PHARMACOLOGY
433

King Saud University
College of Medicine
Foundation Block

Pharmacodynamics I ; 5

Molecular Mechanism of Drug Action.

Objectives :

1	Identify different targets of drug action.
2	Differentiate between their patterns of action; Agonism versus Antagonism
3	Elaborate on drug binding to receptors

NEW TERMS :

*Pharmacodynamics
*Antiporter *Agonist
*Antagonist *Efficacy
*Symporter
*Affinity

Remember That :

Pharmacokinetics: is what the body does to the drug ; (Absorption, Distribution, Metabolism and excretion.)

Pharmacodynamics: is what the drug does to the body.

Pharmacodynamics

Interacts with biological molecules which are known as (targets)

EXCEPTION

- Osmotic Diuretics : مضادات البول
- Purgatives : المسهلات
- Antacids : مضادات الحموضة

Altering their biochemical and /or biophysical activity

response

Depress

Beta blockers (depress the myocardium) reduce the force contraction of the heart.

Activate

Beta agonist (stimulate the myocardium) Increasing the force contraction of the heart.

Replace

Insulin for diabetic patient.

Irritate

Produce locally irritation and increase the blood flow, which will relief the pain.

Destroy

In case of: Cancer we need to kill cells.

Drug Targets :PROTEINS

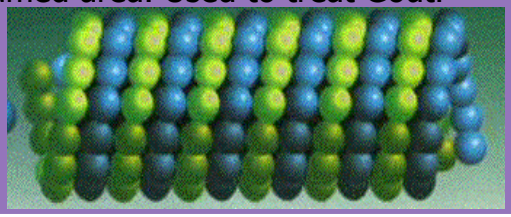
In order of the drug to produce response it has to bind to a certain biological molecule (target)

STRUCTURAL

Tubulin "protein that forms the microtubules in prokaryotic cells"
is target for drugs:

* Vincristine "anticancer drug, inhibit cell division (Mitosis)"

* Colchicine "anti inflammation drug that decrease the protein levels in the body, prevent WBCs to accumulate in the inflamed area. Used to treat Gout."



REGULATORY

- Enzyme
- Ion Channel
- Carrier Molecule
- Receptor

REMEMBER:

Uric acid accumulation causes GOUT
3rd lecture of Pharmacokinetics

Regulatory Proteins : Enzymes

Drug competes with natural substrate for the enzyme.
"competitive inhibition"

	Drug	Competes with:	Enzyme
Reversible (Short duration of action)	Neostigmine	Acetylcholine (Ach) "Drug compete with Ach to prevent hydrolysis"	Cholinesterase at motor end-plates (MEP)
Irreversible (Long duration of action)	Organophosphates	Ach "Drug compete with Ach to prevent hydrolysis"	Cholinesterase

Regulatory Proteins : Carrier Molecules

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

Antiporter

ANTIPORTER the transport of two different molecules or ions across a lipid bilayer membrane in <u>opposite directions</u>.

Symporter

SYMPORTER movement of two or more different molecules or ions across a lipid bilayer membrane in the <u>same direction.</u>

Drug	Transport	Regulation
Cocaine	**Passive**	**Blocks** transport of catecholamine (Epinephrine and Norepinephrine) at synaptic cleft.
Digitalis (treat heart failure)	**Active**	**Blocks** efflux "exit" of Na by Na pump. Na will accumulate in the cell and will exchange with Calcium and the level of calcium inside the cell will increase causing increased force of contraction.

Regulatory Proteins : Ion Channels

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 machinery.

Drugs can act as

1.Channel blocker

Local Anesthetics

Block Na influx through Na channel in nerve fibers.
They are **Na** channel Blockers.

The patient will not sense the pain because we closed the channel so the conduction of the pain will decrease.

2.Channel modulator

Sulfonylurea

Drugs block K^+ out flux via the K channels in pancreatic cells.
They are **K** Channel Modulator.

Used for the treatment of diabetes
It causes release of insulin by modulating the K channel in the pancreas.

Regulatory Proteins : Receptors

Responsible for selectively sensing & binding of a stimulus (ligand) & its coupling to a response via a set of signal transduction machinery.
Drugs bind and alter R signal transduction machinery.

ENDOGENOUS LIGAND + RECEPTOR = Physiological RESPONSE

DRUGS + RECEPTOR = Pharmacological RESPONSE (Agonist)
or NO RESPONSE (Antagonist)

Agonist

- A drug that possesses **BOTH affinity and efficacy**
- Pharmacological RESPONSE
- e.g. **ACh**

Antagonist

- A drug that possesses an **affinity but no efficacy**
- NO RESPONSE
- e.g. **Tubocurarine**

Affinity: is The tendency of a drug to bind to the receptors.

