Pharmacodynamics

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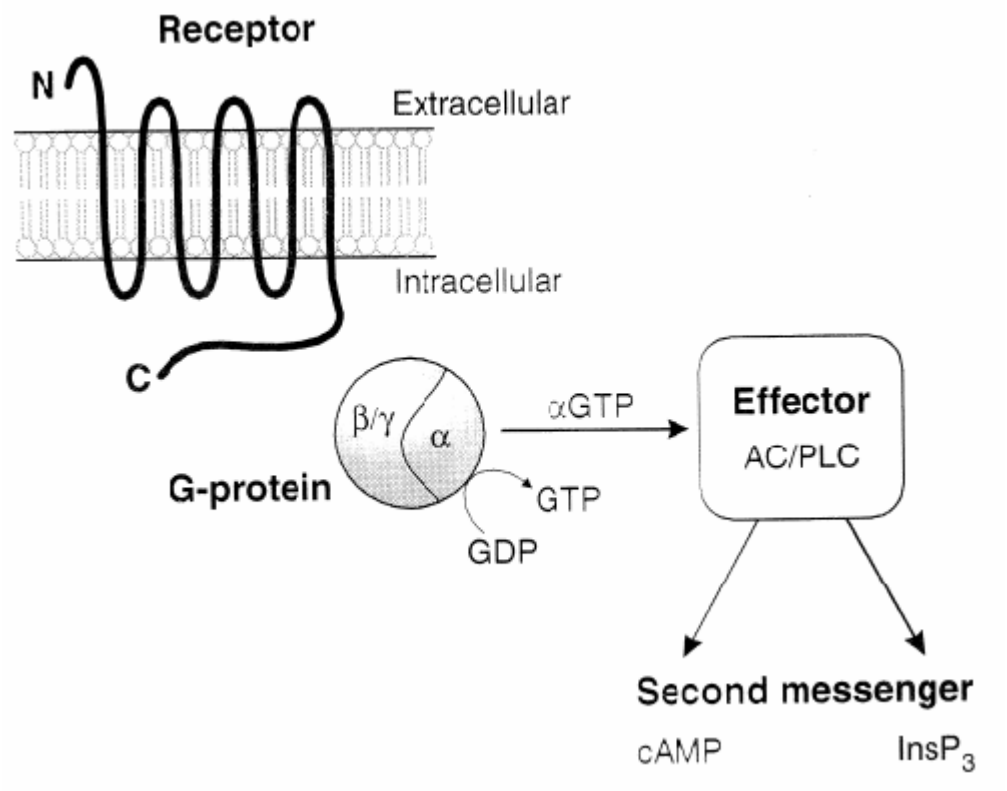
Introduction

- Pharmacodynamics describe the relationship between the concentration of a drug and its pharmacological effect
- Drugs are basically chemicals that bind receptors thereby affecting function

