PHARMACODYNAMICS

Khder Hussein Rasul

Pharmacology, MA 411

Spring Semester

6th week

08/04/2025

Outline

- Pharmacodynamics

Objectives

At the end of the lesson, the students should be able to understand:

1. Introduction to pharmacodynamics
2. Describe drug-receptor interactions.
3. Learn about dose-response relationships.
4. Being familiar with therapeutic and toxic effects of drugs.

Introduction to pharmacodynamics

- **Pharmacodynamics** is the study of how drugs exert their effects on the body, including the biochemical and physiological responses they produce.
- It explains the mechanism of action of drugs at the molecular, cellular, and systemic levels.
- In simple terms, pharmacodynamics answers the question: "What does the drug do to the body?"

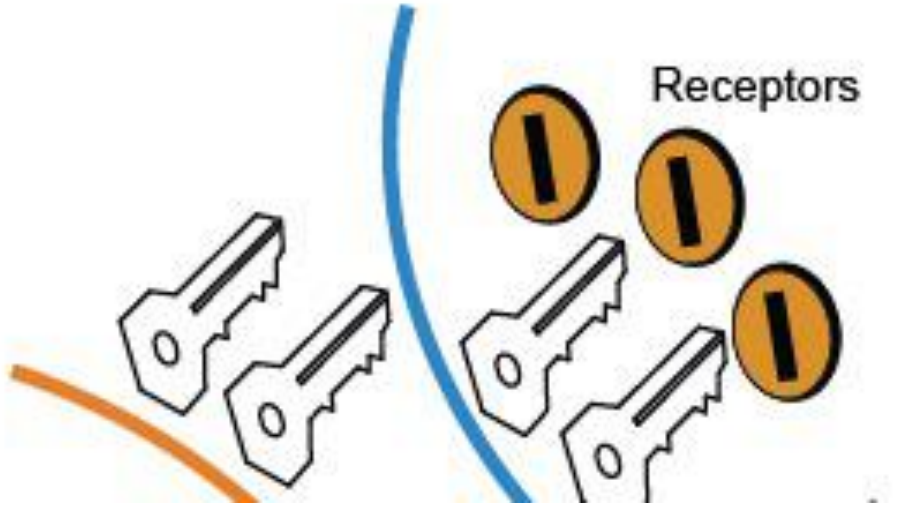
Introduction to pharmacodynamics

➢ **Pharmacodynamics involves key concepts such as:**

1. Drug-receptor interactions (binding to receptors, enzymes, or ion channels)
2. Dose-response relationships (how the drug effect changes with concentration)
3. Therapeutic and toxic effects

Drug-receptor interactions

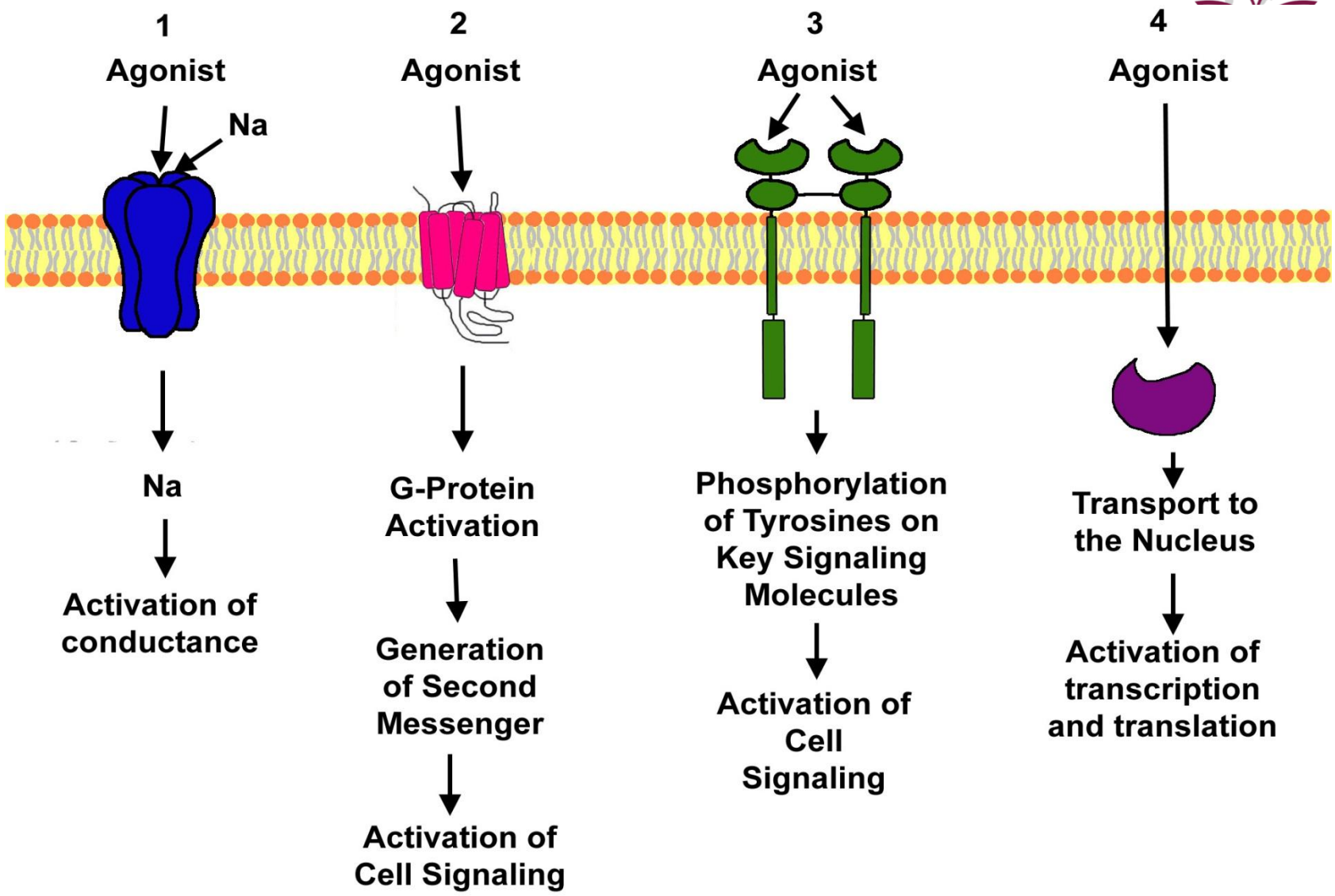
- **Drug-receptor interactions** refer to the binding of a drug to a specific receptor in the body, leading to a biological response.
- **Receptor:** A specific protein (on the cell surface or inside the cell) that a drug binds to, triggering a response.



