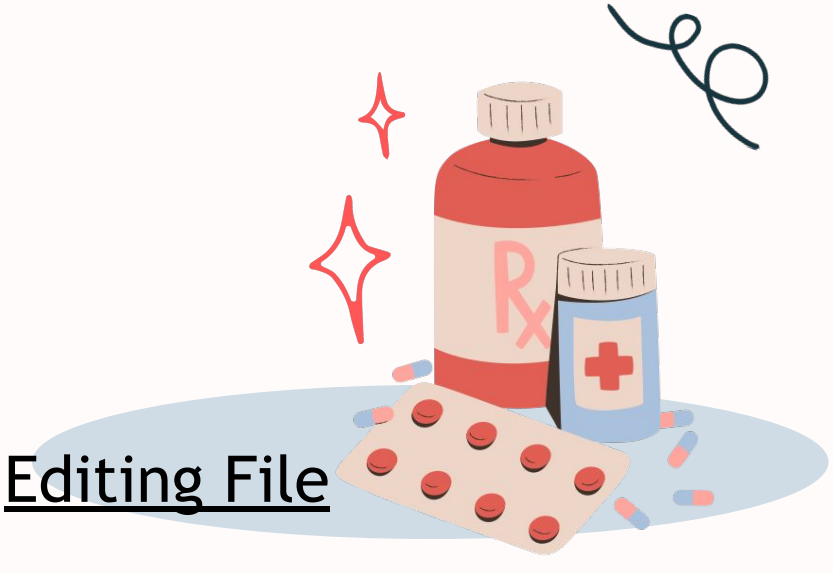
Drug Administration and Absorption

Lecture no. 1

Color Index:

- Main Text
- Important
- Females' Slides
- Males' Slides
- Drs' Notes
- Extra info.



Editing File

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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.

What is Pharmacology?

From the Greek pharmakon (drug), and legein (to speak or discuss).

Broadly defined as the study of how chemical agents affect living processes.
e.g. Hormones, Neurotransmitters and drugs

Pharmacology studies the effects of drugs and how they exert their effects.

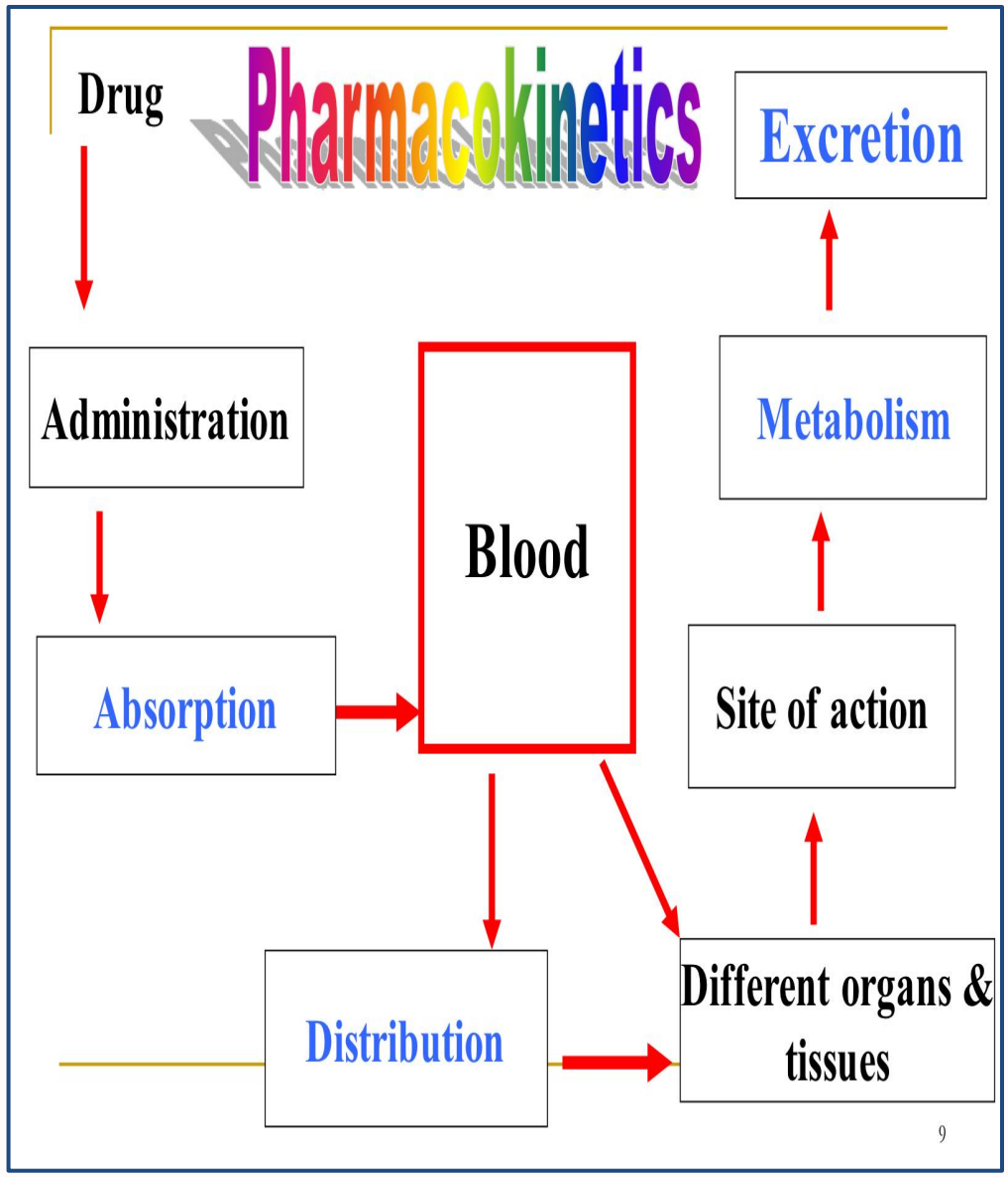
Acetylsalicylic acid (ASA) or Aspirin can reduce inflammation, pain and fever through inhibition the action of a human cell membrane enzyme known as cyclooxygenase.

