PHARMACOLOGY
TEAM 439

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Mechanism of drug action

If you didn't understand any part from this lecture Click here!

- Important
- In male and female slides
- Only in male slides
- Only in female slides
- Extra information

Objectives

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

Any Future corrections will be posted on the editing file.
make sure to check it frequently

Click Here

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

Drugs can produce their actions by one of the following mechanisms:

Receptor-mediated mechanism (binding with biomolecule):

Receptors= Biomolecules =Target Targets are mostly **protein** in nature

Drugs can produce actions by binding with biomolecules (Protein Targets):

- Regulatory proteins
  - Receptor
  - Ion channel
  - Carrier molecule
- Structural proteins
  - Enzyme

Non receptor- mediated mechanism:

Depends on:
Physicochemical properties of drugs.

- By **chemical** action: E.g. Neutralization of gastric acidity by Antacids.(antacids are bases)
- By **physical** action: E.g.
  -Osmotic diuretics(increase of urination rate),
  -purgative effect of MgSO4 (treatment of constipation)

Binding forces between drugs and receptors

- Van-Dar-Waal
- Ionic Bond
- Covalent Bond
- Hydrogen Bond

Protein

Structural

Tubulin is the target for drugs as anticancer drugs and antigout drugs and it is required for microtubules formation (cytoskeleton)

Target for

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

Colchicine : used in treatment of gout, it binds to tubulin and inhibits microtubule formation, preventing neutrophil motility and decreasing inflammation

Regulatory

Receptor

Is a special target **macromolecule** that binds the drug and mediates its pharmacological actions

located in

Cell membrane - Cytoplasm - Nucleus

Enzymes

The drug competes with the natural endogenous substrate for the enzyme

E.g. Anticholinesterases inhibit acetylcholinesterase thus producing cholinomimetic action

reversibly

Neostigmine reversibly compete with ACH for acetylcholinesterase enzymes at motor end plate (neuromuscular junction)

irreversible

Organophosphate irreversibly competes with ACH for acetylcholinesterase enzyme

Ion Channels

-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.

Local anesthetics

Act by blocking sodium (Na+) influx through Na channel in nerve fibers (Na Channel Blockers)

Sulfonylurea drugs (Antidiabetic drugs)

Block potassium outflux via the K channel in pancreatic beta cells resulting in depolarization and opening of calcium channels and insulin secretion

Carrier Molecules

Responsible for transport of ions and small organic molecules between intracellular compartments, through cell membranes or in extracellular fluids.

Drugs bind to such molecules to alter their transport ability.

Digoxin

Blocks efflux of Na+ via Na+ / k+ pump (Na+ / K+ -ATPase) used in the treatment of heart failure

more Na+ in the cytosol less export of ca++ stronger heart muscle contraction

Cocaine

-Blocks transport of 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

Definition

Is a drug that binds with a receptor and elicit a response. It has Affinity and Efficacy.

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.

The ability of the drug once bound to the receptor to trigger response.

The value of Intrinsic Activity ranges from 0 to 1.

E Max: Maximal response produced by a drug.

For better understanding click here

#Team436:

كأن عندنا مفتاحين لقفل ، مفتاح أصلي يدخل ويفتح ومفتاح ثاني تقليد يدخل لكن ما يفتح القفل لكنه يمنع المفتاح الاصلي من الدخول

Types

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) acts upon muscarinic receptors

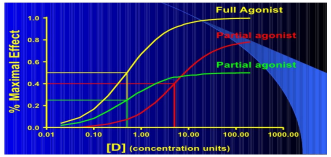
Partial Agonist

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.

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



Antagonist

Is a drug that combines with the receptor without producing a response (**It blocks the action of agonist**)). e.g. Atropine, blocks the action of Ach on muscarinic receptors.

It has a similar chemical structure to the Agonist

It has Affinity but No Efficacy or zero efficacy.

Only in female slides

Terms	Definitions
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 -The value of intrinsic activity ranges from 0 to 1
Full agonist	Having a full affinity to the receptor and 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
Antagonist	Having full affinity to the receptor but no intrinsic activity (0) e.g. atropine

SUMMARY:

Drug	Mechanism of action
antiacids	Neutralization of gastric acidity
Neostigmine (**reversible cholinesterase inhibitor**)	competes with ACh for acetylcholinesterase enzyme at motor end plate (neuromuscular junction).
Sulphonylurea (**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 **causing euphoria**
vincristine	**Anticancer agent**
colchicine	**Drug for gout treatment**
Purgatives (MgSO4)	Used for treatment of constipation
Atropine (**anticholinergic**)	a drug that combines with a receptor without producing responses. It blocks the action of the agonist
Organophosphates	Competes with ACH for acetyl Cholinestrase enzyme (**Irreversible**)
Pindolol (**Beta blocker**)	a partial agonist, produces less decrease in heart rate than pure antagonists

MCQ

Check out the questions made by MQ Team439 about this lecture here!!

1) Receptors are located in all of the following except			
A) Nucleus	B) Cell membrane	C) Cytoplasm	D) Ribosomes

2) The Study of biochemical and physiological effects of drugs and their mechanism of action, referred to:			
A) Pharmacodynamics	B) Pharmacokinetics	C) Pharmacology	D) None

3) Receptors are ?			
A) micromolecules	B) macromolecules	C) none	D) both

4) Sulfonylurea drugs also called as ?			
A) antiseptic drugs	B) antigout drugs	C) Anticancer drugs	D) antidiabetic drugs

ANSWERS

1	C
2	B
3	B
4	D

MCQ

5) Tubulin is a good target for ?

A) Anticancer drugs	B) antiseptic drugs	C) antigout drugs	D) A&C

6) What channels do local anesthetics work on to block signals on a nerve axon ?

A) Na+ channels	B) k+ channels	C) H+ channels	D) Ca+ channels

7) Dopamine accumulation in the synaptic cleft produces ?

A) euphoria	B) fatigue	C) decreased in heart rate	D) A&C

8) Efficacy =1 when the drug is:

A) Full Agonist	B) Antagonist	C) Partial Agonist	D) None

ANSWERS

5	D
6	A
7	A
8	A

SAQ

1) How do drugs produce their effects?

2) What are the 4 major protein targets for drugs?

3) What are receptors? where are receptors located ?

4) What vincristine is used for?

5) How does cocaine produce its effects?

6) What is the main mechanism of action of digoxin ?

7) Explain by giving examples the difference between full agonist and partial agonist ?

8) Describe the affinity and efficacy of Agonist, Antagonist, Full Agonist, Partial Agonist.

ANSWERS:

1- by binding to protein molecules (95%)
2- slide 3
3- slide 4
4- slide 4
5- slide 4
6- slide 4
7- slide 5
8- slide 5&6

GOOD LUCK!

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