



Adverse drug reactions

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Intended learning outcomes (ILOS):



- **Identify types of adverse drug reactions.**
- **Interpret differences between different types of drug interactions.**
- **Discuss synergism and antagonism.**
- **Identify net results of addition of drugs.**

ADVERSE DRUG REACTION

*A noxious and unintended response to a medicine.
(European Medicines Agency definition)*

- Are harmful effects of a drug at doses used in therapy, which calls for

Decrease dosage, Stop drug & or immediate treatment

Types of adverse drug reactions

- 1- **Type A** = **A**ugmented and Predictable = Related to the normal pharmacology of the drug.
- 2- **Type B** = **B**izarre and unpredictable = Not related to the normal pharmacology of the drug.
- 3- **Type C** = **C**hronic effects after long use of drugs.
- 4- **Type D** = **D**elayed effects of the drugs.
- 5- **Type E** = **E**nd of dose effects.
- 6- **Type F** = **F**ailure of therapy.

I) TYPE A (Augmented or predictable undesirable adverse effects):

Predictable undesirable effects related to the normal pharmacological actions of the drug:

1- Side Effect

2- Secondary Effect

3- Over-dose

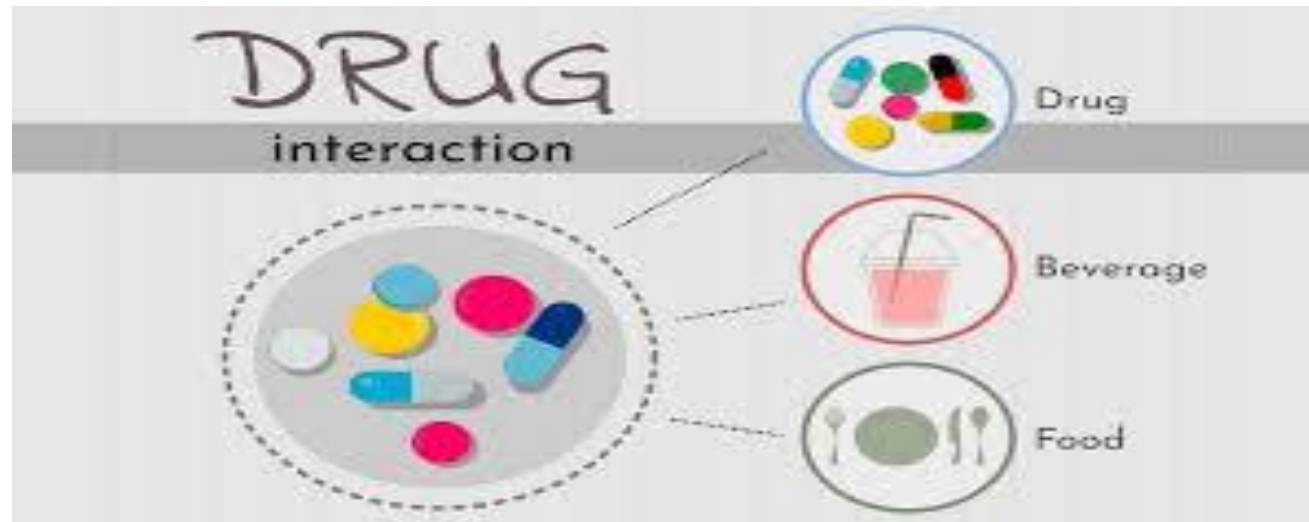
4- Super-sensitivity

5- Drug Intolerance

6- Direct Cytotoxic Effects

7- Drug Interactions

Drug interactions



Drug interactions

- Drug Interactions are altered pharmacological responses due to multiple drugs acting concurrently (**Polypharmacy**).

