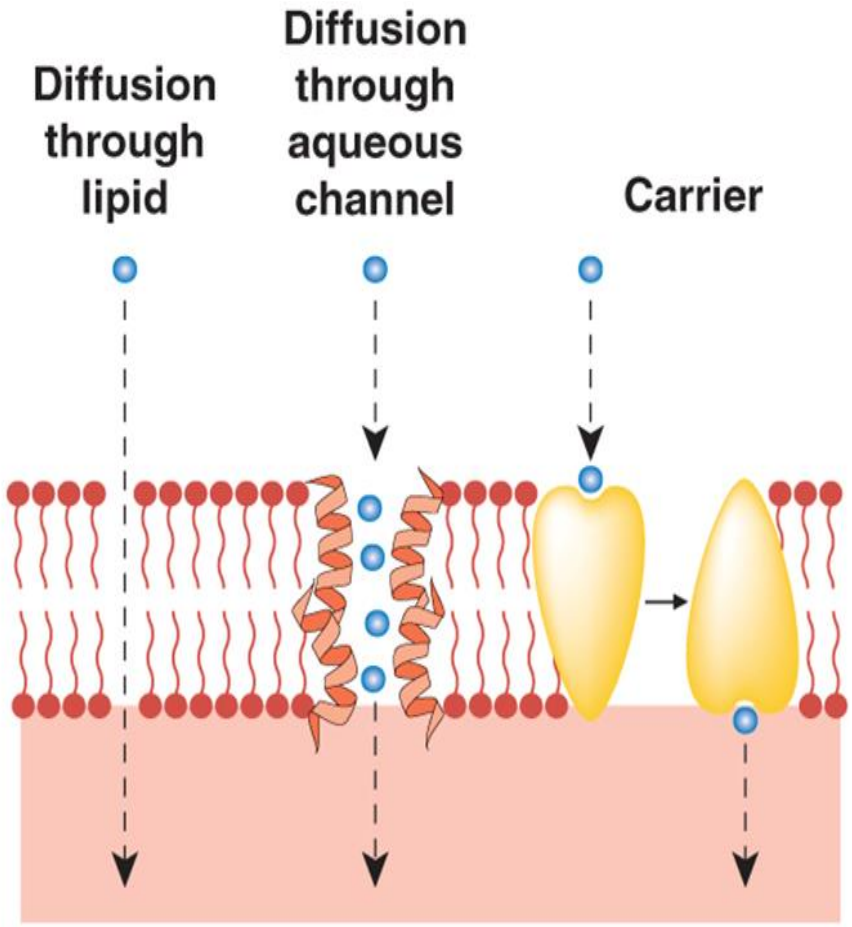
CORE SUBJECT

PERMEATION

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

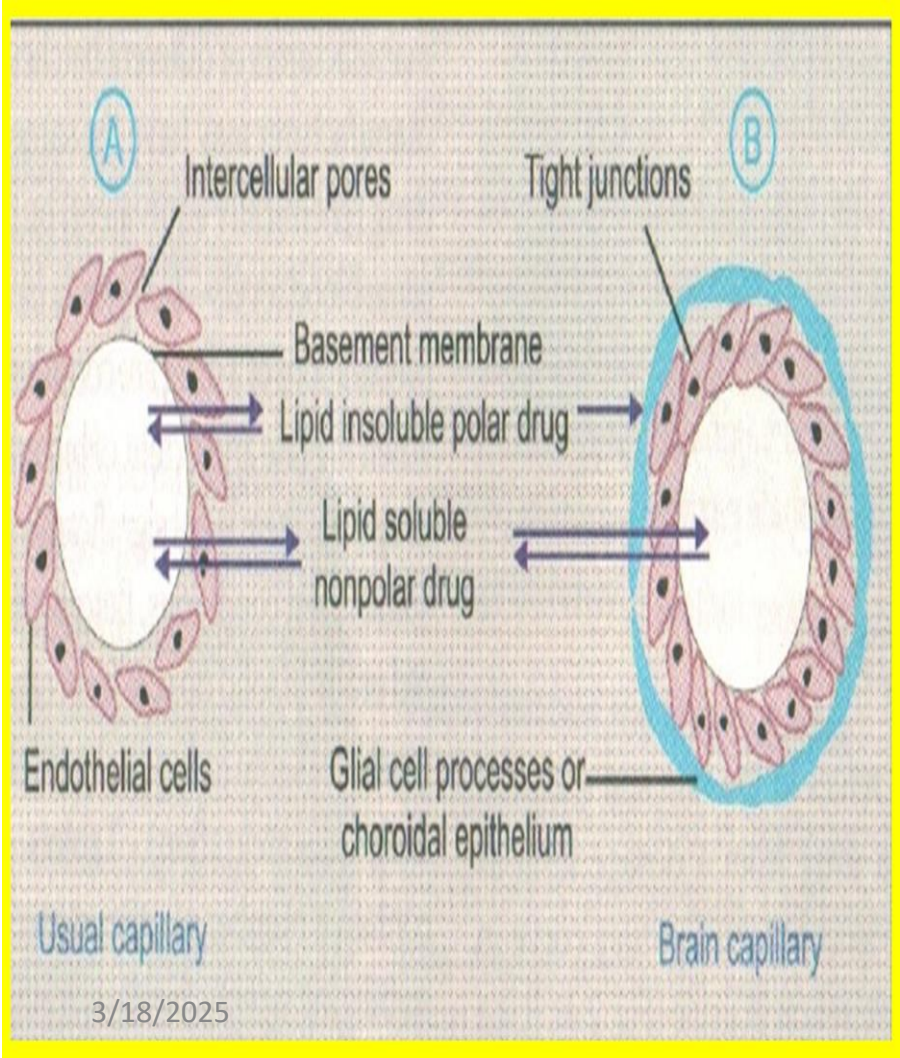
CORE SUBJECT

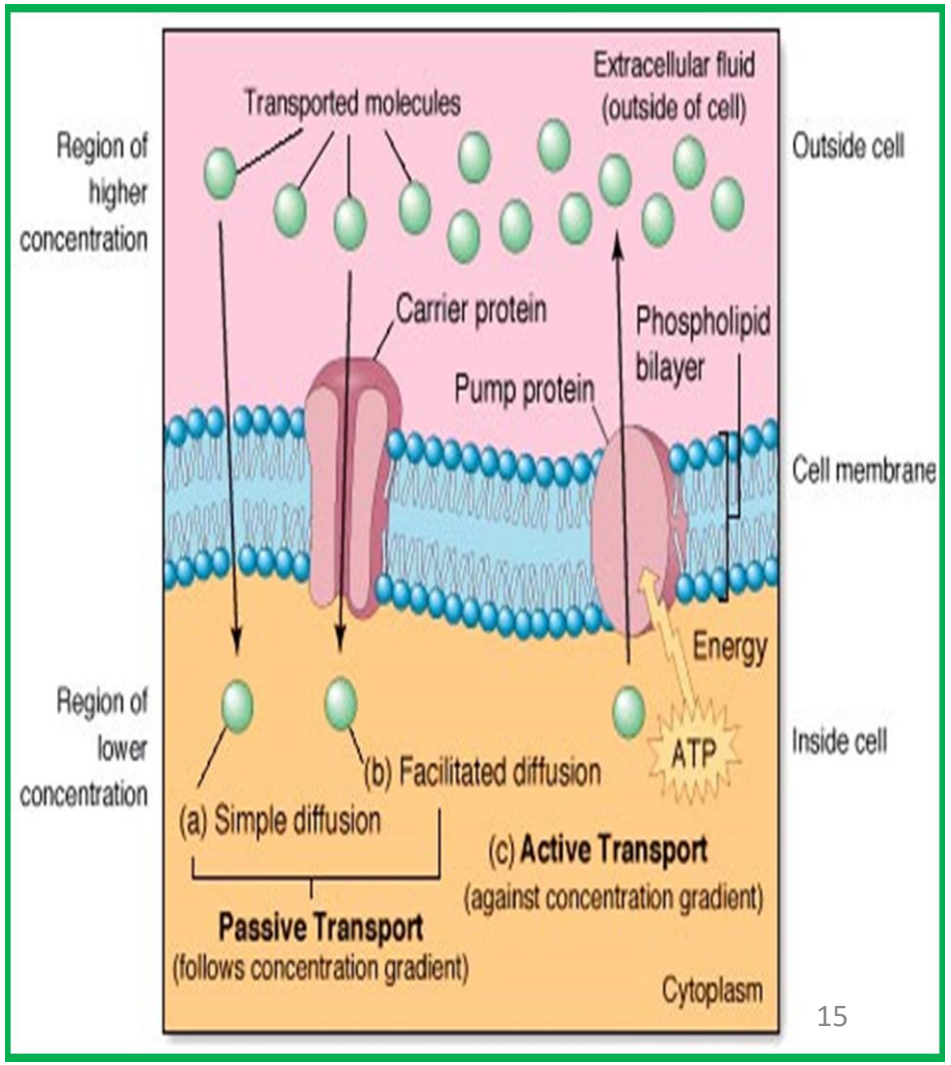




SPIRAL INTEGRATION

VERTICAL INTEGRATION





FACTORS AFFECTING DIFFUSION

1. Concentration Gradient Across Membrane:

- Fick's law of diffusion

- Flux (molecules/unit time) =

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

CORE SUBJECT

FACTORS AFFECTING DIFFUSION

CONT--

2. Molecular/ Particle Size

3. Membrane Surface Area

4. Lipid :Aqueous Partitian Coefficient

CORE SUBJECT

CONT--

5. **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

CORE SUBJECT

FACTORS AFFECTING DIFFUSION

- Henderson-Hasselbalch equation

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

- Weak Acids
- Weak bases

CORE SUBJECT

