MECHANISMS OF DRUG ACTION

Physical action

Drug can produce a therapeutic response because of it's physical properties.

e.g:

1- Mannitol as diuretic because it increase osmalerity,

2- Radio-isotopes : emit ionizing radiation

Simple chemical reaction

Drug may act through a chemical reaction.

e.g:

1- Gastric antacids work by neutralizing the stomach acidity with a base,

2- Chelating agents that bind heavy metals in body.

Receptors

- Def: is a specialized target macromolecule mostly protein,
- Location: present on the cell surface or intracellular,
- Fun:binds a drug and mediates it's pharmacological actions.
- Nature of receptors: can either be enzymes, nucleic acids or structural proteins to which drugs may interact.

- Def of ligand: A molecule that binds to a receptor , and can be a peptide or another small molecule like a neurotransmitter, hormone, or drug, or endogenous substance

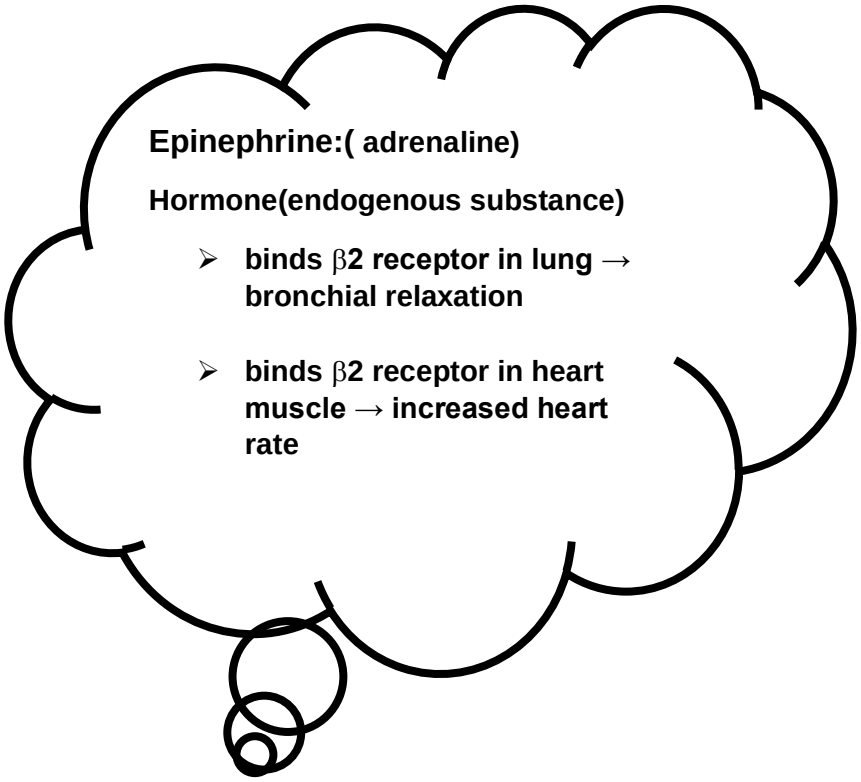
- What is the endogenous substance? It is a natural materials inside the body, like

1- steroid hormone 2- progesterone 3- testosterone

4- acetylcholine 5- adrenaline 6- histamine

- What happens after ligand binding in a receptor? Ligand binding changes the conformation (three -dimensional shape) of the receptor molecule. This alters the shape at a different part of the protein, changing the interaction of the receptor molecule with associated biochemicals, leading in turn to a cellular response mediated by the associated biochemical pathway.

TYPES OF LIGAND-RECEPTOR INTERACTIONS: Not every ligand that binds to a receptor also activates the receptor. The following classes of ligands exist:				
From where	**1. (Full) agonists**	**2. Partial agonists**	**3. Antagonists**	**4. Inverse agonists**
Def	**able to activate the receptor and result in a maximal biological response. The natural endogenous ligand with greatest efficacy for a given receptor is by definition a full agonist (100% efficacy).** **- EX: Isoproterenol: important therapy in asthma**	**do not activate receptors thoroughly, causing responses which are partial compared to those of full agonists (efficacy between 0 and 100%).**	**bind to receptors but do not activate them. This results in receptor blockage, inhibiting the binding of agonists and inverse agonists.** **- EX: propranolol: control heart beat**	**is a drug that binds to the same receptor as an agonist (negative efficacy).** **- EX: Nearly all antihistamines acting at H1 receptors and H2 receptors have been shown to be inverse agonists**



TYPES OF DRUG-RECEPTOR BONDING: Drugs interact with receptors by means of chemical forces or bonds. These are of three major types:			
From where	**1. Covalent**	**2. Electrostatic**	**3. Hydrophobic**
Char	**1- It is very strong** **2- in many cases not reversible under biologic conditions.** **3- Thus, the duration of drug action is frequently, but not necessarily, prolonged (*irreversible*)**	**1- is much more common than covalent bonding in drug-receptor interactions.** **2- These vary from (Types) 1- relatively strong linkages between permanently charged ionic molecules to 2- weaker hydrogen bonds and 3- very weak induced dipole interactions such as van der Waals forces.** **3- Electrostatic bonds are weaker than covalent bonds. (*reversible*)**	**1- are usually quite weak** **2-are probably important in 1- the interactions of highly lipid-soluble drugs with the lipids of cell membranes perhaps in 2- the interaction of drugs with the internal walls of receptor "pockets."**

- Why the Drugs which bind through weak bonds to their receptors are generally more selective than drugs which bind through very strong bonds? This is because weak bonds require a very precise fit of the drug to its receptor if an interaction is to occur

DURATION OF DRUG ACTION: Termination of drug action at the receptor level results from one of several processes			
1. The effect lasts only as long as the drug occupies the receptor, so that dissociation of drug from the receptor automatically terminates the effect.	**2. The action may persist after the drug has dissociated, because, for example, some coupling molecule is still present in activated form.**	**3. Drugs that bind covalently to the receptor, the effect may persist until the drug-receptor complex is destroyed and new receptors are synthesized.**	**4. Many receptor-effector systems incorporate desensitization mechanisms for preventing excessive activation when agonist molecules continue to be present for long periods**