List the different mechanisms of drug actions with examples (23% pass)

7 methods by which drugs cause their action include: PEFsPdCpRsig (almost PEEPd CpR sig)

1. PHYSICOCHEMICAL ACTIONS
   - Antacids exert their effects by neutralizing gastric acid
   - Chelating agents reduce the concentration of certain metallic ions within the body (e.g., desferoxamine and iron, or activated charcoal)
   - CaCl₂, KCl, blood, Mg, replase alter or supplement endogenous primary substrates

2. ACTIONS ON ENZYMES
   - Enzymes are biological catalysts, and most drugs that interact with enzymes are inhibitors
   - Increased concentration of the substrate and decreased concentration of the product (e.g., ACE inhibitors (captopril, enalapril) prevent the conversion of ACEI to ACEII and bradykinin to various fragments)
   - Neostigmine inhibits acetylcholinesterase reversibly

3. DRUGS WHICH ACT AS FALSE SUBSTRATES FOR ENZYMES
   - Fluorouracil act as "false substrate", replaces uracil as an intermediate in purine biosynthesis but cannot be converted into thymidylate

4. PRODRUGS
   - Require conversion to activated form by metabolic pathway
   - Levodopa → Dopamine
   - Parecoxib → Valdecoxib

5. ALTERATION OF CARRIER PROTEIN PROPERTIES
   - Cardiac glycosides (such as digoxin) inhibits Na-K pump
   - Loop diuretics inhibits Na/K/Cl co-transporter in loop of Henle
   - Cocaine inhibits noradrenaline re-uptake

6. 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
     - local anaesthetics (e.g., lignocaine) block Na channels,
     - calcium channel blockers (e.g., diltiazem) acts on vascular smooth muscle ion channels

7. RECEPTORS
   - Definition:
     - A protein, often integral to a membrane, containing a region to which a ligand binds specifically to elicit a response.
     - Binding may be allosteric (at a site distant to the receptor).
     - Grouped into three classes based on mechanism of action:
       1. Altered ion permeability (ion channels / ionotropic)
          - Membrane spanning complexes with the potential to form a channel through the membrane
          - Three families:
            1. Pentameric
               - nicotinic Ach receptor at the NMJ → allows an Na channel to form
               - GABA A receptor which allows a Cl channel to form,
               - 5HT3 receptor
            2. Ionotropic glutamate - NMDA ligand gated ion channels.
               - They form Na, K and (NMDA only) Ca channels when glutamate binds
            3. Purinergic receptors activated by ATP, permeable to Na, K and Ca, and are associated with mechanosensation and pain.
       2. Production of intermediate messengers

Gladwin 2016
• 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:
  1. G proteins (most common) - eg, Nad and Adr
  2. Tyrosine kinase - eg, insulin
  3. Guanylyl cyclase - eg, NO, atrial natriuretic peptide

3. 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.

Examiner Comments

A good answer to this question required candidates to think broadly about how drugs act and have a system for classifying their actions. One possible classification is action via receptors or non-receptor actions. Many candidates used categories such as physiochemical, receptor and enzymes. Common problems were failure to mention a whole class of drug actions e.g. drugs acting via voltage-gated ion channels or gene transcription regulation. Candidates also gave far too much detail in some sections e.g. a description of zero order and first order kinetics is not required. Candidates often did not give examples of the drug action they described.