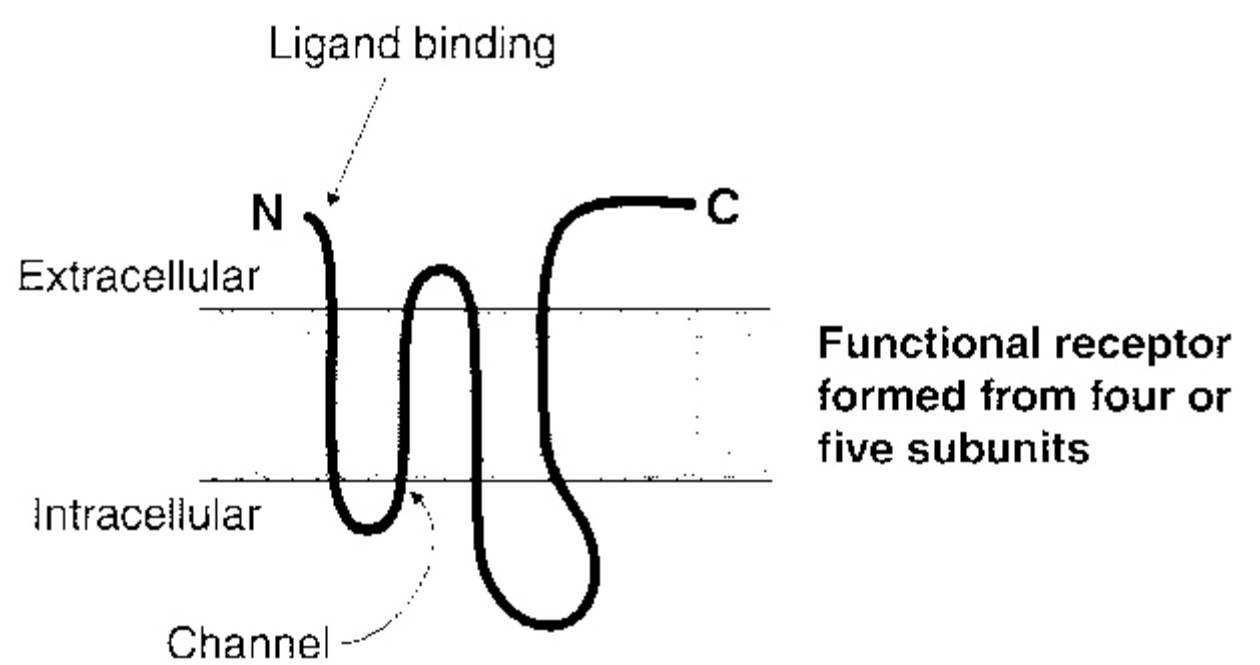
G-Protein coupled receptors



Ligand- gated channels

- Found on the plasma membrane
- Composed of 4 or 5 subunits
- Protein can double as a receptor and an ion channel
- When activated, ions can flow in or out of the cell following their concentration gradients