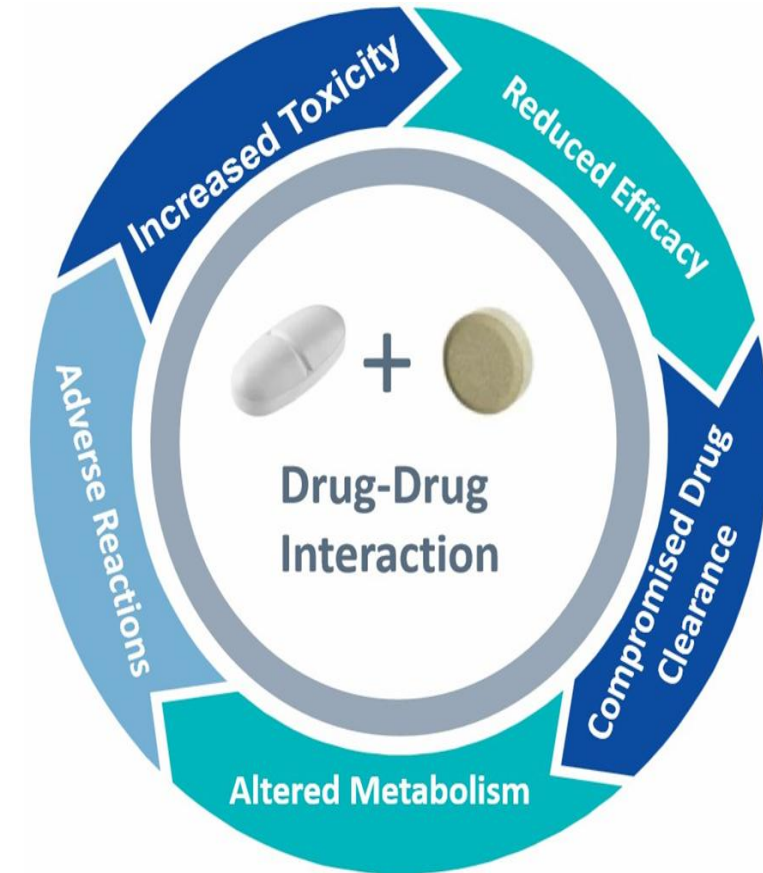
- These can be:

- Beneficial DI:

Are obtained by combining drugs with **different mechanisms** or **drugs that correct adverse effects of each other** e.g. in treatment of cancer and TB.

- Harmful DI:

Can be in the form of predictable (**type A reaction**), an **unpredictable toxicity (type B reaction)**.



- Most clinically important DI involve drugs with narrow safety margin
e.g. Phenytoin, theophylline.



** Types of drug interactions:*

I- Pharmaceutical

II - Pharmacokinetic

III -Pharmacodynamic

DRUG INTERACTIONS

MADE EASY

- PHARMACOKINETIC INTERACTIONS
- PHARMACODYNAMICS INTERACTIONS
- FOOD AND DRUG INTERACTIONS
- HERB AND DRUG INTERACTIONS
- DRUG AND DISEASE INTERACTIONS

I- Pharmaceutical drug interactions

*These are drug interaction occurring **outside the body before drug administration (in vitro).**

*Due to physical or chemical reaction between the drugs.

e .g **Mixing drugs with IV infusion fluids.**



I- Pharmaceutical drug interactions

Alert! Do not mix Ceftriaxone with Calcium Containing IV Products

P

<https://pakistanisurgeon.blogspot.com>

Don't Mix in the Same Infusion!

