PHARMACODYNAMICS I
MECHANISMS OF DRUG ACTION

Sary Alsanea, Ph.D.

Assistant Professor at the Department of Pharmacology and Toxicology,

Pharmacy College, KSU

salsanea@ksu.edu.sa

(Slides are adopted and modified from Prof. Hanan Hajar)

Mechanisms of Drug action

By the end of this lecture, you should:

- Identify different targets of drug action
- Differentiate between their patterns of action; agonism versus antagonism
- Elaborate on drug binding to receptors

What is Pharmacodynamics?

- Pharmacodynamics is a branch of pharmacology that deals with the study of the biochemical and physiological effects of drugs and their mechanisms of action.

What are the mechanisms of drug action?

Drugs can produce their actions by:

1) Binding with biomolecules (Receptor-mediated mechanisms):
   - Biomolecules = Targets=Receptors
   - Mostly protein in nature (protein target).
2) Non receptor-mediated mechanisms Physiochemical properties of drugs (e.g. Neutralization of gastric acidity with antacids).

What are the mechanisms of drug action?

Drugs can produce their actions by:

- Binding with biomolecules (Receptor-mediated mechanisms):

  Protein targets for drug binding

  - Physiological receptors
  - Enzymes
  - Ion channels
  - Carriers
  - Structural protein

Receptors

- A receptor is a special target macromolecule that binds the drug and mediates its pharmacological actions.

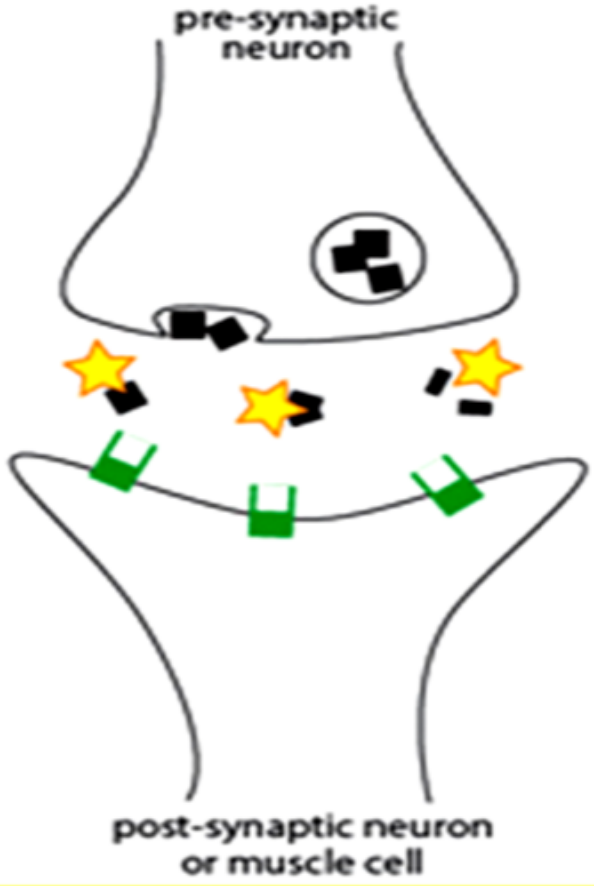
Where are receptors located?

- Cell membrane.
- Cytoplasm.
- Nucleus.