Drug-receptor interactions

- **Receptor families include**

1. Ligand-gated ion channels
2. G protein-coupled receptors
3. Enzyme-linked receptors
4. Intracellular receptors



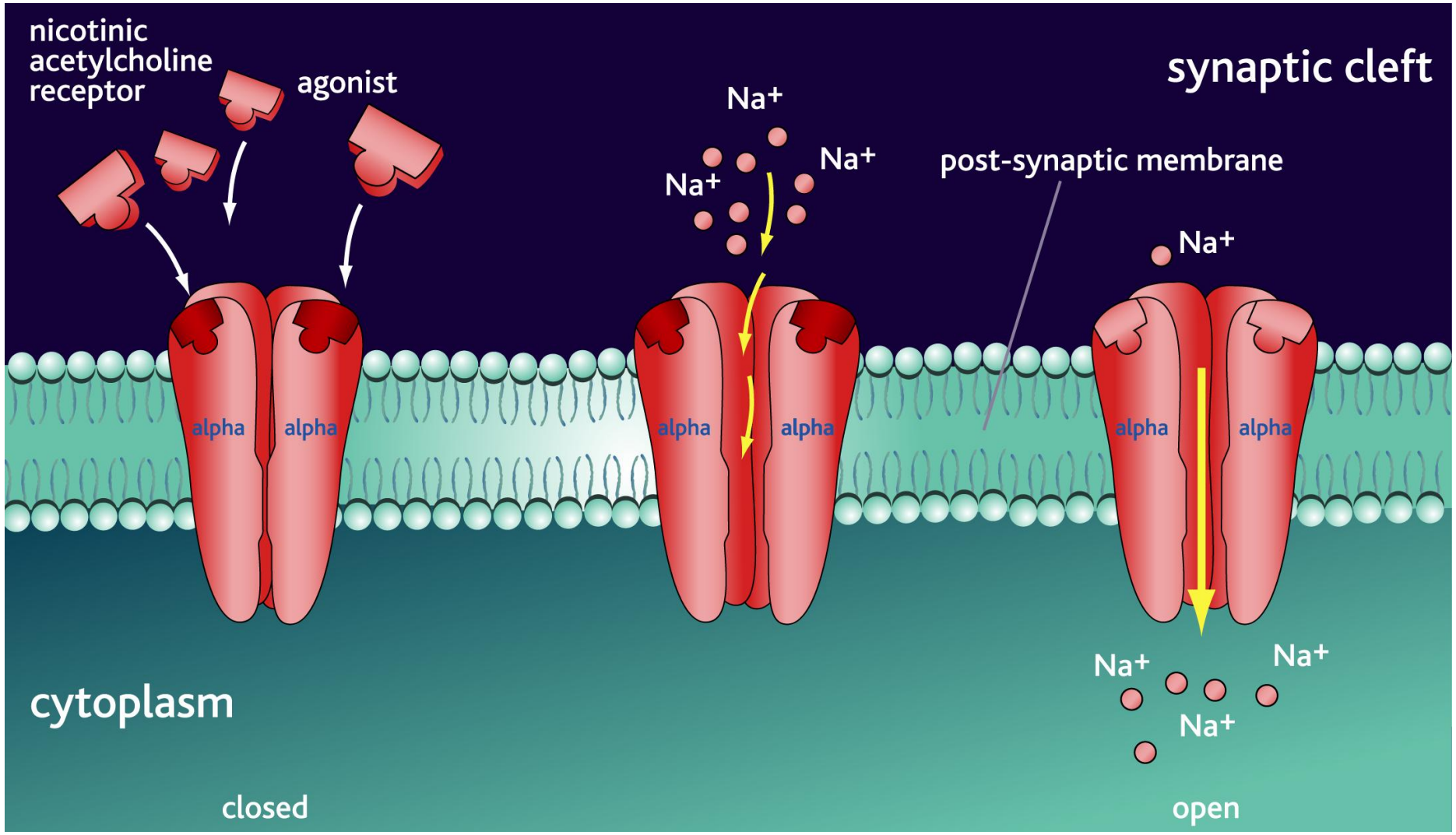
Ligand-gated ion channels

- **Ligand-gated ion channels** are responsible for regulation of the flow of ions across cell membranes.
- Response to these receptors is very rapid.
- Have role in;

1. **Neurotransmission**
2. **cardiac conduction**
3. **muscle contraction etc...**

