PHARMACOLOGY
433

King Saud University
College of Medicine
Foundation Block

Pharmacokinetics 1 ; Drug Administration and Absorption

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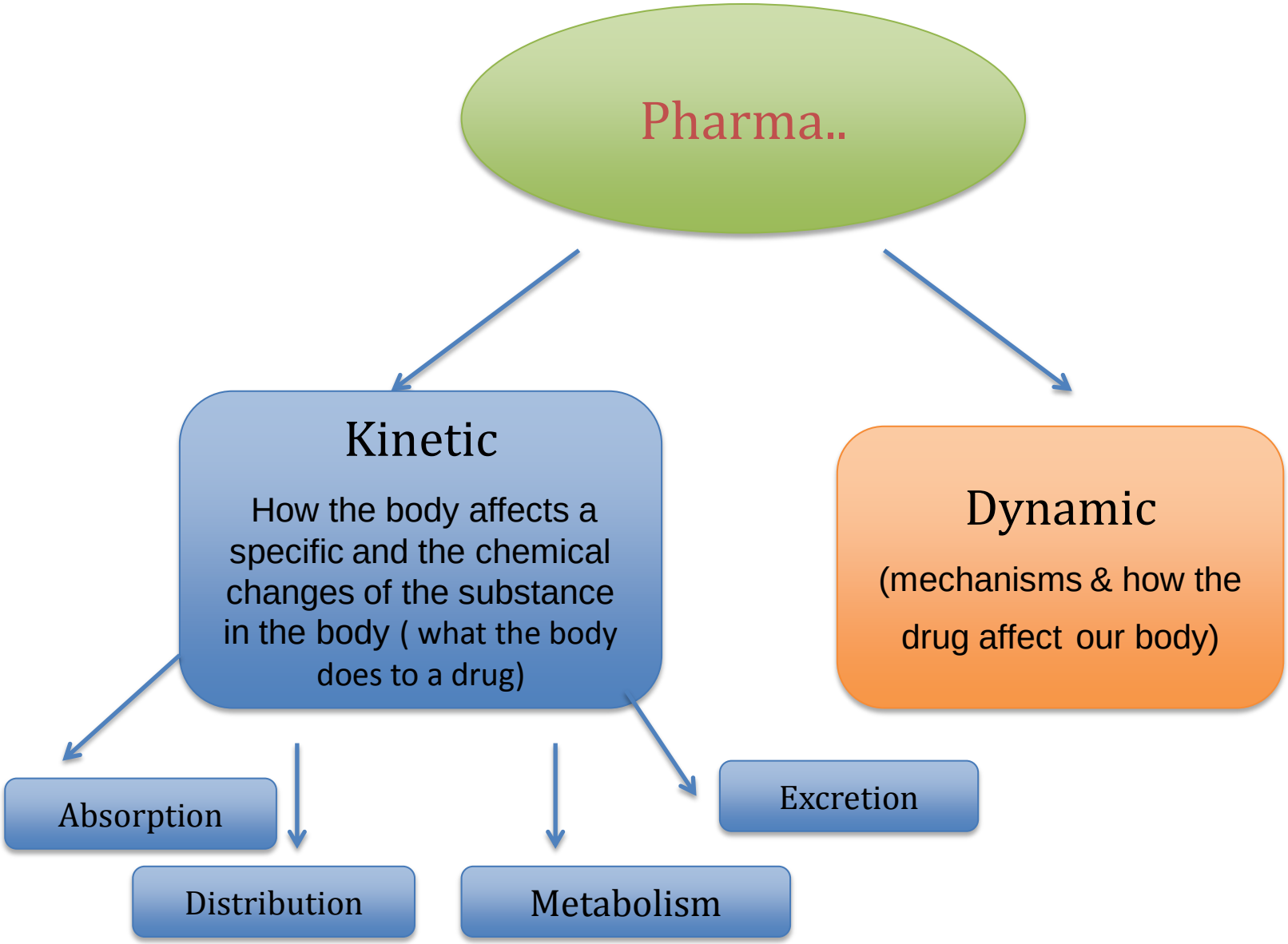
Objectives

