PRINCIPLES OF DRUG ACTION:

- Drugs do not impart new functions to any system,organ or cell.They only alter the pace of on going activity.
- The basic types of drug action can be broadly classed as:

1.Stimulation

2.Depression

3.Irritation

4.Replacement

Principle:

Drugs acts by virtue of PHYSICAL & CHEMICAL properties.

Eg:

DRUG	PROPERTY
Antacid	Neutralisation
Activated charcoal	Adsorbent in heavy metal poisoning
$KMnO_4$	Oxidising property

Majority of drugs produce their effects by interacting with a discrete target biomolecule,which is usually a protein.

- Functional proteins that are targets of drug action can be grouped into four major categories that is:

1.ENZYMES

2.IONCHANNELS

3.TRANSPORTERS

4.RECEPTORS

1.Enzymes:

Almost all biological reactions are carried out under catalytic influence of enzymes.Hence enzymes are very important target of drug action.

- Eg:Levodopa →Dopamine catalysed by Dopa

Stimulation of an enzyme increases its affinity for the substrate so that rate constant (kM)of the reaction is lowered.

- Apparent increase in enzyme activity can occur by enzyme induction i.e. synthesis of more enzyme protein.
- Inhibition of enzyme is a common mode of drug action.

A)Non specific inhibition

B)Specific inhibition

a.competitive , compititive

b.non

A]COMPETITIVE:

The drug being structurally similar competes with the normal substrate for the catalytic binding site of the enzyme so that the product is not formed or a non functional product is formed.

Eg:Captopril competes with angiotensin –I for ACE .

B]NONCOMPETITIVE:

Inhibi & not with cata uch a way that

NON COMPETITIVE INHIBITOR	ENZYME
LOVASTATIN	HMG-CoA reductase
DIGOXIN	Na+k+ATPase

2.IONCHANNELS:

Proteins which act as ion selective channels participate in transmembrane signaling un regulate intra cellular ionic composition.

- This makes them a common target of drug action.
- Drugs can affect ion channels either through a specific receptors,G-protein operated ion channels.
- In addition, certain drugs modulate opening & closing of channels.

Eg:QUINIDINE blocks myocardial Na+ channels.

NICORANDIL open ATP-sensitive K+ channel.

3.TRANSPOTERS:

Several substrates are translocated across the membrane by binding to specific transporters which either facilitate diffusion in the direction of the concentration gradient or pump the metabolite/ion against the concentration gradient using metabolic energy .

eg:Furosemide inhibits the $Na^+k^+2cl^-$ co transporter in the ascending limb of loop of Henle.

- Hydrochlorothiazide inhibits the Na^+cl^- symporter in the early distal tubule .

