**Drug drug interaction**

**Drug Combination**

Two or more drugs are taken at the same time ( Drug drug interaction )

**TYPES of Drug drug interaction**

**1**. Harmful

**2.** Useful ( multidrugs treatment of T.B.)

**Clinically important D -D interactions:**

**1.** Patients with impaired liver or kidney functions.

**2**. Elderly patients.

**3.** Drugs known a enzyme inducers and inhibitors.

**4.** Drugs with small therapeutic index **(digoxin -Lithium).**

**5.** Drugs used for prolonged time and precise plasma levels **(lithium -antiepileptics ).**

**Drug Combination Where :**

**1-** Outside the body.

**2-** Inside the body.

**Drug interaction outside the body**

1. Soluble insulin and protamine zinc → delayed absorption
2. **incompatibility**

Diazepam or phenytoin **+** Infusion fluid (saline) →Precipitation .

Carbenicillin **+** Gentamycin → Inactive gentamycin

Thiopental **+** Suxamethonium → Precipitation**.**

**Drug INTERACTION INSIDE THE BODY**

**Mechanisms :**

**Pharmacokinetic interactions:**

1. Absorption
2. Distribution
3. Metabolism
4. Elimination

**Pharmacodynamics Interactions**

1. Synergism
2. Potentiation
3. Addition
4. Antagonism

**I. Interactions During Absorption**

**A. Direct chemical interaction**

1. Iron and tetracyclines form complex.
2. Antacids**:** Aluminium or magnesium chelate

with tetracyclines ↓ bioavailability of tetracycline **(2 hr apart).**

1. Cholestyramine interfere with absorption of:
2. **-**Digoxin
3. **-**Warfarin .
4. **-**Thyroxine

**B -Alteration of GIT Motility**

1. Purgatives ↓ absorption
2. Antidepressants & anticholinergic drugs e.g. Atropine ↓ gastric emptying & delay absorption.
3. Prokinetics e.g. Metoclopramide ↑ gastric emptying and absorption**.**

**C- Alteration in GIT Flora**

Broad spectrum antibiotics potentiates anticoagulants→ ↓ bacterial synthesis of Vit K.

**D- Absorption from other sites**

Local anesthetic (lidocaine) + Adrenaline delay in absorption → ↑duration of action

**II. Distribution**

**A)** Displacement from plasma protein binding sites.

Sulphonamide + Bilirubin → Kernicterus

**B)** Displacement from other tissue binding sites.

Quinidine + digoxin→ more digoxin → toxicity

**III.Biotransformation**

**A)** Enzyme Induction.

Rifampin + Contraceptives→ Failure of conception

Barbiturates + Warfarin → ↓ Anticoagulant effect

**B)** Enzyme Inhibition.

Cimetidine → potentiates effects of Warfarin , theophylline

**IV. Interaction During Excretion**

1. **Interference with active transport.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| |  | | --- | | Primary Drug | | |  | | --- | | Competing Drug | | |  | | --- | | Result | |
| |  | | --- | | Penicillin | | |  | | --- | | Probenicid | | |  | | --- | | ↑ Penicillin Level | |
| |  | | --- | | Salicylates | | |  | | --- | | Probenicid | | |  | | --- | | Salicylate toxicity | |
| |  | | --- | | Indomethacin | | |  | | --- | | Probenicid | | |  | | --- | | Indomethocin toxicity | |

**Pharmacodynamic Interactions**

* DRUG SYNERGISM.
* DRUG ANTAGONISM.

**Synergism**

When the therapeutic effect of one drug is enhanced by another drug.

**Types:**

Addition.

Potentiation

**Addition :**

**1-**When the effect of two drugs having similar action are additives

**2-**The net effect of two drugs used together is equal to the sum of the individual drug effect.

**1 + 1 = 2**

Thiazide diuretics + Beta blocker have an additive antihypertensive action.

**Potentiation:**

1. When the net effect of two drugs used together is greater than the sum of the individual drug effects.

**1 + 1 > 2 or 1 + 0 > 2**

1. when one drug increases the action of other drug e.g. sulphamethoxazole + trimethoprim → cotrimoxazole **(bactericidal)** 1 + 1 > 2
2. or when drug has no effect as own but increases the effect other drugs

**(1 + 0 >2)** L-dopa and carbidopa

**Antagonism**

The effect of one drug is decreased or abolished by the administration of another one

1. Physiological antagonism.
2. Chemical antagonism
3. Pharmacological antagonism