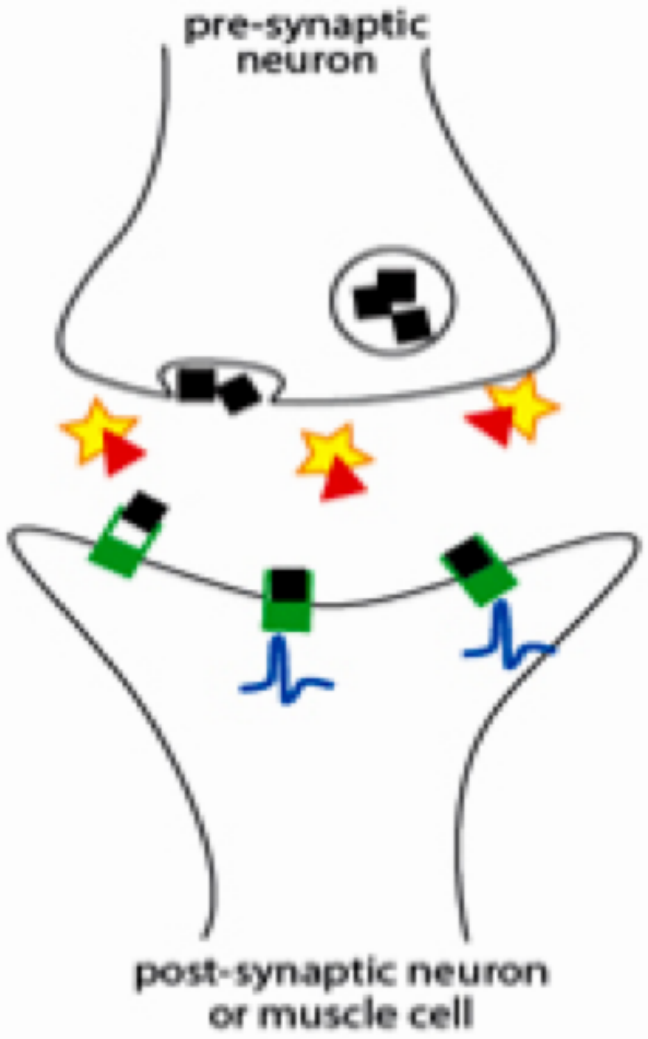
Enzymes

- The drug competes with the natural endogenous substrate for the enzyme.
  - Anticholinesterases inhibit acetylcholinesterase thus producing cholinomimetic action.
    - E.g. Neostigmine competes with ACh for acetyl cholinesterase enzyme at motor end plate (neuromuscular junction).

ACh Esterase STOPS signaling process



- ACh
- ACh Receptor
- Signal transmission
- ACh Esterase



- ACh
- ACh Receptor
- Signal transmission
- ACh Esterase

What are targets for drug binding ?

