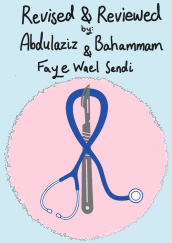


MED441
KING SAUD UNIVERSITY

Drug administration and absorption

Important
Main Text
Male slides
female slides
Extra information
Doctors notes

For any future corrections Editing file

If you didn't understand any part from this lecture Click here

Objectives

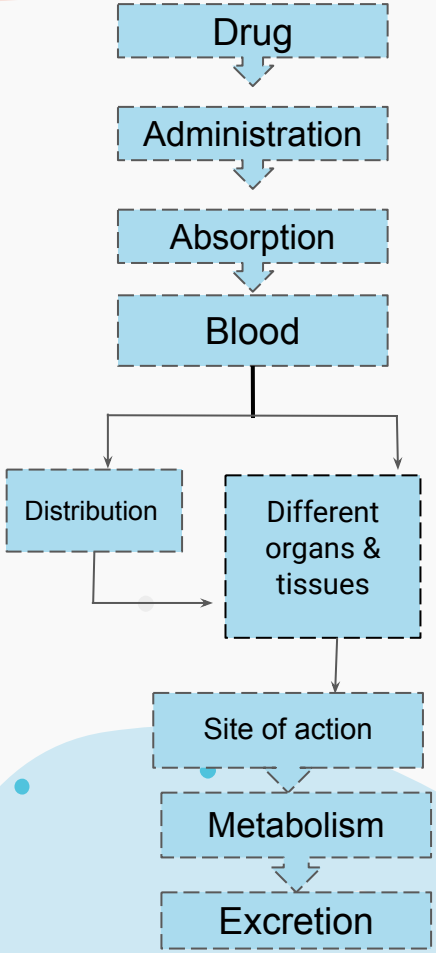
- Know the meaning of pharmacology and its branches.
- Discuss the different routes of drug administration.
- Identify the advantages and disadvantages of various routes of drug administration.
- Know the various mechanisms of drug absorption.
- List different factors affecting drug absorption.
- Define bioavailability and factors affecting it.

Pharmacology
Pharma : drug
Logos: Science
:is the science that deals with the drugs regarding names, pharmacokinetics, pharmacodynamics, side effects and uses.

Pharmacodynamics :
Are studies of
- Mechanisms of drug action.
- Pharmacological effects of drugs.
(what the drug does to the body?)

Pharmacokinetics :
are studies of the [**ADME**]
[**DEMA**]
absorption, **d**istribution, **m**etabolism & **e**xcretion of drugs.
(what the body does to a drug?)

Pharmacokinetics



Acetylsalicylic acid (ASA) or Aspirin can reduce (inflammation, pain and fever)

It inhibits the action of a human cell membrane enzyme known as cyclooxygenase

Penicillin cures certain bacterial infections disrupt the synthesis of cell walls in susceptible bacterial strains by inhibiting a key enzyme.

(Boys slides)

Routes of drug administration:

1. Enteral via GIT *GIT=gastrointestinal tract*
   - Oral
   - Sublingual (تحت اللسان)
   - Rectal

2. Inhalation (respiratory system)

3. Parenteral administration (Injections)

4. Topical application - Locally applied-
(غرض تجميلي او علاجي)

Routes of drug administration Enteral via GIT:	Advantage	Disadvantage
Oral Administration	• Common • easy • self use • convenient • cheap • no need for sterilization	• Slow effect, GIT irritation *It can not be used for emergencies* • Destruction by pH & enzymes e.g. penicillin , insulin • Food -drug or drug-drug interactions • First pass effect metabolism • No complete absorption *because of the pH, enzymes,food-drug interaction* • Low bioavailability *The concentration of the drug in the blood* Not suitable for : vomiting & unconscious patient emergency & bad taste drugs
Sublingual	• Rapid effect • can be used in emergency • High bioavailability * directly to blood circulation* • No first pass effect. • No GIT irritation • No food drug – interaction • Dosage form:friable tablet HINT: ال Advantages تبع sublingual هي عكس ال oral ال تبع disadvantages	not suitable for: Irritant drugs or Frequent use
Rectal	Suitable for • children, vomiting, • unconscious patients • Irritant & bad taste drugs • less first pass metabolism (50%) • Dosage form: suppository or enema	• Irritation of rectal mucosa • Irregular absorption & bioavailability

