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PHARMACODYNAMICS

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2023-2024
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PHARMACODYNAMICS

- In Greek

Pharmacon = Drug

Dynamics = Action/Power

It covers all the aspects relating to **“What a drug does to the body”**

- Action: How and Where the effect is produced is called as Action.

- Effect: The type of response producing by drug.

Principles of Drug Action

- The basic types of drug action can be broadly classed as:
- Stimulation
- Depression
- Irritation
- Replacement
- Cytotoxic action

Stimulation

- Selective enhancement of the level of activity of specialized cells.

- Adrenaline stimulates heart.
- Pilocarpine stimulates salivary glands.

Depression

- Selective diminution of activity of specialized cells.
- Barbiturates depress CNS
- Quinidine depresses heart
- Omeprazole depresses gastric acid secretion.

Irritation

- A nonselective, often noxious effect and is particularly applied to less specialized cells (epithelium, connective tissue).
- Strong irritation results in inflammation, corrosion, necrosis and morphological damage.

Replacement

- Use of natural metabolites, hormones or their congeners in deficiency states.

- Insulin in diabetes mellitus
- Iron in anaemia.

Cytotoxic action

- Selective cytotoxic action on invading parasites or cancer cells, attenuating them without significantly affecting the host cells.
- Utilized for cure/palliation of infections and neoplasms.
- e.g. penicillin, chloroquine, zidovudine, cyclophosphamide, etc.

Mechanism of drug action

- Only a handful of drugs act by virtue of their simple physical or chemical property; examples are:

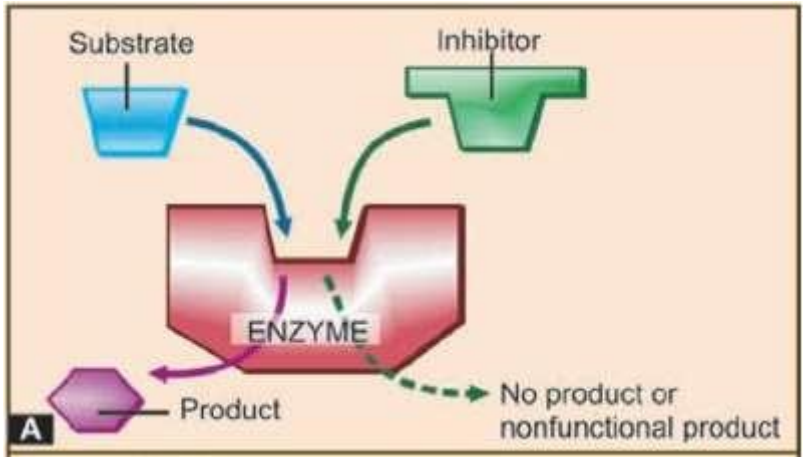
- Bulk laxatives (ispaghula)—physical mass
- Paraamino benzoic acid—absorption of UV rays
- Activated charcoal—adsorptive property
- Mannitol, mag. sulfate—osmotic activity
- ^{131}I and other radioisotopes—radioactivity
- Antacids—neutralization of gastric HCl
- Pot. permanganate—oxidizing property
- Chelating agents (EDTA, dimercaprol)—chelation of heavy metals.

- Majority of drugs produce their effects by interacting with a discrete target biomolecule, which usually is a protein. Such mechanism confers selectivity of action to the drug.

- Functional proteins that are targets of drug action can be grouped into four major categories, viz.
- Enzymes,
- Ion channels,
- Transporters and
- Receptors.

Enzymes

- Almost all biological reactions are carried out under catalytic influence of enzymes;
- Drugs can either increase or decrease the rate of enzymatically mediated reactions.