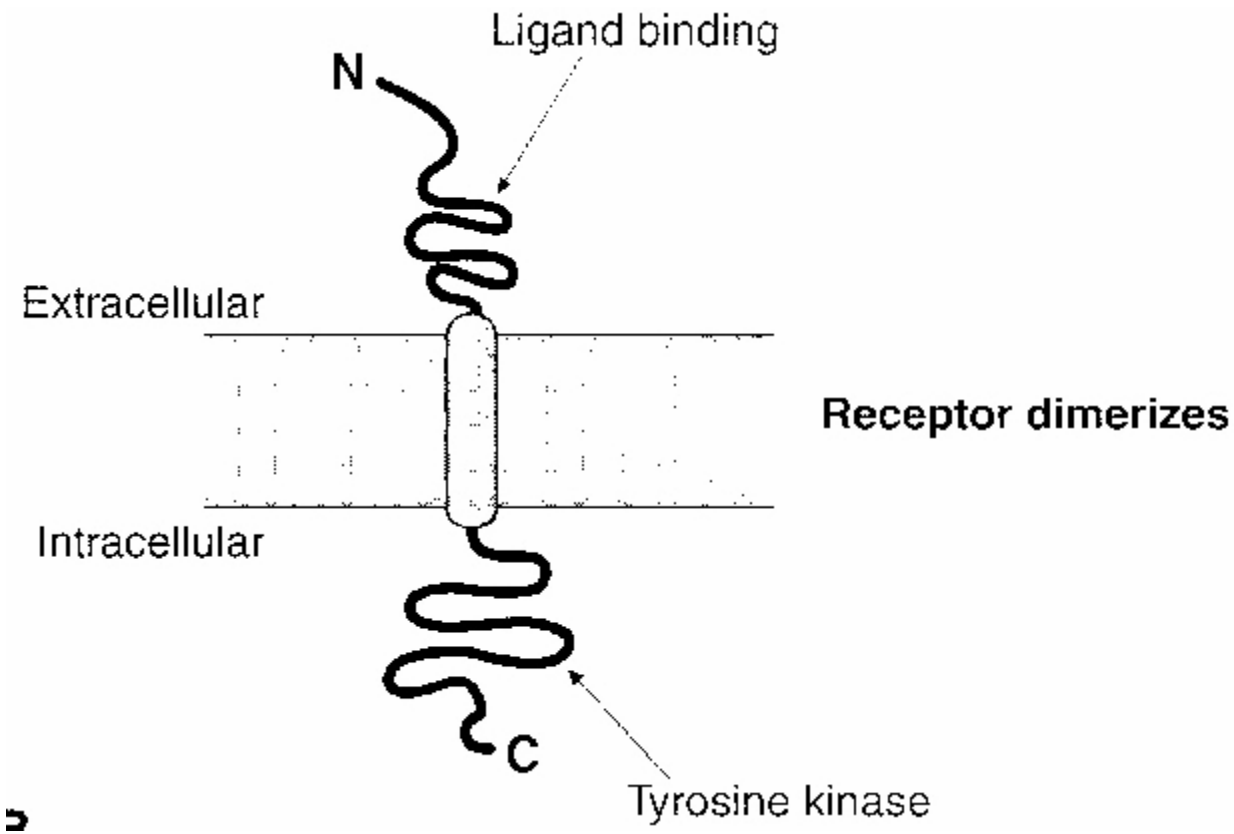
Ligand- gated channel



Tyrosine kinase coupled receptor

- Monomer that spans the membrane only once
- Extracellular portion binds ligand and intracellular portion possesses the tyrosine kinase activity
- When activated, the receptor dimerises and activates intracellular target proteins

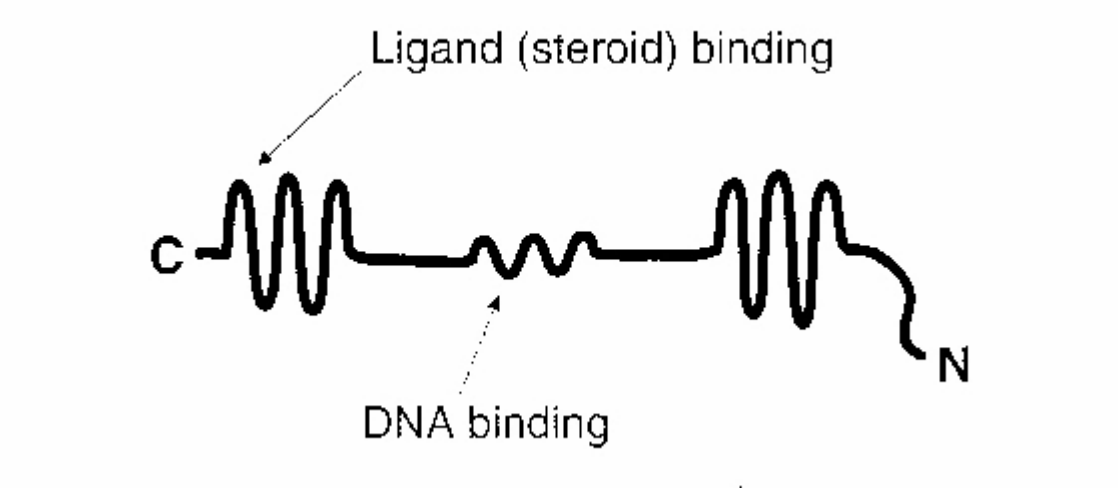
Tyrosine kinase coupled receptor



Intracellular steroid receptors

- Monomeric receptors not found on the plasma membrane
- Possesses a ligand binding domain, a catalytic domain and a set of ‘zinc fingers’
- When inactive, receptor is in the cytosol of the cell
- When activated, it moves to the nucleus and binds to DNA via the ‘zinc fingers’ initiating gene transcription and protein synthesis

