

Types of drug concentration– response relationship

A. Graded drug concentration-Response Relationships

- As the dose of a drug is increased, the response (effect) of the tissue or organ is also increased.
- The efficacy (E_{max}) and potency (ED_{50}) parameters are derived from these data.

GRADED DOSE-RESPONSE CURVE

QUANTAL DOSE-RESPONSE CURVE

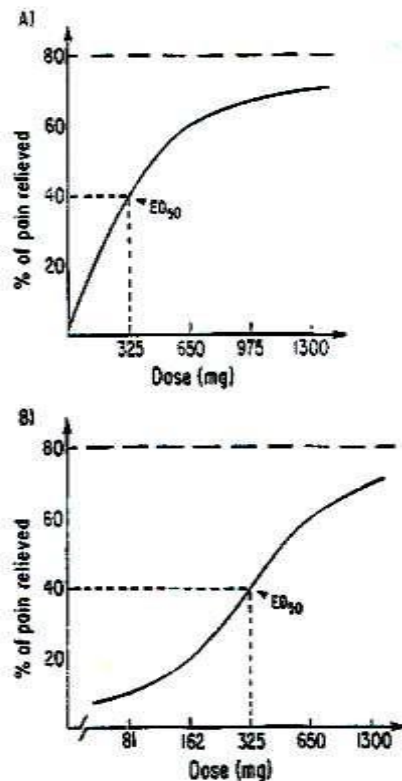
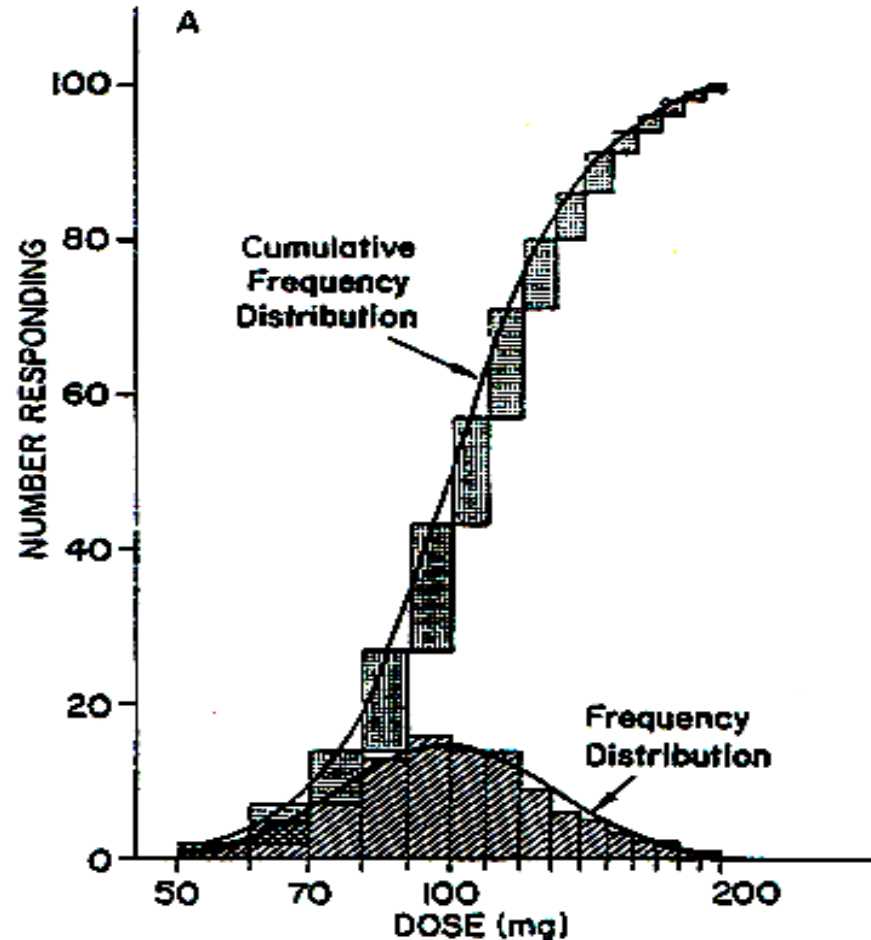


Fig. 1-2. A dose-response curve obtained in one patient relating the dose of aspirin ingested to the percentage of headache pain relieved. (A) A linear plot: the abscissa (dose in milligrams) has a linear scale. (B) A semilog plot: the abscissa (dose in milligrams) has a logarithmic scale.



B. Quantal or all or none dose response relationship.

- ✓ The Plot of the fraction of the population that responds at each dose of the drug versus the log of the dose administered.
- ✓ responses follow all or none phenomenon – that means the individual of the responding system either respond to their maximum limit or not at all to a dose of drug and there is no gradation of response.
- ✓ population studies.
- ✓ relates dose to frequency of effect .
- ✓ The median effective (ED50), median toxic (TD50) ,and median lethal doses (LD50) are extracted from experiments carried out in this manner.

Median effective dose (ED_{50}):the dose at which 50% of individuals exhibit the specified quantal effect.

Median toxic dose (TD_{50}) :the dose required to produce a particular toxic effect in 50% of animals.

Median lethal dose (LD_{50}): is the lethal dose that causes death in 50% animal under experiment.

1. Excretion

- Alteration of urine PH.

e.g. Phenobarbitone + NaHCO_3

- Alteration of active tubular secretion

e.g. Probenecid + penicillin.

II – Pharmacodynamic interaction

- It occurs by modification of pharmacological response of one drug by another without altering the concentration of the drug in the tissue or tissue fluid.

1. Additive – Occurs when the combined effect of two drugs is equal to the sum of the effects of each agent given alone.

$$2 + 2 = 4$$

e.g. H_1 antagonist + CNS depressant

2. Potentiation:-

- a situation where by one drug enhance the action another drug without having an effect by itself.

e.g. $0 + 1 > 1$

e.g. Caffeine +ergot alkaloid

3. Synergism

- when the combined effects of two drugs are much greater than the sum of the effects of each agent given alone.

e.g. $1 + 1 >>> 2$

penicillin + aminoglycosides

4. Antagonism

a) Pharmacological antagonism

- It is due to opposite effects of two drugs binding to the same receptor. It can be competitive antagonism or non – competitive antagonism.

Competitive antagonist

- **Produce receptor blockade by competing with an agonist for the same receptor.** The binding of agonist and antagonist is mutually exclusive, possibly because both agents bind to the same receptor site.
- Reversibly bind to the receptor usually the concentration of the agonist.
- **The effect can be overcome by increasing the concentration of the agonist.**

E.g. diazepam (agonist) and flumazenil antagonist.

→ acetylcholine (agonist) and atropine.

d – tubocurarine (antagonist).

Non – competitive antagonist

- **bind at different site from agonist binding site**
brings conformational change.
- binding is **irreversible**. The irreversible mechanism reduces the total number of receptors available for an agonist action. The irreversible binding doesn't last forever.

b) Chemical antagonism

Occur when antagonist react chemically with agonist and inactivate it independently from receptor interaction.

E.g. - **Neutralization**

- Antacids

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c) Physiological antagonism

- It is due to opposite effects of two drugs on the same physical function.

E.g. – Histamine and adrenaline

- Insulin and glucagon.

d) Physical antagonism

- It is due to physical properties of drugs.

E.g. activated charcoal in alkaloidal poisoning

B – Drug – food interaction

e.g. - MAOI + Tyramine

- TTC + milk

C

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e.g. Grape fruit juice +
saquinavir / **BDZ/ Ca⁺²**

channel blocker (grape fruit juice
is inhibitor)