# Lecture (5)

## Pharmacodynamics I

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pharmacology
Team 438

MED438
KING SAUD UNIVERSITY

- Red : important
- Black : in male / female slides
- Pink : in girls slides only
- Blue : in male slides only
- Green : notes, Extra

Editing File:

https://docs.google.com/document/d/1WvdeC1atp7J-ZKWOUSukSLsEcosjZ0AqV4z2VcH2TA0/edit?usp=sharing

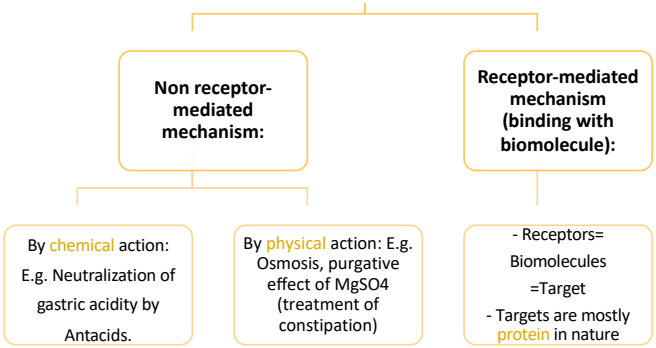
# Objectives:

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

## What is Pharmacodynamics?

Study of biochemical and physiological effects of drugs and their mechanism of action.

## The mechanism of action Based on the drug target site:



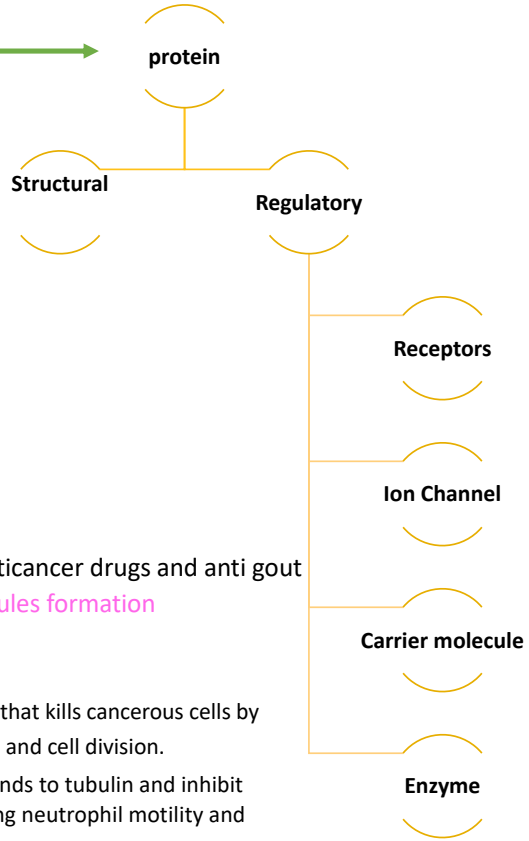

**Receptor:** a special target macromolecule that binds to the drug to produce pharmacological actions.

## Where are receptors located?

- Cell membrane
- Cytoplasm
- Nucleus

## Receptor-mediated mechanism:

**Target = Receptor = Biomolecules = Site of action**




Binding forces between Drugs and Receptors:

1. Ionic Bond
2. Van-Dar-Waal
3. Hydrogen Bond
4. Covalent Bond

**1- STRUCTRAL:**

**Tubulin:** is target for drugs such as anticancer drugs and anti gout drugs. Tubulin is required for microtubules formation (cytoskeleton).

target for :

**Vincristine :** Anticancer drug that kills cancerous cells by inhibiting microtubule formation and cell division.

**Colchicine :** Anti gout drug binds to tubulin and inhibit microtubule formation preventing neutrophil motility and decreasing inflammation

## 2- REGULATORY:

### 1-ENZYMES:

**The drug competes with the natural substrate for the enzyme.**

**E.g. Anticholinesterases inhibit acetyl cholinesterase thus producing cholinomimetic action.**

A- **Reversible: Neostigmine** reversibly competes with **ACH** for acetyl cholinesterase at motor end plate (neuromuscular junction). (Effect lasts for short duration of time)

B- **Irreversible: Organophosphates** irreversibly competes with **ACH** for acetyl cholinesterase.
(Effect lasts forever)

### 2-ION CHANNEL:

- **Responsible for influx or out-flux of ions through cell membranes.**
- **They are activated by alteration in action potential.**
- **Drugs bind to alter channel function (opening or blockade) E.g.:**

A-**Local Anesthetics:** block sodium $Na^+$ **influx** through $Na^+$channel in nerve fibers. ($Na^+$channel Blockers)

B-**Sulfonylurea drugs (Antidiabetic drug):** Block potassium $K^+$channel in pancreatic beta cells, resulting in depolarization and opening of calcium channels and insulin secretion.