Bioavailability

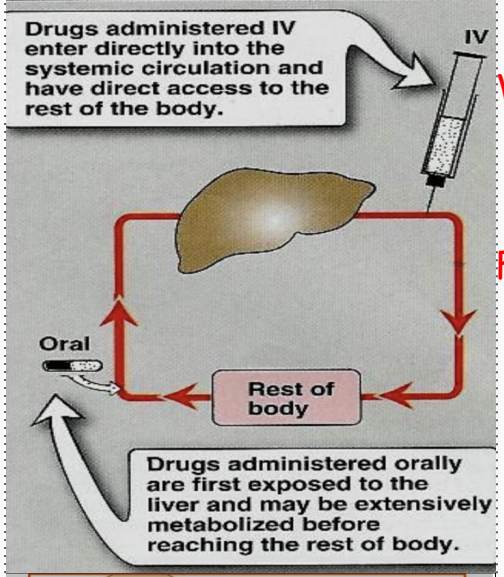
Is the amount of unchanged drug that enters systemic circulation after administration and becomes available to produce pharmacological actions

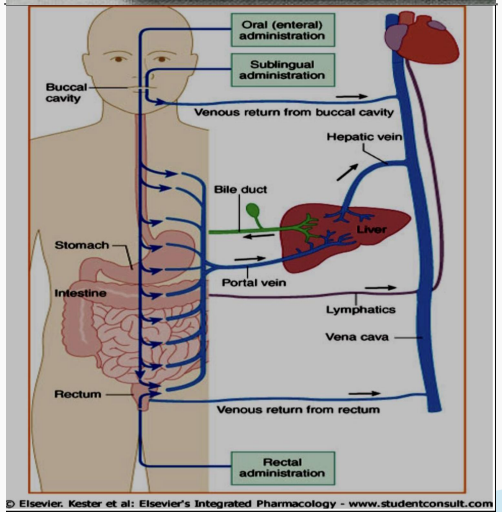
Bioavailability is the concentration of the drug in the blood.

First pass effect*first pass metabolism*:

- Drugs given orally
- Taken to the **liver** (via portal circulation) and metabolized
- Reaching to the blood to be distributed to the body compartment

لما ناخذ دواء orally
راح يروح للكبد ويصير له تكسر ونخسر
جزء من الدواء وتقل bioavailability
ثم يروح للدم ويدخل blood circulation
علشان يصير له absorption
But if we take the drug by
Intravenous injection
First pass effect is avoided.





Where does it occur?

- Liver
- GIT wall
- GIT lumen

First pass metabolism results in:

- Low bioavailability (low conc. of drug in blood).
- Short duration of action (t $\frac{1}{2}$).
- drugs with high first pass effect should not be given orally but parenterally.

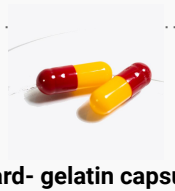
Note : most of the drugs absorbed in the small intestines

Oral Dosage Forms (oral formulations)

Tablets

- Coated tablets: sugar-coated to mask bad taste
- Enteric coated tablets: dissolve only in intestine *it avoids stomach acidity*

Soft- gelatin capsule



Hard- gelatin capsule

Capsules

- Hard gelatin capsules: (contain powder)
- Soft gelatin capsules: (contain liquid)

Spansule

Spansule oral capsule:
a capsule which when swallowed releases one or more medicinal drugs over a set period.
Has a duration of action

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Syrup: e.g. cough syrup*فيها كمية بسيطة من السكر علشان تحسن الطعم خصوصا للاطفال*

Suspension (mixture of solid in liquids e.g. antibiotics).

parentral administration. (INJECTION)

Advantage	Disadvantage
• No gastric irritation • No food-drug interaction • No drug-drug interaction • No first pass metabolism • higher availability than oral	• Need skill • Pain, tissue necrosis or abscess (I.M.) • Anaphylactic or hypersensitivity reaction (I.V.)