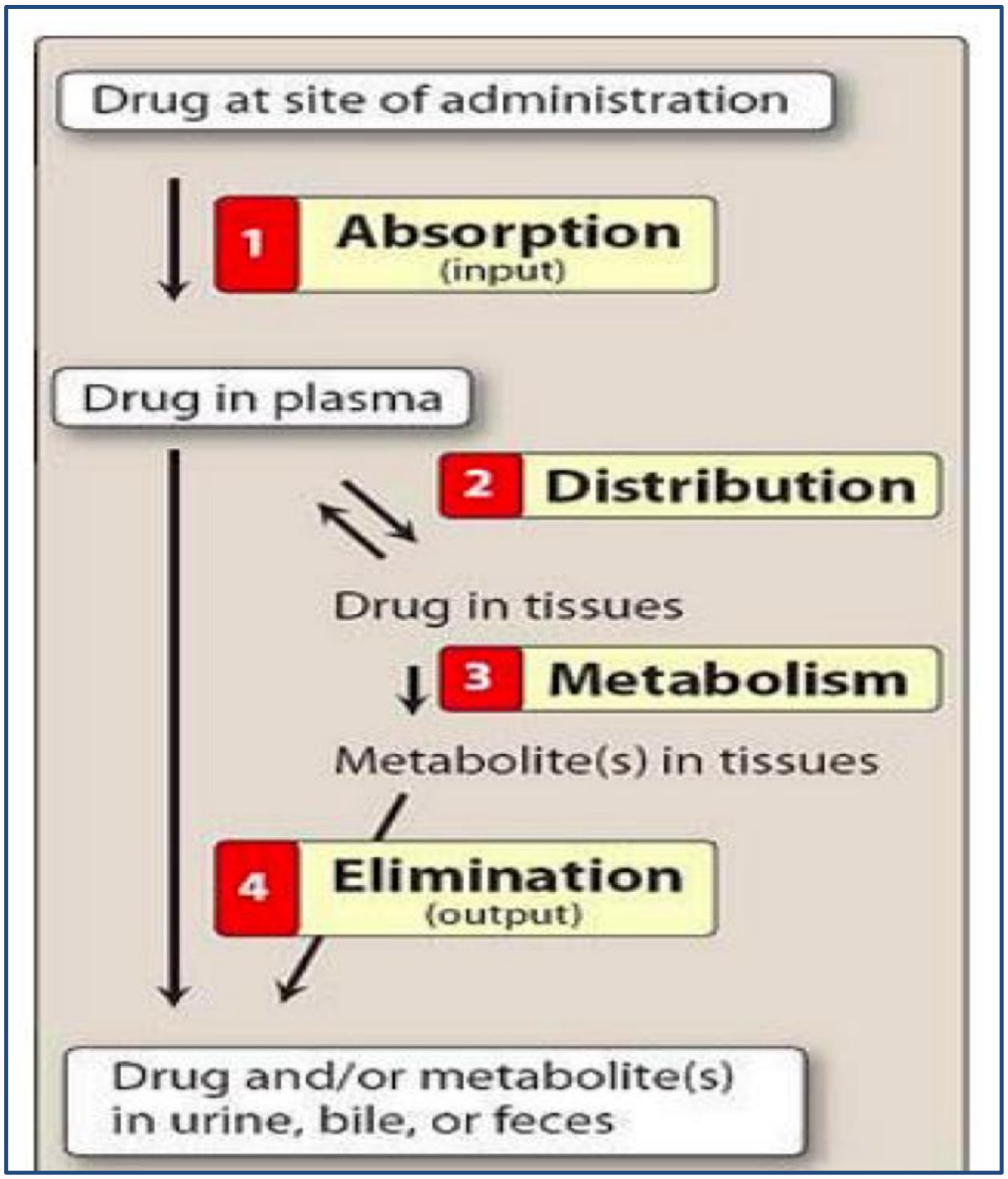
Penicillin cures certain bacterial infections disrupt the synthesis of cell walls in susceptible bacterial strains by inhibiting a key enzyme.

Pharmacology is the science that deals with the drugs regarding classification, pharmacokinetics, pharmacodynamics, side effects and therapeutic uses.

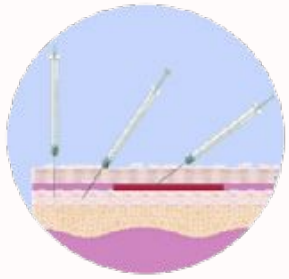
Pharmacokinetics are studies of the ADME: **A**bsorption, **D**istribution, **M**etabolism & **E**xcretion of drugs. (what the body does to a drug?)

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


Drug
Pharmacokinetics
Excretion
Administration
Blood
Metabolism
Absorption
Site of action
Distribution
Different organs & tissues
9


Drug at site of administration
1 Absorption
(input)
Drug in plasma
2 Distribution
Drug in tissues
3 Metabolism
Metabolite(s) in tissues
4 Elimination
(output)
Drug and/or metabolite(s)
in urine, bile, or feces

Routes of drug administration



Parenteral administration (injections)

Inhalation

01

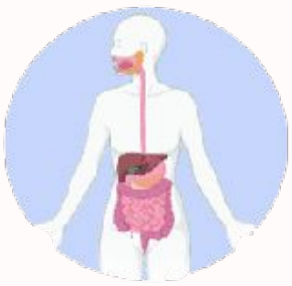
02

03

04

Enteral via gastrointestinal tract (GIT)

- Oral
- Sublingual(under the tongue)
- Rectal



Topical application
Locally applied
(like acne cream)

First Pass Effect

Definition

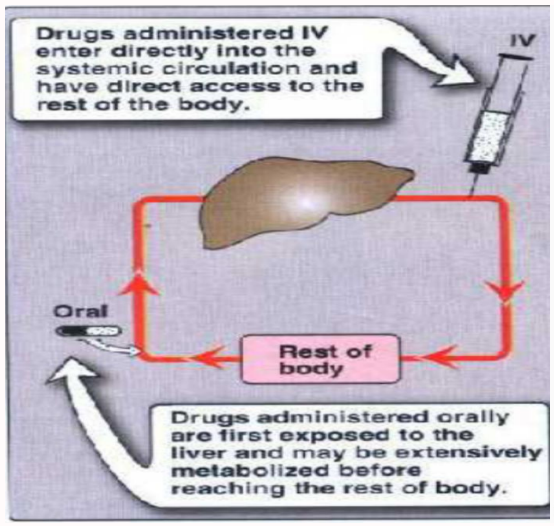
Drugs given orally are first taken to the **liver (via portal circulation)**, where they are metabolized (altered and broken down) before reaching to the blood to be distributed to all other body compartments.