Intracellular steroid receptor

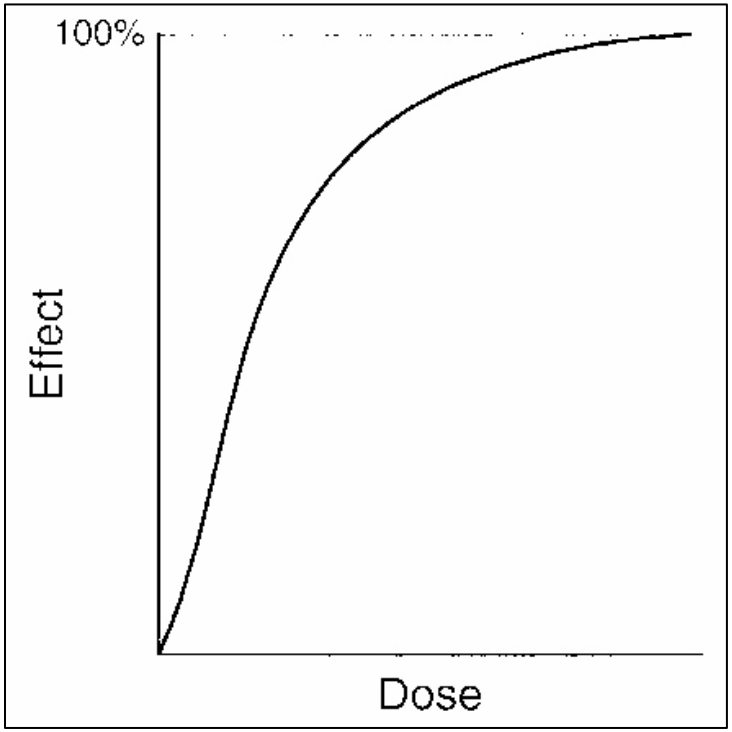


Drug- receptor interactions

- Agonist- ligand binds to a receptor and produces a functional response
  - Full agonist- produces a ‘maximum’ response usually at low levels of receptor occupancy
  - Partial agonist- produces a lower than maximum response even at full receptor occupancy
- Antagonist- ligand binds to a receptor but does not produce a functional response
  - Competitive antagonist- inhibitory effect can be overcome by increasing the amount of agonist i.e. surmountable
  - Non-competitive antagonist- inhibitory effect cannot be overcome i.e. non-surmountable

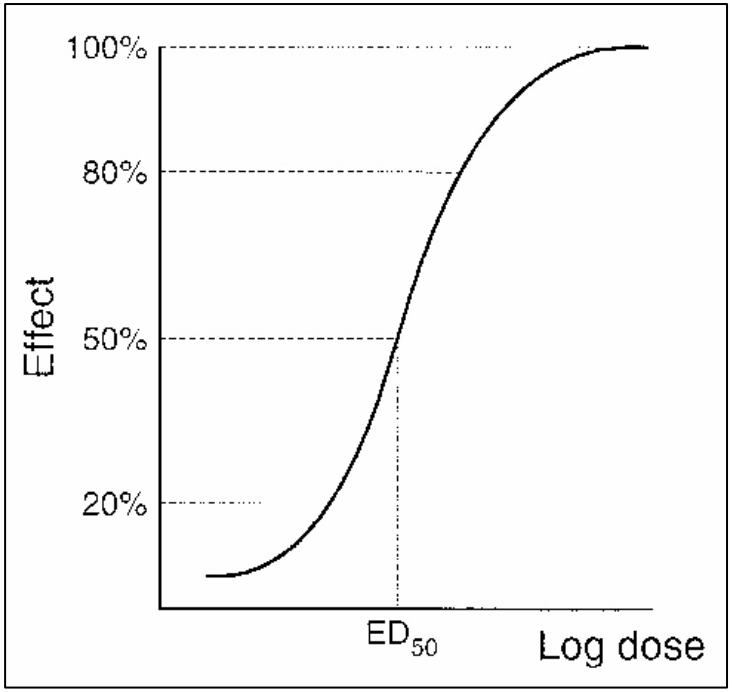
Dose-response relationships

- Relationship between dose and response (effect) experimentally is normally a hyperbola
- However, this relationship is normally expressed as a log dose- response curve



