

\* G-protein-coupled receptor is the most target receptor in Drugs.

↳ 3 subunits → α → is the catalytic one  
↳ β and γ

activate or inhibits

③ Enzyme-linked receptor → Binding of the ligand to extracellular Domain that regulate related cytosolic enzyme  
↳ most common type is receptor that has Tyrosine kinase activity as part of their structure so the result of binding is phosphorylation of tyrosine residues in specific protein.  
↳ Can modify 3D structure of target protein and resulting in molecular switch.

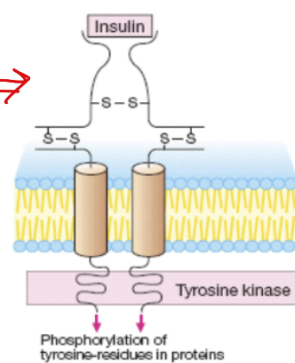
④ intracellular receptors

↳ so the ligand must diffuse into the cell

must have small molecular weight

↳ must have sufficient lipid solubilities to pass the membrane

important example of enzyme-linked receptor

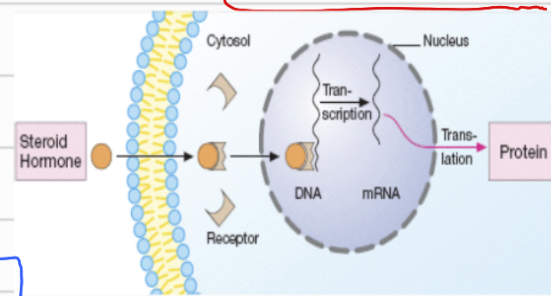


\* Best example is steroids Hormons → bind to the receptor in the cytosol and form ligand-receptor complex

migrate to the nucleus

bind to specific DNA sequences

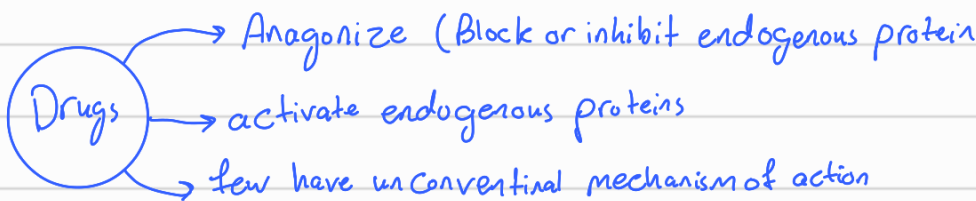
resulting in regulation of gene expression



\* How Drugs work?

most of them interact with endogenous protein

protein within the cell



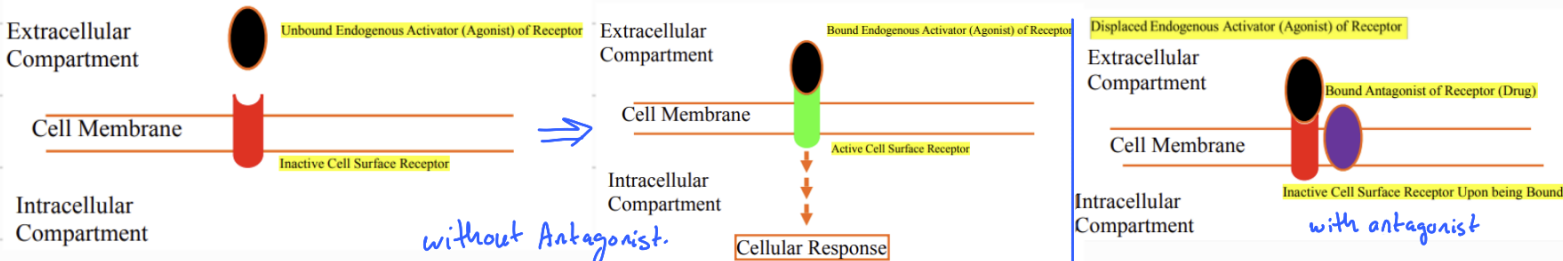
لا تحفظوا  
الأشياء

(A) Antagonism of endogenous protein

↳ Antagonise of cell surface receptor

receptor that is embedded in cell membrane and functions to receive chemical information from the extracellular compartment and transmit that information to intracellular one.