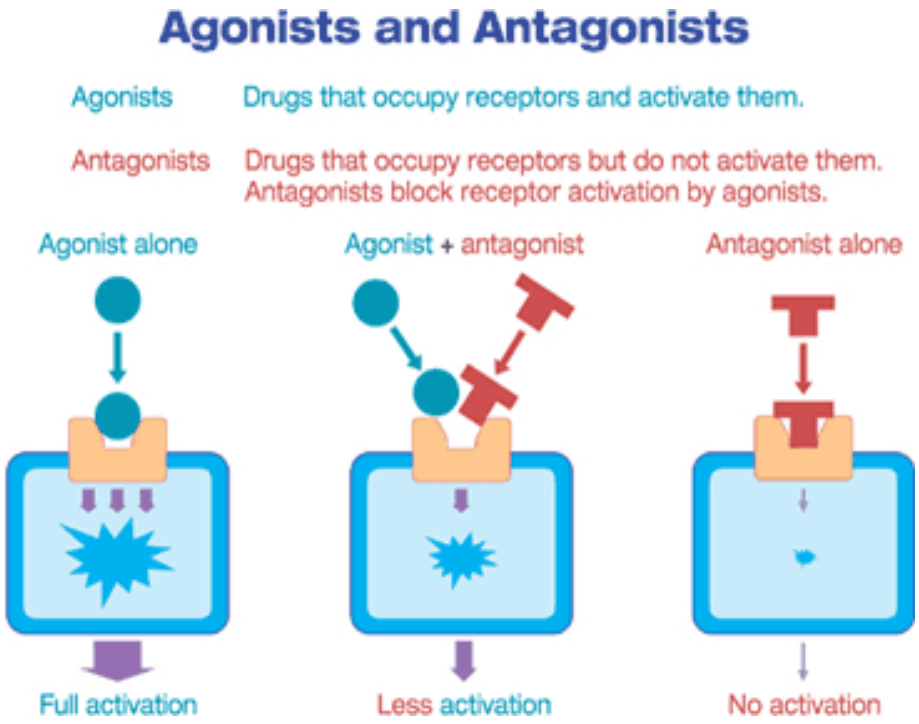
Efficacy: is The ability for it, once bound, to activate the receptor.

Agonist	Antagonist
A drug that possesses **both affinity and efficacy.** Efficacy Is that inherent property *intrinsic* to the agonist that determines how "good" an agonist is.	A drug that possesses an **affinity but no efficacy.**

SUMMARY

✓ **Identify different targets of drug action :**

✓ **Differentiate between targets' patterns of action; Agonism versus Antagonism :**



✓ **Elaborate on drug binding to receptors:**

*** Affinity of a drug for a receptor is:**
a measure of how strongly that drug binds to the receptor.

*** Efficacy is:**
a measure of the biological effect (activation) that a drug can produce as a result of receptor binding.

MCQs

1 **Cocaine acts on:**

a) An ion channel
b) An enzyme
c) A passive transporter
d) An active transporter

2 **One of the drugs that target microtubules is:**

a) Digitalis
b) Neostigmine
c) Tubocurarine
d) Colchicine

3 **Organophosphates compete with ACh:**

a) Reversibly
b) Irreversibly
c) Sometimes both
d) None of the above

4 **Intrinsic activity is a drug's ability to elicit :**

a) Strong receptor binding
b) Weak receptor binding
c) Response
d) Excretion

5 **A drug that has an efficacy more than 0% and less than 100% is considered as:**

a) Full agonist
b) Partial agonist
c) Competitive antagonist
d) Functional antagonist

6 **An example of an antagonist is:**

a) Vincristine
b) Colchicine
c) Acetylcholine
d) Tubocurarine

7 **The function of local anesthetics is that they:**

a) Block transport of catecholamines
b) Block efflux of Na
c) Block influx of Na
d) Block efflux of K

8 **A drug that binds to a cell receptor and affects a response is called :**

a) An agonist
b) An antagonist
c) A receptor blocker
d) A channel blocker

9 **The ability of a drug to bind to the receptors is:**

a) Affinity
b) Efficacy
c) Agonism
d) Antagonism

10 **Pharmacodynamics refers to the relationship of drug:**

a) dose to drug concentration in plasma.
b) dose to drug concentration at the receptor site.
c) concentrations to drug effect.
d) dose to drug effect.

1-C 4-C 7-C
2-D 5-B 8-A
3-B 6-D 9-A
10-C

We hope we made this lecture easier for you.!
Contact us for any questions or comments
Good Luck !

Nada Dammas
Hanan Al-Dossari
Nada Bin Dawood
Malak Alaboudi
Lamees Almezaini
Layan Al Taweel
Norah Alnaeim
Maha Alrajhi
Yara Alenezi

Ahmed Aldakhil
Faris Almoammarie
Mohammed Alnafisah
Abdulmalek Alnujidi
Khalid Alanazi
Yousef Alfadli

Ion Channel Regulatory proteins – Sulfonylurea Medication
(http://www.youtube.com/watch?v=B3GpNRIYNek)

Pharma_433@yahoo.com

@pharma_433