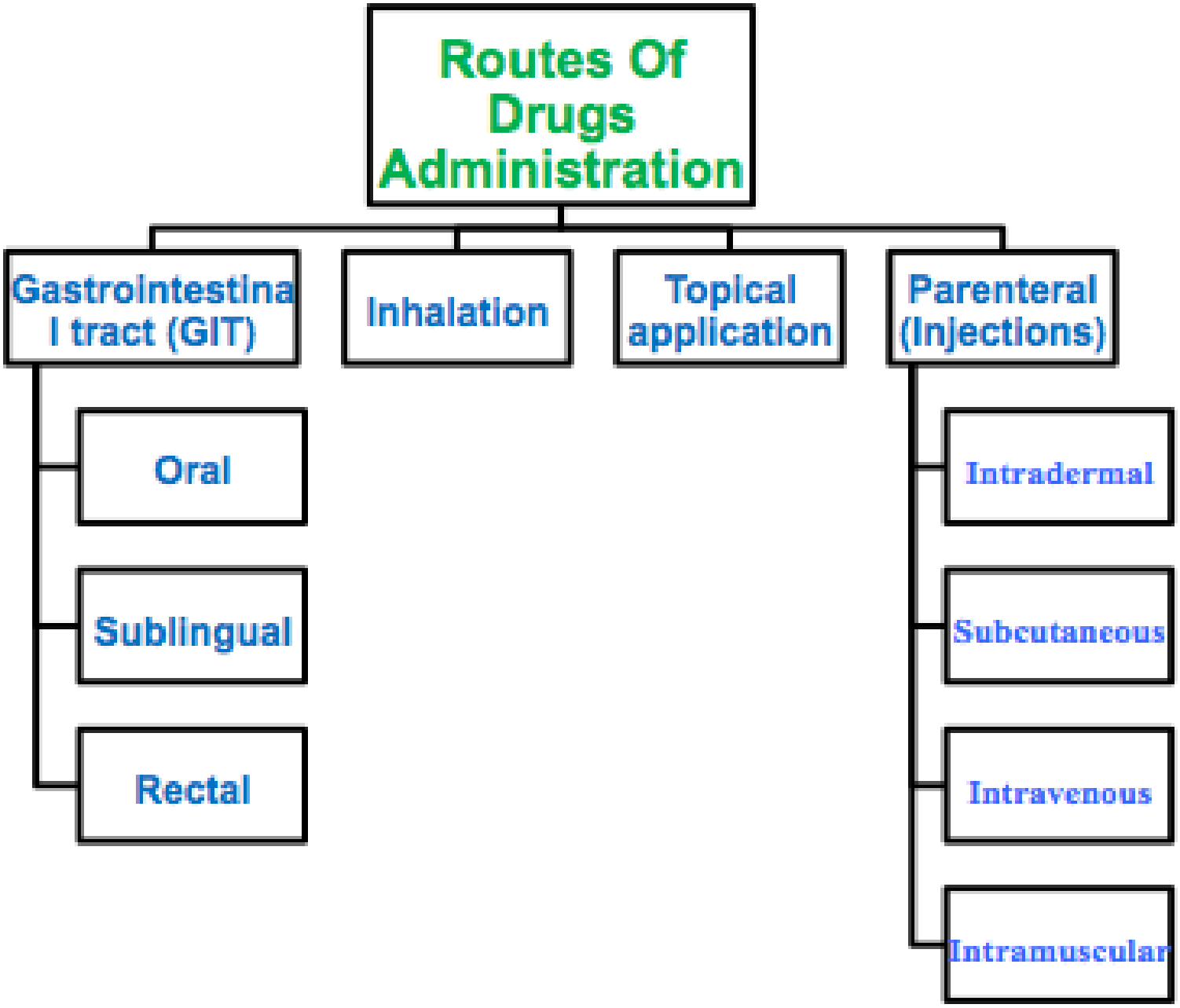
1	Know the meaning of pharmacology and its branches.
2	Discuss the different routes of drug administration.
3	Identify the advantages and disadvantages of various routes of drug administration.
4	Know the various mechanisms of drug absorption.
5	List different factors affecting drug absorption.
6	Define bioavailability and factors affecting it.