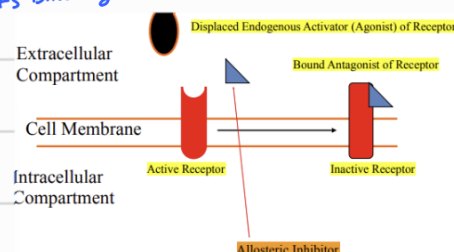
By ↳ Some compound bind to the receptor but does NOT activate it or trigger any response.



\* Most Antagonist attach the binding site of agonist and sterically prevent its binding  
Competitive ← reversible ← irreversible → non-competitive

\* there are some Antagonist Bind remote site

↳ Cause Allosteric displacement of Agonist or preventing it from binding  
↳ it is always Non-competitive



\* there is allosteric activator such as the inhibitor

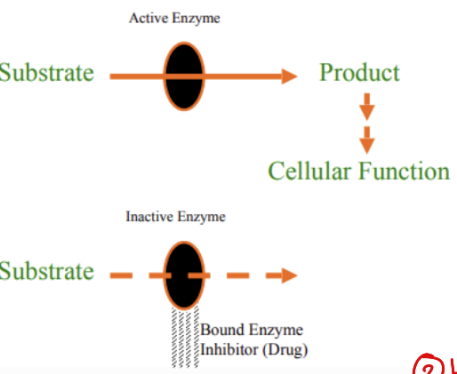
example of cell receptor Antagonism ① → Angiotensin Receptor blocker (ARB) for high Blood pressure (HBP), heart failure, chronic renal insufficiency

②  $\beta$ -Adrenoceptors → for Angina, myocardial infarction, heart failure HBP, performance anxiety

③ Antagonism of Nuclear receptors as ① Mineralocorticoid Antagonism for edema from Cirrhosis, heart failure

② Estrogen receptor → prevention of breast cancer. But remember that the Drug must pass the membrane.

④ Enzyme inhibitors:



\* enzyme → Catalyze Biosynthesis of product from substrate

\* loss of products due to enzyme inhibition mediates the effect of enzyme inhibitors

الإنزيمات أنزيم نظام التمثيل الغذائي (النتيجة بتأثره أو inhibitor من كيمي)

examples: ① Cyclooxygenase inhibitors for pain and fever

② HMG-CoA reductase inhibitor for hypercholesterolemia

③ Angiotensin Converting Enzyme inhibitors for HBP, heart failure chronic renal insufficiency

④ Ion channel Blockers as ① Calcium channel Blocker → angina, HBP

② Sodium channel Blocker to suppress cardiac arrhythmias and local anesthetic

⑤ transport inhibitors as selective Serotonin Reuptake inhibitors and inhibitors of Na-Cl-K symporter (ممنوع السعادة) and the kidney (المكينة) or skin (الجلد)

⑥ Inhibitors of signal transduction proteins as Tyrosine kinase inhibitors for myelocytic leukemia

and Type 5-phosphodiesterase inhibitors for erectile dysfunction

This is a major focus of Drug development

\* And Vice-versa there is same types of Antagonist for Agonists except last two ⑤ and ⑥

\* How Agonists work?

Agonists for cell surface Receptor  
↓  
as Morphine Agonists and  $\alpha$ -agonists

for Nuclear receptor  
↓  
as steroids for inflammation and HRT

Enzyme Activators  
as Nitroglycerine

Ion channel openers  
for Cl and K

\* some Agonist is endogenous chemical while others mimic them

for more selectivity

## \* Unconventional Mechanism of action.

- Disruption of structural protein as
  - Vinca Alkaloids for cancer
  - Colchicine for gout
- Being Enzymes as streptokinase for thrombolysis
- Covalent linking to Macromolecule as Cyclophosphamide for cancer
- Reacting chemically with small molecule as antacids
- Binding free molecule or atoms as drug for heavy metals poisoning
- Being nutrients as vitamins or minerals
- Exerting Action Due to physical properties as Osmotic pressure for diuretic
- working via an Antisense Action (work on RNA)
- Being Antigens as Vaccines
- Have Unknown mechanism as general anesthetics