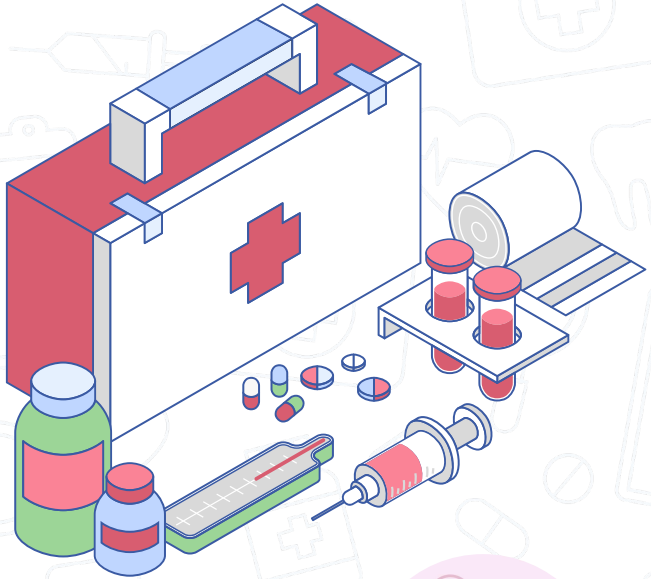
Click for useful **video**!



DRUG ADMINISTRATION AND ABSORPTION 442

EDITING FILE

Important
Main text
Male slide
Female slide
Extra info
Doctor notes

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

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

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

Pharmacokinetics (route\حركة الدواء) : it is (what the body does to a drug ?)
And they are studies of the [ADME] (process)
absorption, distribution, metabolism & excretion of drugs.

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

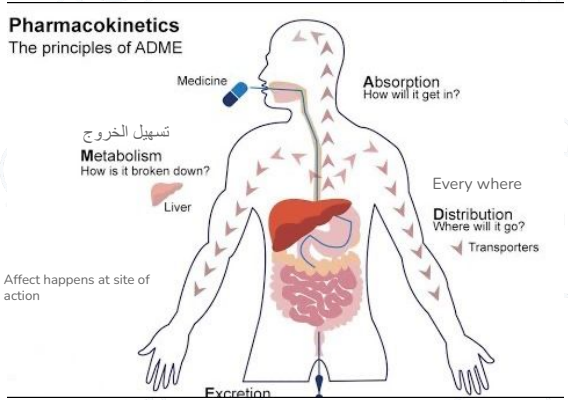
1. Enteral via GIT *GIT=gastrointestinal tract*

- Oral (حبة بالفم)
- Sublingual (تحت اللسان مثلا حبة لإنزال الضغط بسرعة)
- Rectal(من الشرج)

2. Inhalation (respiratory system)

3. Parenteral administration (Injections)

4. Topical application - Locally applied- (مثل الكريم اللتجميل او العلاج)



Click for useful video

BIOAVAILABILITY

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

WHAT IS THE FIRST PASS EFFECT ?

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

Where does it occur?

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

First pass metabolism 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.

Enteral via GIT

	Advantage	Disadvantage
Oral Administration	● Common ● cheap ● easy ● no need for sterilization ● self use	●GIT irritation ● Slow effect *It can not 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 *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 irritating ● 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 first pass metabolism (50%) ● Dosage form : suppository or enema	● Irritation of rectal mucosa ● Irregular absorption ● Irregular bioavailability

ORAL DOSAGE FORMS (formulation)

Tablets:

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

Hard- gelatin capsule

Capsules:

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

Spansule oral capsule :

