Principles of Pharmacodynamics and Pharmacokinetics
Pharmacodynamics: Basic definitions
Pharmacology

- Medicinal pharmacology
- Drug composition and properties
- Interactions
- Toxicology

Pharmacokinetics
- Effect of Body on drug

Pharmacodynamics
- Effect of Drug on body
Pharmacology

Ligand ( = drug )

Receptor

SIGNAL TRANSDUCTION

Effect
**Receptor:**
The component of a cell or organism that interacts with a drug and initiates the chain of biochemical events leading to the drug’s observed effect.

The receptor:

1. Determines the quantitative relations between dose of a drug and pharmacologic effects

2. Responsible for selectivity of drug actions

3. Mediates the actions of both pharmacological agonists and antagonists
**Drug receptor types**

- **Regulatory proteins**
  Examples: neurotransmitters, hormones, etc.

- **Enzymes**
  Examples: ACh esterase, angiotensin converting enzyme, etc.

- **Transport proteins**
  Example: Na⁺/K⁺ ATPase

- **Structural proteins**
  Example: Tubuline
The connection between the drug’s DOSE and the physiological RESPONSE to it can be presented graphically, in a Dose-Response curve, after measuring the effect at various doses of a drug:

In a half-logarithmic scale:
Dose-Response

Relation between drug concentration and receptor-bound drug:

$K_D$ characterizes the receptor’s AFFINITY for binding the drug, reciprocally.
Relation between drug dose and clinical response

- **Potency**: Refers to ED50. The lower it is - the drug’s potency is greater.

  Potency depends on the drug’s affinity to the receptor and on the efficiency of response-coupling.

- **Efficacy**: Reflects the limit of response to the drug (Emax). The greater Emax is, the drug’s efficacy is higher.

  Efficacy is determined by the drug’s mode of interaction with receptors and the effector’s characteristics.
Dose-Response

Facilitates comparison of potency and efficacy among different drugs with the same mechanism of action:

- Potency $\rightarrow$ ED50
- Efficacy $\rightarrow$ Emax
Agonists and Antagonists

Agonists  Drugs that occupy receptors and activate them.
Agonist

Partial agonist

Antagonist

Reversible

Irreversible

Competitive

Non-competitive
**Dose-Response**

**Competitive Antagonism**
Parallel shift to right

\[ E_{\text{max}} \]  
\[ \frac{\uparrow ED_{50}}{ \text{Agonist alone} } \]  
\[ \text{Agonist and antagonist} \]

**Noncompetitive Antagonism**
Nonparallel shift to right

\[ \downarrow E_{\text{max}}, ED_{50}? \]  
\[ \frac{\text{Agonist alone}}{ \text{Agonist and antagonist} } \]
**Physiological antagonists:**

- Sympathetic \( \leftrightarrow \) Parasympathetic
- Epinephrine \( \leftrightarrow \) Acetylcholine

**Neutralizing antagonists:**

- Digoxin \( \leftrightarrow \) Digoxin binding antibody
Dose-Response

Dose-response in a **population**: Number of patients with a defined response produced by a specific dose of drug.
Dose-Response

- Frequency-distribution curve:
- Quantal dose-response curve
Selectivity of drug action

safety/Effectiveness:

ED<sub>50</sub> – minimal effective dose in 50% of the population
TD<sub>50</sub> – minimal toxic dose in 50% of the population

- Therapeutic index:

   \[ TI = \frac{TD_{50}}{ED_{50}} > 1 \]

TD<sub>0.1</sub> – minimal toxic dose for 0.1% of the population

ED<sub>99.9</sub> - minimal effective dose in 99.9% of the population

- Margin of safety:

   \[ TD_{0.1}/ED_{99.9} \]
**Dose-Response**

Enhancement of drug effects

- **Addition:** \[ E_1 + E_2 = E_{\text{sum}} \] \hspace{1cm} (1+1=2)
  
  *Trimethoprim and sulfamethoxazole*

- **Synergism:** \[ E_1 + E_2 = E_{\text{syn}} > E_{\text{sum}} \] \hspace{1cm} (1+1=3)
  
  *Alcohol and benzodiazepines*

- **Potentiation:** \[ E_1 = 0 \hspace{1cm} E_1 + E_2 > E_2 \] \hspace{1cm} (0+1=2,3..)
  
  *Cardidopa and dopa*