

Drug - Receptor and Pharmacodynamics

most drugs exert their effects, both beneficial and harmful by interacting with receptors.

Receptors: special target macromolecules present on the cell surface or intracellular.

receptor ~~bind~~ bind drugs and mediate their pharmacologic action.

Drug may interact with:

- enzymes
- nucleic acids
- membrane receptors

in each case the formation of the drug receptor complex leads to a biologic response.

Drug + receptor \rightleftharpoons Drug-receptor complex \rightarrow Biologic effect

* Chemistry of Receptors

interaction of receptors with ^{drug} ligands involves the formation of chemical bonds, most commonly

- electrostatic and hydrogen bonds

major Receptor (types)

Pharmacology define a receptor = any biologic molecule to which a drug bind and produces a measurable response.

This enzyme and structural Proteins can be considered to be pharmacologic receptors.

These receptors may be divided into 4 families:

1- Ligand-gated ion channels

ex cholinergic nicotinic receptors

regulation of the flow of ions across cell membrane

2- G Protein-coupled receptors

ex: α and β adrenoreceptors

3- Enzyme-linked receptors:

ex: Insulin receptors

4- Intracellular receptors:

ex: steroid receptors

Dose-Response relationships

agonist is defined as an agent that can bind to a receptor and elicit a response. The magnitude of the drug effect depends on its concentration at the receptor site.

A- Graded dose-response relation-

- The concentration of a drug increases the pharmacologic effect also increases.
- The relationship between dose and response is a continuous.



- The response is a graded effect, meaning that the response is continuous and gradual.

B- Quantal response \rightarrow all-or-nothing response.

A graph of the relationship is known as a **graded dose-response curve**.

1- Potency:

Two important properties of drugs can be determined by a graded dose-response curve.

The first is Potency, a measure of the amount of drug necessary to produce an effect.

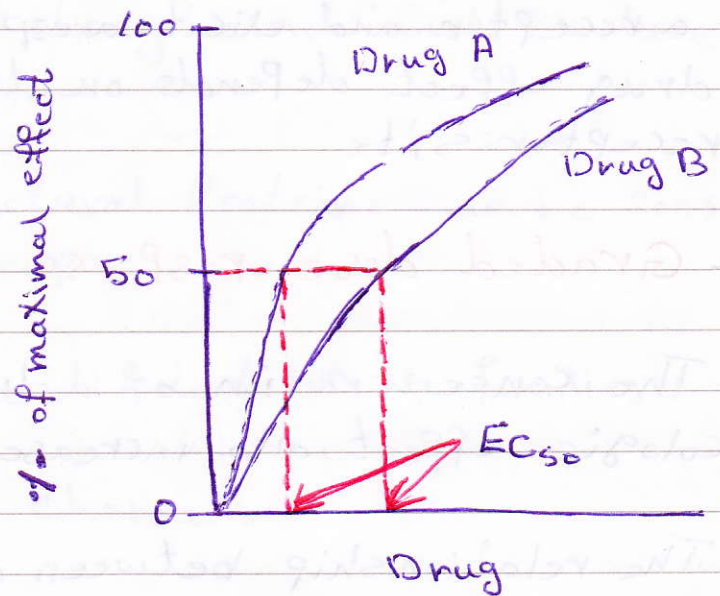
The conc. Producing effect that is fifty percent 50%.

of the maximum is used to determine Potency

$= EC_{50}$

Drug A is more
Potent than Drug B

EC_{50} - is the affinity
of the drug for the
receptor.