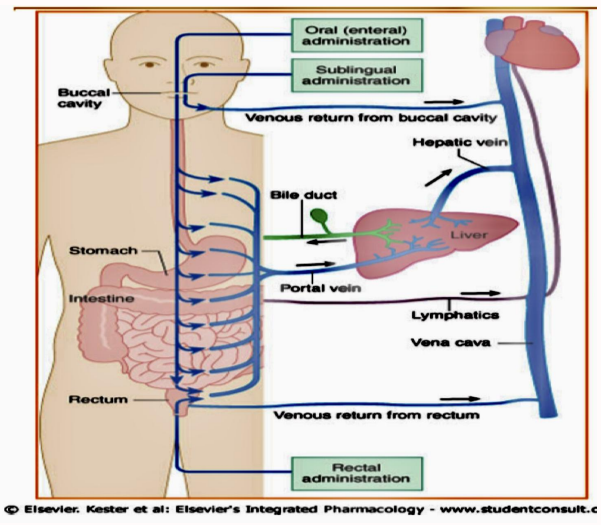
Where does it occur?

- Liver (to metabolize)
- GIT wall (before liver)
- GIT lumen (interact with normal flora bacteria)

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.





BIOAVAILABILITY

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

special thx to team 442 for this amazing diagram

Enteral via GIT

	Advantages	Disadvantages
Oral Administration	• common • cheap • easy • no need for sterilization • self use • convenient • painless	• GIT irritation, Slow effect (It cannot be used for emergencies) • Destruction by pH & enzymes e.g. penicillin, insulin • Food -drug(Reduce absorption) or drug-drug interactions(when two drugs been taken at the same time) • First pass effect metabolism • No complete absorption (because of the pH) • Low bioavailability Not suitable for : vomiting & unconscious patient emergency & bad taste drugs
Sublingual Placement under the tongue allows a drug to diffuse into the capillary and network, therefore, to enter the systemic circulation directly.	• Rapid effect, can be used in emergency (eg.Heart attack) • High bioavailability (directly to blood circulation) • No first pass effect • No GIT irritating • No food drug – interaction • **Dosage form:** friable tablet (easily breaks and dissolves)	Not suitable for: • Irritant drugs • Frequent use
Rectal	Suitable for: - children - vomiting - unconscious patients • Irritant and bad taste drugs • less first pass metabolism (50%) • **Dosage form:** suppository or enema	• Irritation of rectal mucosa • Irregular absorption • Irregular bioavailability (It might go to the liver or directly to the blood)

ORAL DOSAGE FORMS

Tablet:

- ➔ **Coated tablets:** sugar-coated to mask bad taste
- ➔ **Enteric coated tablets** (protects it from GIT): dissolve only in intestine

Capsules:

Hard gelatin capsules

Soft gelatin capsules

Spansule oral capsule

- ➔ Hard gelatin capsules: (contain powder)
- ➔ Soft gelatin capsules: (contain liquid)
  - Spansule oral capsule

A capsule which when swallowed releases one or more medicinal drugs over a set period.
The coat time is different E.g the first half will work in 10min \the other half will work in 30min.

Syrup:

e.g cough syrup

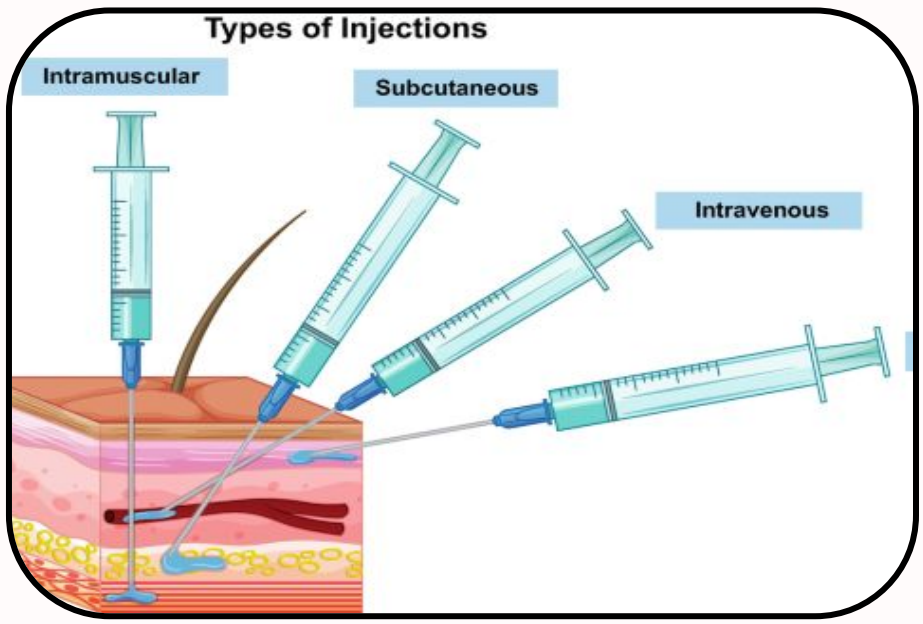
Suspension:

mixture of solid in liquids e.g. antibiotics

(notice how it looks cloudy because it's essentially a solid mixed in a liquid)

Parenteral Administration

- Intradermal **(I.D)** (into skin)
- Subcutaneous **(S.C)** (under skin) insulin
- Intramuscular **(I.M)** (into muscles)
- Intravenous **(I.V)** (into veins)
- Intrathecal **(I.T)** (cerebrospinal fluids)
- Intra-arterial **(I.A)** (into arteries)
- Interaperitoneal **(I.P)** (peritoneal cavity) e.g Rabies vaccine
- Intra-articular (synovial fluid) joint