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

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

CORE SUBJECT

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.**

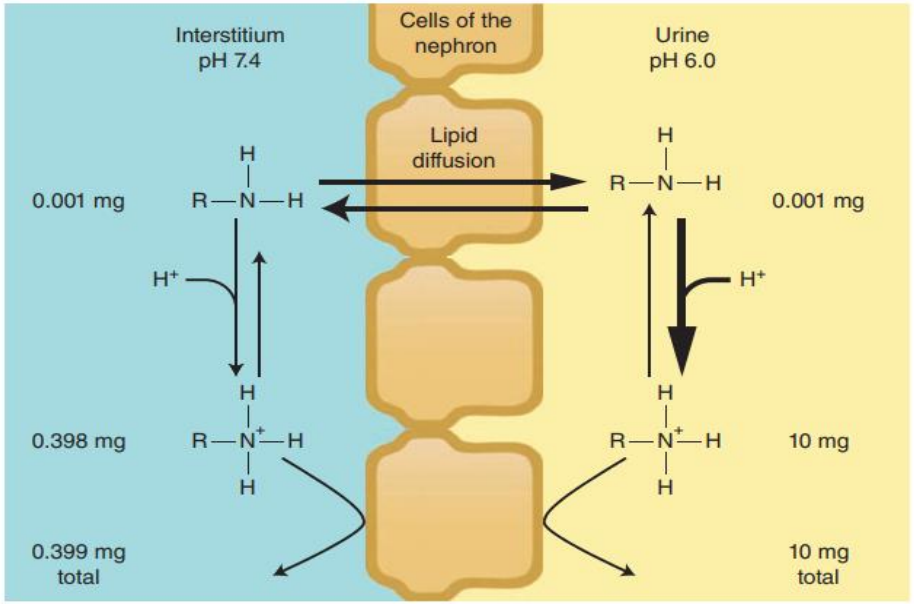
ION TRAPPING

- 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.**

CORE SUBJECT

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.



VERTICAL INTEGRATION

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

CORE SUBJECT

FACTORS AFFECTING ABSORPTION

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

CORE SUBJECT

FACTORS AFFECTING ABSORPTION

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

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

VERTICAL INTEGRATION

How To Access Digital Library

1.Go to the website of HEC National Digital Library.
2.On Home Page, click on the INSTITUTES.
3.A page will appear showing the universities from Public and Private Sector and other Institutes which have access to HEC National Digital Library HNDL.
4.Select your desired Institute.
5. A page will appear showing the resources of the institution
6. Journals and Researches will appear
7. You can find a Journal by clicking on JOURNALS AND DATABASE and enter a keyword to search for your desired journal.

SPIRAL INTEGRATION

FURTHER READING

- Cheng L, Wong H. Food effects on oral drug absorption: application of physiologically-based pharmacokinetic modeling as a predictive tool. Pharmaceutics. 2020 Jul 17;12(7):672.

- Macheras P, Chryssafidis P. Revising pharmacokinetics of oral drug absorption: I models based on biopharmaceutical/physiological and finite absorption time concepts. Pharmaceutical research. 2020 Oct;37:1-3.

SPIRAL INTEGRATION


Thank
you!