Lecture-1-pharmacology

Principle of drugs

Drugs are medications or other substances that have a physiological effect when introduced to the body. There are four basic stages for a medication to go through within the human body: absorption, distribution, metabolism, and excretion

Adverse Effect: An unintended and potentially dangerous pharmacological effect that occurs when a medication is administered correctly.

Receptor, molecule, generally a protein, that receives signals for a cell. Small molecules, such as hormones outside the cell or second messengers inside the cell, bind tightly and specifically to their receptors.

Affinity: The strength of binding between drug and receptor.

Agonist: A drug that binds to a "receptor" and produces an effect.

Antagonist: A molecule that prevents the action of other molecules, often by competing for a cellular receptor; opposite of agonist.

metabolic degradation .

Tachyphylaxis: term is used to describe a decrease in responsiveness to a drug which develops in a few minutes?

Pharmacokinetics of drugs
(ADME)

b) Drug biotransformation in the organism.(effect of body one drug)

- **Absorption**
- **Distribution**
- **Metabolism**
- **Excretion of drugs**

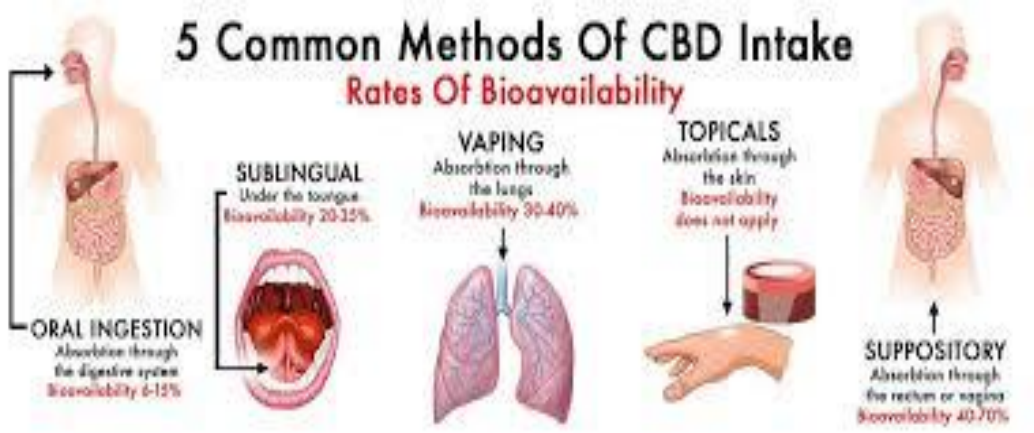
Is the passage of drug through cell membranes to reach its site of action.

Mechanisms of drug absorption

1. **Simple diffusion = passive diffusion.**
2. **Active transport.**
3. **Facilitated diffusion.**
4. **Pinocytosis (Endocytosis).**
    - **water soluble drug (ionized or polar) is readily absorbed via aqueous channels or pores in cell membrane.**
    - **Lipid soluble drug (nonionized or non polar) is readily absorbed via cell membrane itself.**

Bioavailability
is the rate and extent to which an administered drug reaches the systemic circulation. For example, if 100 mg of a drug is administered orally and 70 mg is absorbed unchanged, the bio availability is 0.7 or 70%.

Bioavailability = AUC ORALLY / AUC I.V X 100



Drug distribution is the process by which a drug reversibly leaves the bloodstream and enters the interstitium (extracellular fluid) and the tissues. The distribution of a drug from the plasma to the interstitium depends on cardiac output and local blood flow, capillary permeability, the tissue volume, the degree of binding of the drug to plasma and tissue proteins, and the relative lipophilicity of the drug.

Half life (t ½) is the time required to:

a) Change the amount of a drug in plasma by half during elimination (length of the time required for 50% of drug to be cleared from the body .

