

Q1 List the different mechanisms of drug actions with examples (March 2013)

1. ACTIONS DEPENDENT ON CHEMICAL PROPERTIES

- Antacids exert their effects by neutralizing gastric acid
- Chelating agents reduce the concentration of certain metallic ions within the body (eg, desferoxamine and iron)

2. ENZYMES

- Enzymes are biological catalysts, and most drugs that interact with enzymes are inhibitors
- The results of drug/enzyme interaction are thus - the concentration of the substrate normally metabolized by the enzyme is increased, and that of the product of reaction is decreased
- Eg, ACE inhibitors (captopril, enalapril) prevent the conversion of ACEI to ACEII and bradykinin to various fragments

3. VOLTAGE GATED ION CHANNELS

- Involved in the conduction of action potentials in excitable tissues
- Several groups of drugs have specific blocking actions at these ion channels – eg, local anaesthetics (eg, lignocaine) block Na channels, calcium channel blockers (eg, diltiazem) acts on vascular smooth muscle ion channels

4. RECEPTORS

A receptor is a protein, often integral to a membrane, containing a region to which a ligand binds specifically to elicit a response. They may be grouped into three classes based on mechanism of action:

a. Altered ion permeability (ion channels / ionotropic)

- Membrane spanning complexes with the potential to form a channel through the membrane
- Three families:
 - Pentameric → contain 5 membrane spanning units (eg, nicotinic Ach receptor at the NMJ which allows an Na channel to form, GABA A receptor which allows a Cl channel to form, 5HT3 receptor)
 - Ionotropic glutamate → NMDA, AMPA and kainate ionotropic ligand gated ion channels. They form Na, K and (NMDA only) Ca channels when glutamate binds
 - Purinergic receptors → PX1 and PX2 are activated by ATP, permeable to Na, K and Ca, and are associated with mechanosensation and pain.

b. Production of intermediate messengers

- Membrane bound systems that transduce a ligand gated signal presented on one side of the cell membrane into an intracellular signal transmitted by intermediate messengers. These messengers may be:
 - G proteins (most common) → eg, Nad and Adr
 - Tyrosine kinase → eg, insulin
 - Guanylyl cyclase → eg, NO, atrial natriuretic peptide

c. Regulation of gene transcription

- Steroids and thyroid hormones act through intracellular receptors to alter the expression of DNA and RNA, and indirectly alter the production of intracellular proteins.