MEDICINE
KING SAUD UNIVERSITY

mechanism of drug action

Objectives:

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

Success consists of going from failure to failure without loss of enthusiasm

Titles
Very important
Extra information
Terms

Pharmacology team 436

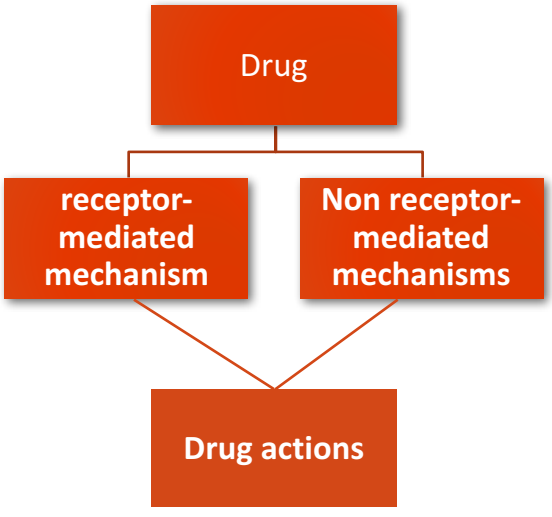
What is Pharmacodynamics?

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

the mechanisms of drug action :

1- Binding with a biomolecule (receptor-mediated mechanisms)	2- Non receptor-mediated mechanisms
Biomolecules = Targets=Receptors Mostly protein in nature (protein target).	Physiochemical properties of drugs.
Protein targets for drug binding : • Structural protein • Regulatory proteins • Physiological receptors • Enzymes • Ion channels • Carriers	**Chemical action** E.g. Neutralization of gastric acidity by antacids. **Physical action** E.g. Osmotic diuretics. Purgatives used in treatment of constipation e.g. MgSO4

What are targets for drug binding ?



Protein (target)

- structural
- Regulatory (regulate specific process inside the cell)
  - enzyme
  - Carrier molecule
  - Ion channel
  - receptor

Binding forces between Drugs and Receptors:

1. Ionic Bond
2. Van-Dar-Waal
3. Hydrogen Bond
4. Covalent Bond (the strogest bond)

Protein → Structural protein → e.g. tubulin which is required for microtubules formation

Tubulin is a target for

anticancer drug e.g. **Vincristine** (anticancer agent) Vincristine kills cancerous cells by inhibiting microtubule formation and cell division	Anti gout drugs E,g, **Colchicine** (used in treatment of gout) **Colchicine** binds to tubulin and inhibits the formation of microtubules, preventing neutrophil motility and decreasing the inflammation.

Receptor-mediated mechanisms:

Receptors : Is a special macromolecule that binds the drug and mediates its Pharmacological action

responsible for selectively sensing and binding of a stimulus (ligand)

And its coupling to a response via a set of signal transduction machinery

location of the receptors:	• cell membrane • cytoplasm • nucleus

Enzymes : The drug competes with the natural endogenous substrate for the enzyme E.g. Anticholinesterases.

reversible : Neostigmine reversibly compete with ACH for acetyl cholinesterase enzyme at motor end plate (neuromuscular junction)	**Irreversible:** Organophosphates irreversibly competes with ACH for acetyl cholinesterase

Ion channels : Drugs bind to alter channel function (by opening or blockade).

Channels are responsible for influx or out-flux of ions through cell membranes along their concentration gradients

They are activated by alteration in action potential and are controlled by gating mechanisms

Blockers : Local anesthetics (block the pain during operation on the patient) Block Na influx through Na channel in Nerve fibers. They are Na channel blockers	**modulation** : Sulfonylurea drugs (use for treatment type 2 diabetes To secrete insulin Block K^+ out-flux via the K channels in pancreatic cells. They are K channels modulator .

Carrier molecule:

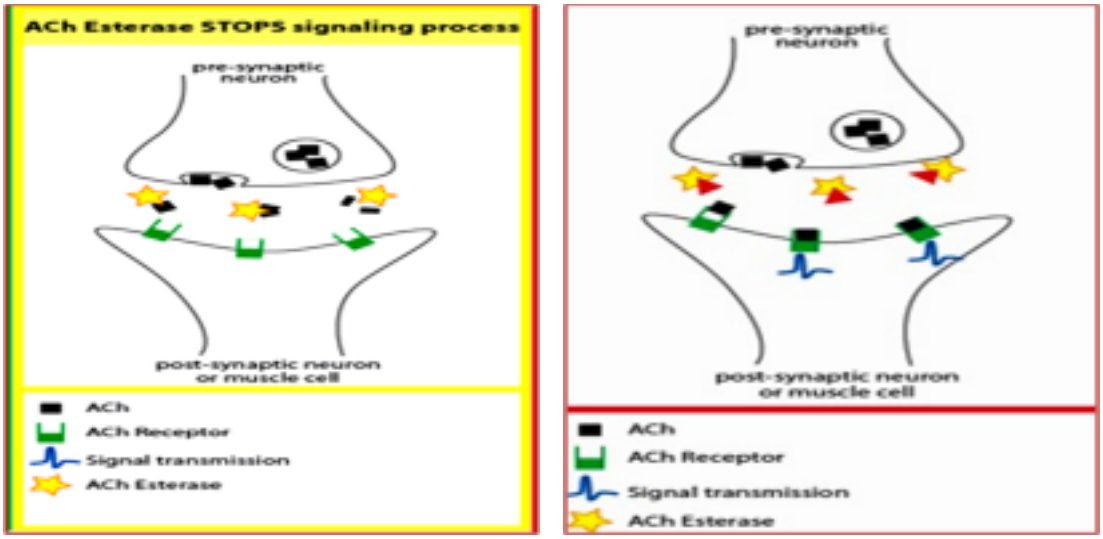
The drug binds to such molecules altering their transport ability