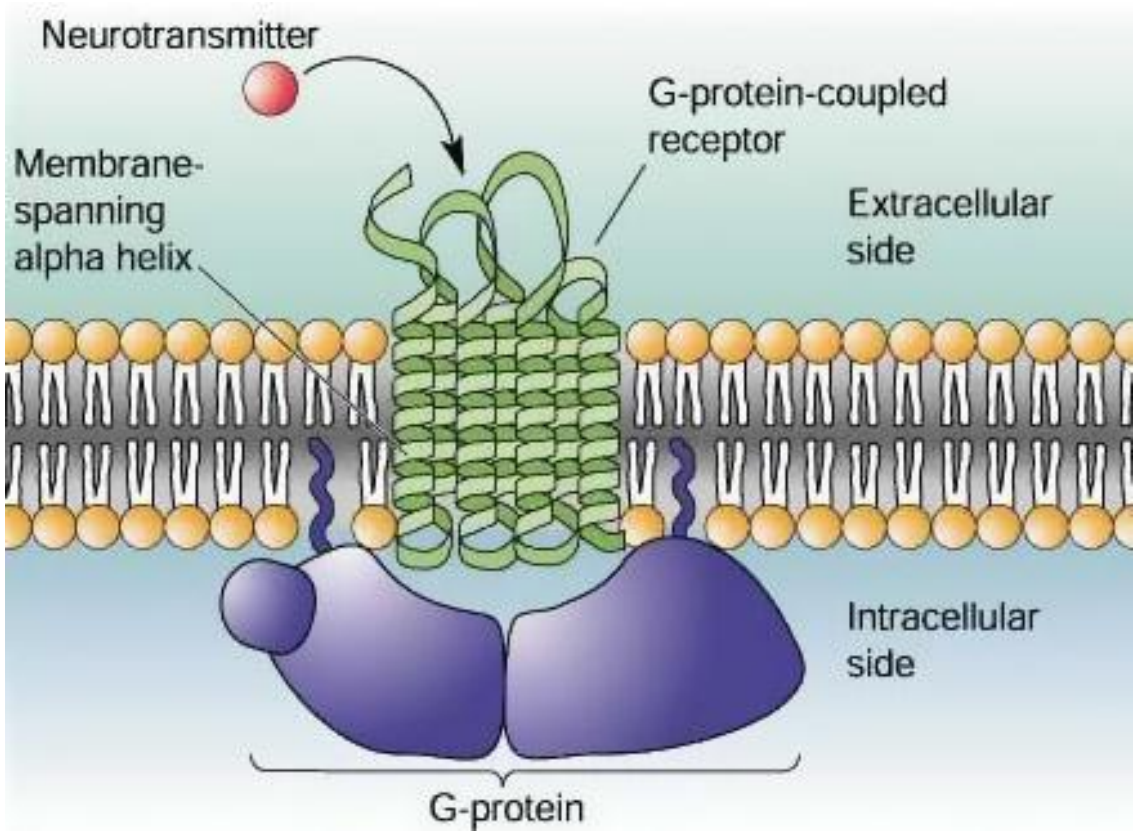
- Cholinergic nicotinic receptors is an example to these type of receptors.

