

# Lec 1: Definition of pharmacology, Drugs: Classification and naming

\*Pharmacology  $\Rightarrow$  it is the science that deals with interaction of drugs with living system.

\*What is drugs  $\Rightarrow$  These are chemical substances that shows biological activity [treatment, diagnosis]

## Division of pharmacology

1. pharmacokinetic

[what the body does to the drug]

this deal with :-

1- administration

2- absorption

3- distribution.

4- elimination

2. pharmacodynamics.

[what the drug does to the body]

this deal with :-

1- action of drug on living system

2- the type or quality of action

3- its quantitative & mechanism of action

4- Adverse effect & safety of drug on body.

\*target organ or tissue  $\Rightarrow$  the main organ or Tissue on which the drug act, and for ~~which~~ which it is used therapeutically.

Other topics linked with pharmacology :-

①  $\rightarrow$  pharmacotherapeutics  $\rightarrow$  proper use of drugs in treatment of disease

②  $\rightarrow$  clinical pharmacology  $\rightarrow$  Drug pharmacology.  
 $\rightarrow$  clinical ~~pharmacology~~ <sup>evaluation</sup> in treating disease

a. clinical trials.

b. surveillance studies  $\leftarrow$  <sup>③</sup>  $\rightarrow$  <sup>④</sup>

③  $\rightarrow$  chemotherapy  $\rightarrow$  use of drug to inhibit <sup>①</sup> growth or <sup>②</sup> kill other.

b. Cancer cell

a. Microbes

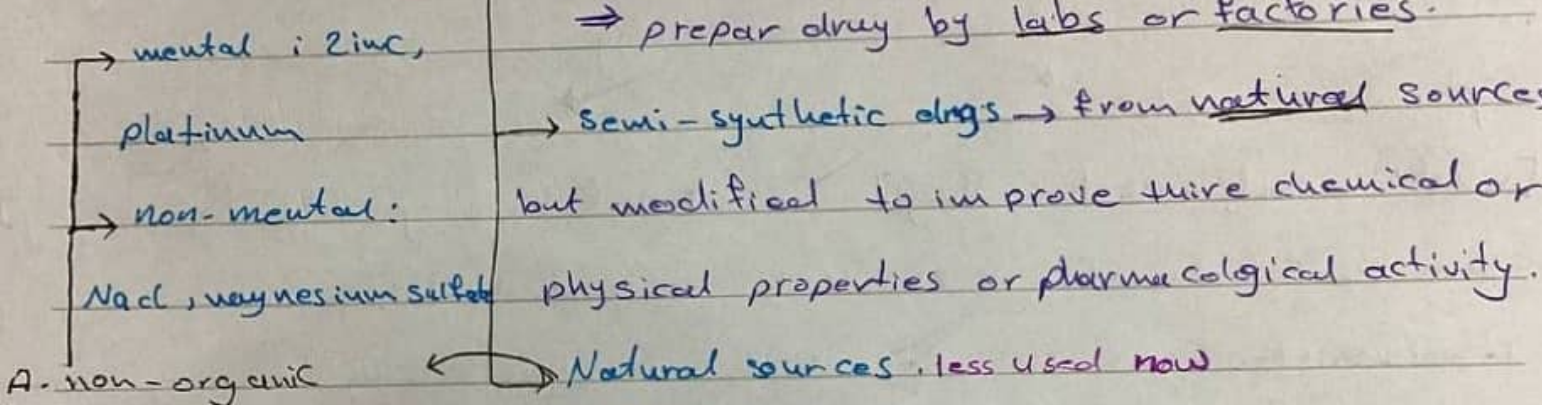
$\downarrow$   
cyto-toxic-anti cancer drugs.

$\downarrow$   
anti-microbial agents

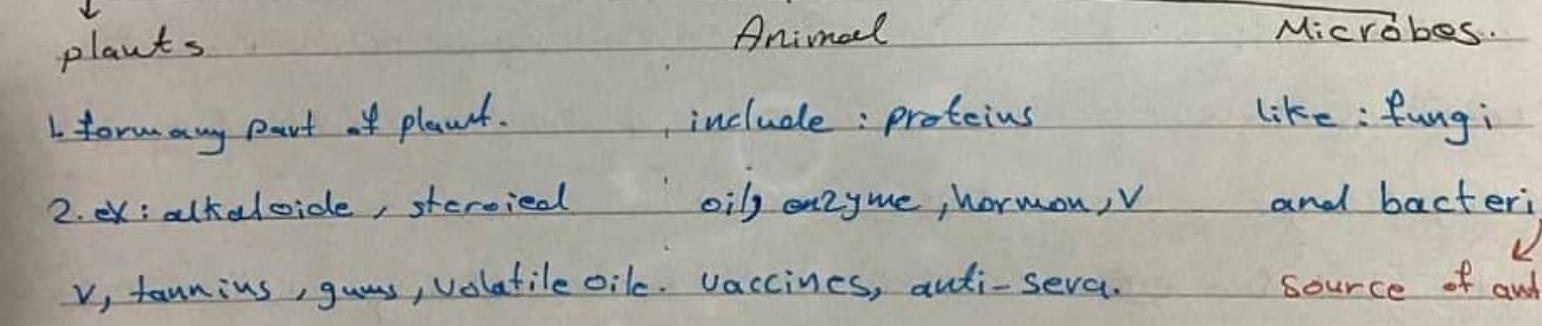
(ii) **pharmacy** → is the science and profession that is concerned with the preparation, storage, dispensing and proper utilization of drug product