Parenteral Administration

Advantages	Disadvantages
• No gastric irritation • No food-drug interaction • No drug-drug interaction • No first pass metabolism • higher availability than oral	• Needs skill • Pain, tissue necrosis or abscess (I.M.) • Anaphylactic reaction (I.V.) • there is no way to retrieve the drug

Parenteral Administration

	Advantages	Disadvantages
Intramuscular (I.M.)	• Moderate volumes (3-5 ml) • Prolonged duration of action • Oily preparations or poorly-soluble substances can be used	• tissue necrosis, pain, abscess may happen • Not suitable: for irritant drugs
Intradermal Administration (I.D.)	• Minute volume of drug (0.1ml) • Suitable for vaccinations • Sensitivity test	• Not suitable: for large volumes
Subcutaneous Administration (S.C.)	• Volume of drug (0.1ml-1ml) • Used for sustained release effect (SR) • Suitable for poorly soluble suspensions e.g. insulin zinc preparation	• Not suitable: for large volumes

Intravenous administration (I.V.)

Advantages	Disadvantages
• Large volume (500ml can be given by infusion) (drips slowly) • Rapid action (emergency) • High bioavailability 100% (the most effective way to get a drug into systemic circulation) • 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 (if not it will lead to blood clotting) • Infection • Anaphylaxis • Sterilization • Expensive • Must be injected slowly • Not suitable: for poorly soluble substance or for oily solutions

Ampoule

Single use (because the glass tip is broken when it's used)

Vial

Repeated use (there's a really small opening in the cap that only allows the needle in)

Summary

Injection	Advantages	Disadvantages
I.D.	Minute volume (0.1 ml) suitable for vaccinations & sensitivity test	Not suitable for large volumes
S.C.	Volume (0.1 ml - 1 ml) suitable for poorly soluble suspensions and for instillation of slow-release implants e.g. insulin zinc preparation	Not suitable for large volumes
I.M.	Suitable for moderate volumes 3-5 ml, for oily solutions or poorly soluble substances	Not suitable for irritant drugs Abscess- necrosis may happen
I.V.	suitable for large volumes and for irritating substances (500 ml can be given by infusion).	Not suitable for oily solutions or poorly soluble substances Must inject solutions slowly as a rule

Topical Application

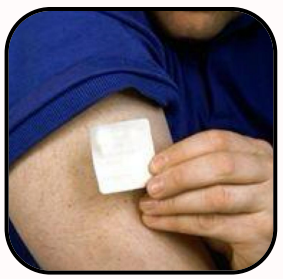
Definition

Drugs are mainly applied topically to produce local effects.
(Any medication applied to a body surface)

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

Transdermal Patch



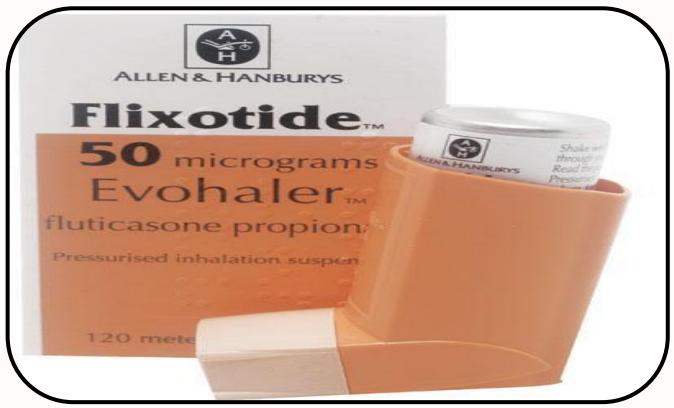
Definition

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).

Inhalation

Advantages	Disadvantages
• Rapid absorption (due to large surface area) • Suitable for emergency • Provide local action • limited systemic effect • less side effects • no first pass effect (doesn't cross the GIT to the liver because its inhaled) • **Dosage form:** - volatile gases e.g. anesthetic - liquids given by aerosol, nebulizer for asthma treatment	• Only few drugs can be used • Not suitable for irritant drug

Nebulizer

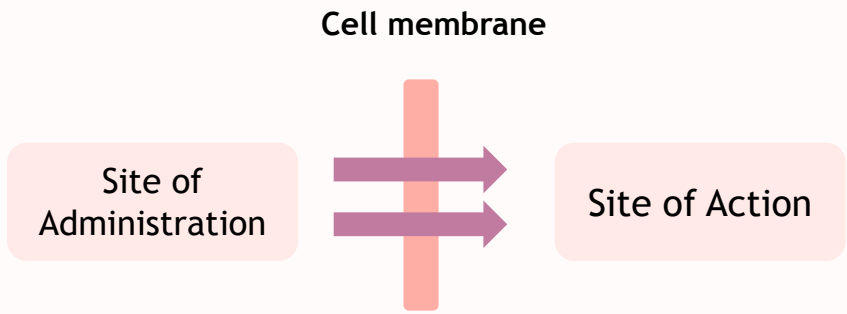


Atomizer

Drug absorption

Definition

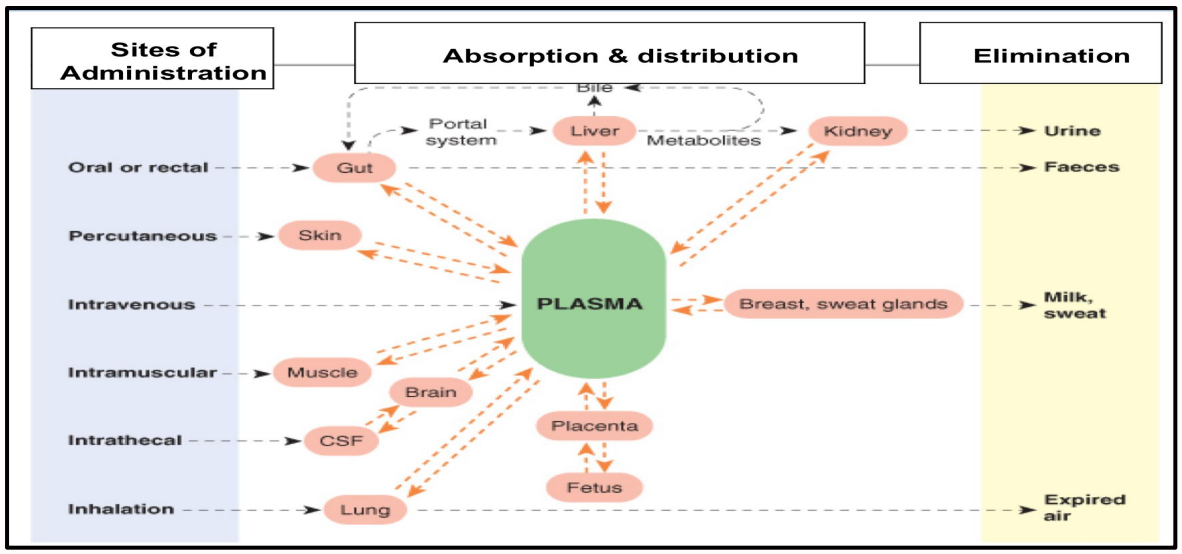
Is the passage of drug from its site of administration to site of action across cell membranes.The rate and efficiency of absorption depends on the route of administration.