من الأبطأ بالاستجابة الى الأسرع

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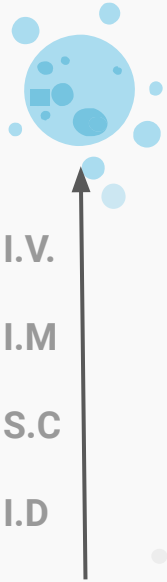


Types of parenteral

Intradermal **(I.D.)** (into skin)	Intramuscular **(I.M.)** (into muscles)	Intravenous **(I.V.)** (into veins)	Intrathecal **(I.T.)** (cerebrospinal fluids)
Subcutaneous **(S.C.)** (under skin)	Intra-arterial **(I.A.)** (into arteries)	Intraperitoneal **(I.P.)** (peritoneal cavity)	Intra - articular (Synovial fluids)

	Advantage	Disadvantage
Intradermal administration **I.D.** "Skin"	• Minute volume of drug (0.1 ml) • suitable for vaccinations • sensitivity test	not suitable for large volumes
Subcutaneous administration **S.C.**	• volume of drug (0.1 ml – 1 ml) • used for sustained release effect • suitable for for poorly soluble suspensions and instillation of slow-release implants e.g. insulin zinc preparation	not suitable for large volumes
Intramuscular administration **I.M.**	• moderate volumes (3-5 ml) • prolonged duration of action • oily preparations or poorly soluble substances can be used	Not suitable for • irritant drugs • pain, abscess, tissue necrosis may happen Abscess- necrosis may happen

Intravenous administration "I.V"

Advantage	Disadvantage
• (500ml can be given by infusion) • suitable for large volumes and • for irritating substances • Rapid action (emergency) • High bioavailability 100% • No food-drug interaction No first pass metabolism • No gastric irritation Suitable for • Vomiting & unconscious • Irritant & bad taste drugs	• used only for water soluble drugs • Infection • Anaphylaxis *الحساسيه المفرطة* • Sterilization • Expensive • not suitable for oily solutions or poorly soluble substances Must inject solutions slowly as a rule

Vial
"Repeated use"

Ampoule
"Single use"

Topical application:

Drugs are mainly applied topically to produce local effects.

They are applied to :

- Skin (percutaneous) e.g. allergy test, topical antibacterial and steroids and local anesthetics.
- Mucous membrane of respiratory tract (Inhalation) e.g. asthma
- Eye drops e.g. conjunctivitis
- Ear drops e.g. otitis externa
- Intranasal e.g. decongestant nasal spray

Inhalation

Advantage	Disadvantage
• rapid absorption (due to large surface area) • suitable for emergency • provide local action • limited systemic effect • less side effects • no first pass effect Dosage form: • volatile gases e.g. anesthetics • liquids given by aerosol, nebulizer for asthma treatment	• Not suitable for irritant drugs • Only few drugs can be used

Nebulizer

Inhalation

Atomizer

transdermal patch:

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, antiemetic for motion sickness).