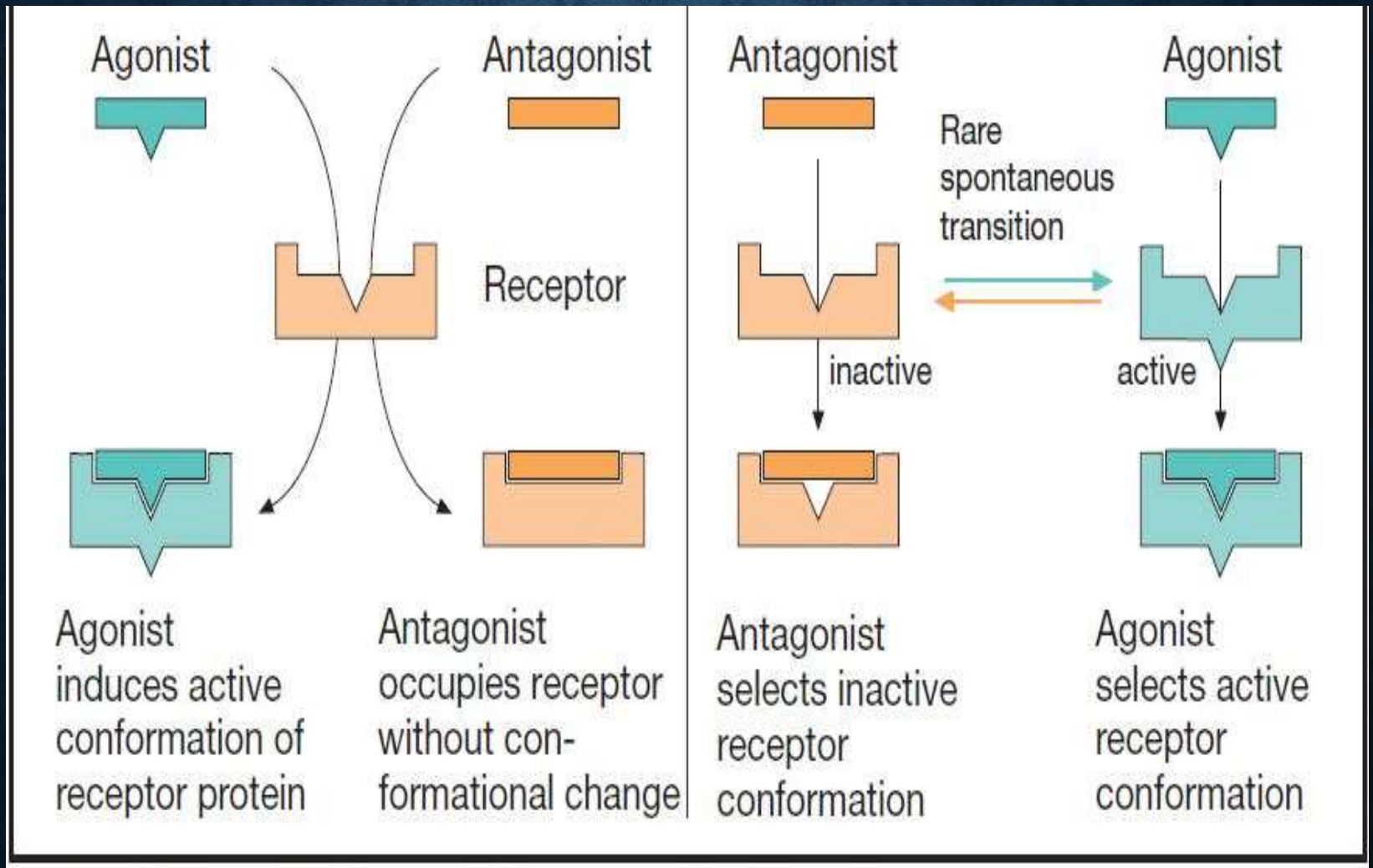
4.RECEPTORS:

Receptor is a macro molecule or a binding site located on the surface or inside the effector cell that serves to recognise the signal molecule but itself has no other function .

- The following terms are used to in describing drug-receptor interaction:

➢ Agonist:An agent which activates the receptor to produce an effect similar to that of the physiological signal molecule.

➢ Inverse Agonist:An agent which activates a receptor to produce an effect in the opposite direction to that of the agonist.



A. Molecular mechanisms of drug-receptor interaction

- Antagonist:An agent which prevent the action of an agonist on the receptor but does not have any effect of its own.
- Ligand:An molecule which attaches selectively to particular receptors of site shows only affinity.

RECEPTOR OCCUPATION THEORY:

This theory states that receptors exsists in dynamic equilibrium some are in active form and some are in inactive form.

- Agonist have both affinity and maximal intrinsic activity.

Eg:Acetylcholine ,Adrenaline.

- Antagonist have affinity but no intrinsic activity.

Eg:Atopine,propanaline .

- Partial agonist have affinity and sub maximal intrinsic activity between 0-1.

Eg:Dichloroisoproterenol-on beta adrenergic receptor.