KEY WORDS :

*Pharmacokinetics
*Pharmacodynamics
*Bioavailability
*First-Pass-Effect
*Parental Administration
*Drug Absorption

Pharmacology Is the science that deals with the drugs




Routes Of Drugs Administration
Gastrointestinal tract (GIT)
Inhalation
Topical application
Parenteral (Injections)
Oral
Sublingual
Rectal
Intradermal
Subcutaneous
Intravenous
Intramuscular

Enteral via (GIT)*

	Advantages	Disadvantages
Oral	Common, easy, self use, safe, convenient, cheap, no need for sterilization.	Slow effect, no complete absorption, destruction by pH & enzymes, GIT irritation, Food-Drug interactions, Drug-Drug interactions, 1st pass effect, Low bioavailability. Not suitable for: vomiting & unconscious patient., emergency & bad taste drugs.
Sublingual	Rapid effect, emergency use, high bioavailability, no 1st pass effect, no GIT irritation, no food drug interaction. *Dosage form:* friable tablet.	Not suitable for: - Irritant drugs - Frequent use
Rectal**	Suitable for: children, vomiting, unconscious patients. Irritant & bad taste drugs. Less 1st pass metabolism (50%) Dosage form: Suppository (تحميلة) or enema. (حقنة شرجية)	- Irregular absorption & bioavailability. - Irritation of rectal mucosa.

*Gastro intestine tract

**شرجية (أي دواء يؤخذ عن طريق فتحة الشرج)

First Pass Metabolism

What is it ?

Drugs where they are metabolized (in liver mostly) before reaching to blood.

Where does it occur ?

- Liver
- Gut wall
- Gut lumen

Results in

-Low bioavailability (low conc. of drug in blood).

-Short duration of action (t ½).

-Drugs with high first pass effect should not be given orally but parenterally.

Oral Formulations

Tablets	Capsules	Syrup	Suspension	Emulsion**
Coated tablets: Sugar-coated to mask bad taste. Enteric coated tablets: Dissolve only in intestine.	Hard gelatin capsules:(contain powder) Soft gelatin capsules: (contain liquid)	Sweet liquid drugs e.g.: Cough syrups	Mixture of solid in liquids. e.g. Antibiotics	*Male's slides * كريم مستحلب
				

Topical Application

Drugs that are applied topically to produce local effects.

Skin (percutaneous) e.g. : local anesthesia. Eye drops e.g. : conjunctivitis.

Ear drops e.g. : otitis externa. Intranasal e.g. : decongestant nasal spray.

Transdermal

Are medicated adhesive patch applied to skin to provide systemic effect (prolonged drug action).

e.g. the nicotine patches (quit smoking)

e.g. Scopolamine (vestibular depressant)

Inhalation

Advantages

Rapid absorption, suitable for emergency, provide local action, limited systemic effect, less side effects, no first pass effect

Disadvantages

Not suitable for irritant drugs

Only few drugs can be used

Dosage Form

-Volatile gases e.g. anesthetics

-Aerosol, nebulizer for asthma

Parental Administration

	Volume	Advantages	Disadvantages
Intradermal (I.D)	0.1 ml	Suitable for vaccinations, Sensitivity tests, No first pass metabolism.	Not suitable for: Large volumes.
Subcutaneous (S.C)	0.1 – 1 ml	Suitable for sustained release effect exp, Insulin zinc prep, Poorly soluble suspensions &slow release implants, No first pass metabolism	Not suitable for: Large volumes.
Intramuscular (I.M)	3 -5 ml	Oily preparations or poorly soluble substances, Prolonged duration of action, No first pass metabolism.	Not suitable for: Irritant drugs, pain, abscess, tissue necrosis may happen
Intravenous (I.V)	500 ml	Rapid action (emergency), High bioavailability, No food-drug interaction, No first pass metabolism, No gastric irritation. Suitable for: Vomiting, unconscious patients, irritant, bad taste Dosage form: -Vial (repeated use) -Ampoule (single use)	Only for water soluble drugs, Infection, Sterilization, Pain, Needs skill, Anaphylaxis, Expensive Not suitable for: Oily solutions or poorly soluble substances

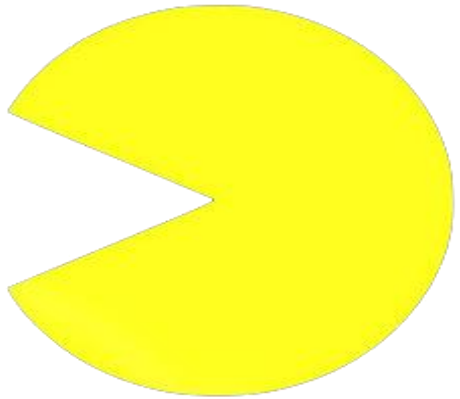
Drug Absorption

It is the passage of drug from its site of administration to its site of action through various cell membranes.