T1/2=0.693XVD/CL

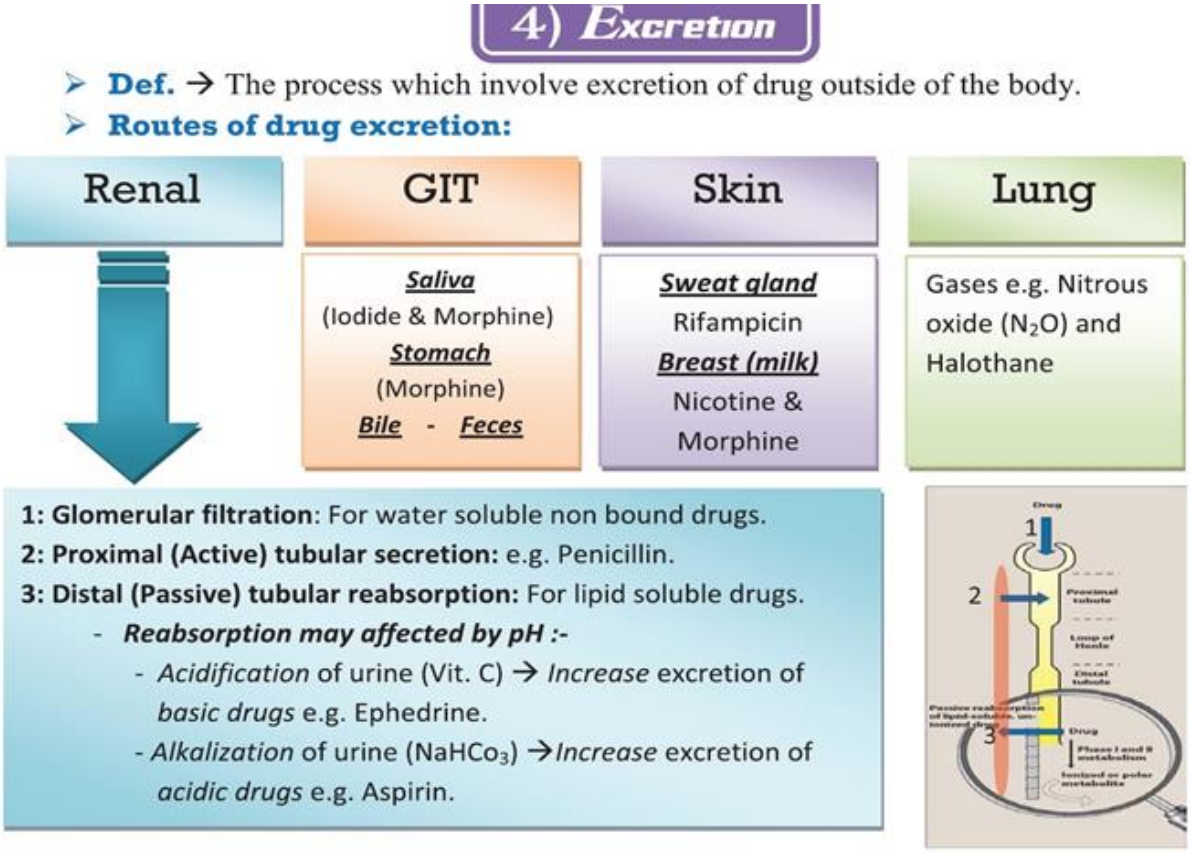
Metabolism

- Liver is the primary site for metabolism .
- Most of the drugs are inactivated by metabolism.
-

Phase I: Phase I reactions convert lipophilic drugs into more polar molecules by introducing or unmasking a polar functional group, such as –OH or –NH2. Phase I

reactions usually involve reduction, oxidation, or hydrolysis. Phase I metabolism may increase, decrease, or have no effect on pharmacologic activity.

Phase II: This phase consists of conjugation reactions. If the metabolite from phase I metabolism is sufficiently polar, it can be excreted by the kidneys. However, many phase I metabolites are still too lipophilic to be excreted. A subsequent conjugation reaction with an endogenous substrate, such as glucuronic acid, sulfuric acid, acetic acid, or an amino acid, results in polar, usually more water-soluble compounds that are often therapeutically inactive.



Pharmacodynamics describes the actions of a drug on the body and the influence of drug concentrations on the magnitude of the response.

Mechanism of Action of Drugs

Drug act either by receptor or by non receptor Drug produce their effect through interacting with some chemical compartment of living organism c/s Receptor.

Receptors are macromolecules Most are proteins Present either on the cell surface, cytoplasm or in the nucleus