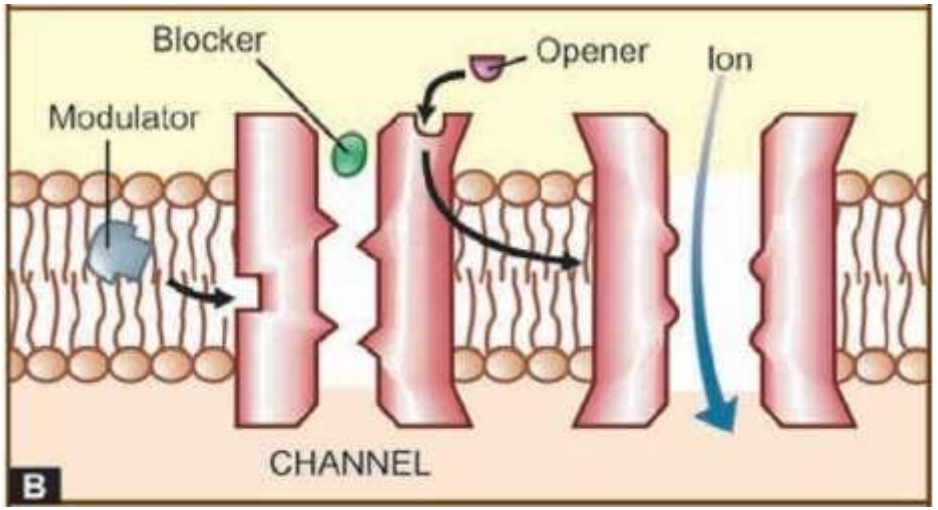
Enzyme inhibition

- Selective inhibition of a particular enzyme is a common mode of drug action.
- Such inhibition is either competitive or non-competitive.

Enzyme	Endogenous substrate	Competitive inhibitor
• Cholinesterase	Acetylcholine	Physostigmine, Neostigmine
• Monoamine-oxidase A (MAO-A)	Catecholamines	Moclobemide
• Dopa decarboxylase	Levodopa	Carbidopa, Benserazide
• Xanthine oxidase	Hypoxanthine	Allopurinol
• Angiotensin converting enzyme (ACE)	Angiotensin-1	Captopril
• 5α-Reductase	Testosterone	Finasteride
• Aromatase	Testosterone, Androstenedione	Letrozole, Anastrozole
• Bacterial folate synthase	Para-amino benzoic acid (PABA)	Sulfadiazine

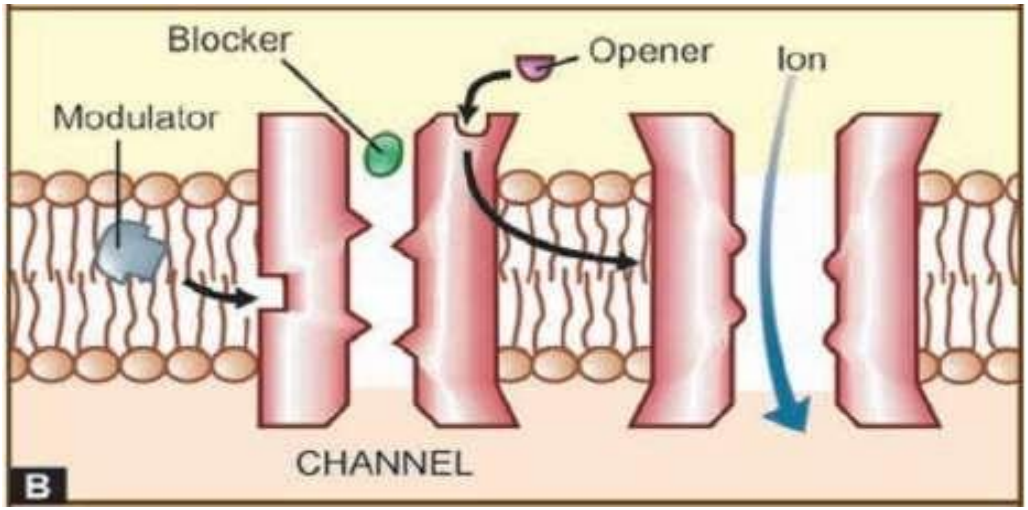
Ion Channels

- *Ligand gated channels* (e.g. nicotinic receptor)
- G-proteins and are termed *G-protein regulated channels* (e.g.cardiacβ1 adrenergic receptor activated Ca2+ channel).



Ion Channels

- Drugs can also act on *voltage operated* and *stretch sensitive channels* by directly binding to the channel and affecting ion movement through it, e.g. local anaesthetics which obstruct voltage sensitive Na+ channels.