Drug-receptor interactions

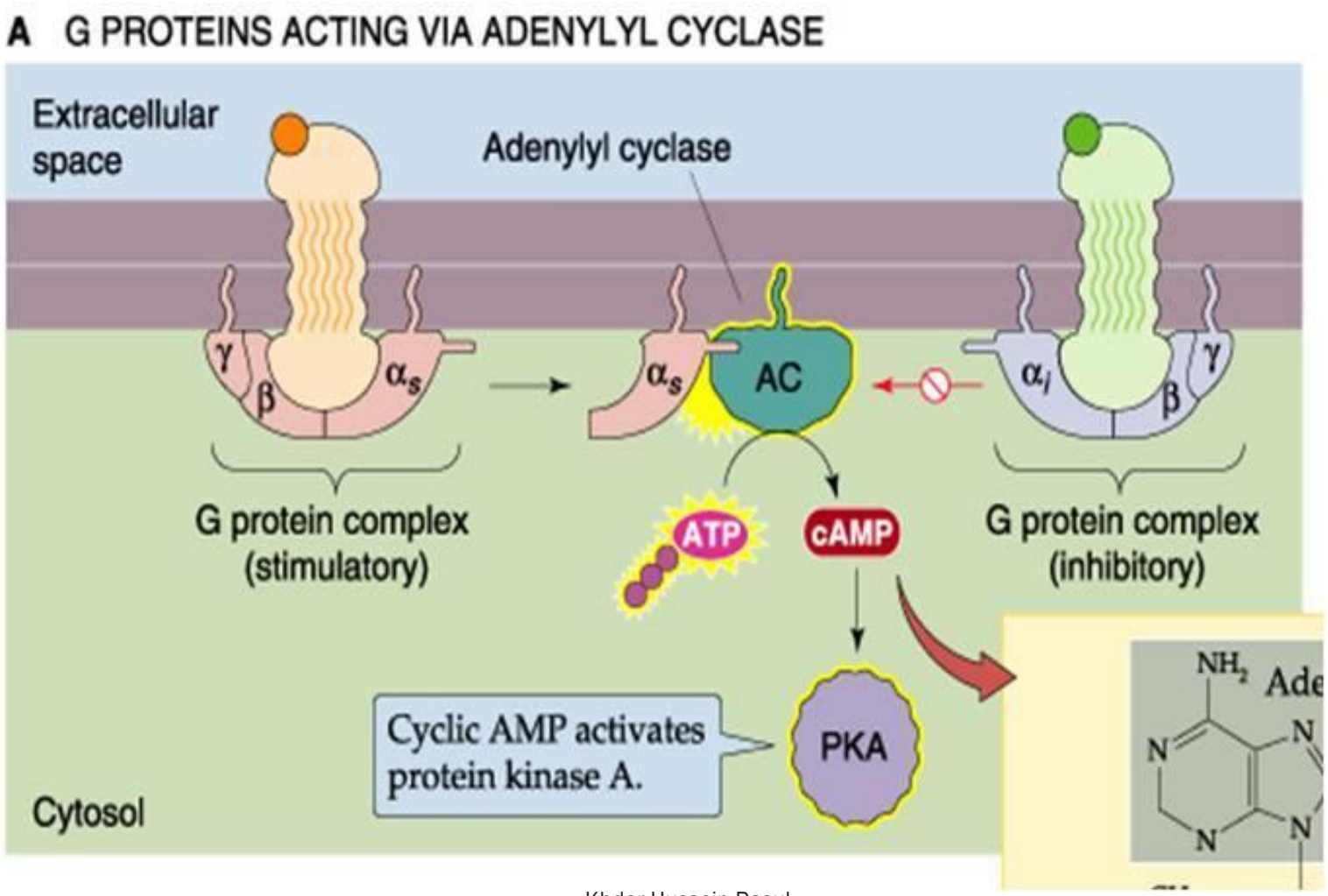


G protein-coupled receptors

- **G protein-coupled receptors** are made of a single α – helical peptide that has seven membrane spanning regions.



G protein-coupled receptors



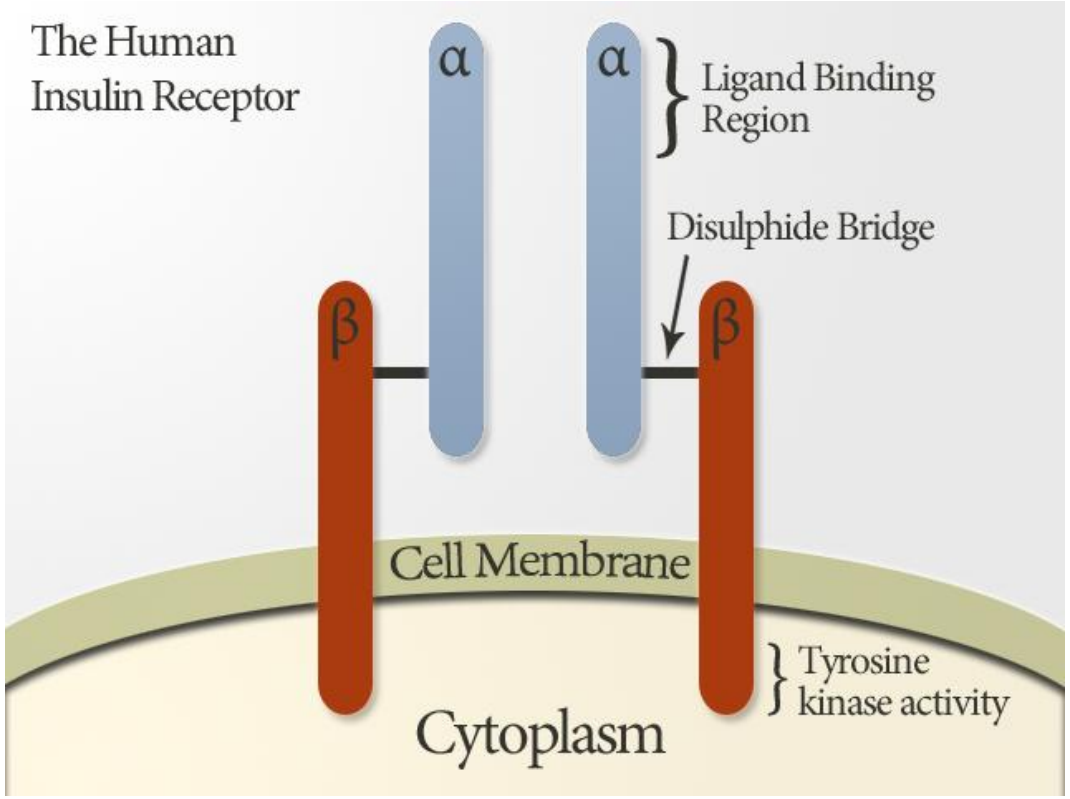
G protein-coupled receptors

- **Second messengers** are intracellular signaling molecules that transmit signals from receptors on the cell surface to target molecules inside the cell, amplifying the effect of the initial signal (first messenger, usually a hormone or neurotransmitter).
- Essential in conducting and amplifying signals from G-protein coupled receptors.
- **Types of second messengers**

1. cAMP (Cyclic Adenosine Monophosphate)
2. cGMP (Cyclic Guanosine Monophosphate)
3. Inositol triphosphate (IP_3) and
4. Diacylglycerol (DAG)
5. Calcium ions (Ca^{2+})

Enzyme-linked receptors

- **Enzyme-linked receptors** are transmembrane proteins that function as both **receptors** and **enzymes**. When drug binds to the extracellular domain, the receptor activates an intracellular enzymatic process, triggering a signaling cascade inside the cell.



Intracellular receptor

- Receptor is entirely intracellular.
- Drug must have sufficient lipid solubility.
- Drugs are mostly attached to plasma proteins in the blood circulation.
- Primary targets of these ligand-receptor complexes are transcription factors.

  DNA → RNA → proteins

- Steroid drugs exert their effects by this receptor mechanism.
- Time course of activation and duration of the response is much longer than the other type of receptors.