## 3-CARRIER MOLECULES:

**Responsible for transport of ions and small organic molecules between intracellular compartments, through cell membranes or in extracellular fluids. The drug binds to such molecules altering their transport ability.**

**A- Digoxin:**

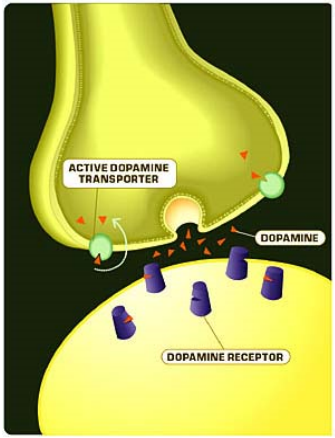
blocks **efflux** of $Na^+$ via $Na^+/K^+$ pump ($Na^+/K^+$-ATPase).

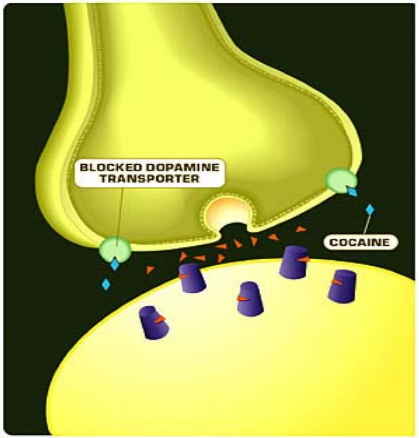
Used in the treatment of heart failure.

(drugs used for treatment of heart Failure increase the contraction of the heart)

**B- Cocaine:**

blocks transport or reuptake of **catecholamines** mainly Dopamine at synaptic cleft. The dopamine transporter can't perform its reuptake function therefore dopamine accumulates in the synaptic cleft producing **Euphoria**.



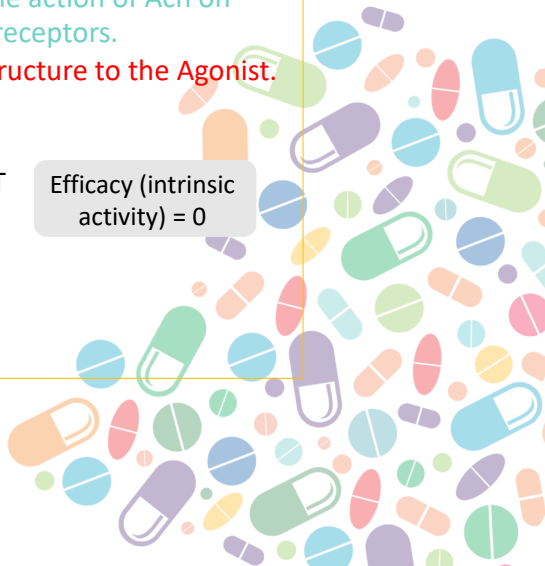
| Agonist | Antagonist |
| --- | --- |
| Is a drug that combines with the receptor and elicit a response<br>E.g. Ach acts upon muscarinic receptors | Is a drug that combines with the receptor without producing a response (0) .<br>It blocks the action of the agonist.<br>E.g. Atropine block the action of Ach on muscarinic receptors.<br>It has similar chemical structure to the Agonist. |
| Affinity + Efficacy (intrinsic activity) | Affinity BUT NO Efficacy (intrinsic activity) = 0 |
| Ability of the drug to combine with the receptor<br>D+R -> D-R complex | -Capacity of a drug receptor complex to produce action<br>- Is the maximal response produced by a drug (E max)<br>- The value ranges from 0 to 1 |

Extra definitions found on girl's slides only :