Route of drug administration

▪ Except for intravenous administration, all routes of drug administration require that the drug be absorbed from the site of administration into the systemic circulation (blood).

• I.V. administration requires no absorption



Mechanisms of drug absorption

The transport of drugs across cell membrane occurs through one or more of the following processes :

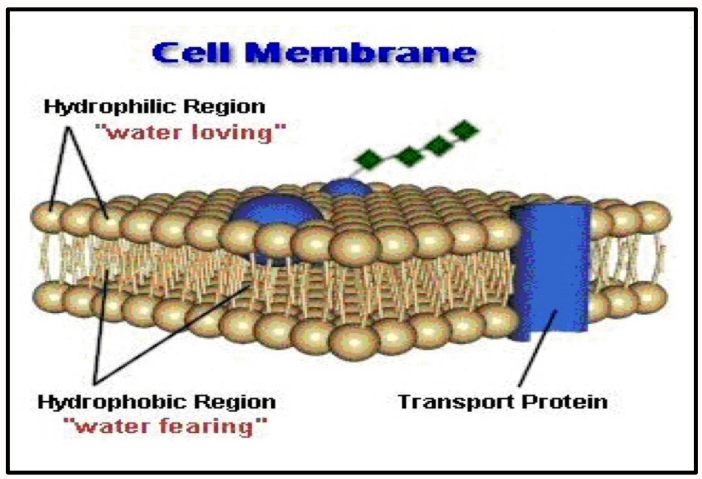
1) Simple diffusion = passive diffusion : (Passive transport)

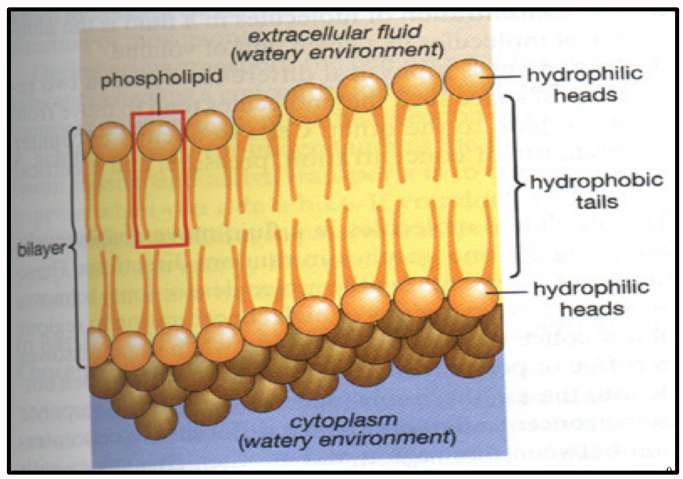
- **Aqueous diffusion:** low molecular weight and water soluble drugs can diffuse through aqueous channels or pores in cell membrane (filtration).
- **Lipid diffusion:** low molecular weight and lipid soluble drugs are absorbed via diffusion through lipid cell membrane itself.

2) Active transport.

3) Facilitated diffusion. (Passive transport)

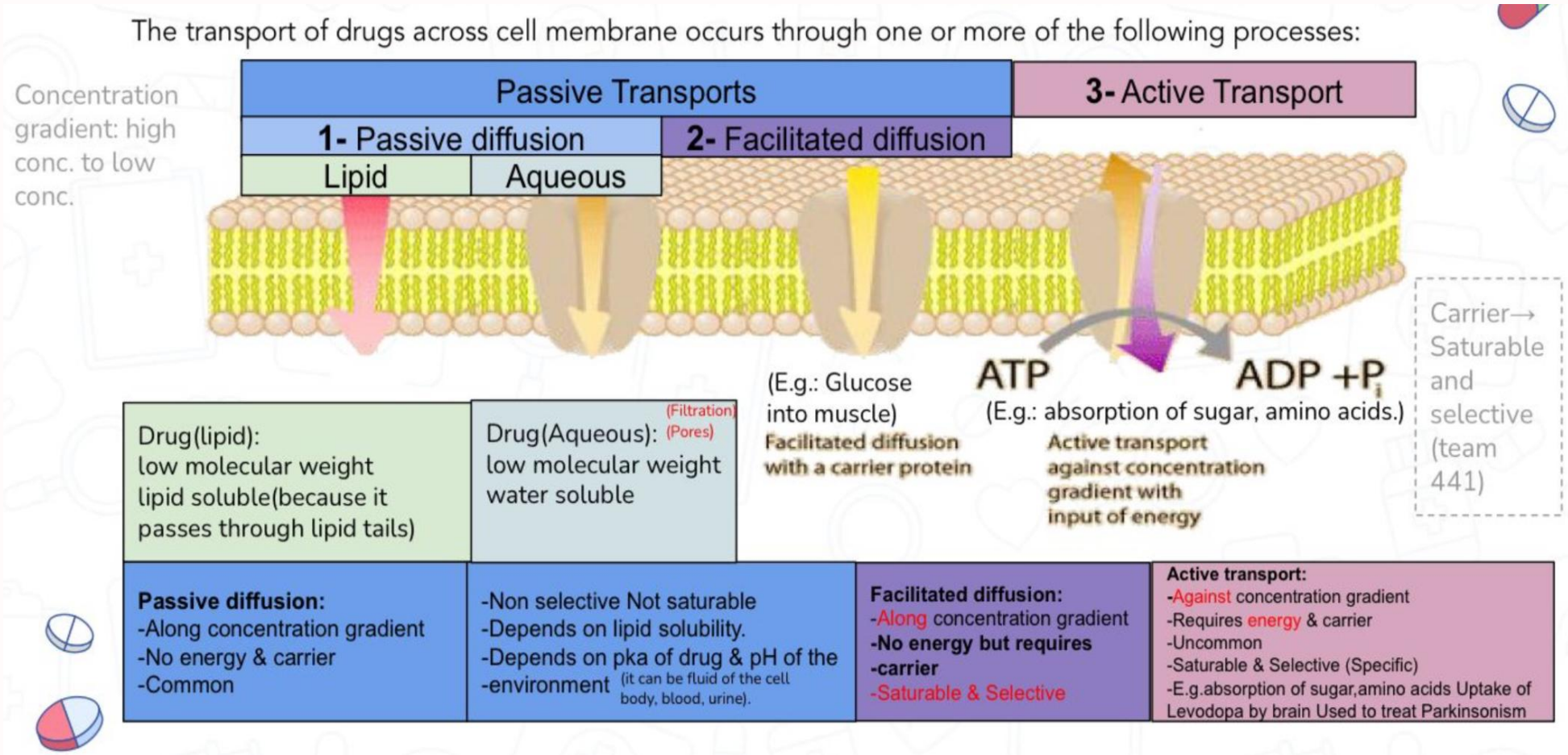
4) Pinocytosis (Endocytosis): Uptake of membrane-bound particles.