Intracellular receptor

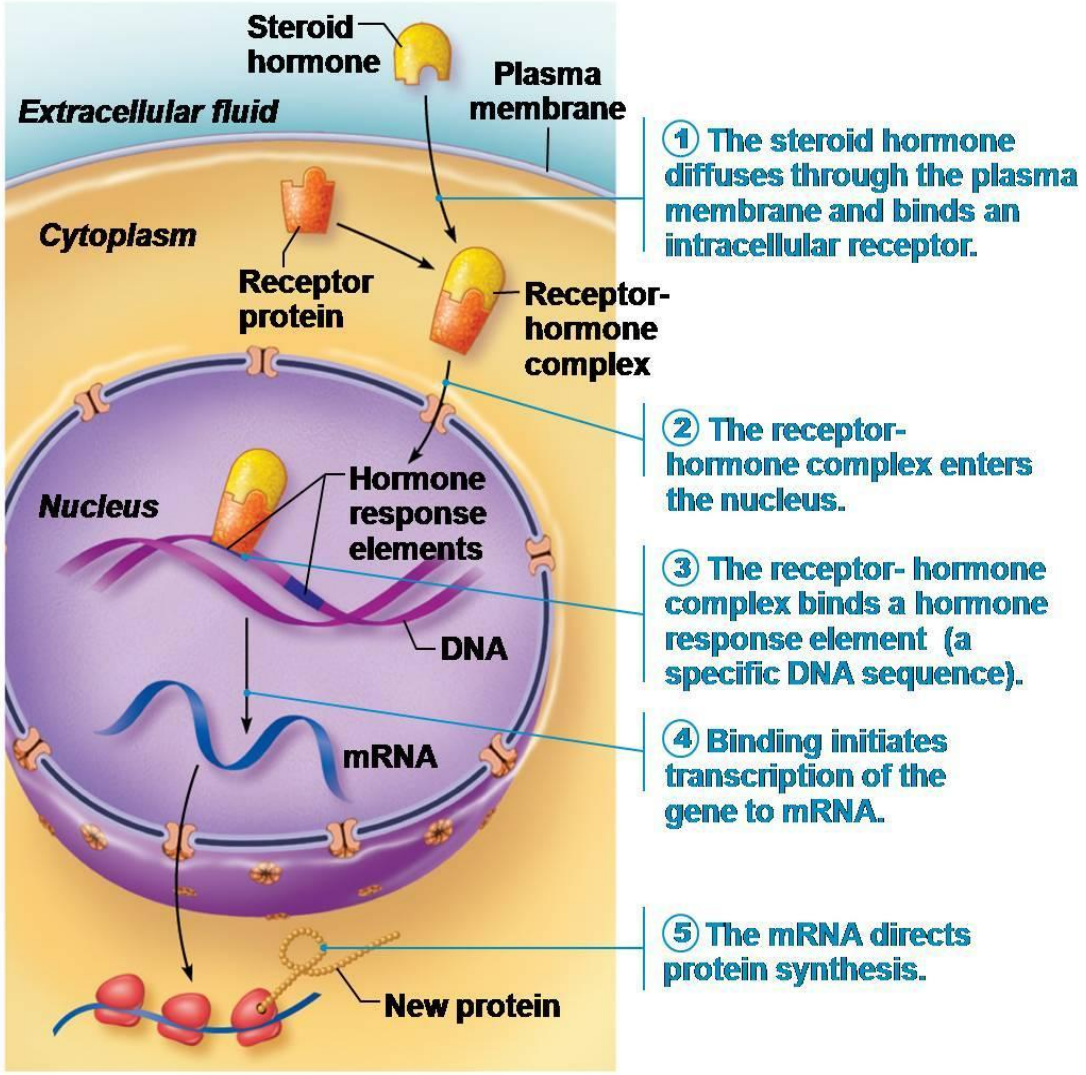
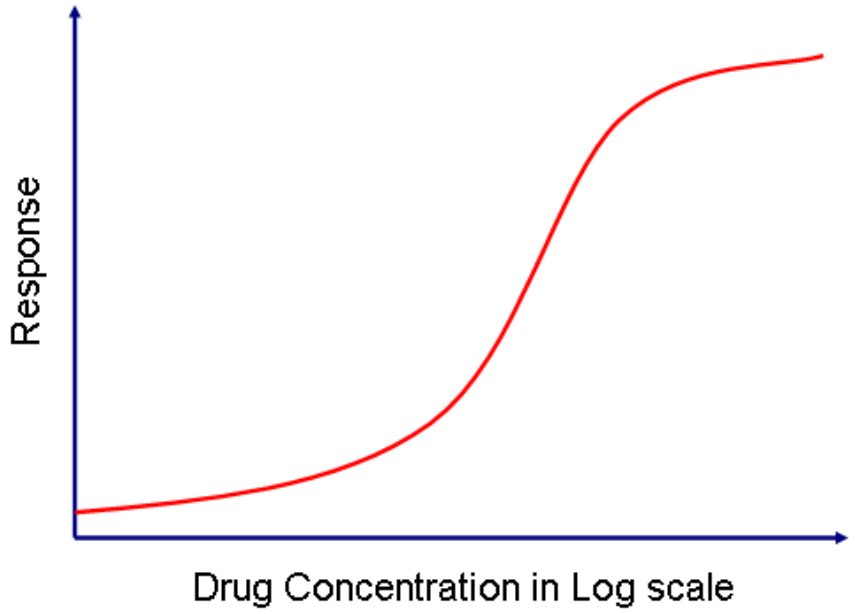


Figure 16.3, step 5

Dose-response relationships

- A dose-response relationship describes how the magnitude of a drug's effect changes as the dose increases.

- As the concentration of a drug increases, the magnitude of its pharmacological effect also increases.



