* Pharmacodynamics-1
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* Learning objectives
* Explain how drugs act
* Classify and describe receptors
* Describe affinity, efficacy and potency of two drugs based on their quantal and graded dose response curve
* Explain full agonist, partial agonist, inverse agonist and antagonist
* By physical action
* By chemical action
* Through antibody production
* placebo effect
* Drug that work without binding to receptor
* Physically
* Osmotically: Mannitol
* Mass (Bulk): isphagula
* Chemically
* Neutralization
* Acidification
* Alkalinization
* What is a Receptor
* Receptor is a macromolecule present on cell surface, cytoplasm or in nucleus where drug binds and interacts to produce cellular changes
* Receptors are Protein and have specificity and selectivity
* Dose response relationship
* The relation between the dose of drug or concentration of drug in plasma and the observed clinical effect can be plotted graphically
* This graph is known as dose response relationship curve (DRC)
* Types of DRC
* Graded DRC:
* This curve when plotted on a graph takes form of a rectangular hyperbola, where as log dose response curve is sigmoid shape
* Quantal dose response curve:
* Certain pharmacological effects which cannot be quantified but can only be said to be present or absent are called quantal responses. e.g drug causing vomiting or ovulation
* Definitions
* Full agonist:
* A drug that when bound to receptor produces 100% of maximum possible biological response or effect.
* Partial agonist
* Drugs which produce less than 100% of the maximum possible biological response no matter how higher their concentration
* Antagonist
* Drugs which bind to receptor but are not capable of producing biological response or effect.
* Inverse agonist
* Drug that binds to receptors but produces biological response opposite to the agonist drug.
* Receptor mediated mechanisms
* Ion channels
* Ion channel
* These are cell surface receptors
* These proteins are selective for a particular ion (Na+, K+, Ca++, Cl–)
* Agonist binding opens these channels and cause depolarization or hyperpolarization
* They are the targets of many important drugs
* Examples of ion channel receptors
* Nicotinic
* These are membrane bound receptors coupled to the effector system (enzyme/channel) through GTP binding proteins called G-proteins.
* Examples:
* Muscarinic cholinergic, adrenoceptors
* Dopaminergic receptors
* Opioid receptors
* GPCR – contd.
* G-proteins and Effectors
* Large number can be distinguished by their α-subunits
* GPCR - 3 Major Pathways  
  (Transducer mechanisms)
* **Adenylyl cyclase:cAMP pathway**
* **Phospholipase C: IP3-DAG pathway**
* **Channel regulation**
* 1. Adenylyl cyclase: cAMP pathway
* 2. Phospholipase C:IP3-DAG pathway
* 3. Channel regulation
* Activated G-proteins can open or close ion channels
* These effects may be without intervention of 2nd messengers – cAMP or IP3/DAG
* Bring about depolarization, hyperpolarization or Ca ++ changes etc.
* Gs – Ca++ channels in myocardium and skeletal muscles
* Go and Gi – open K+ channel in heart and muscle and close Ca+ in neurones
* Enzyme Linked Receptors
* These receptors are directly linked to enzyme like tyrosine kinase or guanylate cyclase
* E.g receptors for peptide hormones like insulin, Atrial Natriuretic Peptide (ANP)
* Intra cellular receptors
* These are intracellular (cytoplasmic or nuclear)
* Receptors for corticosteroids, mineralocorticoids, thyroid hormones, sex hormones and Vit. D etc. stimulate the transcription of genes in the nucleus by binding with specific DNA sequence – called - “Responsive elements”
* Pharmacodynamics-2
* Learning objectives
* Differentiate between different types of antagonists based on its effect on dose response curve with examples.
* Explain the effect of drug concentration on receptor binding
* Compare and contrast the mechanism of cholinergic and adrenergic receptors with distribution and action.
* Explain Therapeutic index and therapeutic window with examples
* Antagonist
* Drugs which bind to receptor but are not capable of producing biological response or effect are called antagonist.
* Drug Antagonism
* The effect of one drug is decreased or abolished in presence of another drug
* Antagonist drug decreases or abolishes the action of agonist.
* Types of antagonism
* Physical antagonism:
* The opposing action of two drugs is due to their physical property
* Example: charcoal adsorbs toxic substances
* Chemical antagonism:
* The opposing action of two drugs is due their chemical property
* Example: antacids neutralize gastric acidity
* Types of antagonism
* Physiological antagonism:
* Two drugs act on different receptors or by different mechanism but have opposite effects on same physiological system
* Examples:
* Histamine and adrenaline on bronchial muscles
* Glucagon and insulin on blood sugar level
* Types of antagonism
* Receptor antagonism: (2 types)
* The antagonist binds to the same receptor as agonist and inhibits its effect
* Competitive antagonism:
* Both agonist and antagonist bind reversibly to same site on receptor
* Non-competitive antagonism:
* The antagonist binds to different site so that agonist cannot displace it from receptor
* Effect of antagonists on dose response curve
* Effect of drug concentration on receptor binding
* The relation is graded drug bound to receptors (B) relates to the concentration of free (unbound) drug (C)
* Contrast between cholinergic receptors & adrenergic receptors
* Cholinergic
* Nicotinic: NN and NM
* Muscarinic: M1, M2, M3, M4 & M5
* Adrenergic receptors
* Alpha receptors
* α1, α2
* Beta receptors
* β1
* β2
* β3
* Mechanism of α receptor action
* Therapeutic index (TI)
* It is index of safety of drug
* TI= Median lethal dose (LD50)

Median effective dose (ED50)

* Wider the value of therapeutic index safer is the drug
* Example penicillin has a high therapeutic index
* Digoxin, lithium, phenytoin have low TI
* Therapeutic window
* The optimal therapeutic range of plasma concentration at which most patients experience desired effect.