Principle &mechanism of drug action

Drugs produce their effects by interacting with the physiological systems of the organisms. By such interaction, drugs merely modify the rate of functions of the various systems. But they cannot bring about qualitative changes, i.e. they cannot change the basic functions of any physiological system. Thus drugs act by:

1. Stimulation
2. Depression
3. Irritation
4. Replacement
5. Anti-infective or cytotoxic action
6. Modification of the immune status.

.

Principle of Drug Action

Principle of drug action means how any drug produce the effect for which it has been administered. These are working methodology of drugs.

Principle	Explanation	Example
Irritation	Senna and some other drug used in constipation irritate the intestine and increase defecation. Other balm in case of headache will irritate the forehead tissue and gives relief from pain for short duration.	Counter Irritant like- drugs for constipation
Stimulation	Stimulation means to increase the function of any specialized organ, which will result in extra work, like in case of fear or fight adrenaline is get secreted and heart rate increase which give FFF response.	Adrenaline. Stimulates heart. pilocarpine stimulates salivary glands
Depression	The simple meaning of depression is the reduction of specialized activity. For example- Barbiturate and benzodiazepine depress the CNS and give depression action. As same Omeprazole reduce gastric acid secretion.	Barbiturate depresses CNS. Quinidine depresses heart. and Omeprazole depress gastric acid secretion
Replacement	When any hormone or biochemical substance is in inadequate quantity and there recovery is not possible then there is one option of replacement. The replacement is done for insulin in case of insulin dependent diabetes; here insulin is given by injection to maintain the requirement	Levodopa in Parkinson's, Insulin in diabetes and Iron in Anemia.
Cytotoxic	When there is entry of any parasite, or there is no other option to control the growth of own body cell then Cytotoxic drugs are used. They kill the microorganism of kill the uncontrolled and excessive growing cells.	Penicillin, Zidovudine, Chloroquine, cyclophosphamide

Modification of immune status: Vaccines and sera act by improving our immunity while immunosuppressants act by depressing immunity, e.g. glucocorticoids.

MECHANISMS OF DRUG ACTION

- through receptors
- through enzymes and pumps
- through ion channels
- by physical action
- by chemical interaction
- by altering metabolic processes.

Through Receptors

Drugs may act by interacting with specific receptors in the body

Through Enzymes and Pumps

Drugs may act by inhibition of various enzymes, thus altering the enzyme-mediated reactions, e.g. allopurinol inhibits the enzyme xanthine oxidase; acetazolamide inhibits carbonic anhydrase, enalapril inhibits angiotensin converting enzyme, aspirin

inhibits cyclo-oxygenase, neostigmine inhibits acetylcholinesterase

Through Ion Channels

Drugs may interfere with the movement of ions across specific channels, e.g. calcium channel blockers, sodium channel blockers, potassium channel openers and GABA gated chloride channel modulators.

Physical Action

The action of a drug could result from its physical properties like:

Adsorption – Activated charcoal in poisoning

Chemical Interaction

Drugs may act by chemical reaction.

Antacids – neutralise gastric Acids

Chelating agents – bind heavy metals making them nontoxic.

Altering Metabolic Processes

Drugs like antimicrobials alter the metabolic pathway in the microorganisms resulting in destruction of the microorganism, e.g. sulfonamides interfere with bacterial folic acid synthesis.

RECEPTOR

Definition A receptor is a macromolecular site on the cell with which an agonist binds to bring about a change.

Affinity is the ability of a drug to bind to a receptor.

Intrinsic activity or efficacy is the ability of a drug to elicit a response after binding to the receptor.