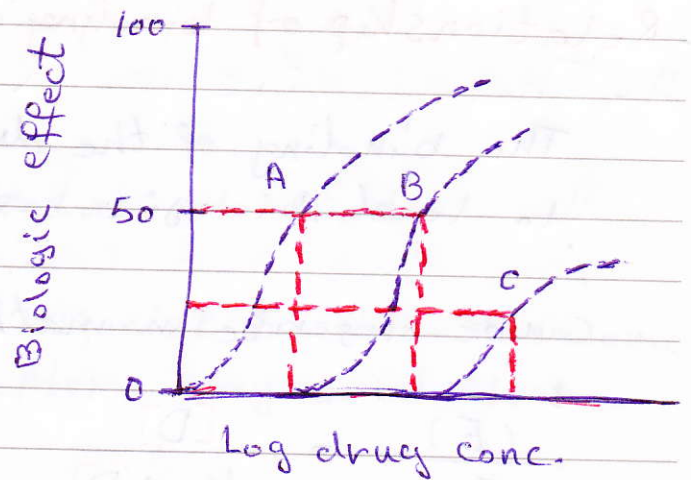


2- Efficacy:

The second Property of drugs

- efficacy can be determined from graded dose-response plots.
- Efficacy is dependent on the number of drug-receptor complexes formed and the efficiency of coupling of receptor activation to cellular response.
- The maximal response (E_{max}) or efficacy is more important than drug potency.
- Drug with greater efficacy is more therapeutically beneficial than one that is more potent.

- Drug A is more Potent than Drug B, but both its Same efficacy.



- Drug C lower Potency and lower efficacy than Drug A and B.

3- Drug receptor binding:

The Quantitative between drug conc- and receptor occupancy.

we can mathematically express the relationship between the Percentage or fraction of bound receptor and the drug conc.

$$\frac{[D-R]}{[R_t]} = \frac{[D]}{K_d + [D]}$$



D = conc. of free drug

$D-R$ = conc. of bound drug

R_t = total conc. of receptor = free receptor + bound receptor

K_d = disassociation constant for the drug from the receptor

$$K_d = \frac{[D][R]}{[DR]}$$

4- Relationship of binding to effect.

The binding of the drug to its receptor initiates to lead biologic response.

Can be describe in mathematical

$$\frac{(E)}{(E_{max})} = \frac{[D]}{K_d + [D]}$$

E = effect of the drug at conc. $[D]$

E_{max} = maximal effect of the drug.

5- Agonists:

drug binds to receptor and produce a biologic response

ex: Phenylephrine is an agonist at α_1 adrenoceptor

because produce effect that resemble to the action of the endogenous norepinephrine.

6- Antagonists:

Drug that decrease the action of another drug or endogenous.

antagonism may occur in several ways:

1- on receptor

2- no intrinsic activity \rightarrow Produce no effect

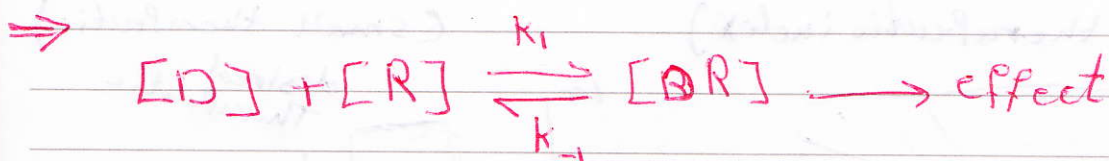
if both the antagonist and agonist bind to the same ~~receptor~~ site on the receptor. they said to be (Competitive)

ex: antihypertensive drug (Prazosin) Competes with the endogenous (norepinephrine) at α_1 adrenoceptor

B. Quantal Dose response relationships

The response are known as quantal response because for any individual the effect either occurs or it dose not.

Dose response Curves



at equilibrium:

$$[D] \times [R] \times k_1 = [DR] \times k_{-1}$$

$k_1 / k_{-1} = \text{affinity const.}$

$k_{-1} / k_1 = \text{dissociation const. (Kd)}$

The lower the Kd the more potent the drug.

A-Therapeutic index:

The Therapeutic index of a drug is the ratio of the dose that produces toxicity to the dose that produces a clinically desired or effective response in a population of individuals.

$$\text{Therapeutic index} = \frac{TD_{50}}{ED_{50}}$$

TD_{50} = The drug dose that produces a toxic effect in half population.

ED_{50} = The drug dose that produces a therapeutic or desired response in half population.

The therapeutic index is a measure of a drug's

safety, because a large value indicates that there is a wide margin between doses that are effective and that doses are toxic.

(Large therapeutic index)

(small therapeutic)