→ **Toxicology** → is the science that deals with harmful effect of chemical [including drugs]

\* **Sources of drugs** → synthetic sources. ((common at present))



B. **organic sources.**



Alkaloids: small organic molecules have nitrogen (ex) atropine, morphine, caffeine, theophylline, quinine

\* **Dose Forms of DRUGS** :- → physical form of drug product that suitable for administration.

- Type of drug dose forms:**
- 1. oral
  - 2. Inhalational
  - 3. Topical
  - 4. parenteral
  - 5. suppository → Vaginal / Rectal
- ↳ IV / IP / IP / SC
- IM / IT.

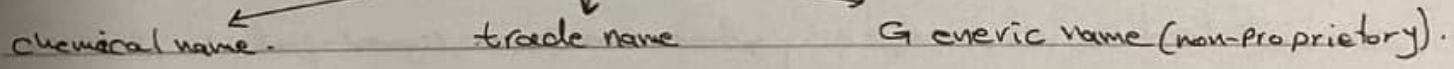
For drug derived from nature the plant species & genus of drug chemistry are included in their name.  
 ex. A. belladonna alkaloids from atropa belladonna.  
 B. digitalis glycosides from Digitalis leaves.

Topical: A. cream, gel, ointment, lotion. B. eye drop (ophthalmic)  
 C. ear drop (otic) D. skin patch. (transdermal)  
 Inhalation: A. Aerosol B. Inhaler C. vaporizer (solutions)  
 oral: A. pill: Tablets and capsules. B. Liquid: syrup or suspension  
 C. powder D. Herbal plant: seeds, leaves etc.. E. pastes.

\* drugs classification there is no fixed role.

- therapeutic use: anti-hypertensive, anti-microbial drugs, anaesthetics, hypoglycaemic, anticoagulants.
- type of pharmacological action: → shaped by precise [local or general anaesthetics]
- according to molecular or cellular site of action in target cell
- physiological system of acting: CNS/GI/RS ...
- chemical nature or source. drug that have similarity in their pharmacological profile classified by common chemical groups or structure ex → steroid, benzodiazepine

« Drugs Names »



- |   |                                    |   |
|---|------------------------------------|---|
| 1. its complex so that is not usually used to name drugs. | 1. given by pharmaceutical company | 1. given by official pharmaceutical bodies                                |
| 2. sometime shorthand name based on a simple chemical.    | 2. drug can have many brand name   | 2. present in (BP/USP) pharmacopoeias.                                    |
|   |                                    | 3. Approved scientific name.  |
|   |                                    | 4. used in scientific publication and prescriptions esp                   |
|   |                                    | 5. may have common name.  |
|   |                                    | ex. alol → beta-blocker   |
|   |                                    | 6. few drug have more one generic name (eg) - Cocaine → local anaesthetic |

A. Noradrenalin / adrenaline → UK but Norepinephrin / epinephrin → USA & WHO



## Lec 2: Pharmacodynamic I

\* Drug can act through :- 1- physical action: product a response by its physical properties. ex 1. Mannitol as diuretic because it  $\uparrow$  osmolarity.  
2. radio-isotopes. ionizing radiation.

2- simple chemical reaction. act through chemical reaction.  
ex 1. Gastric antacids neutralizing the stomach acidity with base.  
2. chelating agent bind heavy metals in body.