Ion channels

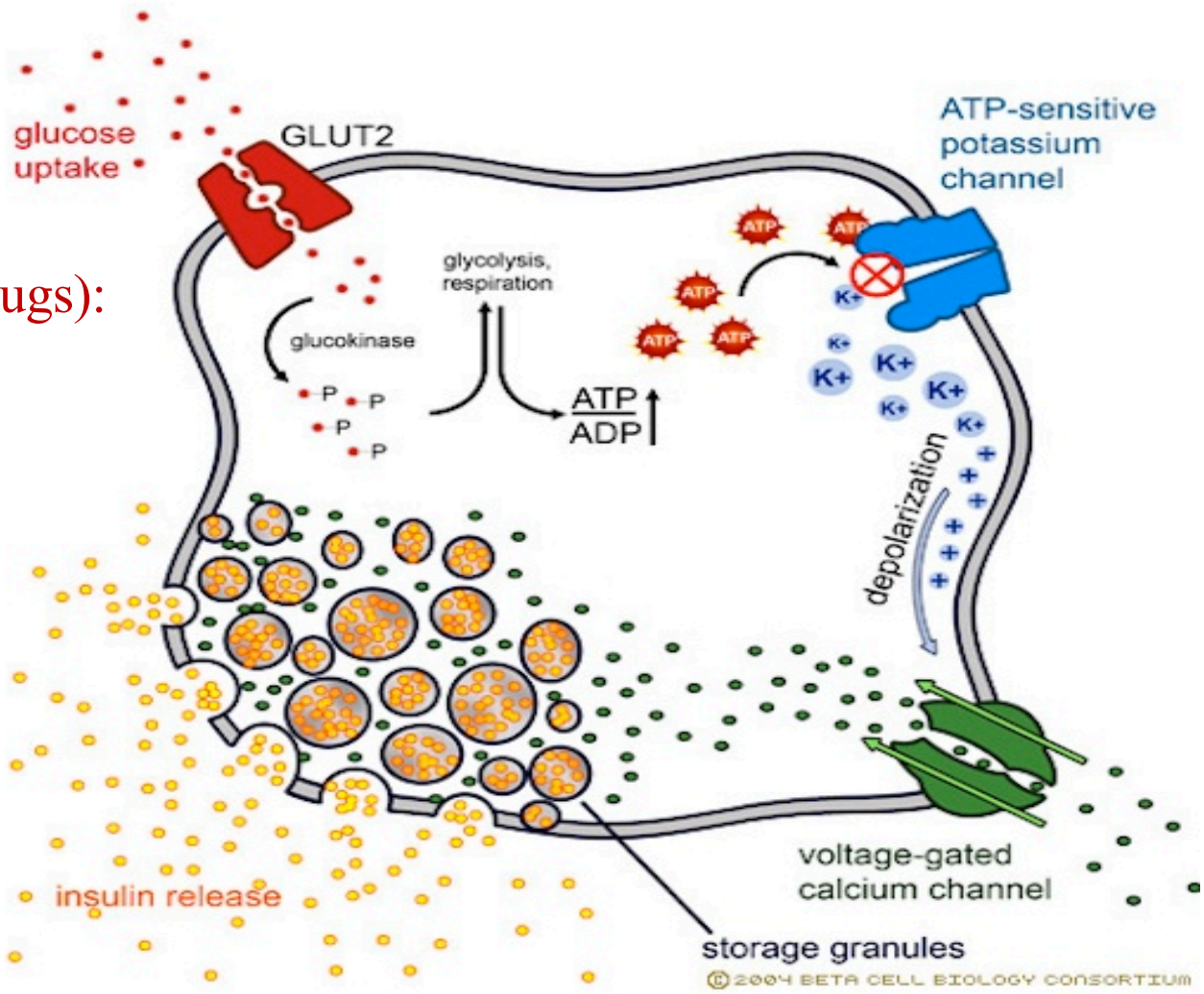
- e.g. Sulfonylurea drugs (antidiabetic drugs): block K^+ outflux via the K channels in pancreatic beta cells resulting in opening of calcium channels and insulin secretion.

What are targets for drug binding ?

Ion channels

- e.g. Sulfonylurea

drugs (antidiabetic drugs):



What are targets for drug binding ?

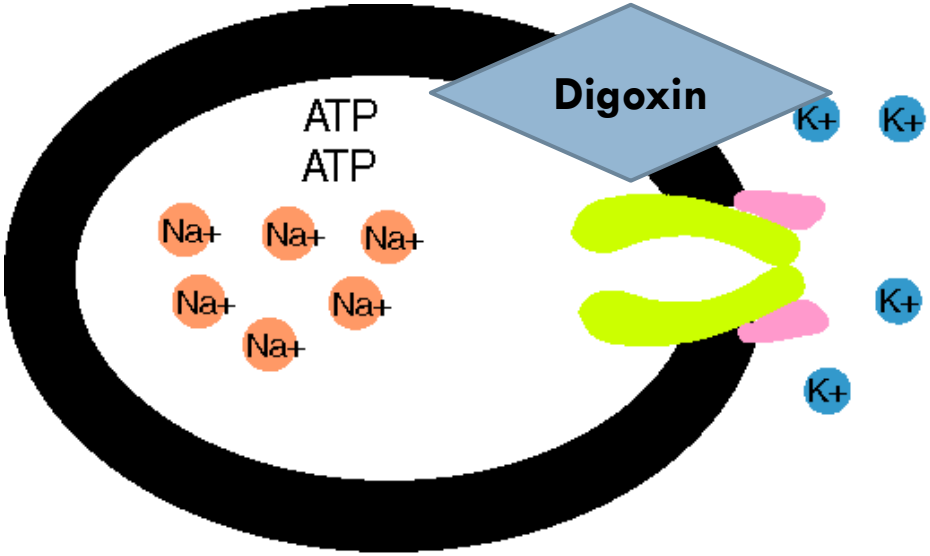
Carrier molecules

- The drug binds to such molecules altering their transport ability
- Responsible for transport of ions and small organic molecules between intracellular compartments, through cell membranes or in extracellular fluids.
- e.g., Na+,K+-ATPase inhibitor

What are targets for drug binding ?