Log dose- response curve

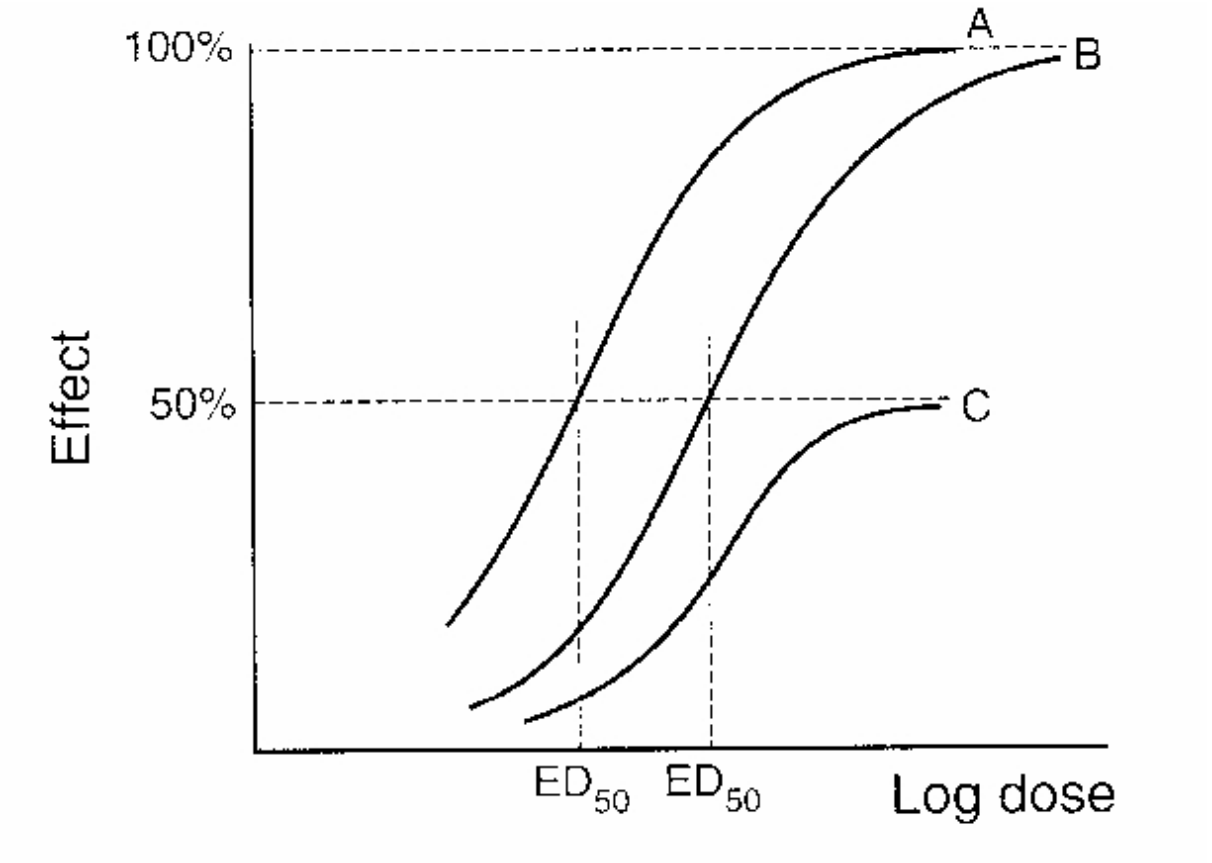
- Typically, a sigmoid curve which is linear between 20% and 80% of maximum effect
- Allows comparison of drugs with large differences in potency (ability to produce a response in terms of concentration of the agonist)



Agonists

- Ligands that bind to a receptor and produces a functional response
- Maximum effect reached as receptors become saturated with rising agonist concentration with regard to full agonists
- Partial agonists produce a full response lower than that of a full agonist

Agonists



Antagonists

- Ligand binds to a receptor but does not produce an effect
- In the presence of a competitive antagonist, maximum effect remains unaltered
- A non-competitive antagonist reduces maximum effect with increasing concentrations

Competitive antagonism

Non-competitive antagonism