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

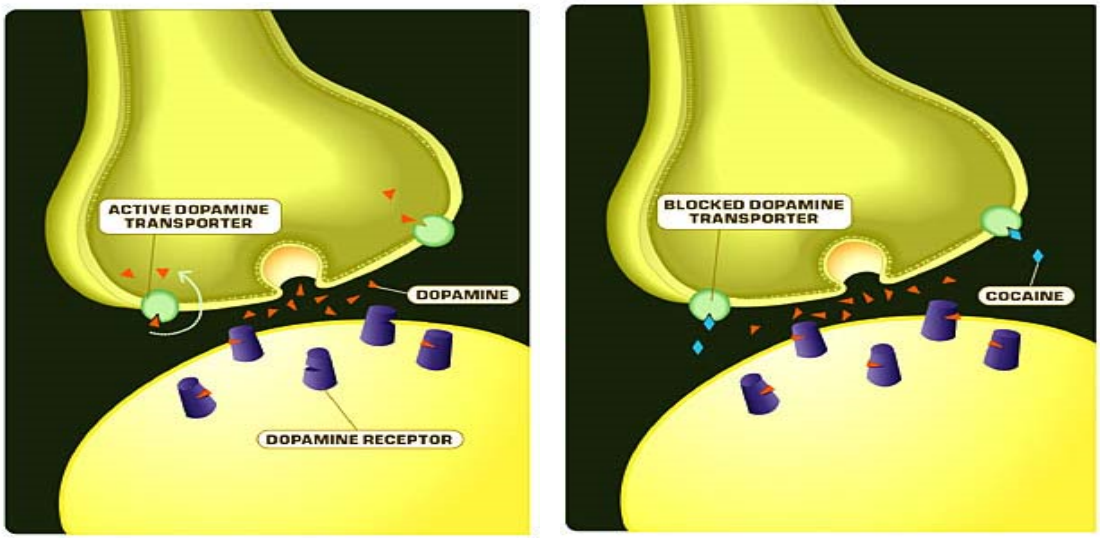
Digoxin: blocks Na efflux via **Na pump**; used in treatment of heart failure.	**Cocaine:** blocks transport or reuptake of **catecholamines** (dopamine) at synaptic cleft The dopamine transporter can no longer perform its reuptake function, and thus dopamine accumulates in the synaptic cleft.

Pictures for more understanding: Anticholinesterases (antiacetylase)



In the normal, the Ach leaves the pre-synaptic neuron to post-synaptic of muscle cell, at the synapse there is enzyme (Ach esterase) will metabolize some of the Ach and degenerate it, when we use drug which is Anticholinesterases it will bind to the Ach esterase and inhibit it, so there will be accumulation of the Ach