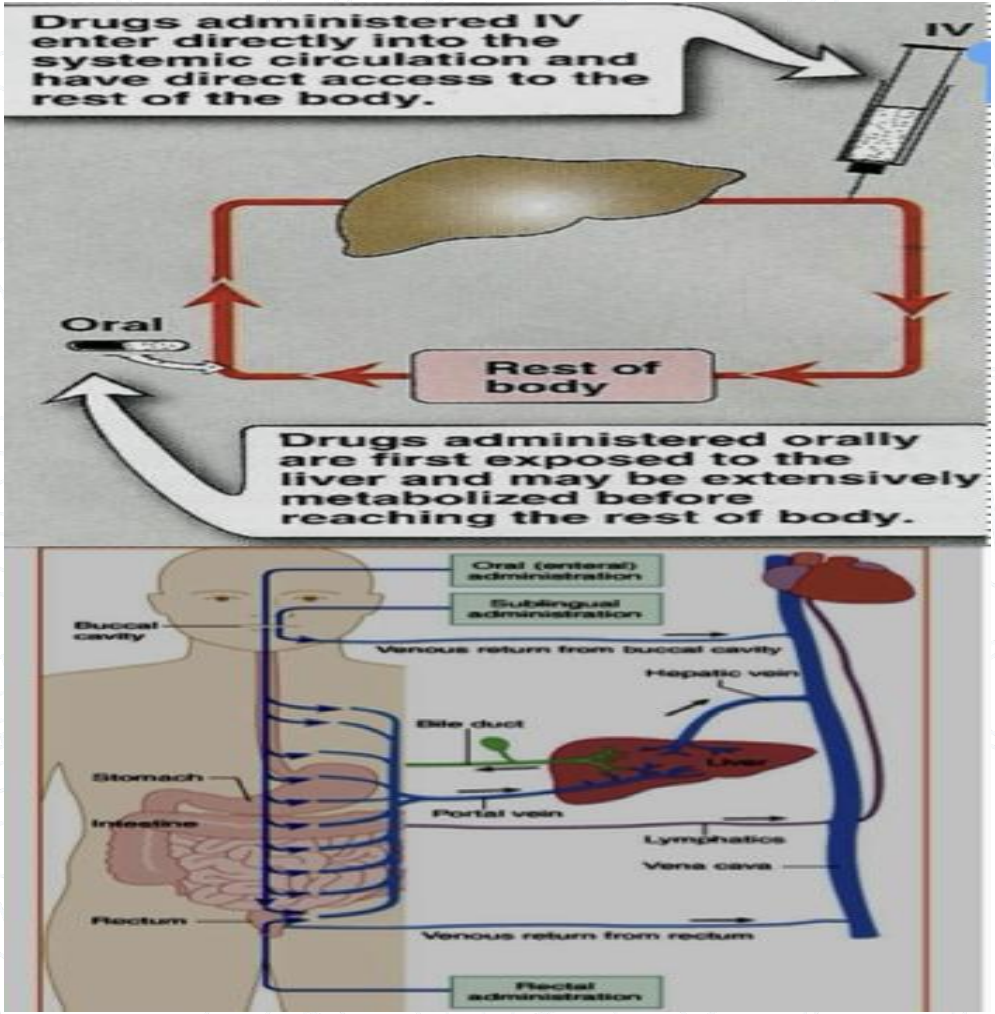
-*a capsule which when swallowed releases one or more medicinal drugs over a set period.

- 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).

Just to understand the concept



TYPES OF PARENTERAL

- Intradermal (I.D) (into skin)
- 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)
- Intra articulation (synovial fluid) joint
- Subcutaneous (S.C) (under skin) insulin

PARENTERAL ADMINISTRATION (INJECTIONS)

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

	Advantage	Disadvantage
Intradermal administration I.D. “Skin”	• Minute volume of drug (0.1 ml) • suitable for vaccinations • sensitivity test نقدر نجرب كمية بسيطة قبل لا نستخدمه	not suitable for large volumes
Subcutaneous administration S.C.	• volume of drug (0.1 ml – 1 ml) • used for sustained release effect(SR) • suitable for poorly soluble suspensions and instillation of slow-release implants e.g. insulin zinc preparation long duration of action	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 -long duration -harder to absorb -slow solubility -can be used again at the same place	Not suitable for • irritant drugs • pain • abscess • tissue necrosis may happen • Abscess- necrosis may happen

INTRAVENOUS ADMINISTRATION "I.V"