Mechanisms of drug absorption

Team 442



Drug(lipid): low molecular weight lipid soluble(because it passes through lipid tails)	Drug(Aqueous): (Filtration) (Pores) low molecular weight water soluble

Passive diffusion: -Along concentration gradient -No energy & carrier -Common	-Non selective Not saturable -Depends on lipid solubility. -Depends on pka of drug & pH of the -environment (it can be fluid of the cell body, blood, urine).	**Facilitated diffusion:** -Along concentration gradient **-No energy but requires -carrier** -Saturable & Selective	**Active transport:** -Against concentration gradient -Requires energy & carrier -Uncommon -Saturable & Selective (Specific) -E.g.absorption of sugar,amino acids Uptake of Levodopa by brain Used to treat Parkinsonism

Phagocytosis (Endocytosis & Exocytosis)

Definition

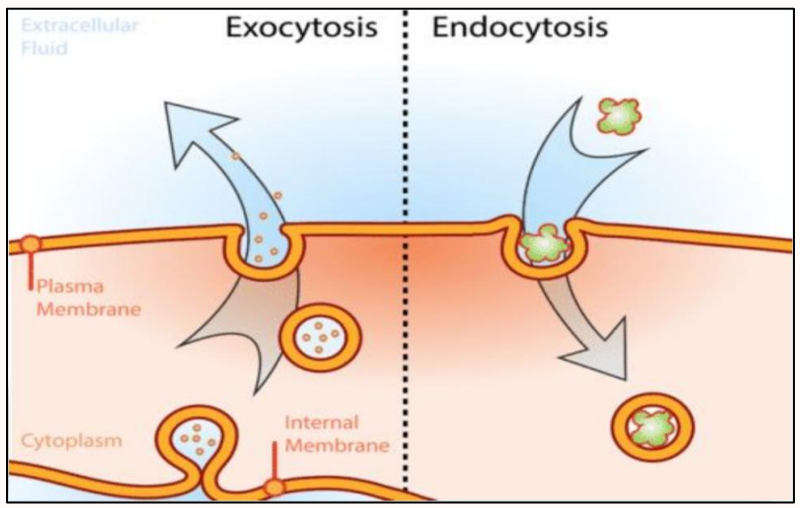
Endocytosis: uptake of membrane-bound particles.

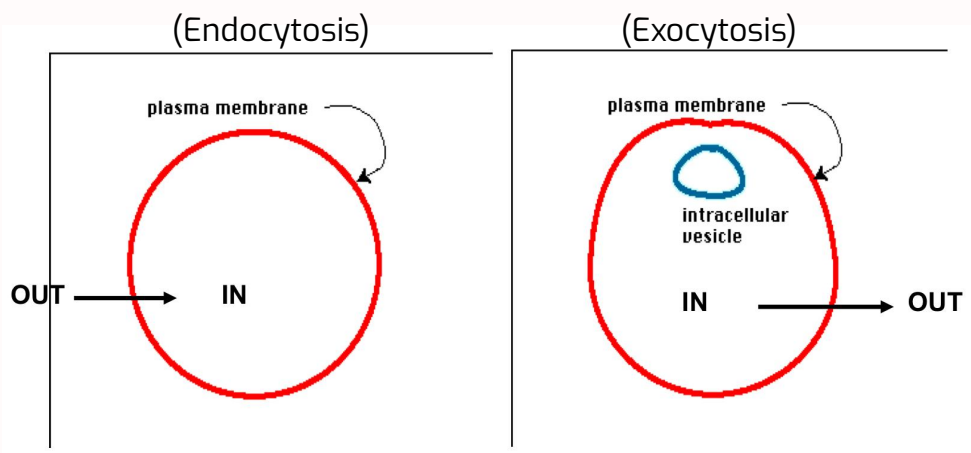
Exocytosis: expulsion of membrane-bound particles

Endocytosis occurs for drugs which are either :

for high molecular weight drugs
- large molecules such as peptides

high polar substances, such as vitamin B12 & iron
- vitamin B12 combines with intrinsic factor.
- iron combines with transferrin.





Mechanisms of drug absorption

Simple diffusion	Active Transport	Carrier-mediated Facilitated Diffusion
Common	relatively uncommon	————————————
Occurs with or along concentration gradient.	occurs against concentration gradient	occurs along concentration gradient
No energy & No carrier	requires carrier and energy	No energy but Require carrier
Non selective	specific or selective	selective
Not saturable	Saturable	Saturable
depends on lipid solubility	absorption of sugar, amino acids	Similar to entry of glucose into muscle.
depends on pka of drug - pH of the environment (it can be fluid of the cell body, blood, urine).	uptake of levodopa by brain. **Levodopa** is used in treatment of **parkinsonism**	————————————

pH Effect on drug absorption

Most drugs are weak acids or weak bases.