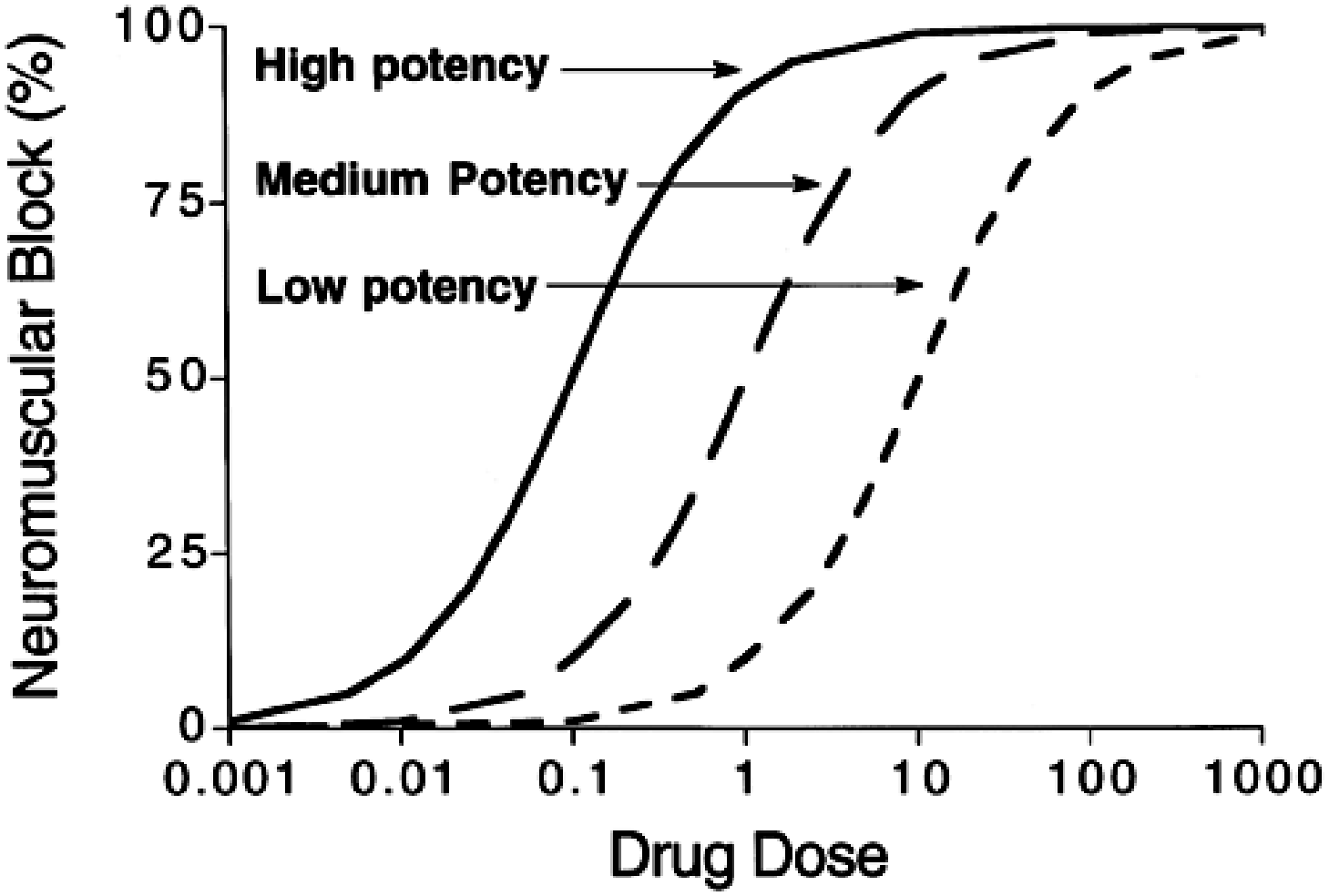
Dose-response relationships

- A dose-response relationship is fundamental in pharmacology for understanding

1. Drug potency
2. Drug efficacy
3. Drug safety

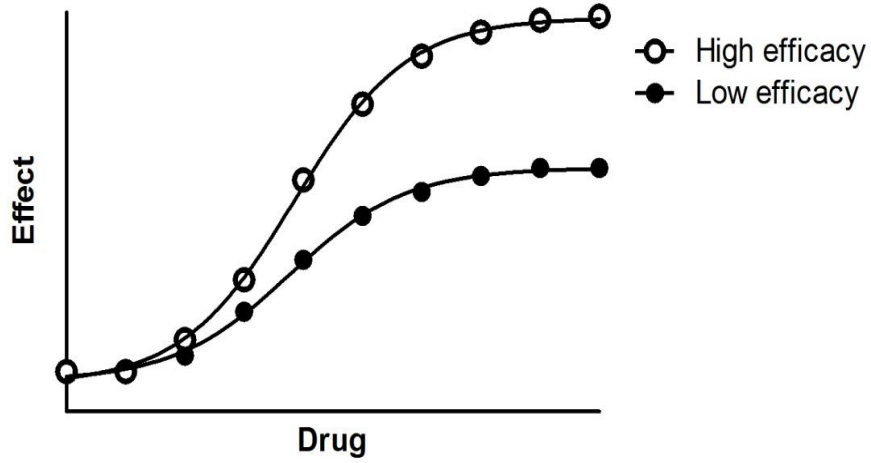
Dose-response relationships

- **Drug potency:** measure of the amount of drug necessary to produce an effect of a given magnitude



Dose-response relationships

- **Efficacy:** The ability of the drug-receptor complex to produce a biological effect.
- Efficacy is dependent on the number of drug-receptor complexes formed
- Maximal efficacy of a drug assumes that all receptors are occupied by the drug and if more drugs are added, no additive response will be observed.
- Maximal response (efficacy) is more important than drug potency.
- A drug with greater efficacy is more therapeutically beneficial than the one that is more potent.



Dose-response relationships

- **Affinity:** The strength of the drug's binding to the receptor.

1. Higher affinity → Drug binds strongly to the receptor
2. Lower affinity → Drug binds weakly and may easily dissociate.

- Measured by: Dissociation constant (Kd)

Lower Kd = Higher affinity (stronger binding).

Higher Kd = Lower affinity (weaker binding).