Carrier molecules

- Digoxin: blocks Na efflux via Na pump; used in treatment of heart failure.



What are targets for drug binding ?

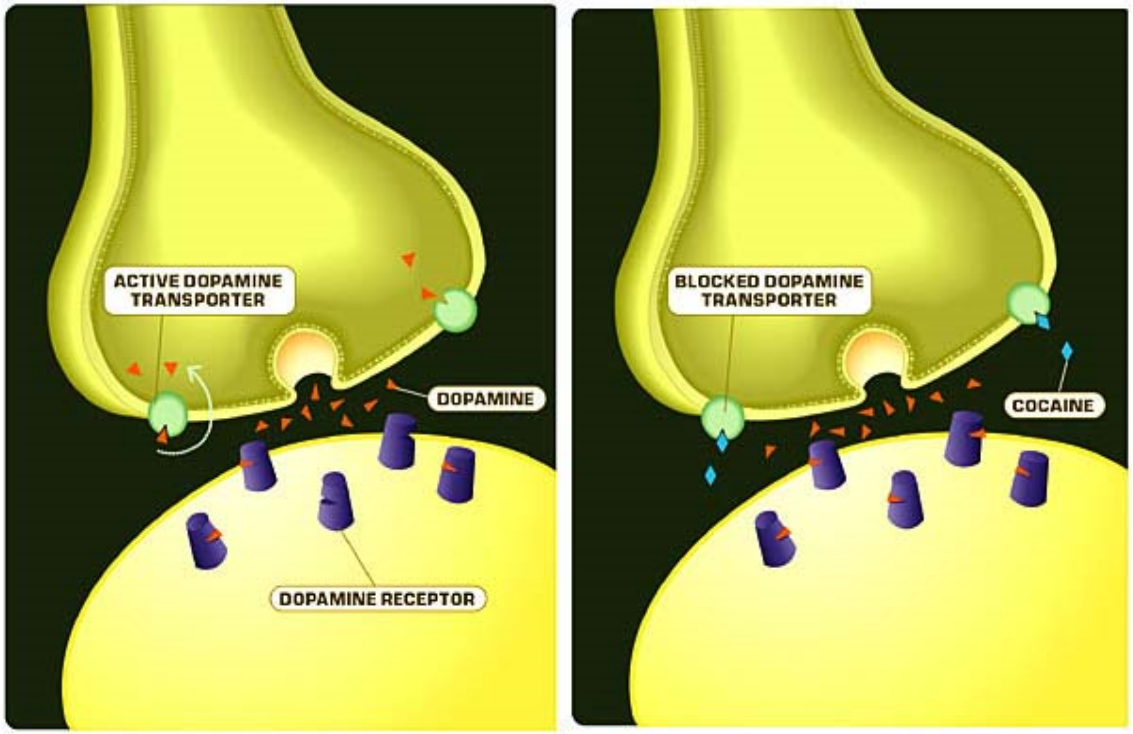
Carrier molecules

- Cocaine: blocks transport or reuptake of catecholamines (dopamine) at synaptic cleft
- The dopamine transporter can no longer perform its reuptake function, and thus dopamine accumulates in the synaptic cleft.

What are targets for drug binding ?

