MEDICINAL CHEMISTRY-I – BP402T

UNIT: 1

CLASS: 7

TOPIC: FACTORS INFLUENCING PROTEIN BINDING OF DRUGS

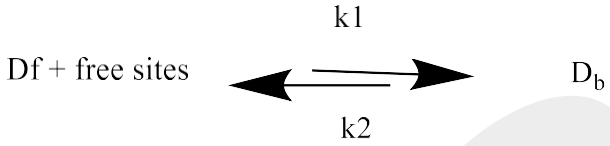
The phenomenon of complex formation with protein is called protein binding of drugs.

- Drug binding to plasma proteins affects drug distribution and elimination as well as the pharmacological effect of a drug.
- The high molecular weight of plasma proteins restrict their passage across capillaries and their low lipid solubility prevents them from crossing the cell membrane.
- Analogously, binding of drugs to plasma proteins restrict their passage across cell membranes.
- Only that fraction of the drug concentration that is freely circulating or unbound can penetrate the cell membrane and be subject to glomerular filtration.
- Because, the interaction of drugs with plasma proteins is a rapidly reversible process, the plasma protein-binding phenomenon as being temporary storage of a drug, subject to instant recall.
- Drug binding to plasma proteins may be attributed to weak chemical bonds namely
    i.) Ionic
    ii.) Vanderwalls
    iii.) Hydrophobic and
    iv.) Hydrogen bonding

The most important contribution to drug binding in the plasma is made by albumin, which comprises approximately 50% of the total plasma protein.

- Albumin binds a wide variety of drug molecules and plays a particularly important role in the binding of weak acidic and neutral drugs.

- α_1 acid glycoprotein is another important binding protein with an affinity for basic drugs.
- The drug protein interaction can be described by applying the law of mass action



D_f and D_B represent free and bound drug
K1 and k2 rate of constant of association and dissociation
Thus,

$$K = \frac{K1}{K2} = \frac{[Db]}{[Df](free\ sites)}$$

$$K = \frac{K1}{K2} = \frac{[Db]}{[Df](nP - Db)}$$

K is equilibrium constant
n is no of available binding sites per mole of protein
[Df], [Db], P molar concentrations of free drug, bound drug and protein respectively

FACTORS AFFECTING PROTEIN BINDING:

1. Drug related factors
   a.) Physico chemical characteristics of drug
   b.) Concentration of drug in the body
   c.) Affinity of a drug for a particular binding component
2. Protein/ tissue related factors
   a.) Physico chemical characteristics of the protein or binding agent.
   b.) Concentration of the protein or binding agent.
   c.) No. of binding sites of the binding agent.
3. Drug interactions
   a.) Competition between drugs for the binding site (displacement innteraction).

b.) Competition between drug and normal body constituents.
c.) Allosteric changes in protein molecules.

4. Patient related factors
   a.) Age
   b.) Inter subject variation
   c.) Disease states