- Drugs can exist in two forms ionized (water soluble) & unionized forms (lipid soluble) in equilibrium.
- Only unionized form is absorbable.
- Ionization of drugs reduce passage of drugs across cell membranes.
- The degree of ionization of drugs is determined by their pKa and pH of the surrounding.

Remember

- Water soluble drugs = ionized = polar = charged are difficult to permeate cell membranes.

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

pH Effect on drug absorption

Affects degree of ionization of drug:

- **Weak acidic drugs** —> best absorbed in stomach (in acidic medium of stomach, drugs exists in unionized form that is lipid soluble and easily absorbed).

- **Weak basic drugs** —> best absorbed in intestine. (in basic medium of intestine, drugs exists in unionized form that is lipid soluble and easily absorbed).

PKa Effect on the drug absorption

(Dissociation or ionization constant): pH at which half of the substance is ionized & half is unionized.

- **The lower the pKa value** (pKa < 6) of the acidic drug, the stronger the acid e.g aspirin (Pka= 3.0).
- **The higher the pKa value** (pKa >8) of a basic drug, the stronger the base e.g propranolol (pKa= 9.4).

Q/ Which one of the following drugs will be best absorbed in stomach (pH=1-2)?

a- Aspirin pka=3.0 ✔

b- Propranolol. pka= 9.4

The answer is Aspirin

Factors affecting absorption

Important

Route of administration
E.g; sublingual > oral

Dosage forms (depending on particle size and disintegration, ease of dissolution). (solution > suspension > capsule > tablet)

Molecular weight of drug:
Small > big

Lipid solubility

Degree of ionization.
Unionized > ionized

Drug solubility (aqueous preparation better than oily, suspension preparations)

Chemical instability in gastric pH
(Penicillin & insulin).

Surface area:
small intestine has large surface area than stomach due to intestinal microvilli.

Blood flow:
- greater blood flow increases bioavailability
- Intestine has greater blood flow than stomach.

Intestinal motility.
Diarrhea reduce absorption

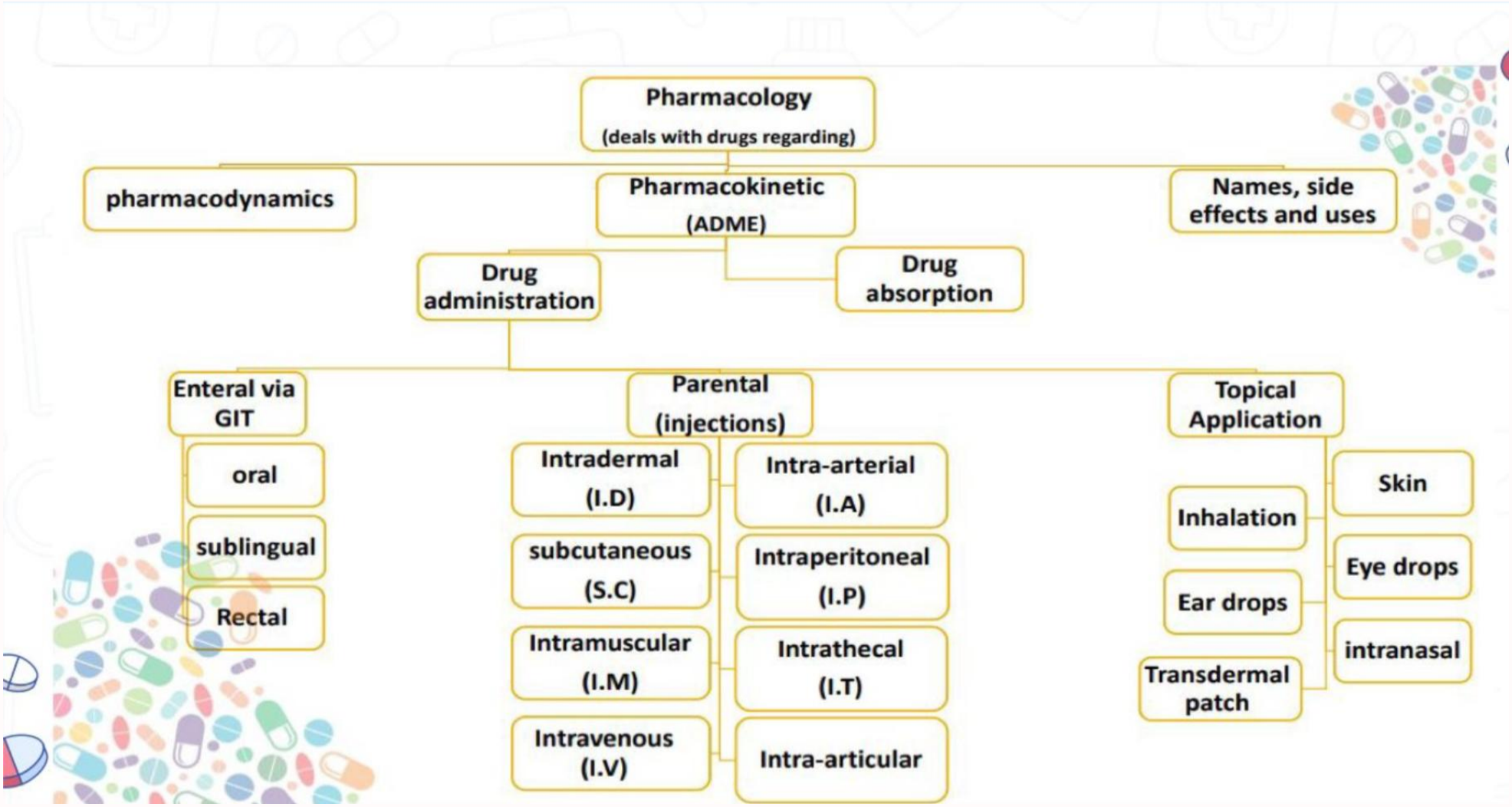
Food.
A fatty meal increase the absorption of fat soluble antifungal drug (e.g. griseofulvin)

Drug interactions.