3- receptor 1. specialized target macromolecule mostly protein  
2. present in the cell surface or intracellular  
3. bind a drug and mediate its pharmacological action.  
4. receptor can be enzymes & nucleic acid & structural proteins

\* Ligand: that molecule bind to the receptor can be peptide hormones and neurotransmitter  $\Rightarrow$  Ligand binding changes the conformation of the receptor leading to cellular response

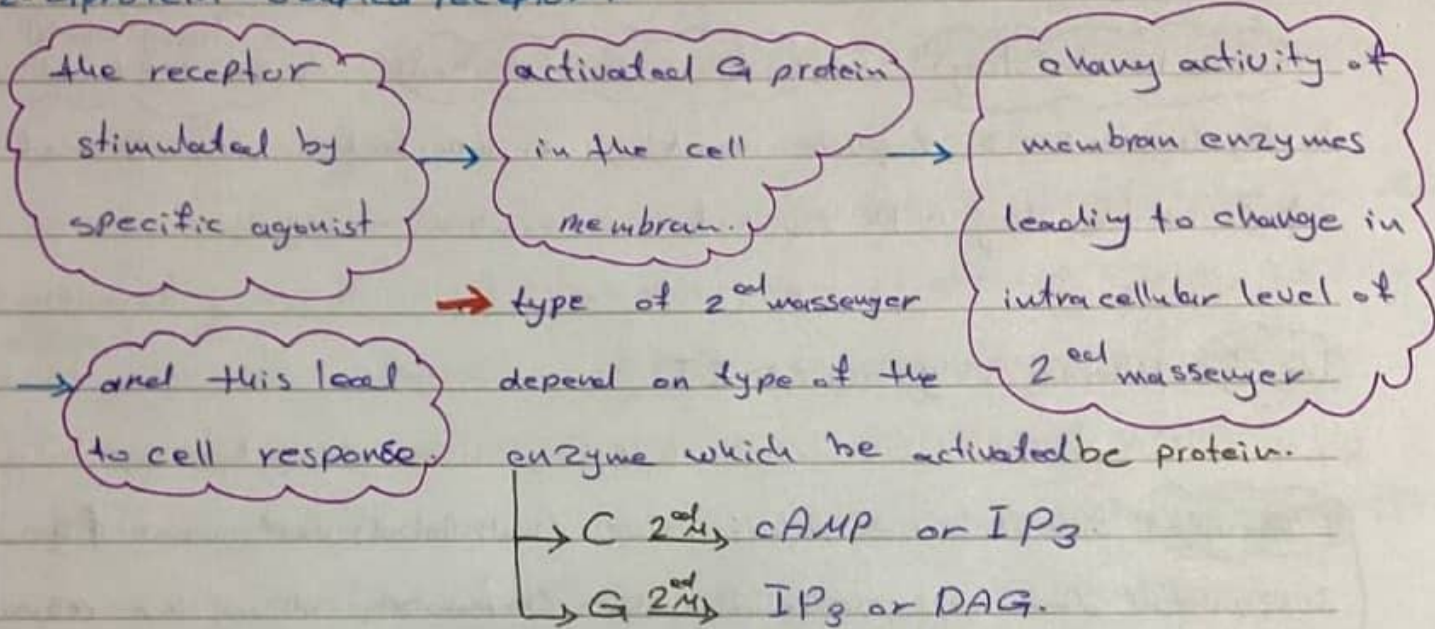
\* classification of receptor

- transmembrane ligand-gated ion channels.
- G-protein-coupled receptor.
- enzyme-linked receptor
- intracellular receptor

### ① Ligand-gated ion channel.

1. present in the wall of ion channel in cell membrane.
  2. when they opened lead to movement of ions across cell membrane.
  3. they activated by specific agonist.
  4. their function including neurotransmitter / cardiac contraction and muscle contraction.
- ex  $\rightarrow$  Nicotinic receptor  
 $\rightarrow$  GABA receptor

## 2. G-protein-coupled receptor:-



## 3. Enzyme-linked receptor:-

- receptor for insulin.
- for growth factor like EGF or PDGF
- receptor for immune cytokines.

## 4. intracellular receptor:- steroid receptor.

1. located in cytoplasm or nucleus → thyroid hormone or VD<sub>3</sub>.
2. the agonist must cross cell membrane to inside of cell. activate it.

## \* Type of ligand-receptor interaction. / not every ligand bind to receptor

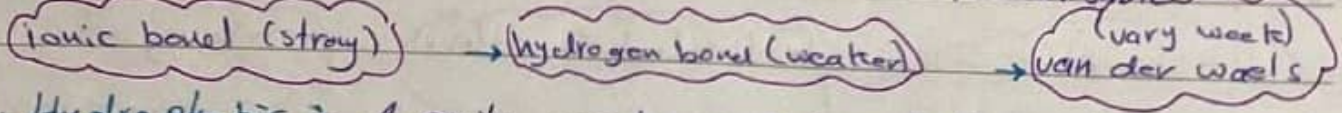
1. Full agonist. 100 efficacy / maximal biological response.
2. partial agonist. between 10-100 efficacy
3. antagonist bind to receptor but don't activate it.
4. Inverse agonist. negative efficacy. / bind to same receptor as agonist.