DRUG ACTION:

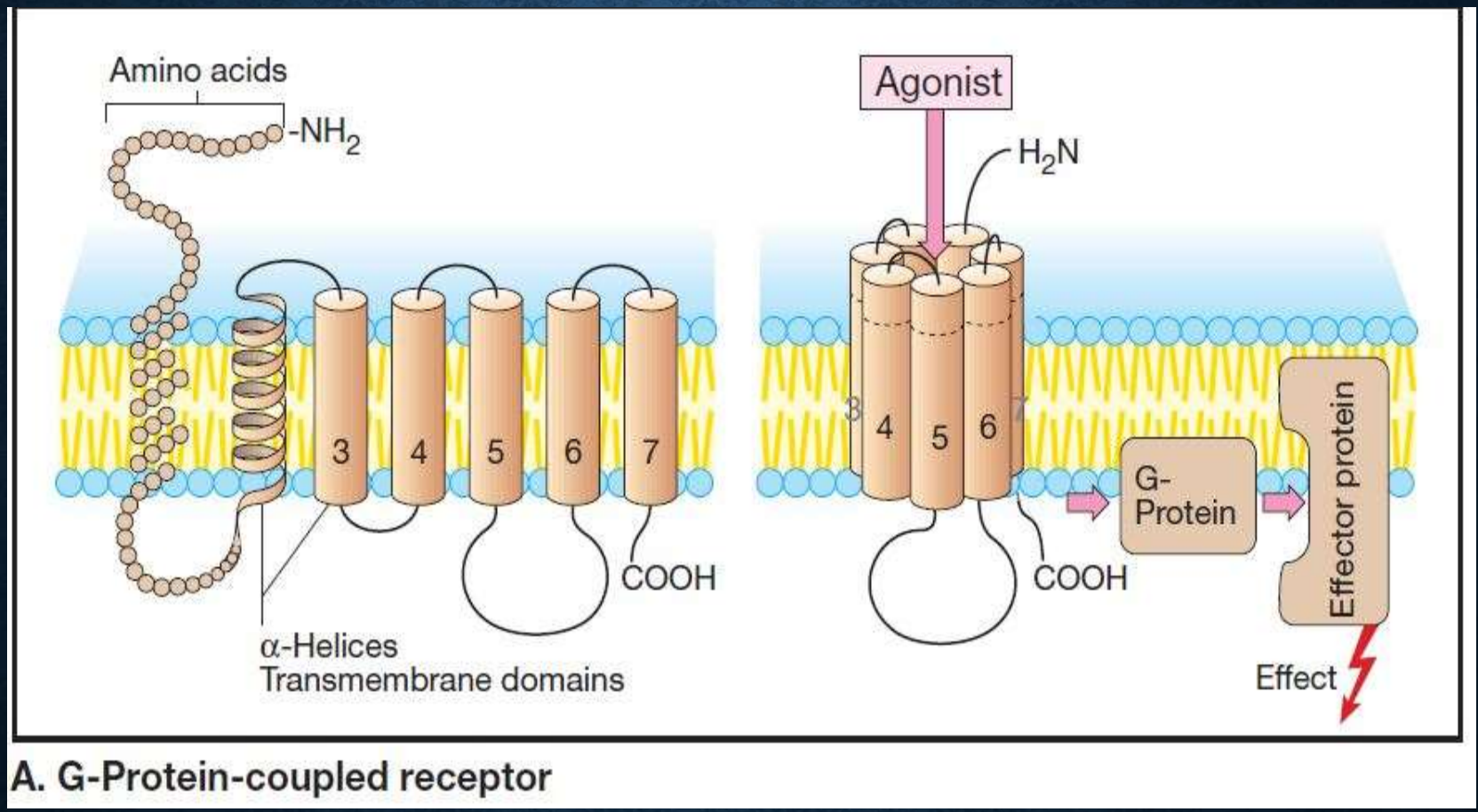
It is the intial combination of drug with a receptor resulting in a conformational change(agonist binding) or prevention of conformational change(antagonist).

