PHA 2022
Drugs and Society

How Drugs Act

Pharmacodynamics and Pharmacokinetics

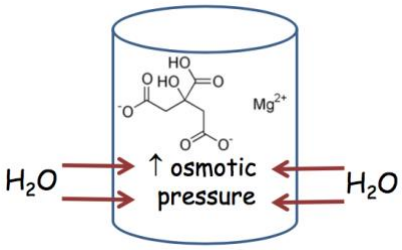
Pharmacodynamics – What a drug does to the body
Pharmacokinetics – Where the drug moves in the body

Non-Specific Mechanisms

Chemical

- Simple drugs
- Direct chemical interaction
- Involve basic inorganic and non complex organic compounds

I.e. Mylanta
Used for hyperacidity – $Mg(OH)_2 + HCl \rightarrow MgCl_2 = H_2O$
I.e. Chelating Agents – Remove heavy metal ions – EDTA



Physical

- Very few drugs work in this way

I.e. Osmosis – Alter fluid balance between body compartments
- GIT – Osmotic laxatives (magnesium citrate)
- Kidney – Osmotic diuretics (mannitol)
I.e. Surfactants –reduce surface tension –Simethicone –decrease pain associated with GI gas

Specific Cellular Targets

- Molecular targets are usually proteins or DNA
- Majority of drugs interact with specific targets

Binding to Protein Targets

- Drugs mimic or block the actions of endogenous factors – compete with ligands
- Ideally, drugs interact with 1 molecular target **– Specificity**
- Reality – Drug has preference for 1 target over others – **Selectivity**

Selectivity of Binding

Dependent on:

- Chemical structure
- Molecular size
- Electrical charge

Selectivity is reciprocal:
The target is selective too, it wont react and bond with anything that passes it
Selectivity is relative:
Related to dose, as an increased dose increases the chance of interacting with other targets

Drugs and Ion Channels

- Ligand gated (receptor)
- Voltage gated
- Maintain voltage gradient and ionic fluxes in excitable cells
- May block or open channels
- Modulates: increasing or decreasing its likelihood

Enzymes

- Drugs may block the active site and compete
- Prostaglandins are mediators of pain and inflammation
- Arachidonic acid (precursor) is synthesised by COX (cyclooxygenase) into prostaglandins and can decrease pain and inflammation

Carrier Molecules

- Transports molecules against their concentration gradient
- Uses active transport
- Can be transporters, symporters or antiporters
- Noradrenaline re-uptake can be inhibited by cocaine

Drugs and Receptors

- Receptors are targets for neurotransmitters and hormones
- Present in either cell membrane, cytoplasm and cell nucleus
- Can block the site for the hormone or neurotransmitter

Example Questions:

- Inhibition of Acetylcholinesterase increases levels of transmitter at receptor
- Blockade of sodium channels reduced paint transmission
- Inhibition of Cyclooxygenase decreased production of inflammatory mediators
- Opening of potassium channels causes relaxing of vascular smooth muscle
- Inhibition of NA transporter protein increases level of transmitter at receptor

Drug and Receptor Interactions

Receptors

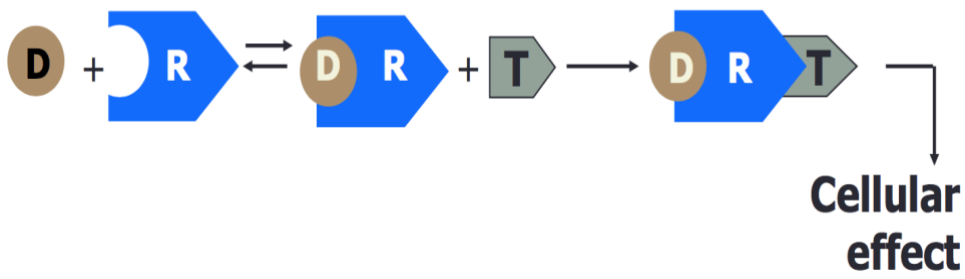
Are chemical mediators that can be neurotransmitters and hormones that interact with specific receptors on the cell membrane, cytoplasm or cell nucleus

Drugs can…

- Mimic endogenous ligand - agonists
- Block action of endogenous ligand – antagonist

First and Second Messenger

- Drug and receptor is a **first messenger system – Lock and Key**
- Drug-Receptor complex and transduction mechanism = **Second Messenger**



4 Super Families of Receptors

Ligand-Gated Ion Channels

- Ionotropic Receptors
- Fast acting hyperpolarises and depolarises
- Nicotinic ACh Receptor

G-Protein Coupled Receptors

- Metabotropic
- Fast acting
- Muscarinic ACh Receptor
- Ca^{2+} release

Kinase-Linked Receptors

- Slow acting (Hours)
- Cytokine Receptors
- Protein phosphorylation and transcription of proteins

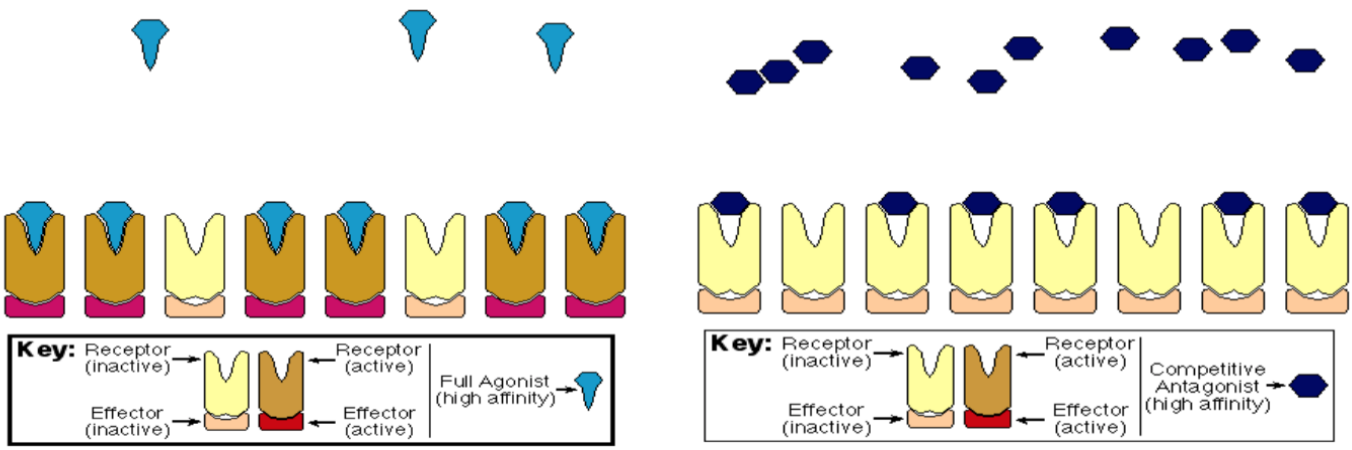
Nuclear Receptors

- Slow acting
- Binds to receptor in the nucleus and causes gene transcription
- Protein synthesis occurs
- Utilises Oestrogen receptors

Lock and Key Model – 3 Possibilities

1. Key does not fit into the lock
2. Key fits into the lock, but it does not unlock it – **Antagonist –** Affinity but no Efficacy
3. Key fits and unlocks the lock – **Agonist –** Affinity and Efficacy

Agonists and Antagonists can be Full or Partial



Effectiveness of a Drug

Dependent on…

- How well it binds to a receptor
- How well it activates the receptor

Affinity – Ability to bind at a receptor site
Efficacy – The consequences of Affinity - Ability of a substance which has bound at a receptor to generate stimulus and produce a biological effect