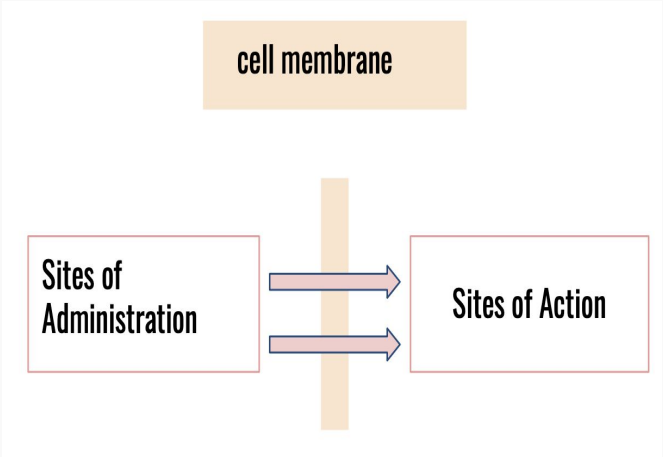
Helpful video

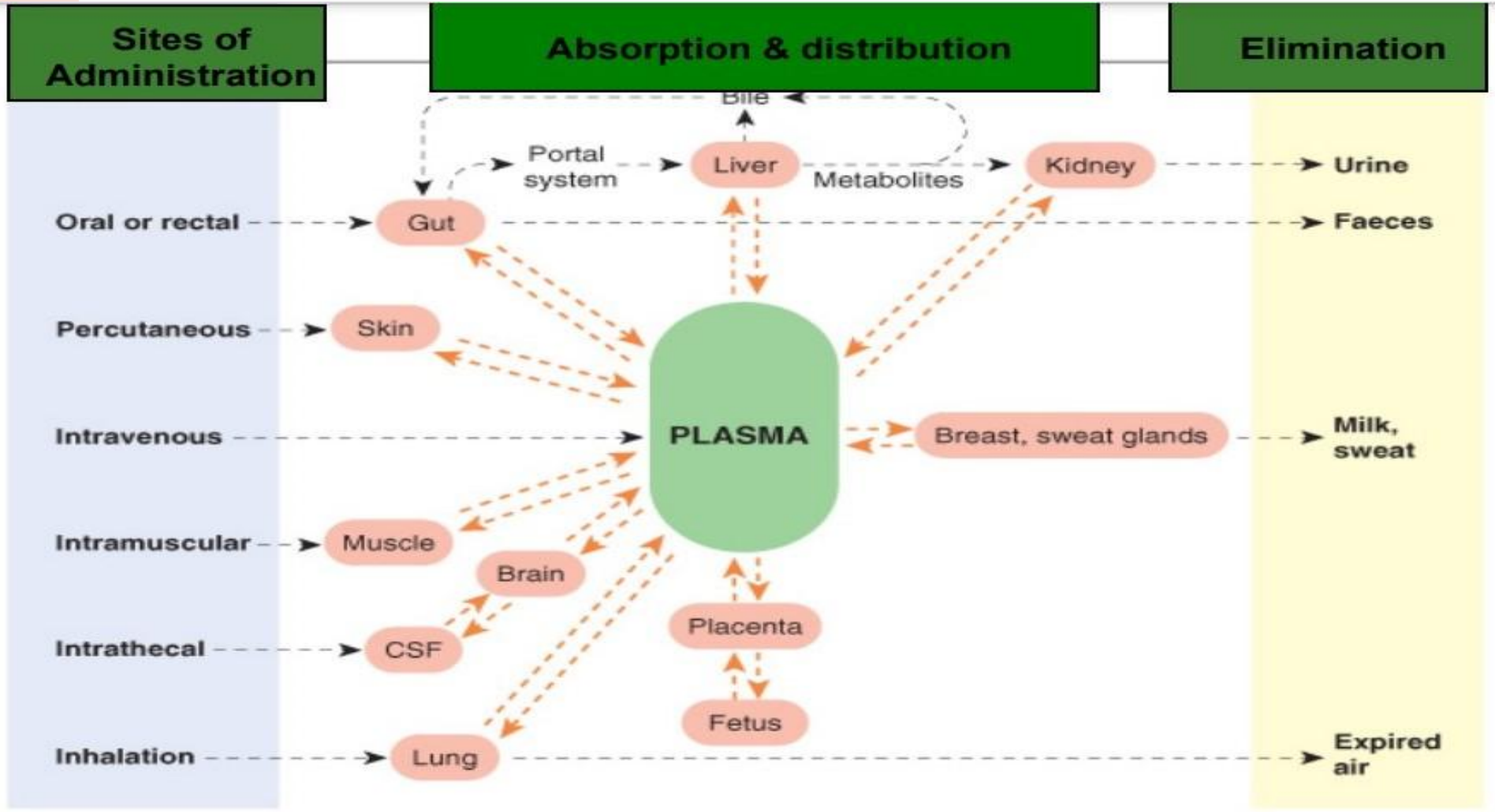
Drug Absorption

Is the passage of drug from its **site of administration** to **site of action** across cell membranes.

