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

*Pharmacology ⟹ it is the science that deals with interaction of drugs with Living system.

*what is drugs ⟹ These are chemical substances that shows biological activity [treatment, diagnosis]

Division of pharmacology.

1. pharmacoKinetic
[what the body dose to the drug]
this deal with :-
1- administration
2- absorption
3- distribution.
4- elimination

2. pharmacodynamics.
[what the drug dose 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- Advers effect & safety of drug on body.

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

Other topics linked with pharmacology :-

① → pharmacotherapeutics → proper use of drugs in treatment of diseases

② → clinical pharmacology → Drug pharmacology.
→ clinical ~~pharmacology~~ evaluation in treating disease
a. clinical trials. b. surveillance studies (done by)

③ → chemotherapy → use of drug to ihibit① growth or ~~kill either~~ ②
b. Cancer cell → cyto-toxic-anti cancer drugs.
a. Microbes → anti-microbial agents

- pharmacy → is the science and profession that is concerned with the preparation, storge, dispensing and proper utilization of drug prod
- Toxicology → is the scince that deals with harmful effect of chemical [including drugs]

* Sources of drugs → synthetic sources. ((common at present))
  ⇒ prepar drug by labs or factories.
  - A. non-organic
    - mental : zinc, platinum
    - non-mental: Nacl, magnesium sulfate
  - Natural sources. less used now
    - semi-synthetic drugs → from natural sources but modified to improve their chemical or physical properties or pharmacological activity.
  - B. organic sources.
    - plants: 1. form any part of plant. 2. ex: alkaloide, steroical, tannins, gums, volatile oils.
    - Animal: include: proteins oils enzyme, hormon, vaccines, anti-sera.
    - Microbes: like: fungi and bacteria ↙ source of anti

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

* Dose forms of DRugs :- → physical form of drug product that suitable form administration.

Type of drug close forms : 1. oral 2. inhalational 3. Topical 4. parenteral 5. suppository → Vaginal / Rectal

↳ IV / ID / IP / SC
IM / IT

:- for drug drived from natur the plant species & genus of drug chemestry are included in there name.

ex. A. baladona alkaloide from → atropa balladona.

B. digitalis glycosides from → Digitalis leaves.

Topical :- A. crame, gel, ointment / lotion. B. eye drop (ophthalmic)

C ear drop ~~otic~~ (otic) D. skin paleh. (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, anasthetics, hypoglycamic, anticoagulants.

→ type of pharmacological action :- → shoted by precise [local or general anaethetics]

→ according to molecular or cellular site of action in target cell

→ physiological system acting :- CNS / GI / RS ...

→ chemical nature or sorce. drug that have similarity in their pharmacology profil classified by common chemical groupe or structure ex → steroied, benzodiazepine

<< Drugs Names >>

chemical name.	trade name	Generic name (non-proprietory).
1. its complex so that is not usualy used to name drugs.	1. given be specific pharmaceutical Company	1. given by offical pharmaceutical bodies
2. Sometime shorthand name based on a simple chemical.	2. drug can have many brand name	2. present in (BP / USP) pharmacopeas.
		3. Approved scientific name.
		4. used in scintific publication and Prescriptions esp
		5. may have Common ending. ex. olol → beta-blocker
6. few drug have more the Generic Name (eg)		-caine → local anaethetic

A. Paradrenalin / adrenalin → UK and 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 ↑ osmolarity.

2. radio-isotopes. ionizing radiation.

2- simple chemical reaction. act through chemical reaction.

ex 1. Gastric anatacids neutralizing the stomach acidity with base.

2. chelating agent bind heavy metals in body.

3. receptor 1. specilized target macromolecule mostly protien

2- present in the cell surface or intra cellular

3 bind a drug and mediate its pharmacological action.

4. receptor can be enzymes & nucleic acid & structural proting

* Ligand :- that molecule bind to the receptor can be peptide hormons and neurotransmitter ⇒ Ligand binding changes the conformation of the receptor leading to cellular response

* classification of receptor → transmembrane ligand-gated ionchannele.
→ G-protien-coupled receptor.
→ enzyme-linked receptor
→ intra cellular receptor

① Ligand-gated ion channel.

1. present in the wall of ion channell in cell membran.

2 when they opened lead to movment of ions across cell membran.

3. they activated by specific agonist.

4 there function including neurotransmitter / cardic contraction and muscle contraction. ex → ~~Nitro~~ Nicotinic receptor
→ GABA receptor

2- Gprotein -Coupled receptor :-

the receptor stimulated by specific agonist → activated G protein in the cell membrane. → change activity of membran enzymes leading to change in intracellular level of 2nd messenger → and this lead to cell response

→ type of 2nd messenger depend on type of the enzyme which be activated bc protein.

- C 2nd → cAMP or IP_3
- G 2nd → IP_3 or DAG.

3. Enzyme -linked receptor :- eg → 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 hormon or VD_3.

2. the agonist Must cross cell membran to inside of cell. activat it.

*Type of ligand - receptor interaction. / not every ligand that 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 activat 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 reversable.
- → Hydrophobic

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

2- Electrostatic 1. much common than covalent 1revarsible.

(Ionic bond (strong)) → (hydrogen bond (weaker)) → (van der waels (very weak))

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

(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 by determined by G-D-R
   → A. potency B. Efficacy

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

- potency affected by:- 1. efficacy 2. Affinity 3. [receptor] 4. efficiency of stimulus-response

⇐ كل ما كانت كمية ال dose يلي احتجتها حتى EC50 أقل (critical number) تكون ال more potent.

Efficacy:- depend on.

1. number drug-receptor complex
2. efficiency of the coupling receptor activation.

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

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

antagonist + agonist → No effect. → بالعكس

* Antagonist :- give dose but ther is No effect. 3 types

1. chemical anagonist : 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

A. competive reversible antagonist & agonist have same chemical structure so that competes for binding with the receptor

↓ [agonist] so that the antagonist bind to receptor and give No effect.

↑ [agonist] agonist is restored and give effect

shifted to Right

↑ [antagonist] → ↑ shifted to Right

ex: 1. Atropine → Ach

2. Beta-blockers → adrenalin.

B. non-competitive.

1. Irreversible antagonist either

A the antagonist bind to agonist receptor by covalent bond

B. dissociate very slowly from receptor

↑ [agonist] → No effect.

different

shifted slightly to the Right.

↑ [antagonist] → ↑ depression (تثبيط) of maximal response.

C. uncompetive.

Alosteric antagonist.

1 antagonist bind to Alostric site of agonist receptor

cause agonist receptor

No effect.

note: drug can bind to another alostric site on agonist receptor lead to ↑ bind the agonist to receptor this called Alostric enhancement → effect

this lead to

ex → Binding of Benzodi.. to GAMA-A receptor can enhance (تعزيز) the GABA effect.

the irreversible non-competitive & uncometitive & Allostric have same dose-respons curve.

c. uncompetive antagonist. antagonist bind on different receptor of agonist so that the effect of agonist is blocked.

* Receptor regulation.

Receptor up-regulation

↑ in number of receptor and affinity of specific receptor (supersensituity)

occur with prolonged use ← receptor antagonist. → disease

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

≠ tolerance.

Receptor down-regulation.

↓ number and affinity of available receptor due to Prolonged occupation by agonist & continued use of receptor agonis

↑ 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 $\xrightarrow{\text{due to.}}$ Pharmacokinetic factor

2. abnormality in receptor number or function $\xrightarrow{\text{due to}}$ up or down regulation

3. post-receptor defect inside cell

4. variation in concentration of an endogenous receptor Ligand