Agonists

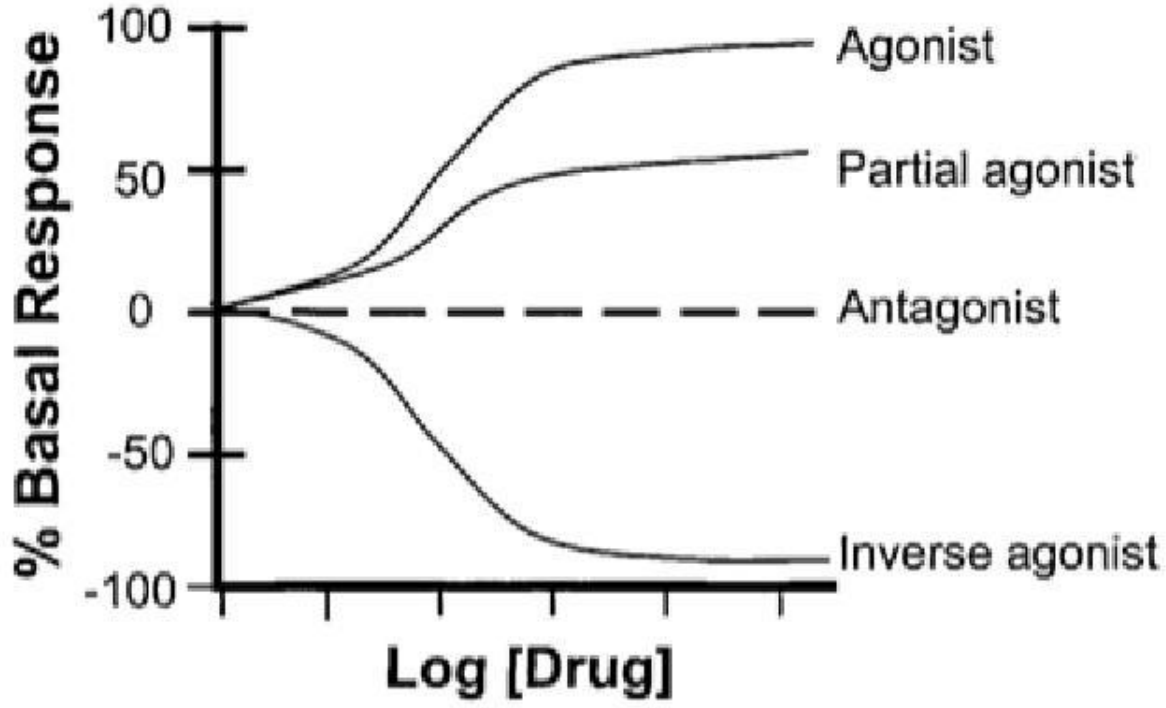
- An **agonist** binds to a receptor and produces a biological response.

1. **Full agonists**
2. **Partial agonists**
3. **Inverse agonists**

- **Full agonist:** If a drug binds to a receptor and produces a maximal biological response that mimics the response to the endogenous ligand, it is known as a full agonist.

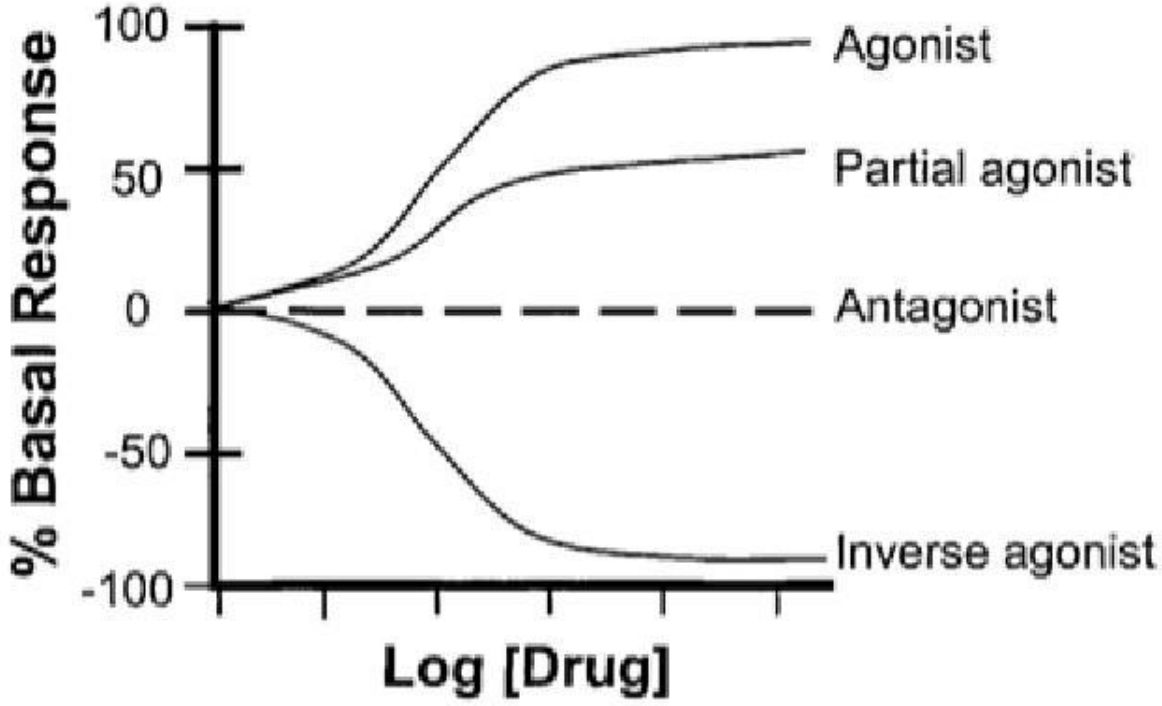
Agonists

- **Partial agonist:** Have efficacies greater then zero but less then that of a full agonist.
- **Inverse agonist:** produce a response below the baseline responses measured in the absence of drug.