Advantage	Disadvantage
• suitable for large volumes (500ml can be given by infusion) drip مثل المغذي • 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 has no contact with tissue	• used only for water soluble drugs (if not it will lead to blood clotting • Infection • Anaphylaxis تحسس • Sterilization • Expensive • not suitable for oily solutions or poorly soluble substances Must inject solutions slowly as a rule

INHALATION

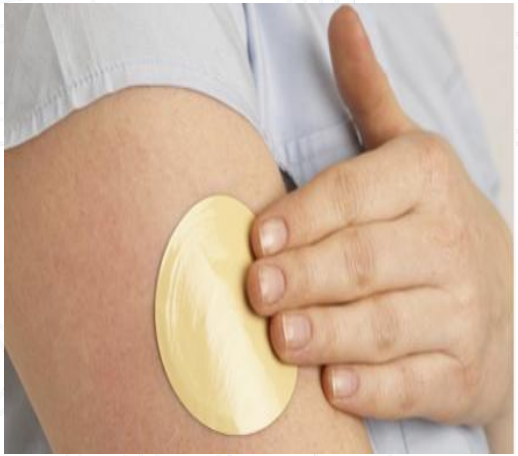
Advantage	Disadvantage
• rapid absorption (due to large surfaces area) with blood supply • suitable for emergency • provide local action • limited systemic effect • less side effects • no first pass effect Dosage form : • volatile gases e.g. anesthetics • liquids given by aerosol, nebulizer for asthma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

TOPICAL APPLICATION :

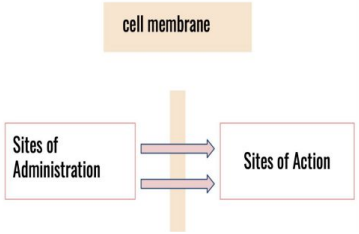
Drugs are mainly applied topically to produce local effects.
They are applied to :

- 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

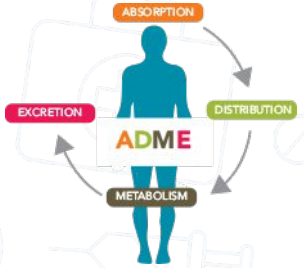
TRANSDERMAL PATCH :



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).



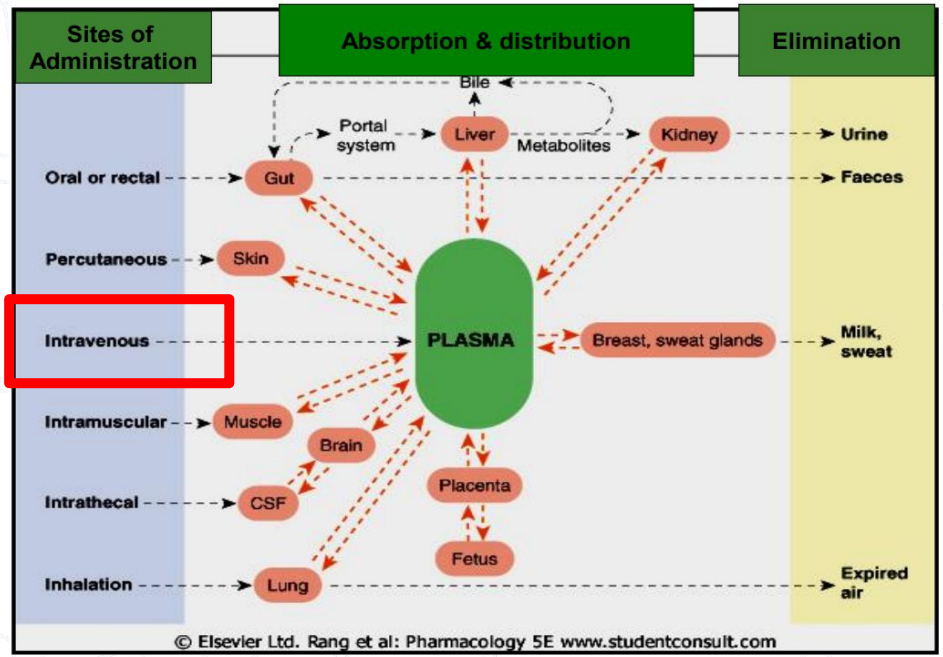
DRUG ABSORPTION



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

- **Except for intravenous administration** (directly into the bloodstream, no absorption needed), all routes of drug administration require that the drug be absorbed from the site of administration into the **systemic circulation (blood)**.