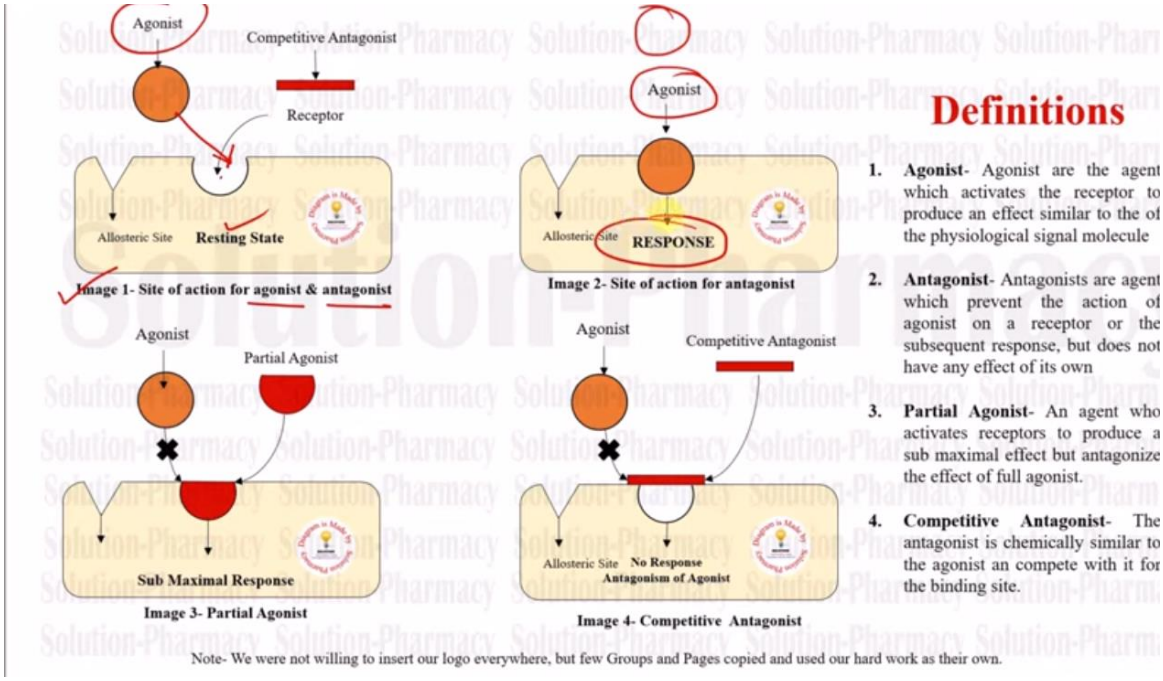
Agonist An agonist is a substance that binds to the receptor and produces a response. It has affinity and intrinsic activity. E.g. adrenaline is an agonist at adrenergic receptors.

Antagonist An antagonist is a substance that

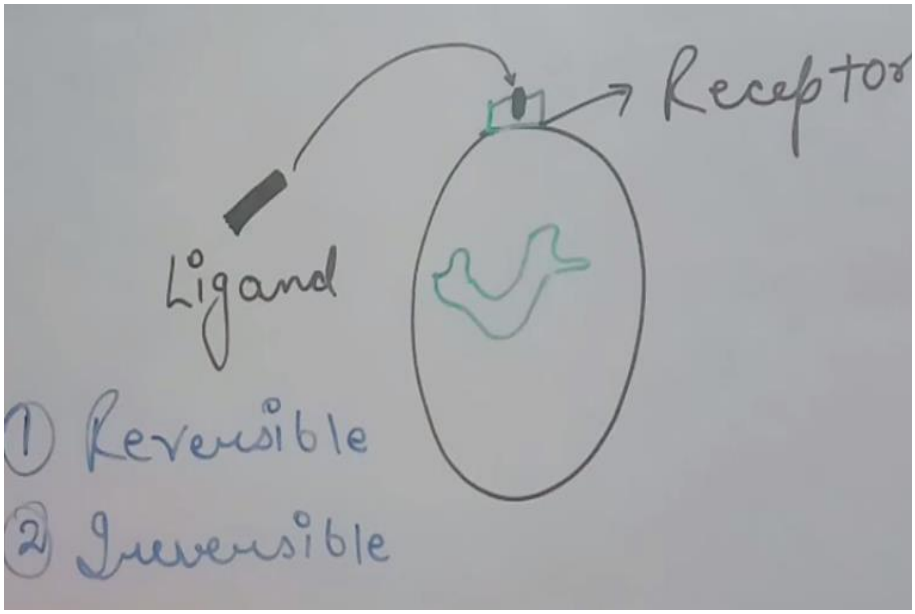
binds to the receptor and prevents the action of the agonist on the receptor. It has affinity but no intrinsic activity. E.g. Tubocurarine is an antagonist at nicotinic receptors.