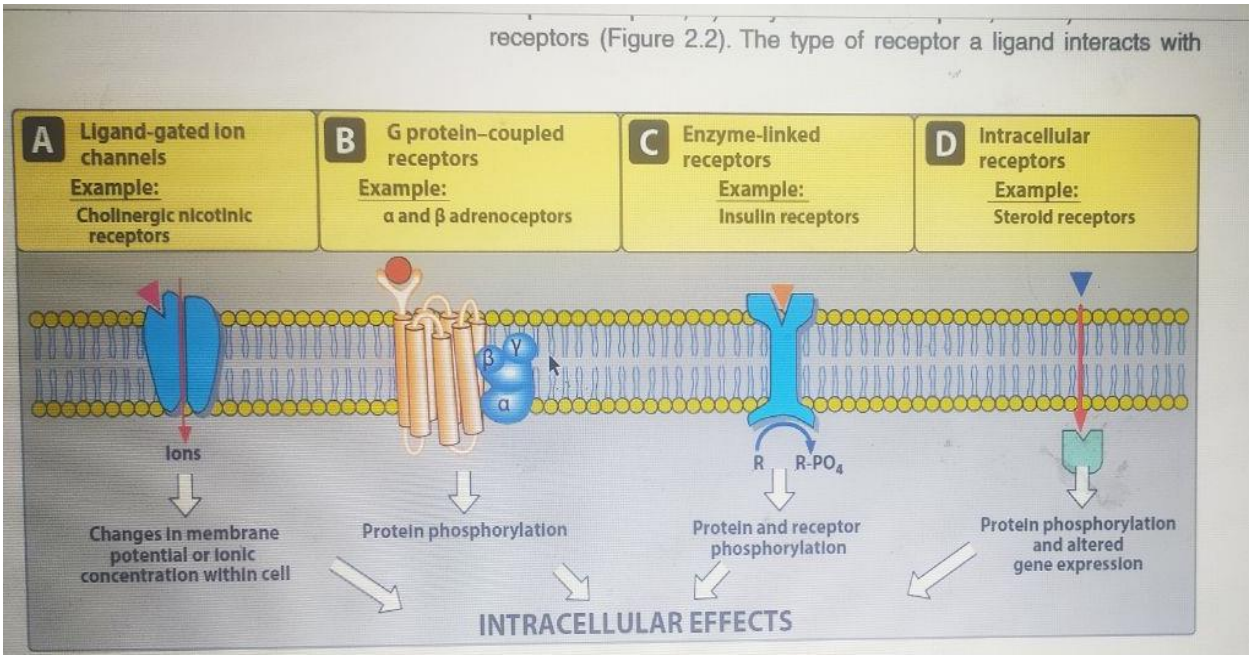
1. Selectivity:- Degree of complimentary co relation between drug and receptor.

Ex:- Adrenaline Selectivity for α, ß Receptor

2. Affinity:- Ability of drug to get bound to the receptor.

3. Intrinsic activity (IA) or Efficacy:- Ability of drug to produce a pharmacological response after making the drug receptor complex.

