# D.P.VIPRA COLLEGE BILASPUR

DEPARTMENT OF CHEMISTRY

## M.Sc- 4rth semester

Subject- Medicinal chemistry

**A Presentation on-** Theories of drug activity

Presented by –

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## DRUG

- It is a natural or synthetic substances which has a physiological effects when administered into the body.

## RECEPTOR

- It is a specific binding site present on the cell surface made up of protein or nucleic acid where a ligand can bind and initiates a characteristic response.

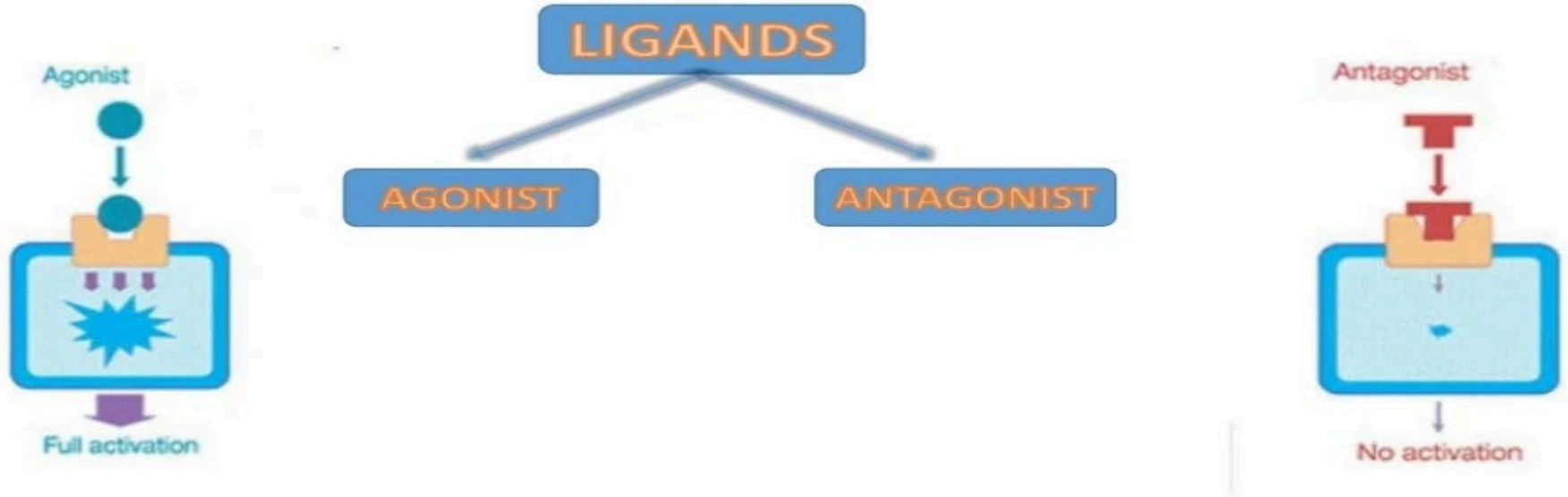
# TYPES OF RECEPTORS

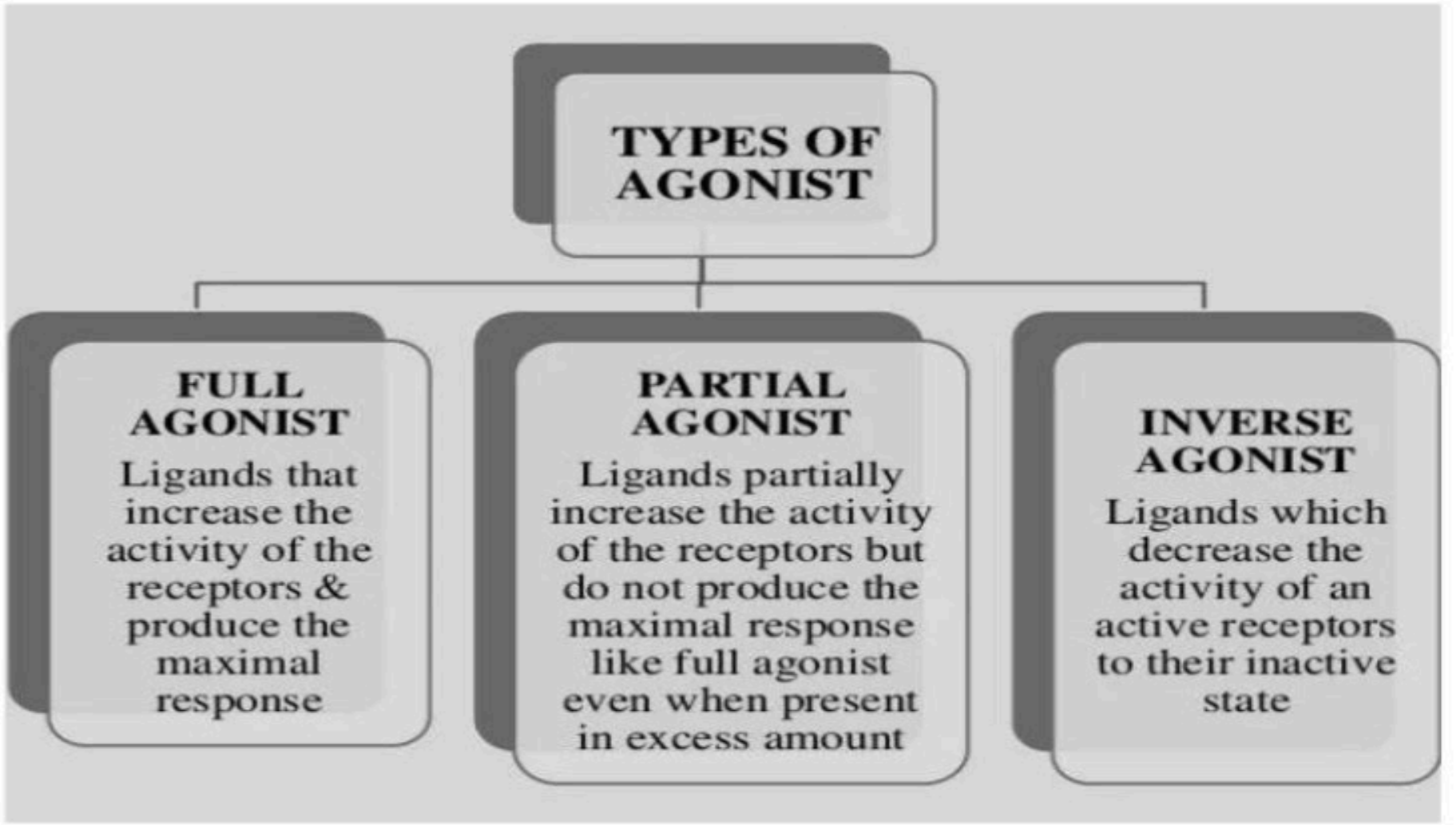
- Intracellular Receptors
- Cellular Receptors :-

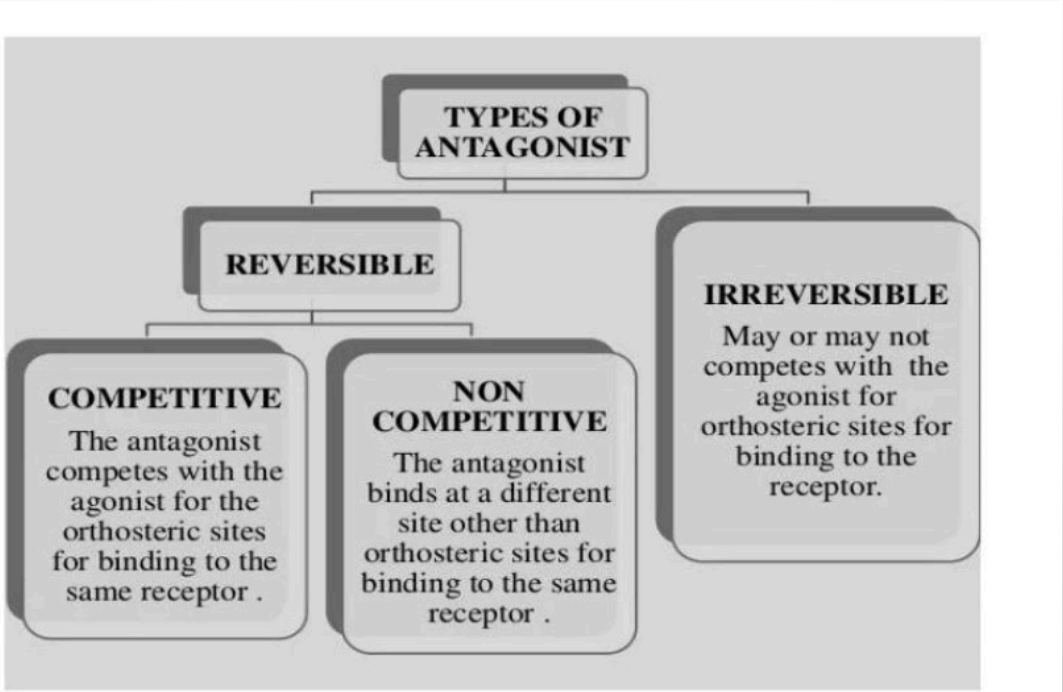
1. Ligand-gated ion channels
2. G protein-coupled receptors
3. Tyrosine kinases receptors