- DRUG EFFECT:

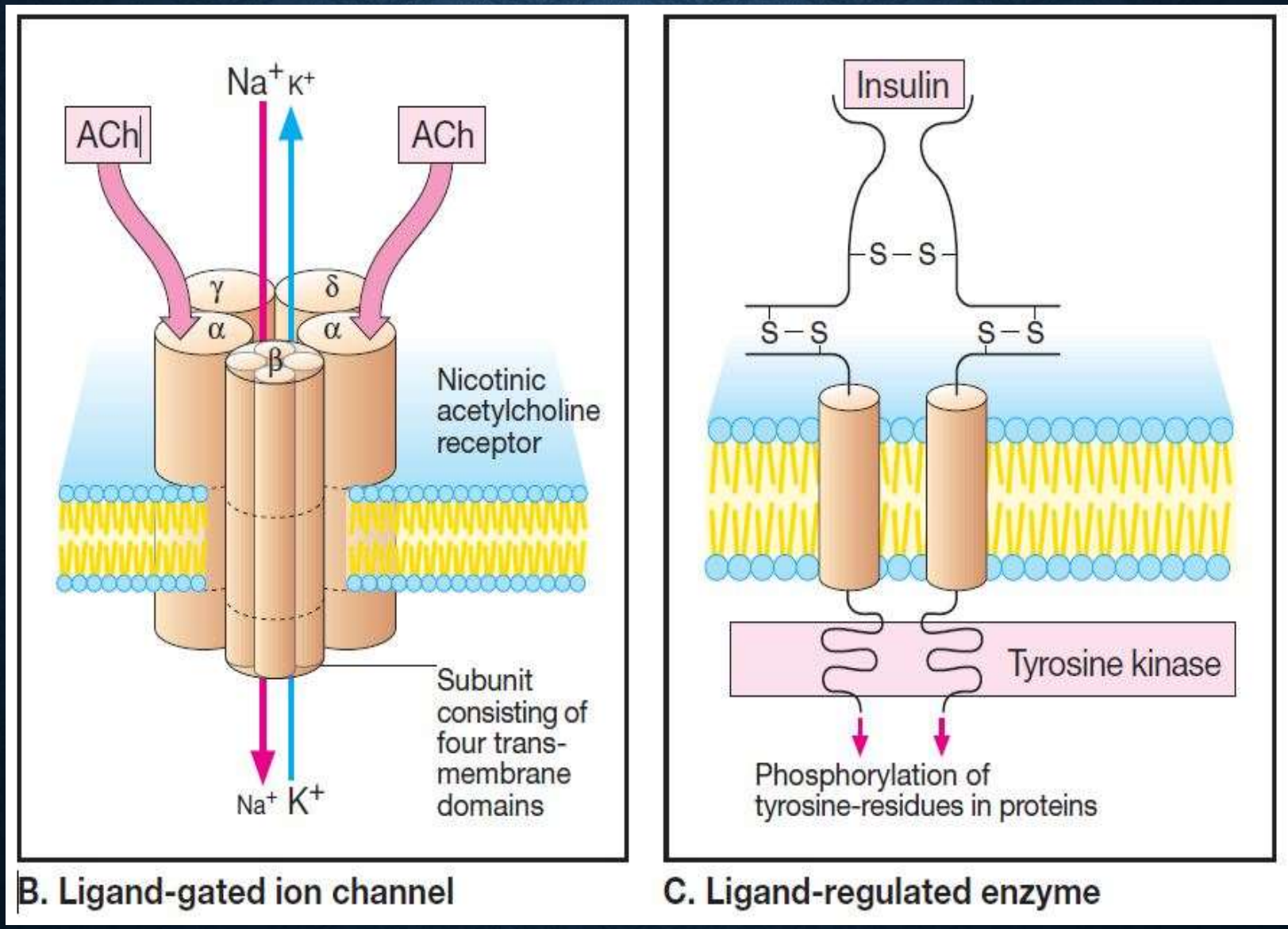
  It is the ultimate change in biological functions brought about as a consequence of drug action,through a series of intermediate steps i.e transducer.