## \* Type of drug-receptor binding. drug interact with receptor by chemical

- forces or bond
- Covalent. strong & not reversible
  - Electrostatic reversible.
  - Hydrophobic

→ Drug with which bind by weak bond their receptor more selective than drug bind by very strong bond. because weak bond require very precise fit at the drug to its receptor if interaction is to occur

2. Electrostatic 1. much common than covalent / reversible.



3. Hydrophobic :- 1. quite weak 2. important in interaction of highly lipid-soluble drug with lipid of cell membrane.

lec 3 Pharmacodynamics II



\* The relation between dose and response exhibited as following:

1. Graded dose-response relationships (individual) continuous & gradual

2. Quantal dose-response relationships (population) all or non response

1. the magnitude of drug effect depend on [drug] at receptor site.

2. ↑ [drug] → ↑ the magnitude of its pharmacologic effect

3. the Graded D-R curve described as a rectangular hyperbola.

4. 2 important properties of drug can be determined by G-D-R

- ↳ A. potency B. Efficacy

Potency :- the [drug] producing an effect that 1/50 of maximum used to determine potency as EC50

Efficacy :- depend on 1. number drug-receptor complex 2. efficiency of the coupling receptor activation.

- potency affected by :- 1. efficacy 2. Affinity 3. [receptor]

maximal efficacy (E<sub>max</sub>) of a drug assumes that all receptor are occupied by the drug, and no ↑ in response will be observed if more drugs are added.

critical number of EC50 is more potent.

→ A drug with greater efficacy is more therapeutically beneficial than a drug that is more potent.

antagonist + agonist → No effect. → الغالب

\* Antagonist: give dose but there is No effect. 3 types

- 1. chemical antagonist:
  - A. alkaline antacids → neutralize HCl in stomach of peptic ulcer patient.
  - B. protamine (basic) neutralize the anti-coagulant heparin (acidic) in plasma
  - C. chelating agent. bind with heavy metal to prevent tissue toxicity.

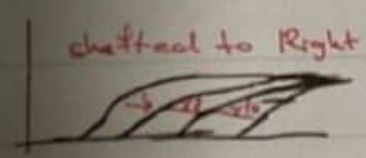
2. physiological antagonist. ex Adrenalin act antagonist to histamine

agonist A + agonist (not give oppsite effect to A) → No effect.

3. pharmacological antagonist. Ligand interact with receptor but give No effect

<p>A. competitive reversible</p> <p>antagonist &amp; agonist have same chemical structure so that competes for binding with the receptor</p> <p>↓ [agonist] so that the antagonist bind to receptor and give No effect.</p>	<p>B. non-competitive</p> <p>1. Irreversible antagonist either</p> <p>A. the antagonist bind to agonist receptor by covalent bond</p> <p>B. dissociate very slowly from receptor</p>	<p>C. uncompetitive</p> <p>Allosteric antagonist.</p> <p>antagonist bind to Allosteric site of agonist receptor</p> <p>↓ change agonist receptor</p> <p>↓ No effect.</p> <p><u>note:</u> drug can bind to another allosteric site on agonist receptor lead to ↑ bind the agonist to receptor this called Allosteric enhancement</p>
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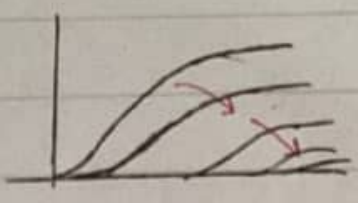
↑ [agonist] agonist is restored and give effect



↑ [antagonist] → shifted to Right

ex: 1. Atropine → Ach

2. Beta-blockers → adrenalin.



# shifted slightly to the Right.

↑ [antagonist]

↓ depression of maximal response.

ex → Binding of Benzodiazepine to GABA-A receptor can enhance the GABA effect.

ex → Binding of Benzodiazepine to GABA-A receptor can enhance the GABA effect.

the irreversible non-competitive & uncompetitive & Allosteric have same dose-response curve.

c. uncompetitive antagonist. antagonist bind on different receptor of agonist so that the effect of agonist is blocked. ~~it is not~~

\* Receptor regulation.

Receptor up-regulation

↑ in number of receptor and affinity of specific receptor (supersensitivity)  
prolonged use ← receptor antagonist → disease

here there is lack of binding of antagonist for long period time

Receptor down regulation. ~~tolerance.~~

↓ number and affinity of available receptor due to prolonged occupation by agonist & continued use of receptor agonist  
↑ dose of agonist → restore the intensity of response.

⇒ Tachyphylaxis = rapidly developing receptor tolerance.

⇒ causes of variation in pharmacologic responsiveness.

1. variation in [drug] that reaches the receptor  $\frac{d_{50}}{d_0}$  Pharmacokinetic factor

2. abnormality in receptor number or function  $\frac{d_{50}}{d_0}$  up or down regulation

3. post-receptor defect inside cell

4. variation in concentration of an endogenous receptor ligand