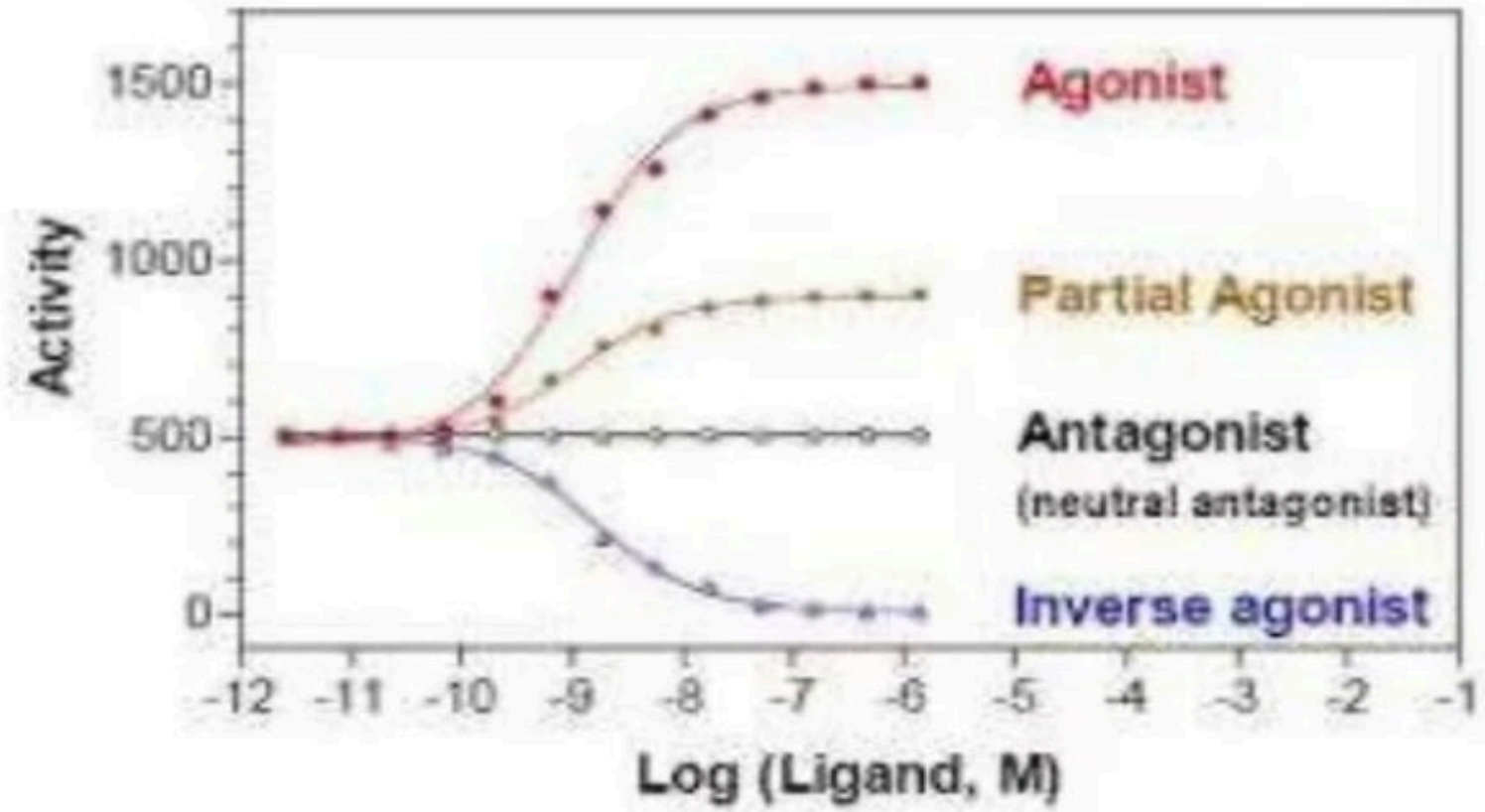
# Classification of ligands

Ligands are classified by effects upon binding to receptors




TYPES OF AGONIST
FULL AGONIST
Ligands that increase the activity of the receptors & produce the maximal response
PARTIAL AGONIST
Ligands partially increase the activity of the receptors but do not produce the maximal response like full agonist even when present in excess amount
INVERSE AGONIST
Ligands which decrease the activity of an active receptors to their inactive state


TYPES OF ANTAGONIST
REVERSIBLE
IRREVERSIBLE
May or may not competes with the agonist for orthosteric sites for binding to the receptor.
COMPETITIVE
The antagonist competes with the agonist for the orthosteric sites for binding to the same receptor .
NON COMPETITIVE
The antagonist binds at a different site other than orthosteric sites for binding to the same receptor .