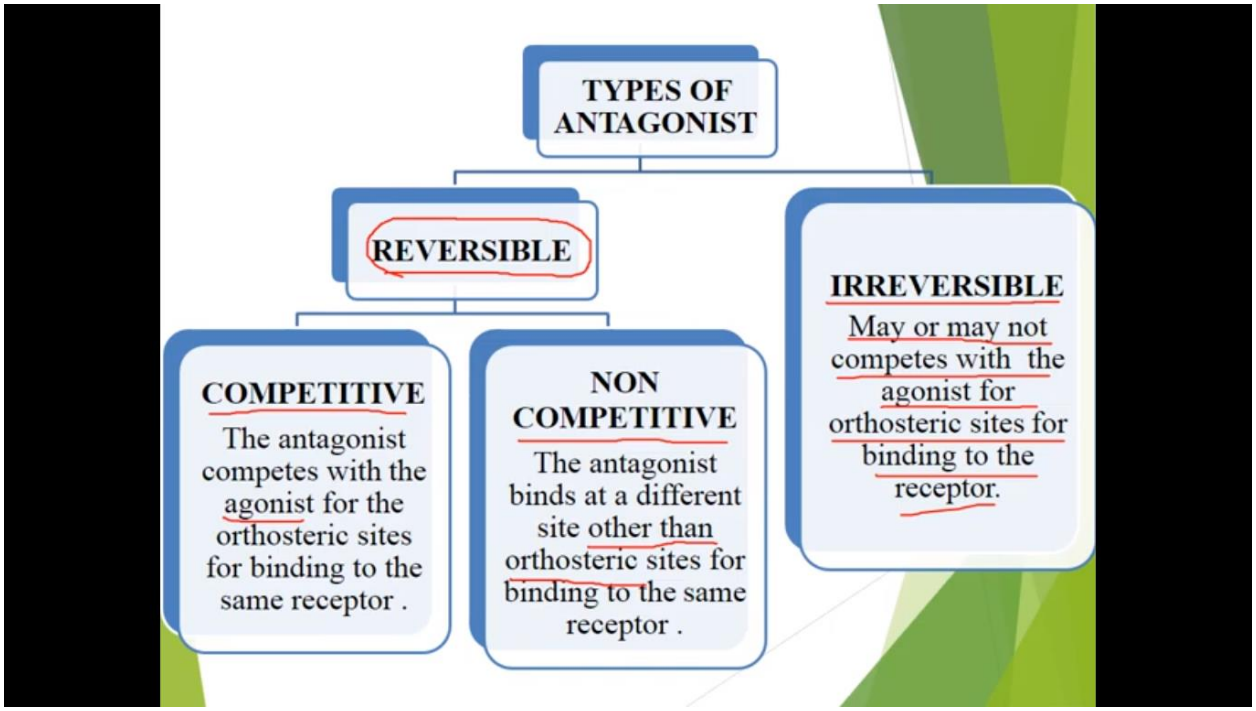
Partial agonist binds to the receptor but has low intrinsic activity. Pentazocine is a partial agonist at ⌈ opioid receptors.

Inverse agonist Some drugs, after binding to the receptors produce actions opposite to those produced by a pure agonist. They are known as inverse agonists, e.g. Diazepam acting on benzodiazepine receptors produces sedation, anxiolysis, muscle relaxation and controls convulsions, while inverse agonists ®-carbolines bind to the same receptors to cause arousal, anxiety, increased muscle tone and convulsions.



Ligand is a molecule which binds selectively to a specific receptor.

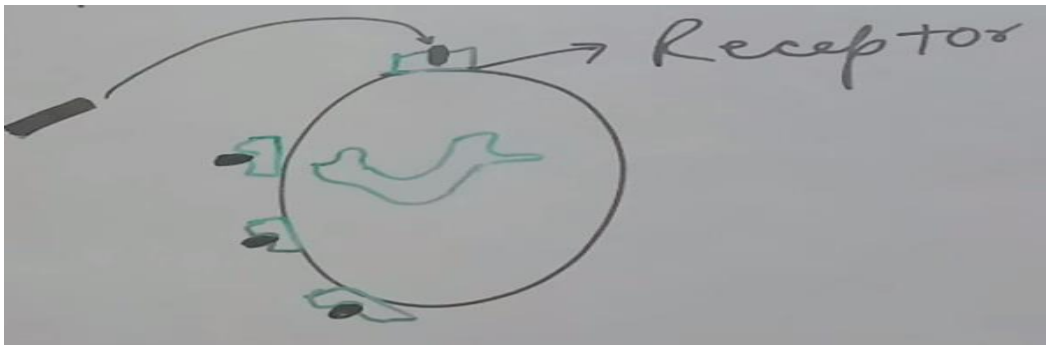




Receptor Theories

Lock and key' --Drug receptor interaction has been considered to be similar to 'lock and key' relationship where the drug specifically fits into the particular receptor (lock) like a key.

T**he occupation theory** suggests that the magnitude of drug response depends on the proportion of the receptors occupied by the drug.



The rate theory -- proposes that the magnitude of response depends on the rate of agonist–receptor association and dissociation.

TWO-STATE (MULTI-STATE) RECEPTOR MODEL

The two-state model is a simple linear model to describe the interaction between a ligand and its receptor, but also the active receptor (R*)

It proposes that ligand binding results in a change in receptor state from an inactive to an active state based on the receptor's conformation.

A receptor in its active state will ultimately elicit its biological response

It was first described by Black and Leff in 1983 as an alternative model of receptor activation

Two state model --- Rr exist in two state ----- Resting & inactive

Dg with higher affinity for activated state = full agonist

Dg with moderate affinity for activated Rr = partial agonist

Types of recepotor

1.Ion channels (inotropic receptor)

2. G-protein coupled receptors (metabotropic receptor)

Enzymatic receptors (kinase linked receptor)

4. Transcription factors (receptors that regulate gene transcription or nuclear receptors

Ion channels **or receptor channels**—are proteins present on the cell surface. Binding of the agonist opens the channel allowing ions to cross the membrane. These are called ligand-gated ion channels. Depending on the ion and the channel, depolarisation/

hyperpolarisation occurs, e.g. nicotinic cholinergic receptor channel permits passage of Na+ ions resulting in depolarisation.