- Transducer mechanism can be grouped into four categories

1. GPCR
2. Receptors with intrinsic ion channel.
3. Enzyme linked receptors.
4. Receptors regulating gene expression.

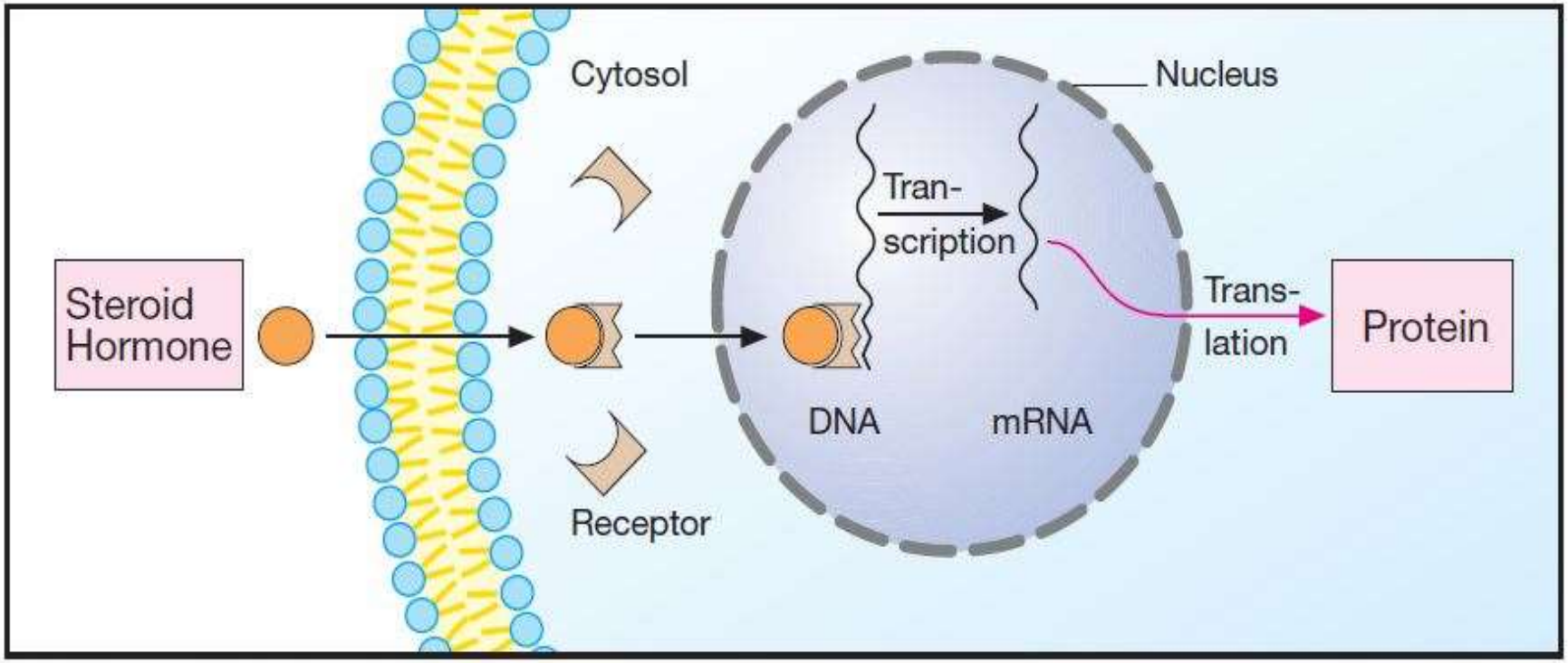


A. G-Protein-coupled receptor



B. Ligand-gated ion channel

C. Ligand-regulated enzyme



D. Protein synthesis-regulating receptor