Except for intravenous administration (I.V), all routes of drug administration require that the drug be transported from the site of administration into the systemic circulation.

Mechanism of Drug Absorption

- Simple (passive) diffusion
- Active transport
- Facilitated diffusion
- Pinocytosis (Endocytosis)



Passive Transport	Active Transport	Carrier-Mediated Facilitated Diffusion
Along concentration gradient (from high to low).	Against concentration gradient (from low to high).	Along concentration gradient (from high to low).
No carriers needed.	Needs carriers.	Needs carriers.
Not saturable.	Saturable.	Saturable.
Not selective.	Selective (Specific).	Selective.
No energy.	Energy is required.	No energy required.
Common.	Relatively unusual.	
Depends on lipid solubility.	e.g.: absorption of sugar, amino acids and iron.**	
Depends on pKa of drug - pH of medium.	Uptake of levodopa by brain.**	

Simple or Passive Diffusion

Water Soluble Drug

(Ionized or Polar)
Is readily absorbed via diffusion through **aqueous channels or pores** in cell membrane if it has small MW*

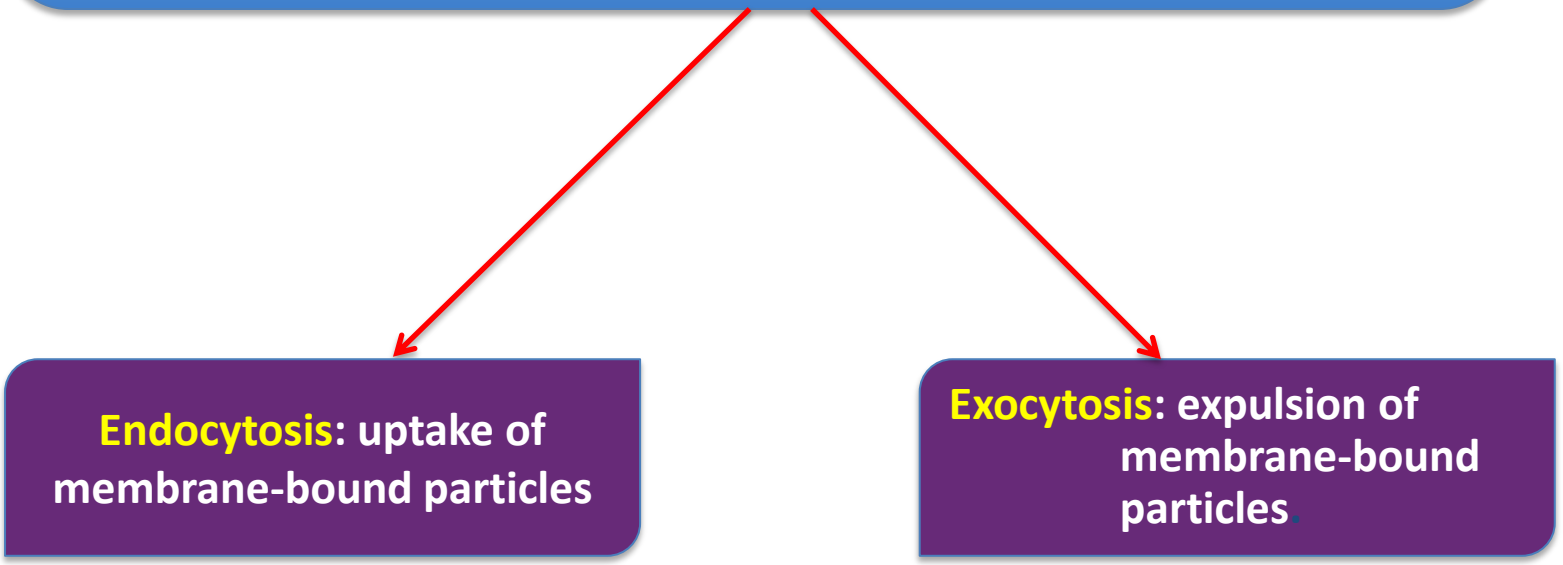
Lipid Soluble Drug

(Non-ionized or Non-polar)
Is readily absorbed via diffusion through **the lipid cell membrane itself.**

*Molecular weight
** Female's slides

Non-ionized / Ionized ratio is determined by pH and pKa**

Phagocytosis :
It occurs for high molecular weight drugs or highly lipid insoluble drugs



PKa of the drug (Dissociation or ionization constant):

pH at which half of the substance is ionized & half is unionized

pH of the medium
Affects ionization of drugs.