Helpful Video (team 441)



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 (water soluble)
    - Passive diffusion (lipid soluble)
2. Facilitated diffusion. (passive transport)
3. Active transport.
4. Pinocytosis (Endocytosis): :uptake of membrane-bound particles.

MECHANISMS OF DRUG ABSORPTION

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

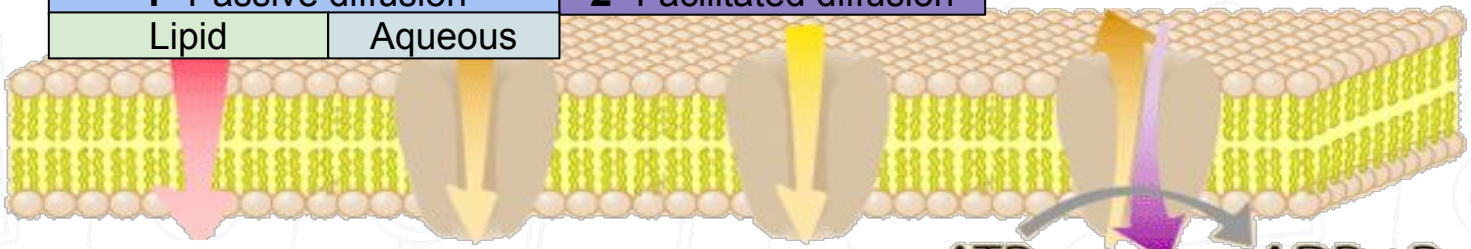
Concentration gradient: high conc. to low conc.

Passive Transports

1- Passive diffusion: Lipid | Aqueous

2- Facilitated diffusion

3- Active Transport



(E.g.: Glucose into muscle)
Facilitated diffusion with a carrier protein

(E.g.: absorption of sugar, amino acids.)
Active transport against concentration gradient with input of energy

Carrier→ Saturable and selective (team 441)