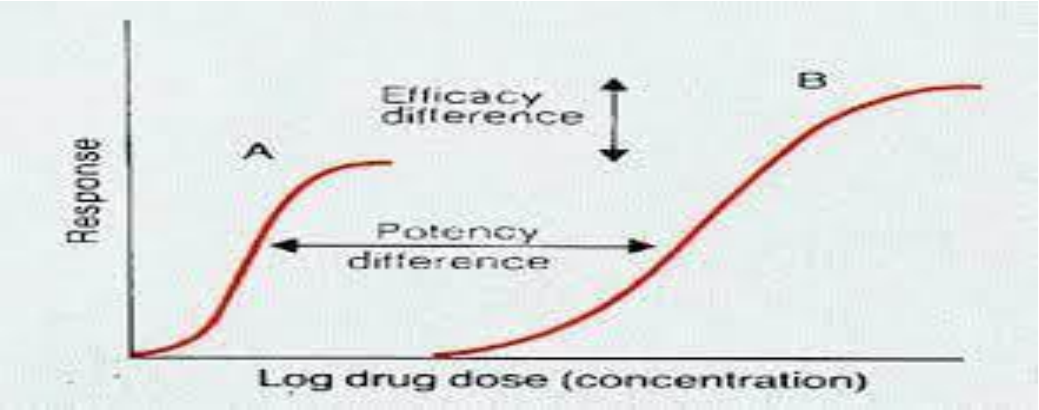
TYPES OF RECEPTORS

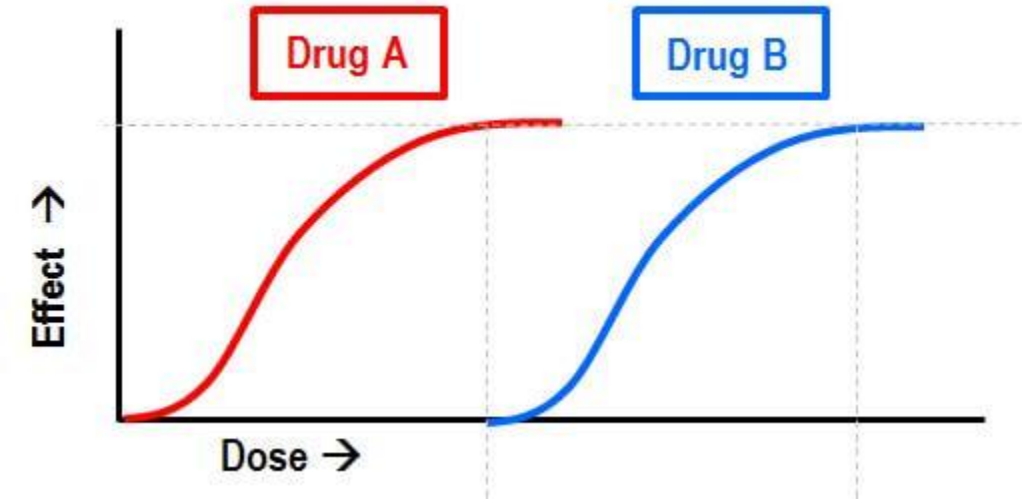


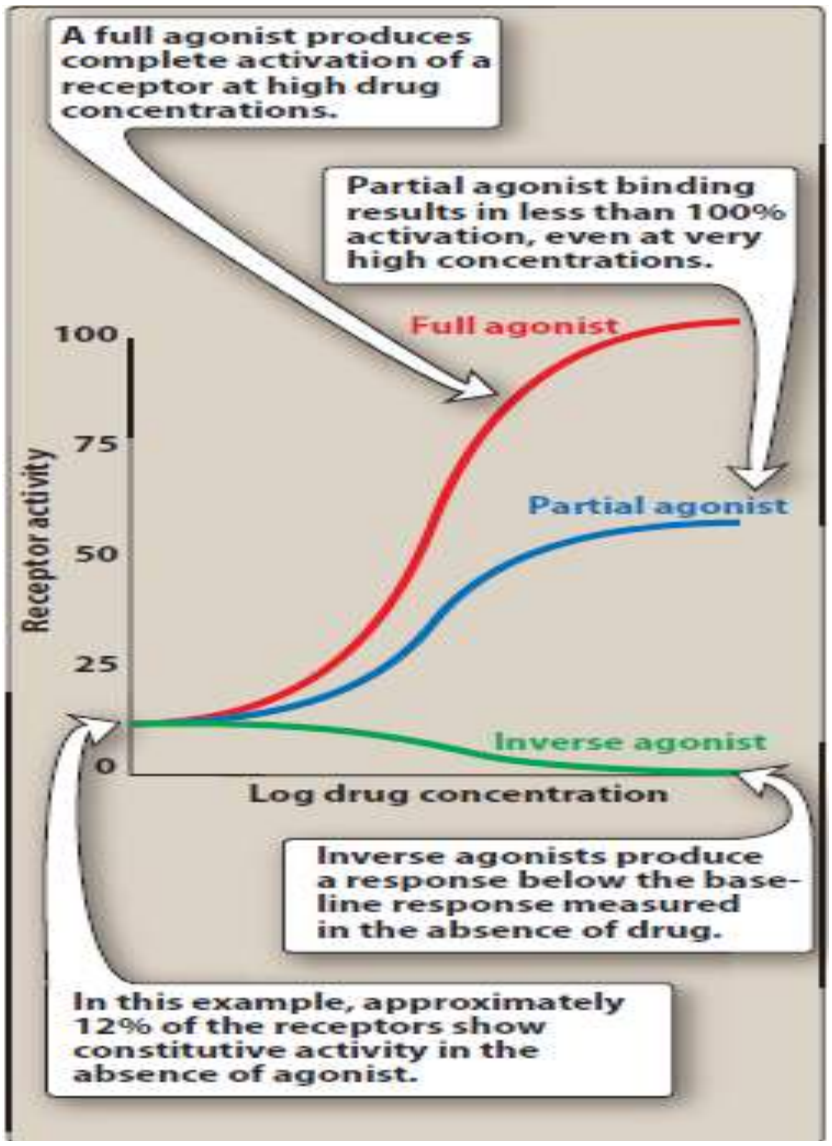
Potency is a measure of the amount of drug necessary to produce an effect of a given magnitude. The concentration of drug producing 50% of the maximum effect

(EC50) is usually used to determine potency. The therapeutic dose range for candesartan is 4 to 32 mg, as compared to 75 to 300 mg for irbesartan.

Efficacy: is the magnitude of response a drug causes when it interacts with a receptor. Efficacy is dependent on the number of drug–receptor complexes formed and the intrinsic activity of the drug (its ability to activate the receptor and cause a cellular response).






A full agonist produces complete activation of a receptor at high drug concentrations.
Partial agonist binding results in less than 100% activation, even at very high concentrations.
Full agonist
Partial agonist
Inverse agonist
100
75
50
25
0
Receptor activity
Log drug concentration
Inverse agonists produce a response below the base-line response measured in the absence of drug.
In this example, approximately 12% of the receptors show constitutive activity in the absence of agonist.