Weak Acids → **best absorbed in** → **Stomach (acidic medium)**
e.g.: acetaminophen*

Weak Bases → **best absorbed in** → **Intestine (basic medium)**

As general, basic drugs are more ionized and less diffusible in a relatively acidic medium, on the contrary basic are more lipid soluble and more diffusible in a relatively alkaline (basic) medium.*

The lower the pKa value (pKa < 6) of the acidic drug, the stronger the acid is.
e.g. aspirin (Pka= 3.0)

The higher the pKa value (pKa >8) of a basic drug, the stronger the base is.
e.g. propranolol (pKa= 9.4)

* Male's slides

Factors Modifying Drug Absorption

GENERAL FACTORS

- Lipid solubility.
- Degree of ionization.
- Drug solubility (aqueous soln. better than oily, susp, soln.).
- Dosage forms (depending on particle size and disintegration: solution > suspension > capsule > tablet).
- Concentration of drugs.
- Circulation at site of absorption. (Greater blood flow increases bioavailability. Intestine has greater blood flow than stomach)
- Area of absorbing surface (small intestine has large surface area due to intestinal microvilli) ,
- Route of administration.

Factors affecting absorption from GIT

- GIT motility changed by drug or diseases.
- Presence of food (slow gastric emptying), Blood flow /surface area
- GIT juices.
- pH of GIT fluids.
- Chemical/drug interactions.
- Dosage form of a drug.

Most of the drug is absorbed with in 1-3 hours , mostly it occurs in small intestine ,rate of absorption depends on lipid solubility ,ionization and pH. (Diarrhea reduce absorption)

Drugs such as the **tetracycline**, **aspirin and penicillin V** which are highly ionized, can complex with Ca++ ions in membranes, food, or milk, leading to a reduction in absorption.

Female's slides.
Male's slides.
Explanations.

Bioavailability

Is the fraction of unchanged drug that enters systemic circulation after administration and becomes available to produce an action

I.V. provides 100% bioavailability

Oral usually has less than I.V.

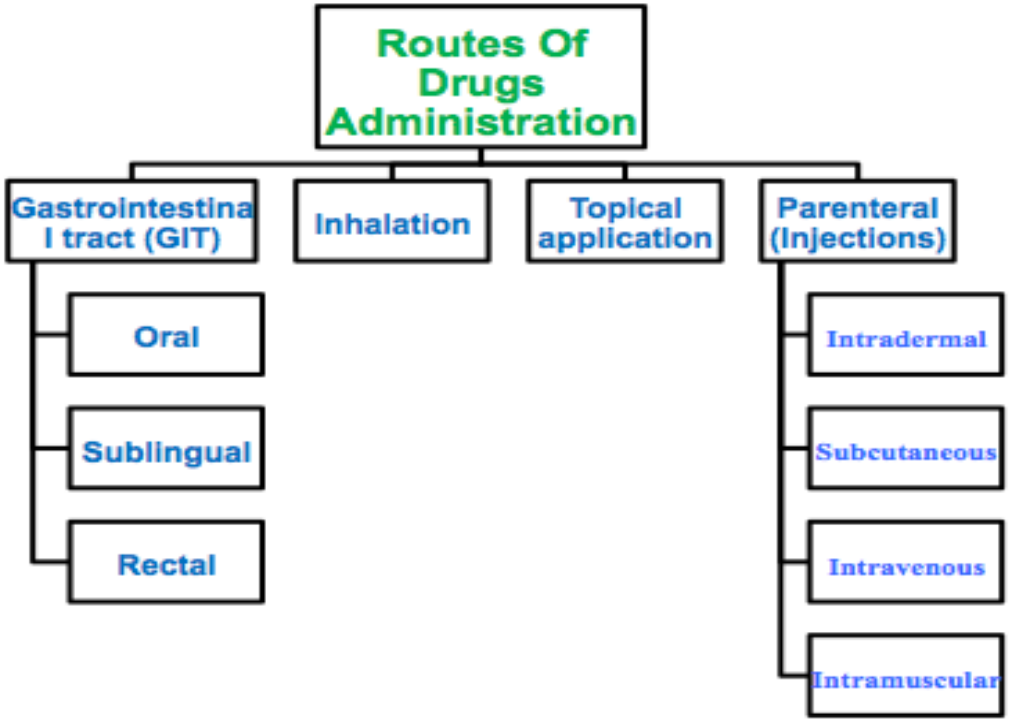
Summary

- ***Know the meaning of pharmacology and its branches.***

Meaning: Study of drugs (uses, names, and side effects)
Branches:
1-Pharmacokinetics:
(ADME) = Absorption, Distribution, Metabolism, and Excretion

2-Pharmacodynamics:
The mechanism and the effects.