Activity
1500
1000
500
0
-12
-11
-10
-9
-8
-7
-6
-5
-4
-3
-2
-1
Log (Ligand, M)
Agonist
Partial Agonist
Antagonist
(neutral antagonist)
Inverse agonist

# THEORIES OF DRUG RECEPTORS INTERACTION

1. Occupation theory
2. Rate Theory
3. The induced-fit theory of enzyme-substrate interaction
4. Macromolecular perturbation theory
5. Activation-aggregation theory
6. Two state model of receptor activation

# OCCUPATION THEORY

- This theory was given by Gaddum and Clark
- This theory states that the intensity of pharmacological effect is directly proportional to the number of receptors that are occupied by the drug
- Drugs act on binding sites and activate them, resulting in a biological response that is proportional to the amount of drug-receptor complex formed.
- The response ceases when this complex dissociates.
- Intensity of pharmacological effect is directly proportional to number of receptors occupied

$$D + R \rightarrow DR \Longrightarrow RESPONSE$$

- Response is proportional to the fraction of occupied receptors
- Maximal response occurs when all the receptors are occupied
- This theory was not acceptable for partial agonist. Hence Arieus and Stephenson modify occupancy theory to account for partial agonist.
- Their concept was based on involvement of two stage during drug receptor interaction

1. There is complexation of drug with receptor known as Affinity.
2. There is initiation of biological effect which Arieus called it as **Intrinsic activity** whereas Stephanson called it as **Efficiency**

- **Affinity** - It is the measure of capacity of drug to bind to receptors dependent on molecular complementarily of drug and receptor.
- **Intrinsic activity** – It is defined as maximum response induced bya compound relative to a reference compound.
- **Efficacy** – It the property of compound that produces the maximum response or ability of drug – receptor complex.

# Rate Theory

- This theory is given by Paton
- Activation of receptors is proportional to the total number of encounters of a drug with its receptor per unit time.
- Therefore this theory suggests that activity is a function of rate of association and dissociation of drug with receptor and not the number of occupied receptor.
- According to this view, the duration of Receptor occupation determines whether a molecule is **agonist, partial agonist.**

# Macromolecular Perturbation Theory

- This theory was given by Bellean
- During the interaction of drug with receptor there are two general types of macromolecular perturbations could result as following:

1. Specific Conformational perturbations which makes possible the binding of agonist.

2. Non-Specific Conformational perturbation which accommodates other types of molecules that do not elicit response.

# Activation – Aggregation Theory

- This theory was given by Monad, Wyman and Changuix and Karlin
- This theory is extension of macromolecular perturbation theory.
- According to which even in absence of drugs receptor is in a state of dynamic equilibrium between $R_o$ and $T_o$

where $R_o$ is Activated form

$T_o$ is Inactive form

Agonist bind to $R_o$ and shift the equilibrium to the activated form whereas antagonist bind to inactive form $T_o$ and partial agonist bind to both.

# Two-State (Multi-state) Receptor Model

- R and R* are in equilibrium (equilibrium constant *L), which* defines the basal activity of the receptor.
- Full agonists bind only to R*
- Partial agonists bind preferentially to R*
- Full inverse agonists bind only to R
- Partial inverse agonists bind preferentially to R

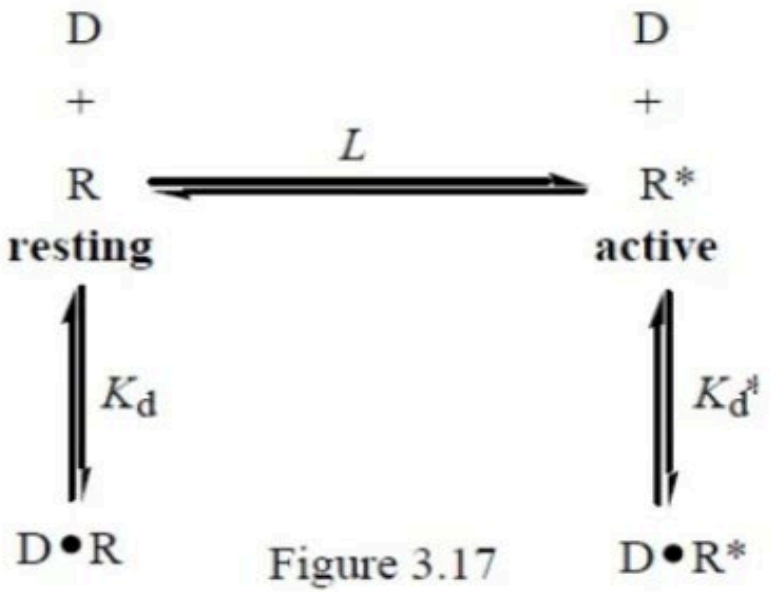



Figure 3.17

- THANK YOU