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

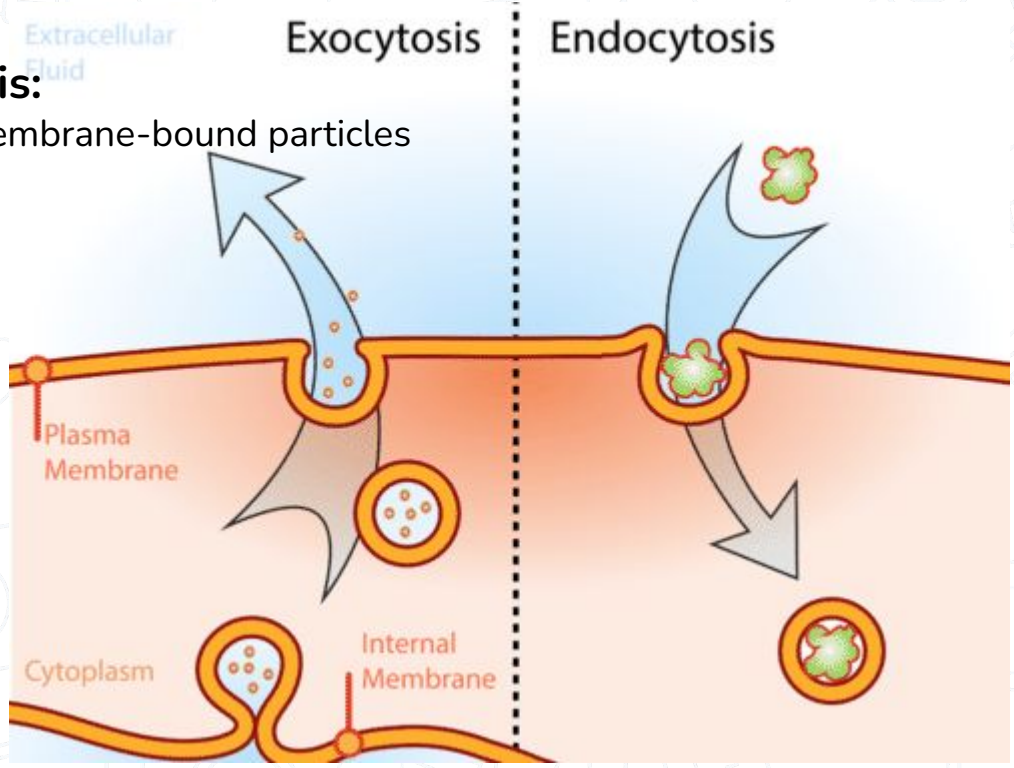
Just understand the concept

MECHANISMS OF DRUG ABSORPTION

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

B-Exocytosis:
Expulsion of membrane-bound particles

(not one of the drug absorption mechanisms)



4.phagocytosis
A-Endocytosis: uptake of membrane-bound particles.

Phagocytosis occurs for drugs which are either:

- **High molecular weight** drugs:large molecules e.g.: **peptides**
- **High polar** drugs:e.g.: >vitamin **B12** combines with intrinsic factor. >**iron** combines with transferrin.

Team438: If an acidic drug entered a *basic* medium the drug will become ionized and the drug won't show its effect Same thing will happen if a basic drug entered an acidic medium

PH EFFECT

Most Drugs are either: weak bases or weak acids
Found in two forms:

Basically the acidic / basic drug stays in acidic / basic medium until the drug becomes unionised (lipid soluble) then absorbed easily

Ionized / water soluble:
Water soluble drugs = ionized = polar = charged are difficult to permeate cell membranes.

Unionized (ABSORBABLE 100%) / Lipid soluble:
Lipid soluble drugs = unionized = non polar = uncharged are easy to permeate cell membranes

The degree of ionization of drugs is determined by their *pKa and pH of the surrounding*.
(Acid with acid, base with base)

Affects degree of ionization of drugs:
Weak acidic drugs best absorbed in **stomach** (in acidic medium of stomach, drug exists in unionized form that is lipid soluble and easily absorbed).
Weak *basic* drugs best absorbed in **intestine**. (*in basic medium* of intestine, drug exists in unionized form that is lipid soluble and easily absorbed).

PKa of the drug (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)

(Team 441)

