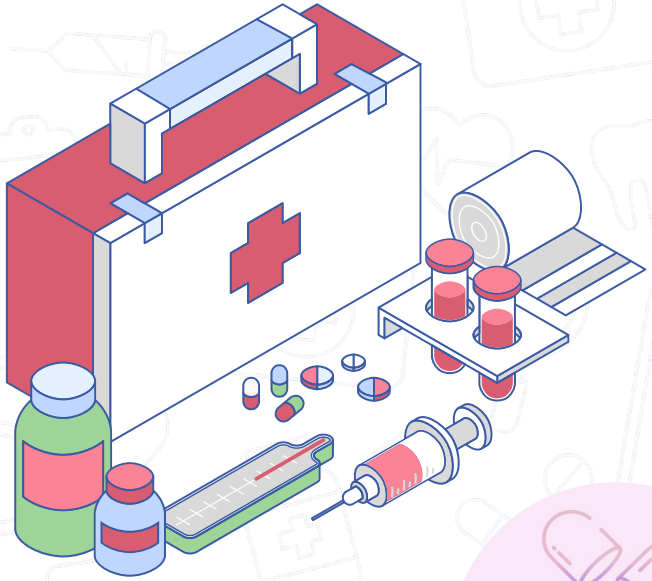


MECHANISMS OF DRUG ACTION 442

EDITING FILE

Pharmacology
Team 442

Important
Main text
Male slide
Female slide
Extra info
Doctor notes

Objectives

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

Click for Useful **video**!!

Pharmacodynamics:

A branch of pharmacology that deals with the study of the biochemical and physiological effects of drugs and their mechanism of action.

Drugs can produce their actions by the following mechanisms (Pharmacodynamics)

Drug actions

Receptor-Mediated Mechanisms (Binding)

Drugs can produce their actions by binding with biomolecules
(Receptors= Biomolecules =Targets)
Targets are mostly protein in nature

Protein targets for drug binding

1-Carrier molecules 2- ion channel 3- Enzymes 4- physiological receptors 5- structural proteins

Non Receptor-Mediated Mechanisms

Physicochemical properties of drugs.

By Chemical action
E.g, Neutralization of gastric acidity(حموضة بالمعدة) by antacids(magnesium hydroxide).

By Physical action
E.g.
-Osmotic diuretics.
-Purgative effect of MgSO4 (treatment of constipation)(-مخذوف-الرمادي)

Important Slide

Protein

You must know
1-e.g names
2-mechanism
3-treatment

Structural Proteins

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

Bind with
Drug-> tubulin->action

Target for

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

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

Regulatory

Physiological 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.

كأنه بلهيه عشان ما يسوي وظيفته

E.g. Anticholinesterases inhibit acetylcholinesterase thus producing cholinomimetic action.

Reversibly

Neostigmine
يدخل في الانزيم ويتكسر بدال
Ach
Result in long life for ACH
Neostigmine reversibly compete with ACH for acetylcholinesterase enzymes at motor end plate (neuromuscular junction)(muscle contraction)

Ion Channels

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

محذوف
Local anesthetics

Act by blocking (Na^+) influx through Na channels in nerve fibers (Na Channel Blockers)

K pump close->high k inside cell->open ca-> insulin

Sulfonylurea drugs (Antidiabetic drugs)

Block potassium channels -outflux via the K channel- in pancreatic beta cells resulting in increase in intracellular potassium & 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

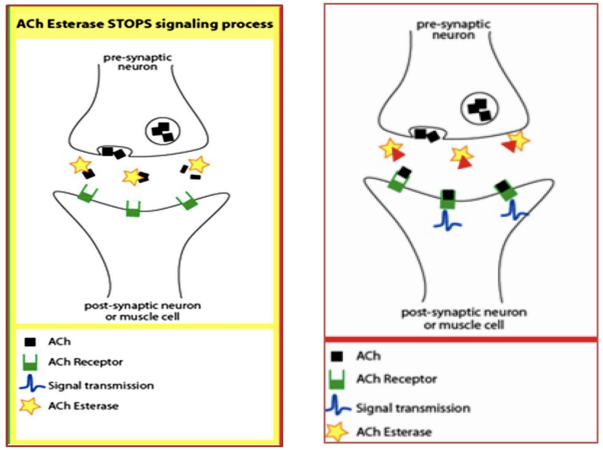
Blocks efflux of Na+ via **Na+/k+ pump (Na+ / K+ -ATPase)** used in the treatment of heart failure
more Na+ in the cytosol less export of ca++ stronger heart muscle
تكدس Na->less ca-> contraction