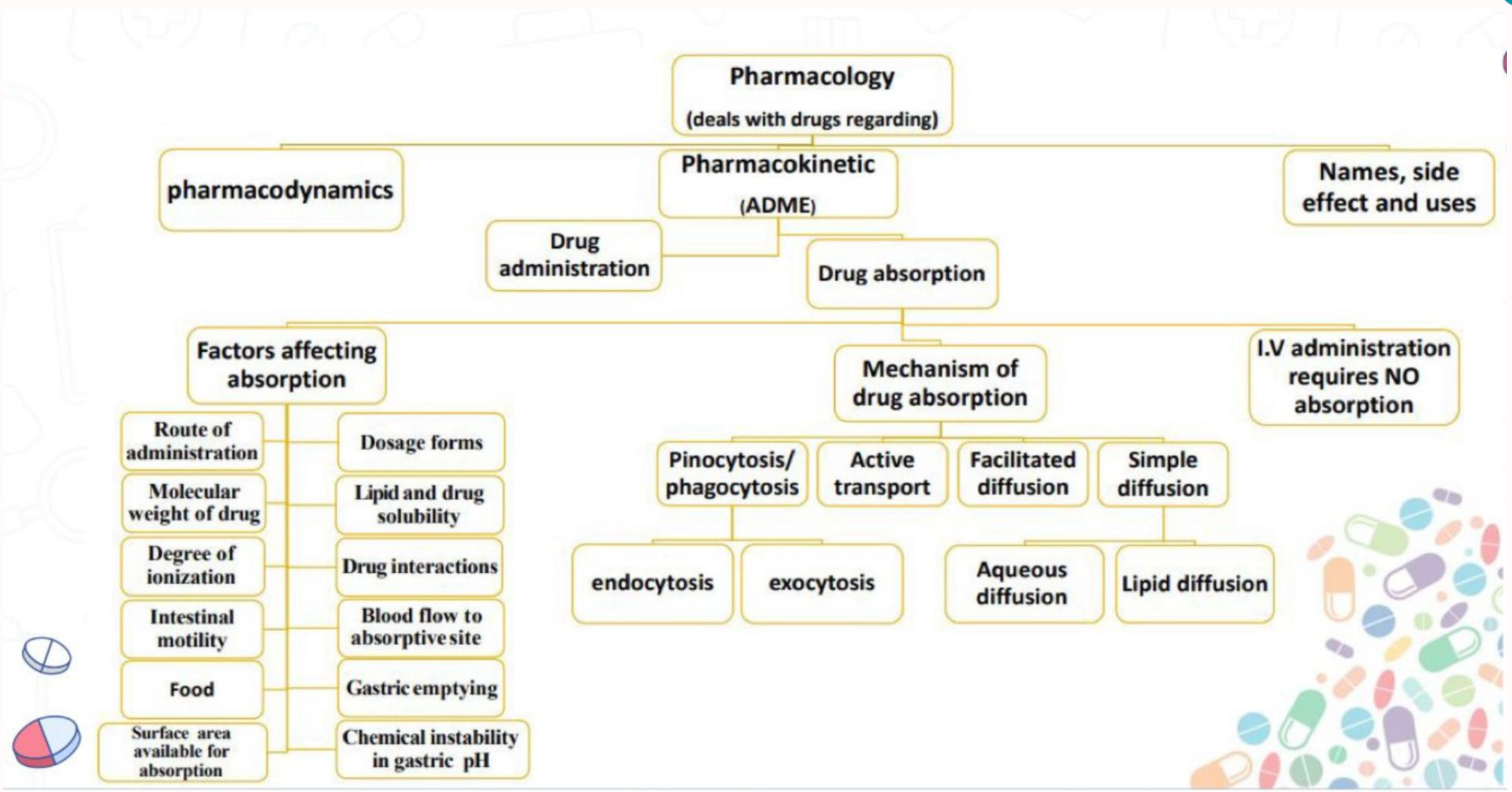
Gastric emptying
drugs that increase gastric emptying enhances absorption (**metoclopramide**).
slow gastric emptying —> generally slow absorption
e.g. Tetracycline, aspirin, penicillin V

part highlighted in yellow is considered under ‘Food’ category in boys’ slides

Summary of Drug Administration (Team 438)



Summary of Drug Absorption (Team 438)



Summaries

Click Here

[Summary (Team 441) Drugs of Pharmacokinetics]

[Summary (Team 441) Lecture 1 Summary]

- Different routes of administration are available.
- Parenteral administration is the suitable route to provide rapid effect.
- I.V. is used in emergency and provide high availability.
- Oral administration is best avoided during emergency or when severe first pass metabolism may occur.
- Drugs may cross any cell membrane by simple diffusion, active transport, facilitated diffusion, and pinocytosis.

MCQs

Q1. What is the most effective route for emergency ?			
a) Oral	b) Intramuscular	c) intravenous	d) intrathecal

Q2. Where does the first pass effect take place?			
a) Liver	b) Kidney	c) Spleen	d) Stomach

Q3. Which of the following parenteral administrations has no first pass effect?			
a) Intradermal	b) Intra-arterial	c) Intravenous	d) Subcutaneous

Q4. A 15-year-old boy who has diabetes and is insulin dependent is brought to the emergency department after collapsing at a baseball game. His blood sugar is 463 mg/dL by finger stick. Which of the following routes of administration would be most efficacious for medications to bring the blood sugar down?			
a) Intramuscular	b) intravenous	c) oral	d) Subcutaneous

Q5. Vitamin B12 is absorbed using?			
a) Facilitated diffusion	b) Endocytosis	c) Active diffusion	d) Passive diffusion

Answers:

1) C
2) A
3) C
4) B
5) B

Not suitable for:

- Irritant drugs
- Frequent use

What are the disadvantages of using the Sublingual administration?

1- Route of administration.
2- Lipid solubility.
3- Drug solubility.
4- Molecular weight of drug.

Mention two factors affecting absorption ?

SAQS

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