Ordered from greatest to least

FACTORS AFFECTING 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

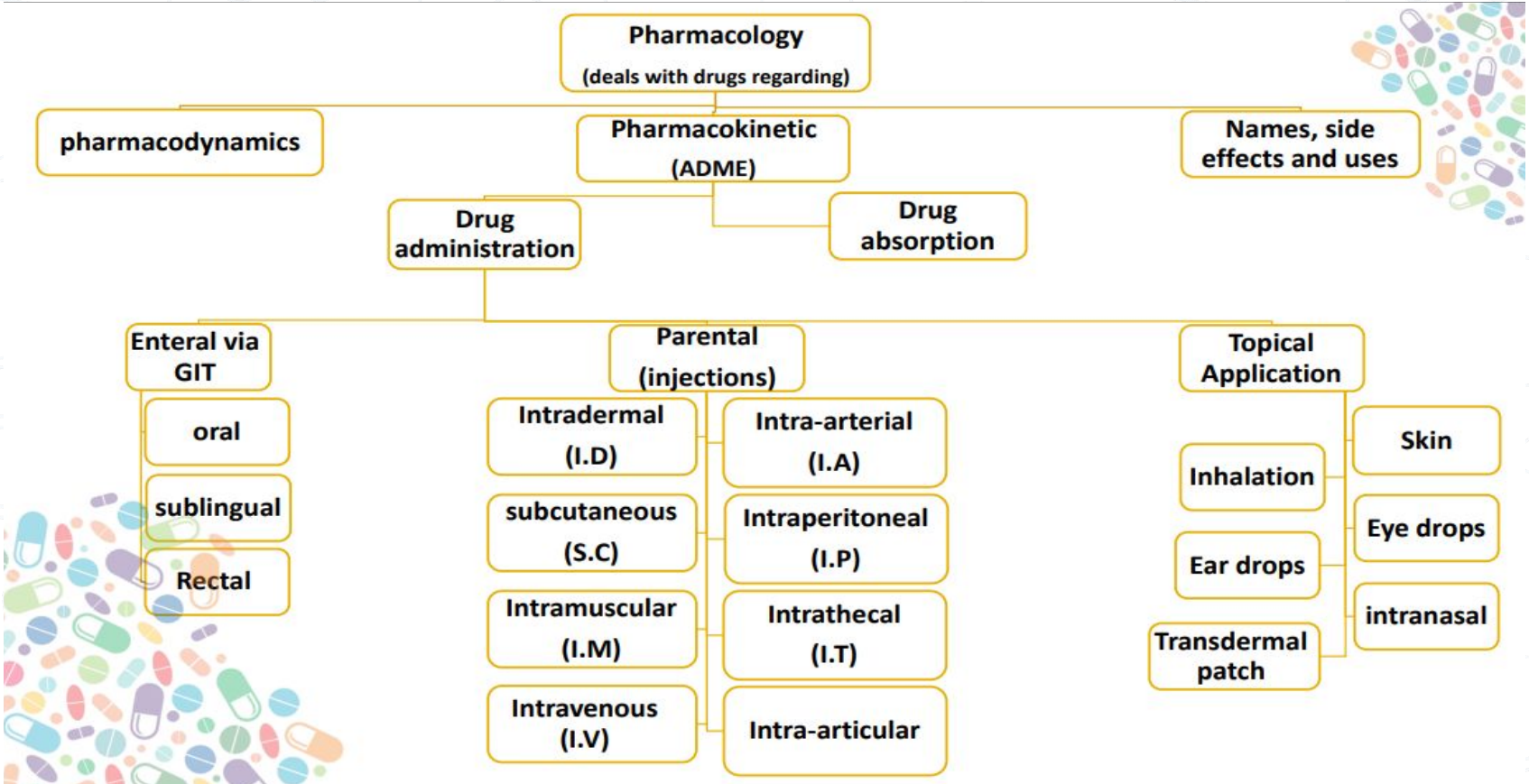
Gastric emptying: Increased gastric emptying → increase absorption (e.g metoclopramide)

