• **References:**
  
  • Basic & clinical pharmacology by Katzung
  • Lippincott’s illustrated reviews by Finkel, Cubeddu & Clark
  • Clinical pharmacology by Laurence
Learning Objectives

At the end of pharmacodynamic lectures you should be able to

1. Describe the relationship between drug dose and response, and between log (drug dose) and response

2. Define ‘competitive’ and ‘non-competitive’ antagonism, and indicate, on appropriate graphs, how these may be distinguished

3. Describe the different types of receptor-effectors coupling with reference to: a) ion channels; b) second messengers; c) protein kinases; and d) intracellular receptors
4. Describe what is meant by the terms ‘efficacy’ and ‘affinity’ in describing agonist potency and how these relate to the concepts of ‘spare receptors’ and ‘partial agonists’.
Pharmacology:

Is the science that studies the manner in which the function of the living system is affected by a chemical agent (drug).

*It's divided into two major categories:*

1. **MEDICAL PHARMACOLOGY:**
   Deals with materials used to "prevent, diagnose and treat" diseases.

2. **TOXICOLOGY:**
   Deals with undesirable effects of chemicals in biological systems.
NATURE OF DRUGS:

A drug is any small molecule that when introduced into the body ALTERS the body's functions by interaction at the molecular level (sub-cellular level).

Note: ALTERS means: causes a change in a certain parameter.
CHARACTERISTICS OF DRUGS:

1. MOLECULAR SIZE:

- (Either small as carbon monoxide or large as enzymes).
- The majority of drugs have molecular weight range of (100-1000) which enables them for convenient administration and efficient absorption and distribution.
2. MOLECULAR SHAPE:

Drugs vary in shape and that's of extreme importance because the majority of drugs interact with specific sites within the target tissue called "RECEPTOTS".

The shape of the receptor site determines what kind of drug molecule may interact with it.

Also the shape of the drug molecule must be "Complementary" to the shape of the receptor site to produce an optimal fit.

As the optimal fit increased, the response to the drug increased too.
3. CHEMICAL NATURE:

Drugs also differ in their chemical nature; they are either highly active or inert substances. Many drugs are either weak acids or weak bases.
• **DRUG-BODY INTERACTION**
  • **PHARMACO-DYNAMIC INTERACTION:**
    • Means the effect of drug(s) on the body.
  • **PHARMACO-KINETIC INTERACTION:**
    • Means the way the body handle the drug(s) i.e. Absorption, Distribution, Metabolism Elimination (Excretion) ... (ADME)
**PHARMACO-DYNAMIC INTRACTIONS:**
Mechanisms of drug action:

1. **ON THE CELL MEMBRANE:**
   Mechanisms:
   
   **A) by acting on specific receptors:**
   For example: agonist and antagonist on adrenoceptors. Histamine Receptors. ACH Receptors.

   **B) by interference with selective passage of ions across membrane:**
   For example: Ca$^{+2}$ entry (channel blockers).
**C-by inhibition of membrane bound enzymes or pumps:**

For example: Membrane bound ATPase is inhibited by "Cardiac Glycoside".

Amine Pump (in nerve cells) is inhibited by "Tricyclic Anti-depressant".

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**D-physiochemical interaction:**

for example : General and Local Anesthetics and Alcohol, they appear to act on lipid constituents of the membrane of the nerve cells.
2. ON METABOLIC PROGRESS (WITHIN THE CELL CYTOPLASM):

A-Enzyme Inhibition:
for example: (MAO "Mono Amino Oxidase") is inhibited by "Phenelizine"
(Cholinesterase) is inhibited by "Pyridostiqmine"
(Xanthine Oxidase) is inhibited by "Allopurinol"

B-inhibition of transport process that carry substances across cells:
For example: Anion Transport is inhibited in the renal tubules by "Probenecid" and this may cause:
*A delay in "Penicilllin" excretion
*enhancing the elimination of Urates by inhibiting reabsorption.
**C-Incorporation into larger molecules:**
For example: 5-flourouracil (which is an anti-cancer) into mRNA in place of amino acid Uracil.
I.e. the drug gets into the structure of the large molecules by taking the place of another group e.g. amino acid.

**D- in case of antimicrobial agents,** they act by altering the metabolic processes unique to the microorganism such as "Penicillin" which interferes with the bacterial cell wall formation (inhibits the wall formation).
3. OUTSIDE THE CELL:

A- Direct Chemical Interaction as in case of "Antacids" or "Acid Neutralizers"

Happens in the stomach cavity itself not in the cells...

B- Osmosis as in case of "Purgatives" such as MgSO4 and "Diuretics" such "Manitol".
**RECEPTOR:**

- *Is the component of a cell or a microorganism that interacts with a drug and initiates the chain of biochemical events leading to the drug's observed effect.*

- *Most of the receptors are proteins and when an agonist binds to them these proteins undergo alternation in conformation which induces changes in systems within the cell leading to a response.*
• **DOWN-REGULATION:**
  • When the tissues are continuously exposed to an agonist, the number of receptors decreases, this phenomena is called "Down-Regulation" a causes of "Tachyphylaxis".

• *Tachyphylaxis:* loss of efficacy with frequently repeated doses of a certain drug (only agonist).
• **UP-REGULATION:**

  • Prolonged contact of receptors with antagonists leads to the formation of new receptors.

• For example: {up-regulation} following abrupt withdrawal of β-adrenoceptors blockers causes Angina Pectoris worsening.
• RELATION BETWEEN RECEPTORS AND CLINICAL USES OF DRUGS:

• 1) Receptors determine the "Qualitative" relation between dose or (concentration) of a drug and its pharmacological effect.

• I.e. the receptors' affinity for binding determines the concentration of the drug required while the total number of receptors limits the maximum effect a drug may produce.
2) Receptors are responsible for "Selectivity" of a drug action (Good Drugs are the selective ones i.e. less side effects).

The Molecular SIZE, SHAPE and ELECTRICAL CHARGE of the drug will bind to a particular receptor among the huge number of chemically different binding sites available in a cell, an animal or a patient.

(i.e. the molecular SIZE, SHAPE and the CHARGE determines the "Selectivity"}.
• **3) Receptors mediate the action of pharmacological antagonism; it means that it prevents the action of an agonist.**

• The effect of a pure antagonist on a cell or in a patient depends entirely upon preventing the action of agonist molecule from binding to the receptor.
Thank you