All routes of drug administration require that the drug be absorbed from the site of administration into the **systemic circulation** (blood) except:

I.V. administration requires no absorption (because they are delivered directly into the bloodstream)



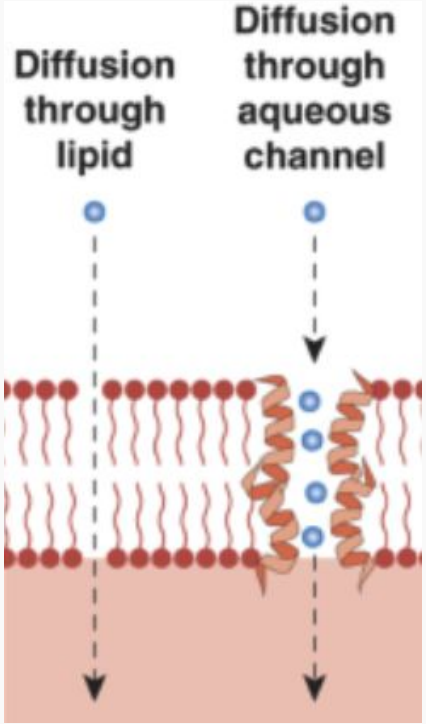

Sites of Administration
Absorption & distribution
Elimination
Bile
Portal system
Liver
Kidney
Metabolites
Urine
Oral or rectal
Gut
Faeces
Percutaneous
Skin
Intravenous
PLASMA
Breast, sweat glands
Milk, sweat
Intramuscular
Muscle
Brain
Placenta
Intrathecal
CSF
Fetus
Inhalation
Lung
Expired air

Mechanisms of Drug Absorption

- Simple/Passive diffusion
  - Aqueous: low molecular weight water soluble drugs diffuse through aqueous channels or pores in the cell membrane (filtration)
  - Lipid: low molecular weight lipid soluble drugs diffuse through the cell membrane
- Facilitated diffusion
- Active transport
- Endocytosis/Pinocytosis. Occurs for:
  - High molecular weight drugs. E.g. peptides
  - High polar drugs. E.g. vitamin B12 → intrinsic factor
    iron → with transferrin

Endocytosis:
Uptake of membrane-bound particles

Exocytosis:
Expulsion of membrane-bound particles



Passive Diffusion	Active Transport	Facilitated Diffusion
Along concentration gradient	Against concentration gradient	Along concentration gradient
No energy & carrier	Requires energy & carrier	No energy but requires carrier
Common	Uncommon	—
Not saturable	Saturable	Saturable
Non selective	Selective	Selective
Depend on **lipid solubility**	E.g. absorption of **sugar** & **amino acids**	E.g. similar to entry of **glucose into muscle**
Depend on **Pka of Drug** and **PH of the environment**	E.g. Uptake of **Levodopa** by the brain Used to treat Parkinsonism	—

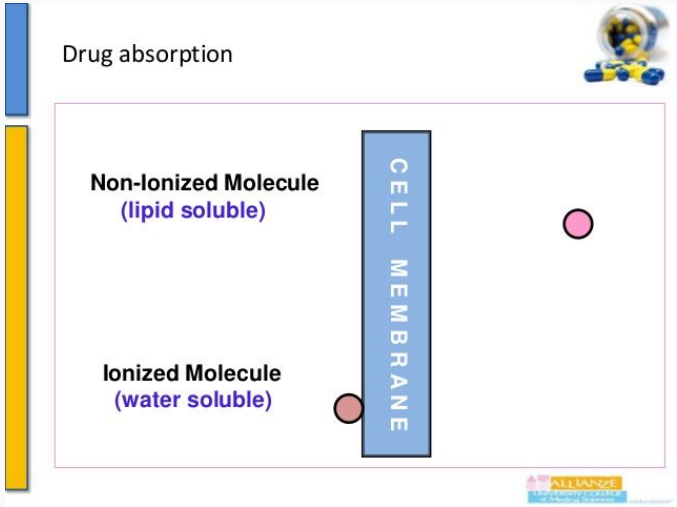
Note: Against concentration gradient> requiers energy