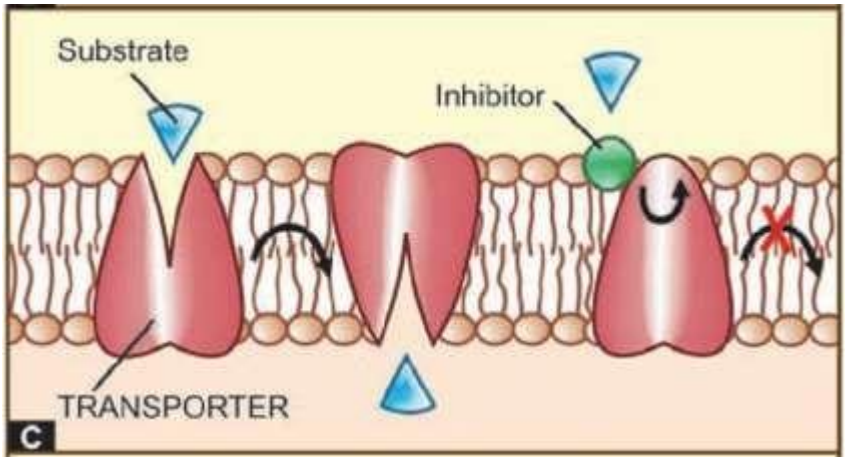


Ion Channels

- Certain drugs modulate opening and closing of the channels, e.g.:
- Nifedipine blocks L-type of voltage sensitive Ca2+ channel.
- Ethosuximide inhibits T-type of Ca2+ channels in thalamic neurones.

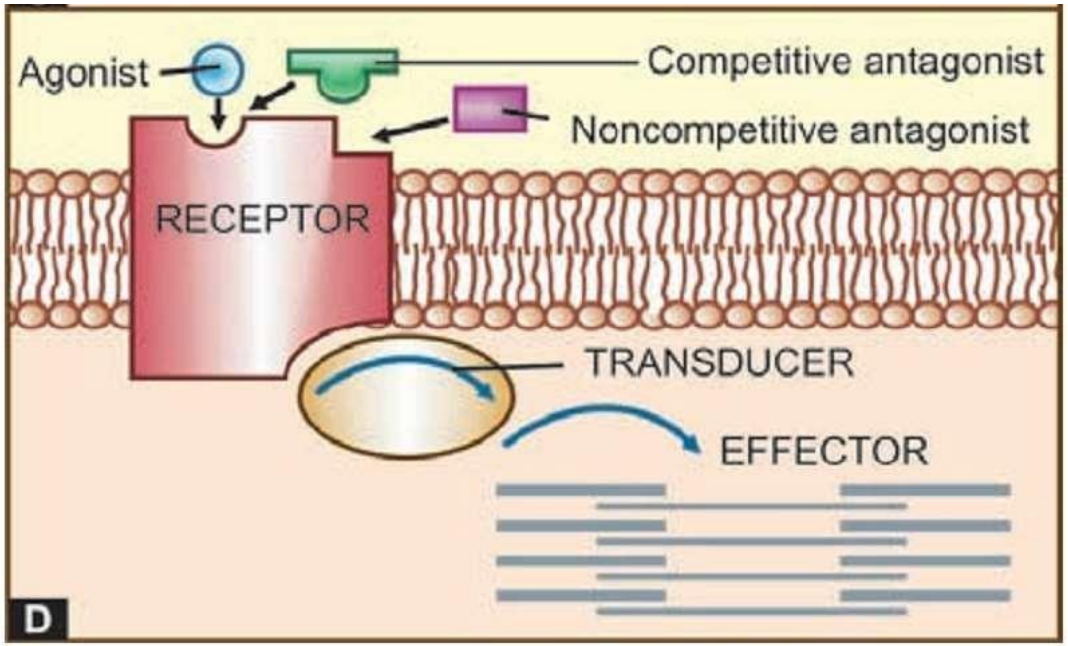
Transporters

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



Receptors

- Macromolecule or binding site located on the surface or inside the effector cell that serves to recognize the signal molecule/drug and initiate the response to it, but itself has no other function.



describing drug-receptor interaction:

- **Agonist:** An agent which activates a 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.
- **Antagonist:** An agent which prevents the action of an agonist on a receptor or the subsequent response, but does not have any effect of its own.
- **Partial agonist:** An agent which activates a receptor to produce submaximal effect but antagonizes the action of a full agonist.

- **Agonists** have both affinity and maximal intrinsic activity (IA = 1), e.g. adrenaline, histamine, morphine.

- **Competitive antagonists** have affinity but no intrinsic activity (IA = 0), e.g. propranolol, atropine, chlorpheniramine, naloxone.

- **Partial agonists** have affinity and submaximal intrinsic activity (IA between 0 and 1), e.g. Dichloro-iso-proterenol (on β adrenergic receptor), pentazocine (on μ opioid receptor).

- **Inverse agonists** have affinity but intrinsic activity with a minus sign (IA between 0 and –1),e.g. chlorpheniramine (on H1 histamine receptor).

Thank You