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

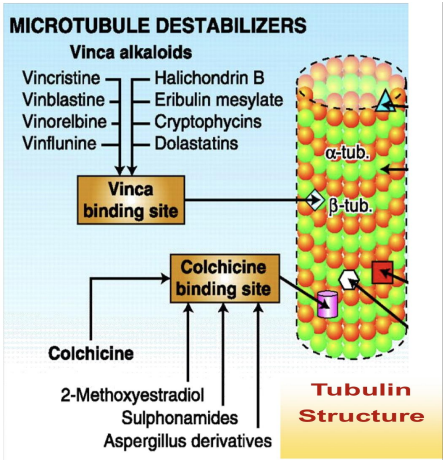
Nerve1 transport dopamine ->nerve2 take it ->cocaine block nerve1->reuptake can't occur ,dopamine stays ->produce euphoria

Enzymes

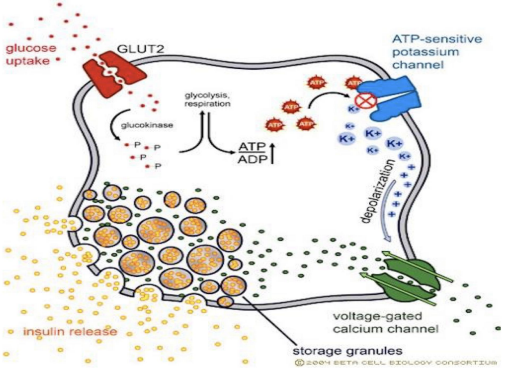


فهم الصورة
للتوضيح

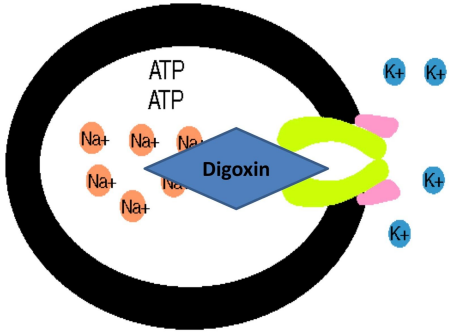
Structural proteins



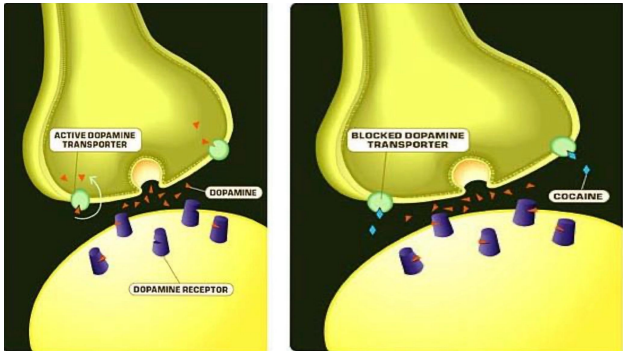
Ion Channels

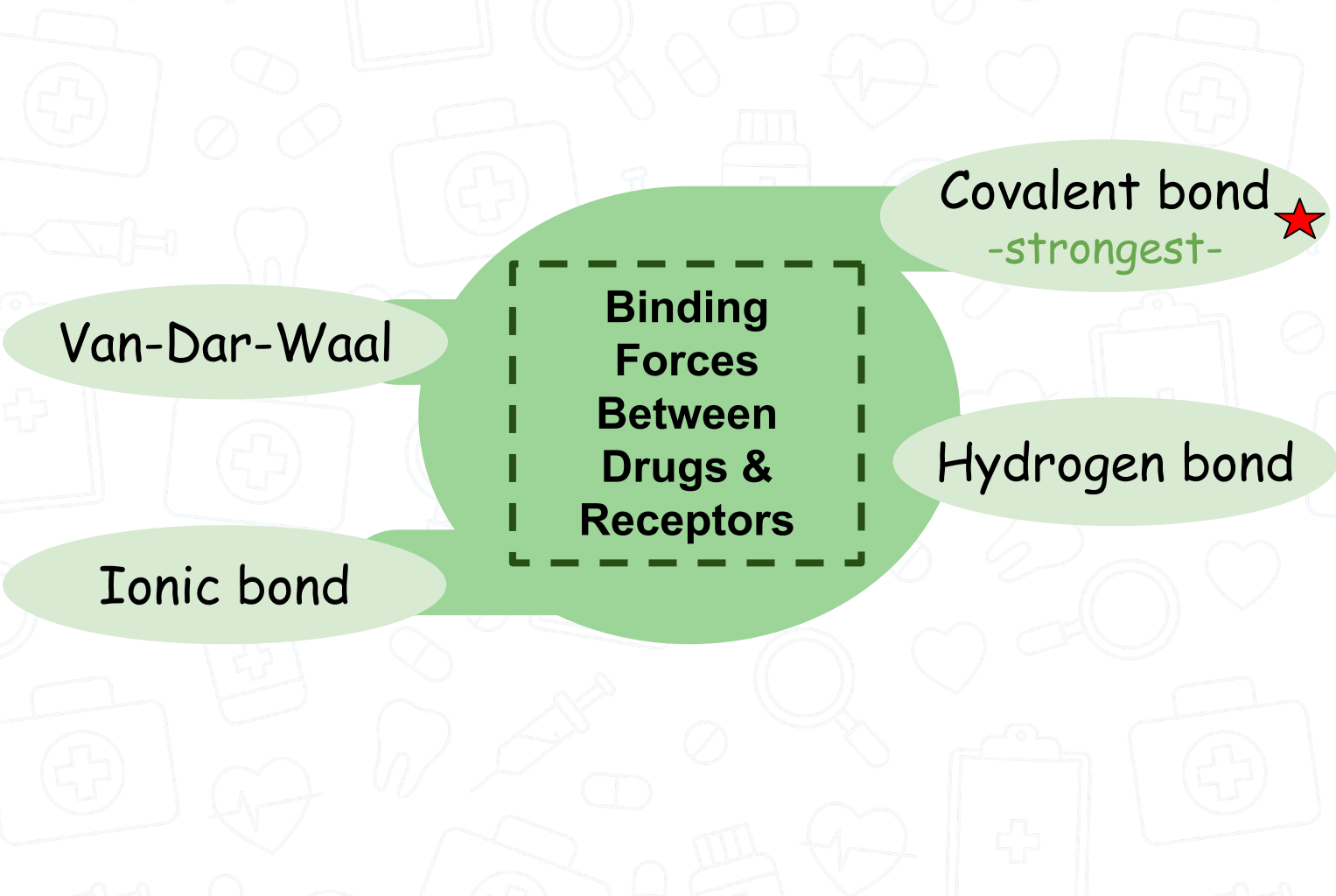


Carrier Molecules (Digoxin)



Carrier Molecules (Effect of cocaine)




Binding Forces Between Drugs & Receptors
Covalent bond
-strongest-
Hydrogen bond
Van-Dar-Waal
Ionic bond

Affinity and Efficacy

Affinity	Ability of a drug to combine with the receptor D(drug) + R(receptor) -> D-R complex -> Effect
Efficacy (Intrinsic Activity)	Capacity of drug receptor complex to produce an action. **E-Max:** Is the maximal response produced by a drug

A drug could have both or just one of them(مو شرط يشتغلون مع بعض)

You must know the definition (explain saq)

Agonist and Antagonist

it is a blocker for agonist
-same structure-
If I had overdose antagonist will be the cure-ترياق-

Click for Useful **video**!!

Agonist

Is a drug that binds with a receptor and elicit a response.

It has Affinity and Efficacy.

There are Two types (next slide):

- Full Agonist
- Partial Agonist

Antagonist

Is a drug that combines with the receptor without producing responses (**It blocks the action of agonist**)

It has Affinity but No Efficacy or zero efficacy.

(Blocks receptor)