Effect of cocaine



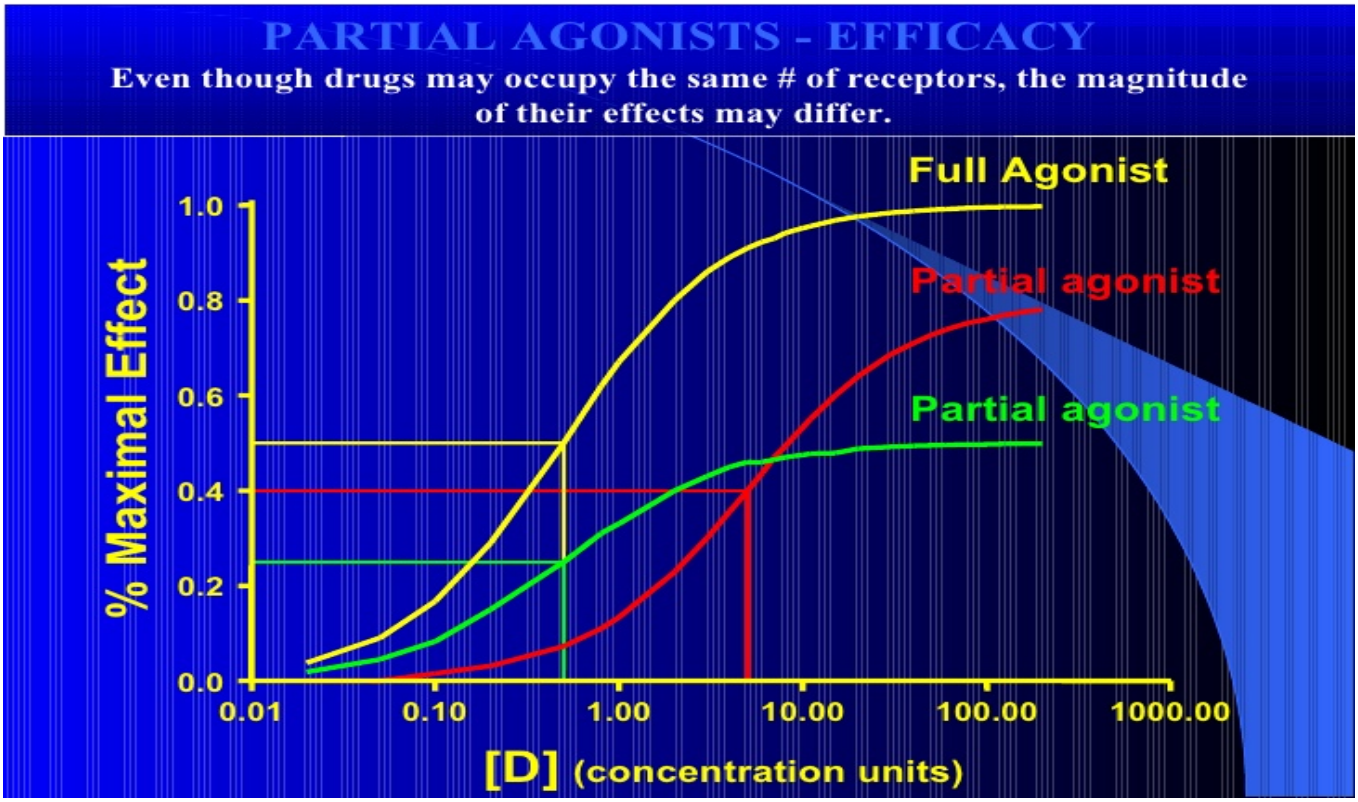
In the normal, the dopamine leave the neuron and some of the dopamine binds with the receptor (the Purple in the picture) and produce effect, and some of the dopamine will reuptake by the transporter (the green in the picture) . If the patient uses cocaine the cocaine will inhibit the transporter so the dopamine will not reuptake and all the receptors will be bind with dopamine which will give high dopamine effect

Terms definition:

The term	The definition	Other definition	Explanation
Affinity	Ability of a drug to combine with the receptor.	is the capacity of a drug to form a complex with the receptor(DR complex)	D + R → D-R complex → Effect. * *D = drug , R = receptor
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).	the ability of the drug once bound to the receptor to trigger response	The value of intrinsic activity (efficacy) ranges from 0 to 1 (the intrinsic activity of antagonist drugs is 0 **e.g. atropine**)
Agonist	is a drug that combines with receptor and elicit a response (affinity + efficacy).	-	كأنها قفل ومفتاحين، كل المفتاحين لهم نفس الشكل، لكن واحد هو المفتاح الأصلي والثاني مو المفتاح الأصلي، كلهم بيدخلون بفتحة القفل لكن الأصلي راح يفتح القفل واللي مو أصلي ما راح يفتح القفل لكن بيمنع المفتاح الأصلي من إنه يدخل بالقفل ويفتحه
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).	having full affinity to the receptor but no intrinsic activity(0) e.g. atropine	
Full agonist	having a full affinity to the receptor and **Affinity** is the capacity of a drug to form a maximal intrinsic activity (1) e.g. acetylcholine	-	-
Partial agonist	having a full affinity to the receptor but with low intrinsic activity (<1) e.g. pindolol	-	-

Agonist	
Full agonist	**Partial agonist**
A drug that combines with its specific receptor to produce maximal effect by increasing its concentration (affinity & high efficacy). e.g.ACh	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 produce less decrease in heart rate than pure antagonists such as propranolol.

The value of intrinsic activity (efficacy) ranges from 0 to 1
(the intrinsic activity of antagonist drugs is 0 **e.g. atropine**)



The full agonist has the maximal effect (1), and after it reaches to the maximal effect there will be no increasing in the effect (constant)
The partial agonist will have effect (Efficacy) but it will not reach to the maximal effect (1) but it has its own maximal effect, and when the partial agonist reach to its own maximal effect there will be no increasing in the effect (constant)

Quick exam

https://www.onlineexambuilder.com/pharmacology-l5/exam-109362

Pharmacology Team

Boys	Girls
عبدالرحمن ذكري	اللولو الصليهم
عبدالعزيز رضوان	روان سعد القحطاني
عبدالرحمن المالكي	أميرة نيازي
فيصل العباد	جواهر أبانمي
فارس النفيسة	رانيا العيسى
خالد العيسى	غادة المزروع
معاذ الفرحان	لمى الفوزان
عبدالرحمن الجريان	نورة الشبيب
محمد خوجة	أسيل ناصر بادخن
عمر التركستاني	أنوار نجيب العجمي