Antagonists

- An **antagonist** is a drug that binds to a receptor but does not activate it. Instead, it blocks or reduces the effect of an agonist.
- Antagonists produce no effect by themselves.



Therapeutic and toxic effects

- **Therapeutic effects:** The desired and beneficial effects of a drug used to treat a disease.

Mechanism: Occurs when the drug interacts with target receptors, enzymes, or pathways to achieve its intended function.

Examples:

1. Paracetamol (Acetaminophen) → Reduces fever and pain.
2. Insulin → Lowers blood glucose levels in diabetes.
3. Antibiotics (e.g., Amoxicillin) → Kills bacteria causing infections.

Therapeutic and toxic effects

- **Toxic effects:** The harmful or dangerous effects of a drug that occur at **high doses** or due to **prolonged use**.

Mechanism: Results from overactivation of drug targets, non-specific interactions, or accumulation of toxic metabolites.

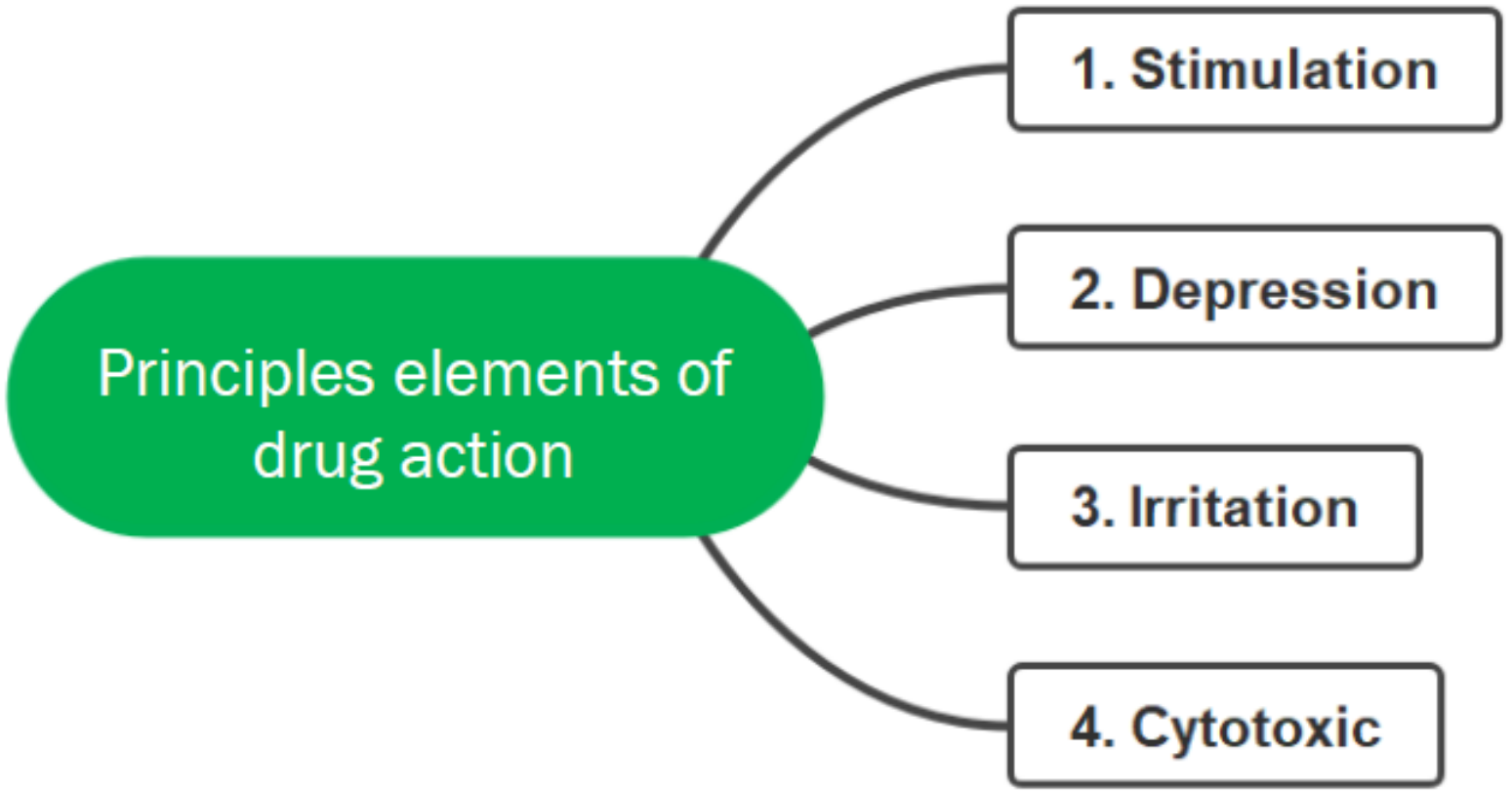
Examples:

Paracetamol overdose → Liver toxicity.

Warfarin excess → Severe bleeding.

Gentamicin → Kidney toxicity.

Principles of drug action



Stimulation and depression

- **Stimulation:** Administered drug selectively enhances the activity of the specialized cell.

Example. **Adrenaline** selectively enhances the activity of the heart.

- **Depression:** is the opposite of Stimulation. When a drug is administered it selectively decreases the activity of the specialized cell.

Example. **Quinidine** depresses the heart cells.

Irritation and cytotoxic

- **Irritation** is an unwanted noxious effect, undesirable to the human body.
  - The non-selective and noxious effect occurs on non-specialized cells such as epithelial cells and connective tissue.
  - **Production of bitterness that increases salivary and gastric secretions.**

- **Cytotoxic action** refers to the process of producing harmful effect(s) by a drug against only the affected cell(s), not the normal cell.
  - This is seen in cancer therapy, where the drug shows its significant effect on the cancerous cell only and most other cells are unaffected or have minimal effect.