It has a similar chemical structure to the Agonist

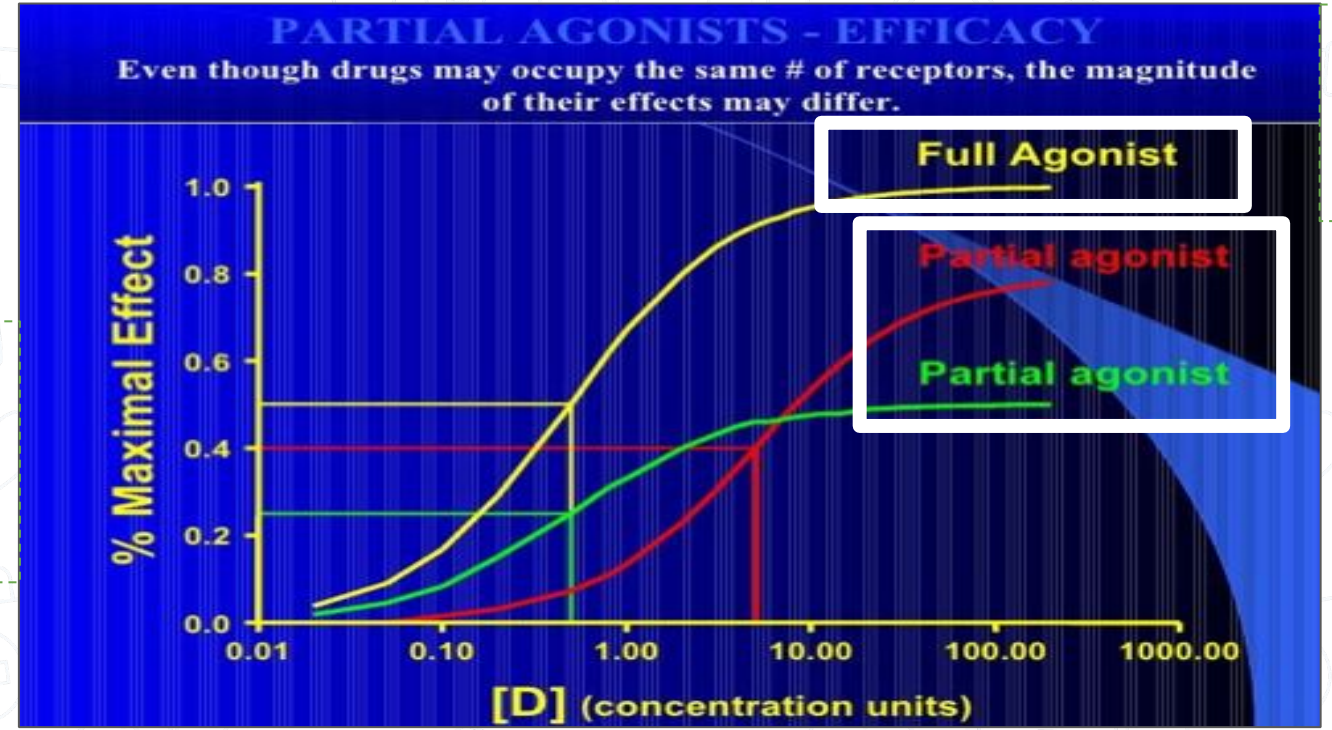
e.g. حفظAtropine: block the action of Ach on muscarinic receptors.

-No need to memorise example
-Must know the difference between full/partial

Types of Agonist

Full Agonist	Partial Agonist
A drug that combines with its specific receptor to produce maximal effect by increasing its concentration.	Combines with its receptor & evokes a response (submaximal effect) as a full agonist regardless of concentration. (Even though the drugs may combine with the same number of receptors, the magnitude they can produce may differ) max مهما زدت الجرعة ماراح اوصل
Affinity & High Efficacy	Affinity & Partial efficacy
e.g. Acetylcholine(ACH): acts upon muscarinic receptors	e.g. Pindolol: A beta blocker which is a partial agonist, produces less decrease in heart rate than pure antagonists such as propranolol

Just Understand the concept



-max(100%)
-if we increase the dose won't change

-submax
-will increase with more dose

Found Only in Female Slides

TERMS DEFINITIONS:

Affinity	is the capacity of a drug to form a complex with the receptor (DR complex) (D= Drug , R= Reseptor)
Efficacy	(Intrinsic activity) the ability of the drug once bound to the receptor to trigger response
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)

The Value of intrinsic activity range from 0 to 1

Summary

Drug:	Mechanism of Action:
Antacids	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/K pump
Cocaine	blocks transport or reuptake of catecholamines (dopamine) at synaptic causing euphoria
Vincristine	Anticancer agent
Colchicine	Drug for gout treatment
Pindolol (Beta blocker)	a partial agonist, produces less decrease in heart rate than pure antagonists

MCQ

Q-1 sulfonylurea drugs is a treatment for what?

A) Antidiabetic drugs B) heart failure. C) cancerous D) None

Q-2 Tubulin is a good target for ?

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

Q-3 Receptors are ?

A) micromolecules. B) macromolecules. C) none D) both

Q-4 The Study of biochemical and physiological effects of drugs and their mechanism of action, referred to:

A) Pharmacodynamics. B) Pharmacokinetics C) Pharmacology. D) None

1-A
2-D
3-B
4-A

SAQ

Q-1 What vincristine is used for?

Q-2 compare between agonist and antagonist

Answers

1- Slide 5

2- slide 9

SAQ

Q-3 What are the 5 targets for drug binding ?

Q-4 what are the two mechanisms of drug action?

Answers

1-Slide 4

2-Receptor-mediated mechanism (binding)
-Non Receptor-mediated mechanism

SAQ

Q-3 what is the definition for agonist? From the dr

Q-4 explain the mechanism for carrier molecules digoxin?

Answers

1-slide 9

2-slide 5

DONE BY THE AMAZING TEAM

You GOT THIS!

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