Incompatible Mixture

- ⚠ Risk of Precipitation
- ⚠ Reduced Effect

Safe Practice

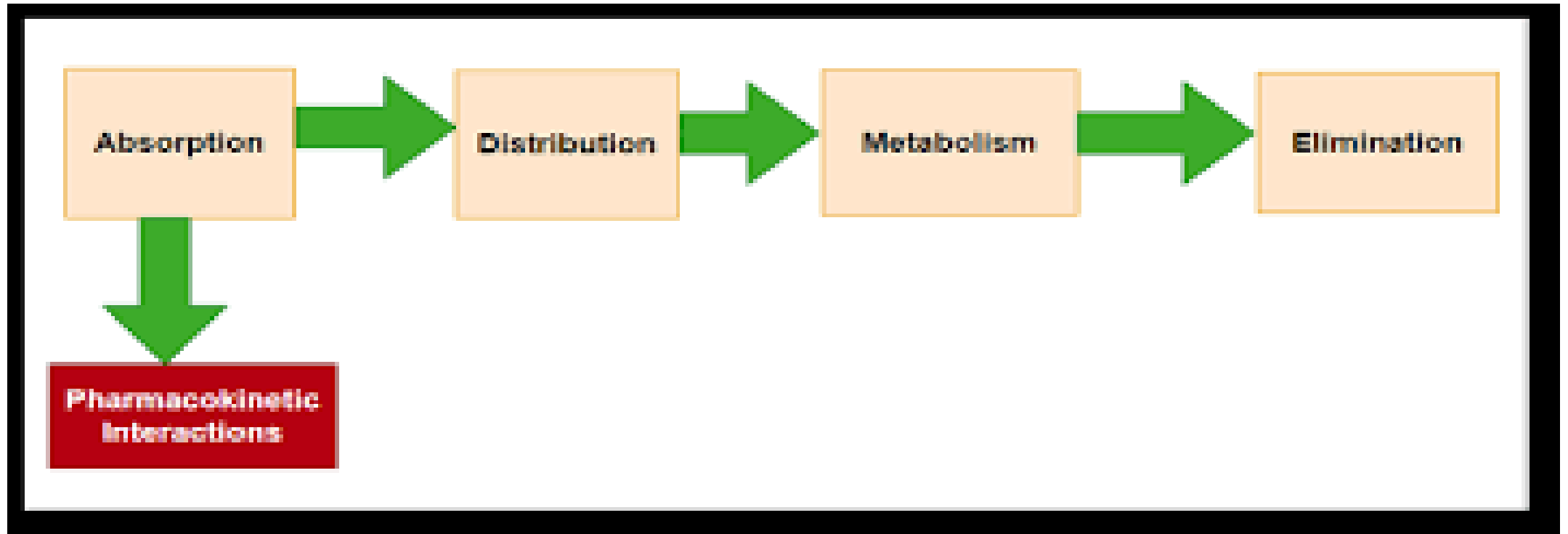
- ✓ Give Separately
- ✓ Same IV Line, Flush with Saline

Omeprazole = Alkaline

Ondansetron = Acidic

Same IV Bottle = **NO** ❌ Same Line, One by One = **YES** ✓

II- Pharmacokinetic drug interactions (Affect ADME)

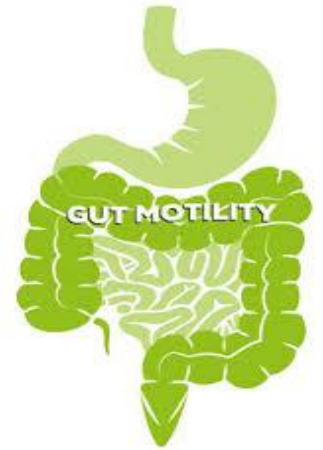


II- Pharmacokinetic drug interactions

1- Drug interaction affecting GIT absorption:

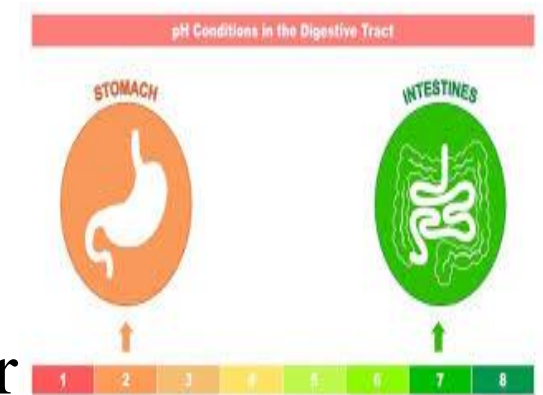
a) Drugs affecting gut motility

- **Motility changes** (↑ by metoclopramide & ↓ by atropine) affect absorption of other drugs .



b) Drugs affecting gut pH:

- Gastric acidity ↑absorption of acidic drugs as aspirin.
- Intestinal alkalinity ↑absorption of basic drugs as ephedrine.



c) Drug binding, adsorption or chelation:

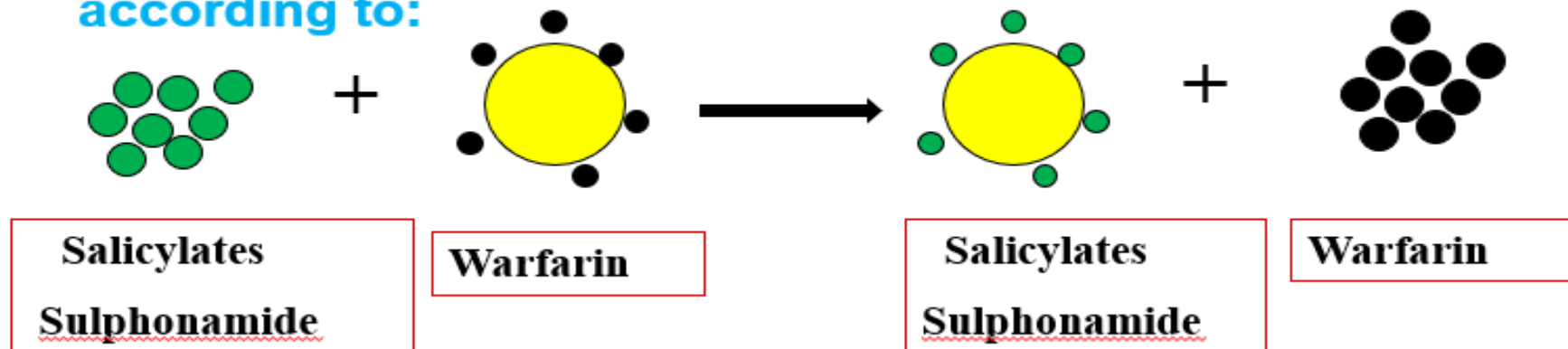
- **Tetracyclines** chelate metals as Ca, Mg, Al & Fe, & ↓ their absorption.

II- Pharmacokinetic drug interactions

2- Drug Interactions affecting Distribution

*Drugs with high affinity binding to plasma proteins as aspirin, sulfa can displace other drugs bound to plasma proteins as Warfarin leading to **↑ free concentration and toxicity.**

The amount of drug bound to plasma protein will change according to:



II- Pharmacokinetic drug interactions

3-Drug interactions affecting Metabolism :

a) Enzyme Induction:

- HME Inducers \uparrow metabolism & \downarrow activity of the inducer & administered drugs. They include: phenobarbitone, phenytoin and tobacco-smoking.

b) Enzyme Inhibition:

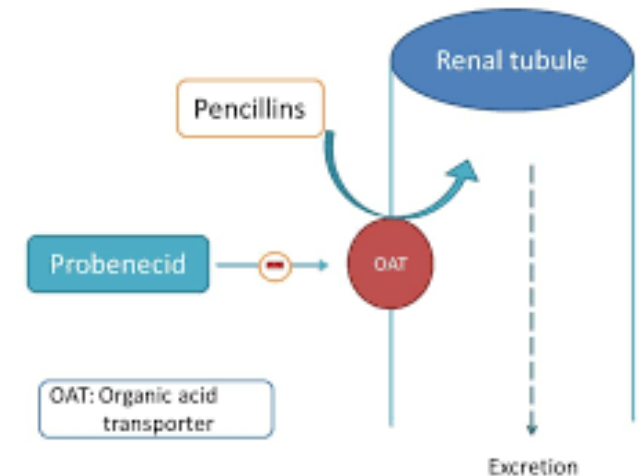
- HME Inhibitors \downarrow metabolism & \uparrow activity of their own & co administered drugs. They include: estrogen and chloramphenicol.

II- Pharmacokinetic drug interactions

4- Drug interaction affecting Renal Excretion:

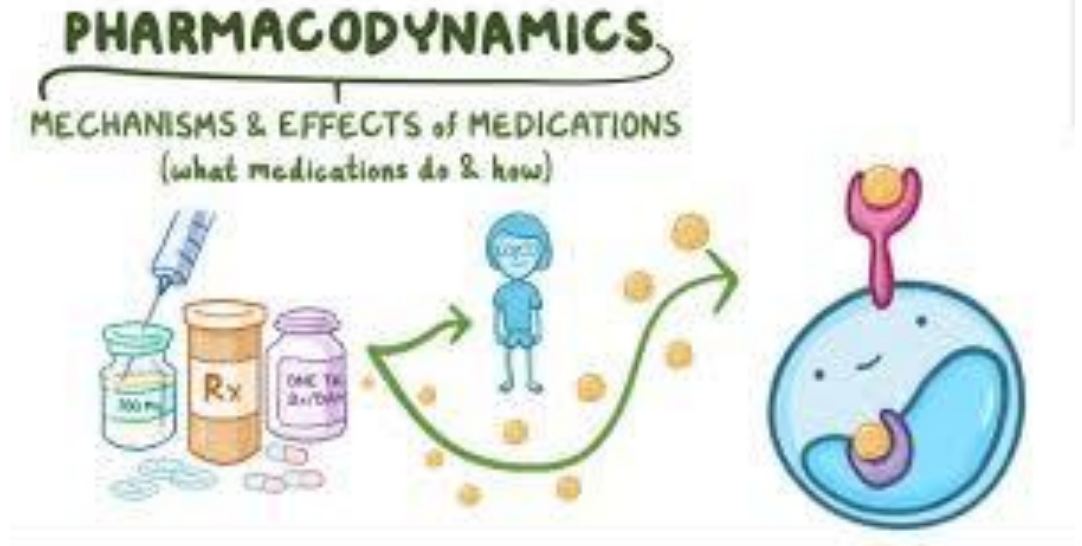
a) Competition for active renal tubular secretion:

- **Probenecid** blocks excretion of weak acids; **penicillin**



b) Changes in urinary PH

- **Acidification of urine** by NH_4Cl or vit C: \uparrow excretion of basic drugs.
- **Alkalization of urine** by NaHCO_3 : excretion of acidic drugs.



III- Pharmacodynamic drug interactions

III- Pharmacodynamic drug interactions

- Drug interaction occurring at **sites of action, receptor sites or secondary physiological mechanisms**; leading to changes in drug responses. **They may be synergistic or antagonistic.**



III- Pharmacodynamic drug interactions

1- Drug interactions at specific receptor sites:

(Pharmacological Antagonism = 2 drug acting on 1 receptor)

Types of Pharmacological Antagonism:

a- Competitive Antagonism: (antagonist displaced by the excess agonist)
e.g.- Acetylcholine & Atropine (M)

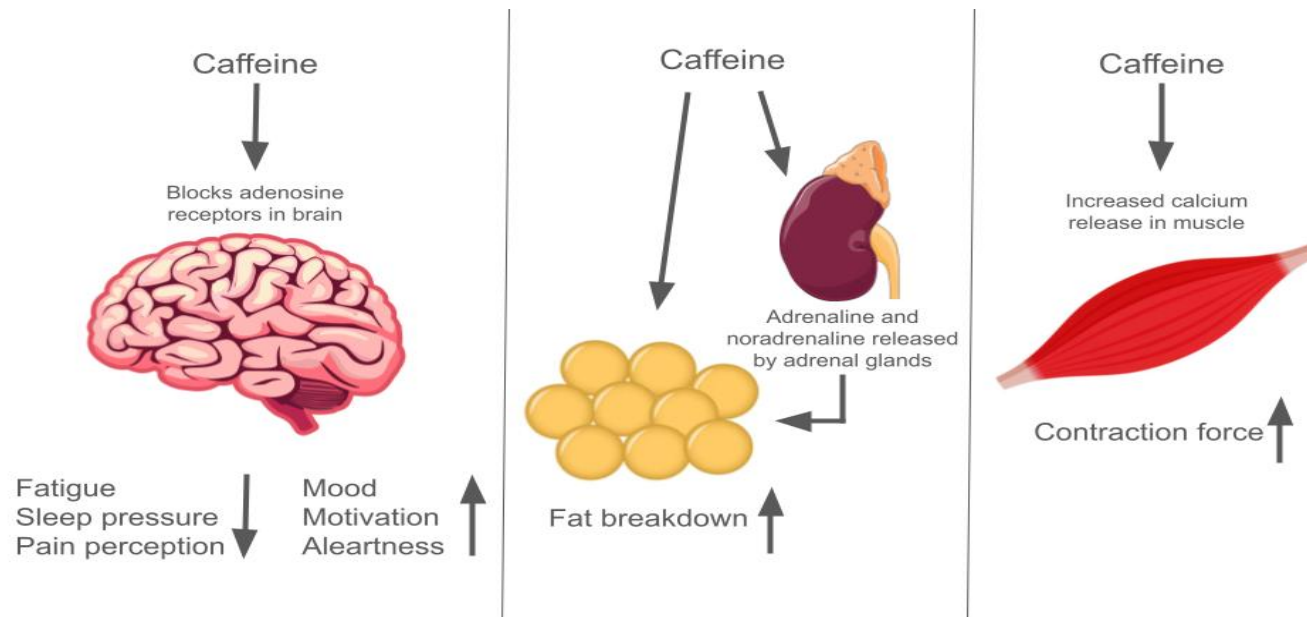
b- Non competitive Antagonism: (antagonist not displaced by the excess agonist)

- **Reversible:** Block end by metabolism of antagonist.
- **Irreversible:** Bind covalently , block end by resynthesize of new receptors.