- ***Discuss the different routes of drug administration***



- ***Identify the advantages and disadvantages of various routes of drug administration***

	Advantages	Disadvantages
Oral	Common and self-use and cheep.	Slow effect and no complete absorption, goes through first pass metabolism.
Sub-lingual	Rapid effect, high bioavailability, no first pass effect.	Not suitable for: Frequent use.
Rectal	Suitable for children, vomiting. Less first pass metabolism (50%).	Irregular absorption. Irritation of rectal mucosa.
Inhalation	Rapid absorption, provide local action, limited systemic effect.	Only few drugs can be used.

Summary

- *Know the various mechanisms of drug absorption*

ABSORPTION

Simple diffusion = passive diffusion
(No energy, along concentration gradient, no carrier, Non selective, depends on Lipid sulobilty and (Pka of the drug + PH of the medium) , non saturable

Active transport
ATP and carries are required, against concetration gradient, saturable, specific

Facilitated diffusion
along concentration gradient, Requires carriers, Selective, saturable ,No energy is required

Phagocytosis (Endocytosis= uptake) & (Exocytosis=expulsion)
occurs for: -high molecular weight Drugs
- highly lipid insoluble drugs.

- *Define bioavailability and factors affecting it.*

- **Bioavailability:** is the fraction of the drug that reaches the blood without any changes.

- *List different factors affecting drug absorption.*

Route of administration.
Dosage forms

- Molecular weight of drug.
- Lipid solubility
- Degree of ionization
- Drug solubility
- Chemical instability in gastric pH
- Surface area available for absorption.
- Blood flow to absorptive site
- Intestinal motility (transit time)
- Drug interactions.
- Food.

MCQs

1. Which one of the following routes of administration is used in a case of no emergency?
A. Sublingual administration
B. Oral administration
C. Rectal administration
D. Parenteral administration
E. Both B and D

2. Which one of the following routes of administration that mostly has no systemic effect?
A. Parenteral administration
B. Topical application
C. Inhalation
D. Both B and C
E. Both A and B

3. …… are studies of mechanisms and effects of drug action.
A. Pharmacodynamics
B. Pharmacokinetics
C. Pharmacogenomics
D. None of the above.

4. Route of administration that avoid "first-pass" hepatic effects:
A. Sublingual
B. Oral
C. Transdermal
D. Rectal
E. Both A and C

5. ……. is not suitable for oily solutions or poorly soluble substances.
A. Intravenous administration
B. Subcutaneous administration
C. Intradermal administration
D. Intramuscular administration

6. Which one of the following is a character of active transport?
A. Unspecific and not saturable
B. Requires no energy and no carrier
C. Absorption of amino acids
D. Occurs along concentration gradient

1-B , 2-D , 3-A , 4-E, 5-A, 6-C

MCQs

7. Drug is most absorbable if it is:
A. Non ionized
B. Ionized
C. Water soluble
D. Both B and C

8. Penicillin (pKa: 2.74) is best absorbed in the:
A. Small intestine
B. Large intestine
C. Stomach
D. None of the above

9. Most drugs are either ____ acids or ____ bases.
A. Strong; Strong
B. Strong; Weak
C. Weak; Weak
D. Weak; Strong

10. Which of the following drug permeation mechanisms involves polar substances too large to enter cells by other means, such as iron or vitamin B12?
A. Aqueous diffusion
B. Lipid diffusion
C. Carrier molecules
D. Endocytosis and exocytosis

11. The order of hardest absorbed drug forms (from most to least) is:
A. Capsule>tablet>suspension>solution
B. Tablet>capsule>suspension>solution
C. Capsule>tablet>solution>suspension
D. Tablet>capsule>solution>suspension

7-A , 8-C , 9-C, 10-D, 11-B

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We hope that we made this lecture easier for you

THANK YOU ☺

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