**Affinity** is the capacity of a drug to form a complex with the receptor(DR complex)

**Efficacy**(Intrinsic activity) the ability of the drug once bound to the receptor to trigger response

**Antagonist** having full affinity to the receptor but no intrinsic activity



# Types of Agonist:

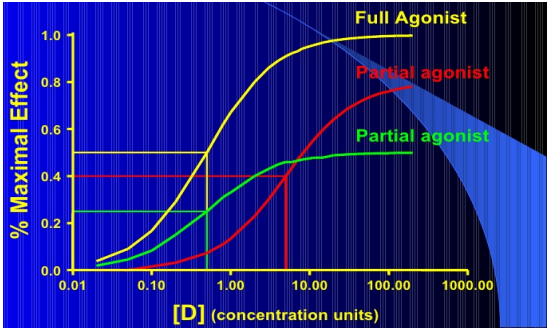
| Full Agonist | Partial Agonist |
| --- | --- |
| A drug that combines with its specific receptor to produce maximal effect (1) by increasing its concentration<br>E.g. Ach<br><br>Affinity + **HIGH** Efficacy | Combines with its receptor & evokes a response that's submaximal effect (< 1) regardless of its concentration<br>E.g. pindolol<br>Is a beta blocker which is a partial agonist, produces less decrease in heart rate than pure antagonist such as propranolol.<br><br>Affinity + **PARTIAL** Efficacy |

Extra definitions found on girl's slides only :

**Full agonist** having a full affinity to the receptor and a maximal intrinsic activity

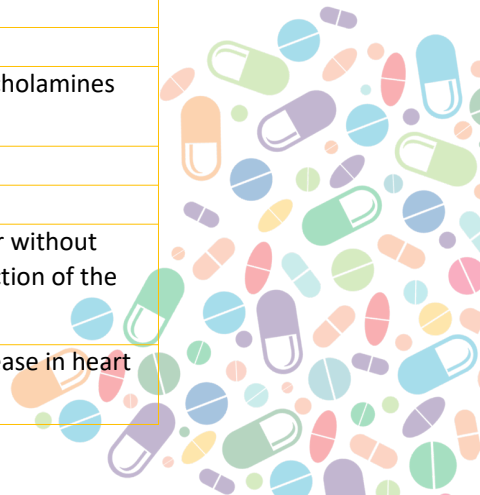
**Partial agonist** having a full affinity to the receptor but with low intrinsic activity

**Partial Agonist:** Even though the drugs may combine with the same number of receptors, the magnitude they can produce may differ



# SUMMARY

| Drug | mechanism of action |
|---|---|
| **antiacids** | Neutralization of gastric acidity |
| **Neostigmine (cholinesterase inhibitor)** | competes with ACh for acetyl cholinesterase enzyme at motor end plate (neuromuscular junction). |
| **Sulphunylurea (anti diabetic)** | block K+ outflux via the K channels in pancreatic beta cells resulting in opening of calcium channels and insulin secretion. |
| **Digoxine ( drug of heart failure)** | blocks Na efflux via Na pump |
| **Cocaine** | blocks transport or reuptake of catecholamines (dopamine) at synaptic cleft |
| **vincristine** | Anticancer agent |
| **colchicine** | Drug for gout treatment |
| **Atropine (anticholinergic)** | a drug that combines with a receptor without producing responses. It blocks the action of the agonist |
| **Propranolol (Beta blocker)** | a partial agonist, produces less decrease in heart rate than pure antagonists |



# QUIZ

| | | | |
|---|---|---|---|
| Q1/ Receptors are located on all of the following except: | | | |
| A- nucleus | B- cell membrane | C- ribosomes | D- cytoplasm |
| Q2/ Digoxin is a drug used for treatment of heart failure , its mechanism of action is: | | | |
| A- blocking Ca efflux | B-Blocking K efflux | C-Blocking Na efflux | |
| Q3/ Tubulin is a target for which of these drugs? | | | |
| A-Cocaine | B- Colchicine | C- Propranolol | D- Digoxin |
| Q4/ dopamine accumulation in the synaptic cleft produces: | | | |
| A- Heart contraction | B-Euphoria | C- Decreased heart rate | |
| Q5/ Efficacy = 1 when the drug is: | | | |
| A- Full Agonist | B- Antagonist | C- Partial Agonist | |

1-C 2-C 3-B 4-B 5-A

# Good luck

Thanks to the pharma team 435

PHARMACOLOGY 435

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