III- Pharmacodynamic drug interactions

2. Drug interactions on the same physiologic system:

Caffeine antagonizes CNS depressant effect of **barbiturates**.



Barbiturates

The diagram shows the chemical structure of a barbiturate (a pyrimidine-2,4,6-trione) and its interaction with a GABA_A receptor. The barbiturate binds to a specific site on the receptor, which leads to a calming effect in the brain. Chloride ions (Cl⁻) are shown entering the cell through the receptor channel.

They are primarily used as

- 1) Sedatives
- 2) Hypnotics
- 3) Anticonvulsants

Calming effect !!

Barbiturate binding site

GABA_A receptor

Barbiturates

Animal Biology

III- Pharmacodynamic drug interactions

3- Drug interactions involving combined Toxicity:

a) Combined use of 2 or more drugs with toxic effects on the same organ can greatly increase the organ damage.

b) **Examples:** use of 2 nephrotoxic (amino glycoside & cephaloridine).



* Results of *drug interactions*:

DON'T FORGET!

* Results of *drug interactions*:

I- Addition (Summation): (1 + 1 = 2).

The resultant action =sum of individual drug actions.

Example: Aspirin + Paracetamol

II- Synergism: (1 + 1 => 2).

The resultant action More than sum of individual drug actions.

Example: Sulfamethoxazole + Trimethoprim → ↑Antimicrobial activity.

III- Potentiation: (0+1>1).

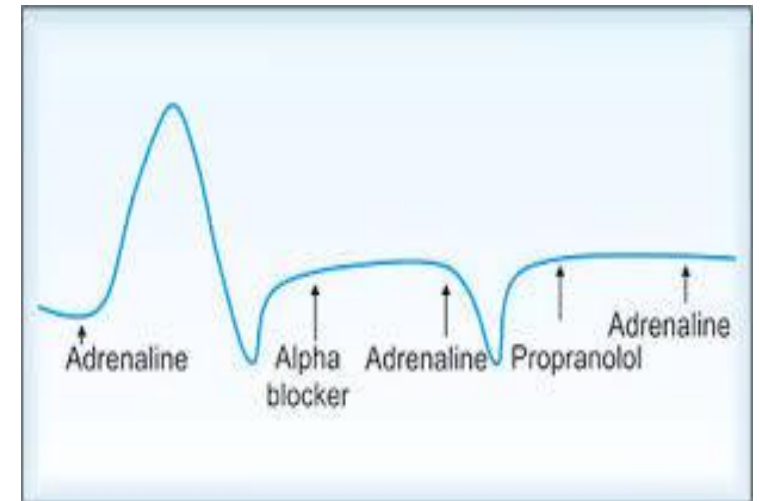
One drug has no action(0) increases the effect of another drug (>1)

Examples: **Barbiturates** (NOT analgesic) potentiate the analgesic effect of **Aspirin**.

IV- Reversal:

Adrenaline after Phentolamine (alpha blocker) →hypotension .

V- Antagonism



* **Results of drug interactions:**

V- Antagonism: occurs when using drugs of opposite actions

Types of antagonism :

1- Chemical:

one drug react chemically with an active drug forming inactive compound Neutralization (Acid + Base)

2- Physiological:

- a- 2 Agonists on 2 Receptors producing 2 Opposing actions.
- b- Example: Adrenaline ($\beta 2$) + Histamine (H1) on bronchi.

3- Pharmacological :

2 drugs acting on 1 receptor A- competitive B- noncompetitive



Questions



Explain:

1. Aspirin can cause bleeding tendency with warfarin.
2. Metoclopramide interferes with digoxin absorption.

Put true or false:

Drug interactions are type C adverse drug reactions.





Thank You