Along concentration gradient >No energy required

Note: If the mechanism requires a carrier, it's also saturable and specific

pKa & pH

- Most drugs are weak acids or weak bases
- pKa of drug (dissociation/ionization constant): pH at which ½ of the drug is ionized & ½ is unionized
- The lower the pKa value of the acidic drug the stronger the acid , pKa < 6
- The higher the pKa value of the basic the stronger the base , pKa > 8
    - Low pKa → acidic (e.g Aspirin, pKa = 3.0)
    - High pKa → basic (e.g Propranolol, pKa = 9.4)
- Only unionized form is absorbable
- Ionization of the drugs reduce passage of drugs across cell membranes
- The degree of ionization of drugs is determined by their Pka and pH of the surrounding (environment)
- Absorption:
    - Acidic → best absorbed in stomach
    - Basic → best absorbed in intestine



Remember:
Water soluble drugs=ionized=polar=charged at difficult to permeate cell membranes

Lipid soluble drugs= unionized=non polar=uncharged easy to permeate cell membranes

Drugs can exist into both forms

Factors affecting absorption

> means better absorption

Route of administration

E.g; sublingual > oral

Dosage forms

Solution > suspension > capsule > tablet

Molecular weight of drug

Small > big

Lipid & drug solubility

Aqueous preparation > oily suspension preparation

Degree of ionization

Unionized > ionized

Chemical instability in gastric pH

E.g; Penicillin & insulin

Surface area

Small intestine>stomach
Small intestine have large surface area than stomach due to intestinal microvilli.

Blood flow

Intestine (more blood flow) > stomach (less blood flow)
Greater blood flow increases Bioavailability

Gastric emptying

Increased gastric emptying → increase absorption (e.g metoclopramide)

Intestinal motility

Diarrhea reduces absorption

Drug interactions

Food

Slow gastric emptying → slower absorption. However, fatty meals increase absorption of fat soluble antifungal drug (e.g griseofulvin)

Much content was either copied or heavily inspired by the work of team 439... their effort is greatly appreciated

Useful Summary

Useful Summary

Quiz

1) What is the most common way of drug administration?

A) Oral
B) Sublingual
C) IV (intravenous)
D) IT (intrathecal)

2)Which type of the drug administration doesn't require absorption?

A-IM(intramuscular)
B-Sc(subcutaneous)
C-IV (intravenous)
D-ID(intradermal)

3)Which type of drug administration has the highest bioavailability?

A) Rectal
B) Oral
C) IV (Intravenous)
D) IT (intrathecal)

4)Where does the first pass effect take place?

A) Lymph nodes
B) Liver
C)Kidney
D) Spleen

Answers :
1-A
2-C
3-C
4-B

Quiz

5) Vitamin B12 is absorbed using?
A. Facilitated diffusion
B. Endocytosis
C. Active diffusion
D. Passive diffusion

6) Levadopa is absorbed using?
A. Facilitated diffusion
B. Endocytosis
C. Active diffusion
D. Passive diffusion

7) Least absorbable oral dosage form
A. Solution
B. Tablet
C. Suspension
D. Capsule

8) Drug that infect gastric emptying?
A. Aspirin
B. Griseofulvin
C. Metoclopramide
D. Conjunctivitis

Answers
5-B
6-C
7-B
8-C

Thank you

Team leaders

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-"Success consists of going from failure to failure without loss of enthusiasm."

Never give up!