Intestinal motility: Diarrhea reduces absorption

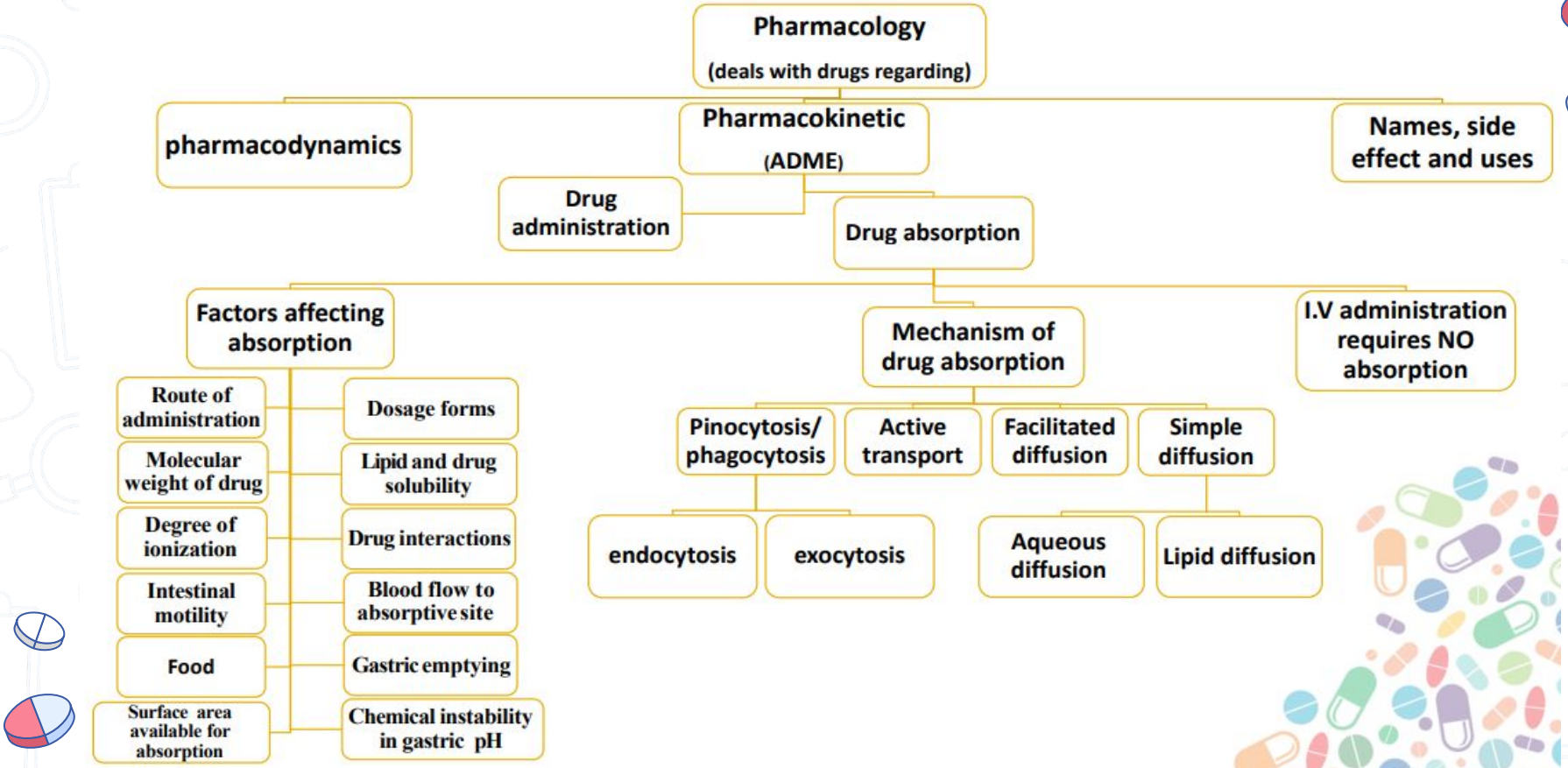
Drug interactions

Food: Slow gastric emptying → slower absorption. However, fatty meals increase absorption of fat soluble antifungal drug (e.g Griseofulvin) Tetracycline(empty stomach), aspirin(with food), penicillin V(empty stomach)

SUMMARY OF DRUG ADMINISTRATION (TEAM 438)



SUMMARY OF DRUG ABSORPTION (TEAM 438)



Summaries:

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.

MCQ

Q-1 what is the most effective route for emergency ?			
A- Oral	B- I.m	C- IV(intravenous)	D- IT (intrathecal)
Q-2 Where does the first pass effect take place?			
A- Kidney	B- Spleen	C- lymph nodes.	D-Liver
Q-3 Which of the following is not absorption affecting factor?			
A) food	B) surface area	C) age	D) intestinal motility
Q-4 Basic drugs are best absorbed in?			
A) Liver	B) Intestine	C) Stomach	D) acid
Q-5 Which mechanism requires an energy ATP?			
A) simple diffusion	B)active transport	C)facilitated diffusion.	D) B&C

1-C
2-D
3-C
4-B
5-B

SAQ

Q-1 list three factors that affect the drug absorption?

Q-2 What is the disadvantages of using the Sublingual administration?

Answers

1-(molecular weight of drug- degree of ionization - surface area). Slide 23

2-Not suitable for :
- Irritant drugs frequent use slide 7

DONE BY THE AMAZING TEAM

You GOT THIS!

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