Date

PROTEIN BINDING :

- The phenomenon of complex formation of drugs with proteins is called as Protein-binding.

- Binding of drugs to plasma proteins is a major determinant in drug distribution.

- This binding is both, reversible & irreversible in nature.

- Reversible binding → weak chemical bonds
  ↓
  Hydrogen bonds
  Hydrophobic bonds
  Ionic bonds
  Vander waal's forces

- Irreversible binding → covalent bond.

⇒ Order of binding :

Albumin > α_1 acid glycoproteins > Lipoproteins
> Globulins.

#

Date

- Albumin : All types of drugs.
- α_1-acid glycoprotein : Basic drugs, imipramine, lidocaine

- Lipoproteins : Basic, Liphophilic drugs, chlorpromarine.

- α_1 globulin : steroids.
- α_2 globulin : Vitamins A, D, E & K
- Heamoglobin : Phenytoin, Pentobarbitol, phenothiazines.

- When the drug appears in circulation, the following things happen:
  (i) A fraction of drug molecules bind with plasma proteins and another fraction remains free.

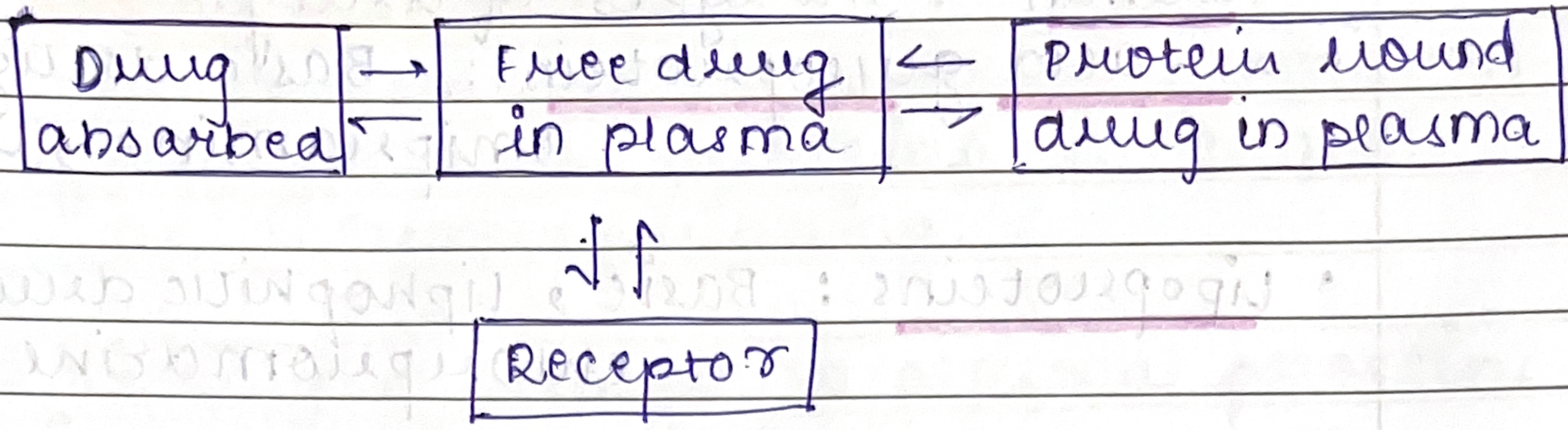
  (ii) There is always an equilibrium between bound and free drug concentration.

  (iii) In general, the binding is reversible and follows law of Mass action.

- The bound drug is kept in the blood stream while the unbound drug is either excreted or metabolized.

#_____

Date


Drug absaribed
Free drug in plasma
Protein round drug in plasma
Receptor
P'carological and therapeutic respanse

#

Date

KINETICS OF PROTEIN - DRUG BINDING :

If [P] represents protein and [D] represents drug,
Then applying law of mass action to reversible protein-drug binding, the equation will be as follows:

$$[P] + [D] = [PD]$$

Protein Drug Protein-drug complex

The association constant [K] can be expressed as follows:

$$ka = \frac{[PD]}{[P][D]}$$

OR

$$ka[P][D] = [PD] \quad \text{—— (1)}$$

where,
[P] = conc. of protein
[D] = conc. of drug
[PD] = conc. of protein - drug complex
ka = Association rate constant.

⇒ If total protein is supposed to be $[P_T]$, then:

$$[P_T] = [P] + [PD]$$

OR

$$[P] = [P_T] - [PD] \quad \text{—— (2)}$$

#

Date

By substituting eqn (2) in eqn (1), we get:

$$[PD] = Ka[D][P_T - PD]$$

$$[PD] = Ka[D][P_T] - Ka[D][PD]$$

$$Ka[D][P_T] = [PD] + Ka[D][PD]$$

$$Ka[D][P_T] = [PD](1 + Ka[D])$$

$$[PD] = \frac{Ka[D][P_T]}{(1 + Ka[D])}$$

$\Rightarrow$ Dividing both sides by $[P_T]$:

$$\frac{[PD]}{[P_T]} = \frac{Ka[D]}{1 + Ka[D]}$$

Here,

r = $\frac{\text{moles of drug bound}}{\text{total moles of protein}}$

$$r = \frac{[PD]}{[P_T]}$$

$$\therefore \frac{[PD]}{[P_T]} = \frac{Ka[D]}{(1 + Ka[D])}$$

From above equation:

$$r = \frac{Ka[D]}{(1 + Ka[D])}$$

#