Carrier molecules

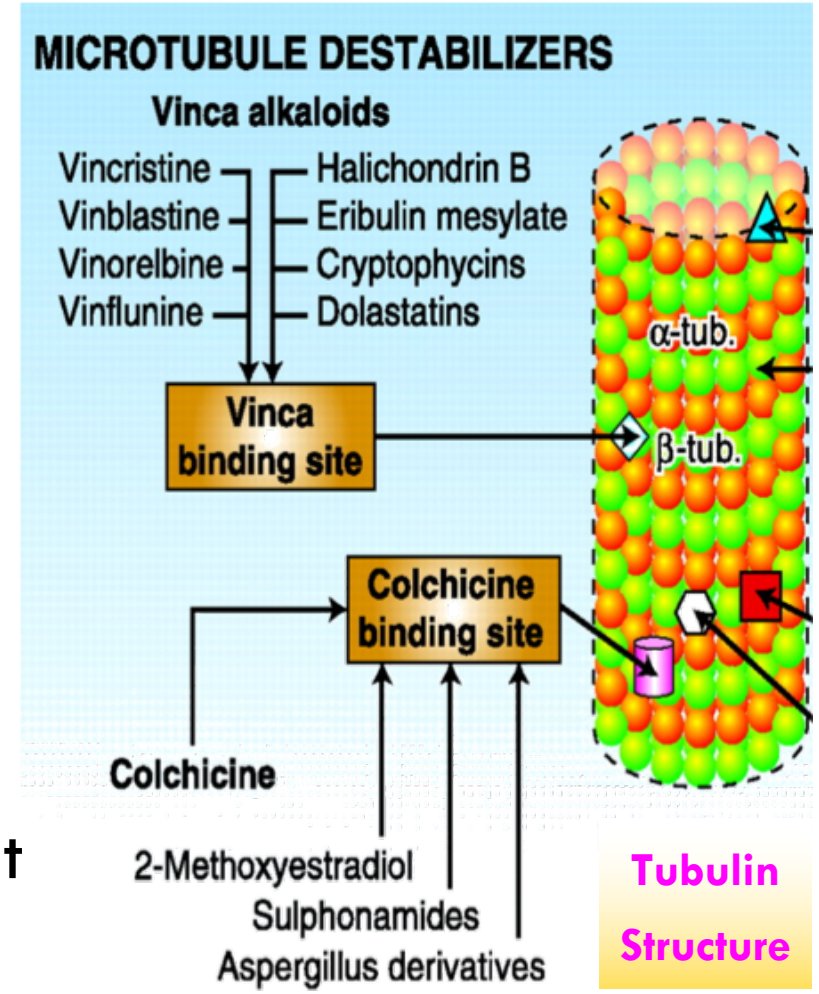
- Effect of cocaine



What are targets for drug binding ?

Structural proteins

- e.g. tubulin is target for:
  - Vincristine
    - anticancer agent
  - Colchicine
    - used in treatment of gout



Drug-Receptor Interaction

- Binding Forces between drugs and receptors
  - Ionic bond.
  - Van-Dar-Waal.
  - Hydrogen bond.
  - Covalent bond.

Drug-Receptor Interaction

- Affinity

  Ability of a drug to combine with the receptor.

  D + R ⟶ D-R complex ⟶ Effect.

- Efficacy (Intrinsic Activity)
  - Capacity of a drug receptor complex (D-R) to produce an action.
  - is the maximal response produced by a drug (E max).

Drug-Receptor Interaction

- Agonist

  is a drug that combines with receptor and elicit a response (has affinity and efficacy).

- Antagonist

  is a drug that combines with a receptor without producing responses. It blocks the action of the agonist (has affinity but no or zero efficacy).

  e.g. atropine

Drug-Receptor Interaction

Agonist and Antagonist

Drug-Receptor Interaction

- Agonist

  Full agonist.

  Partial agonist

  - Full Agonist

A drug that combines with its specific receptor to produce maximal effect by increasing its concentration (affinity & high efficacy). e.g. acetylcholine (Ach).

Drug-Receptor Interaction

- Agonist
  - Partial Agonist

combines with its receptor & evokes a response as a full agonist but produces submaximal effect regardless of concentration (affinity & partial efficacy).

- e.g. pindolol
  - A beta blocker which is a partial agonist, produces less decrease in heart rate than pure antagonists such as propranolol.

Drug-Receptor Interaction