MEDICINAL CHEMISTRY-I – BP402T

UNIT: 1

CLASS: 1

TOPIC: PHYSICOCHEMICAL PROPERTIES AND CHEMICAL ACTIVITY

Introduction:

A drug is a chemical molecule. Following introduction into body, it must pass through many barriers, survive alternate sites of attachment and storage and avoid significant metabolic destruction before it reaches the site of action, usually a receptor or a cell.

The ability of a chemical compound to elicit a pharmacologic/ therapeutic effect is related to the influence of various physical and chemical properties of the chemical substance on the biomolecule that interacts with.

The various physico chemical properties that influence biological activity include

1. Solubility
2. Partition coefficient
3. Dissociation constant pKa
4. Hydrogen bonding
5. Molar refractivity
6. Ionization of drugs
7. Drug shape
8. Complexation
9. Surface activity
10. Protein binding
11. Bioisosterism
12. Isomerism

1. PARTITION COEFFICIENT:

The biological activity of the several groups of the drugs is correlated with their partition coefficient in polar and non polar solvents.

The ability of a drug to dissolve in a lipid phase when an aqueous phase is also present is called lipophilicity, which can be characterized in partition coefficient (the equilibrium constant of drug concentrations for unionisable molecules in the two phases

$$P = \frac{[DRUG]lipid}{[DRUG]water}$$

For ionisable molecules (acids, bases, salts)

$$P = \frac{[DRUG]lipid}{(1-\alpha)[DRUG]water}$$

α—degree of ionization

The partition coefficient describes the

Drug (water,A) $\xrightarrow{PC}$ Drug(oil,N)

Consider the partitioning of a drug between two immiscible phases A and N

More the water molecules around the solute in the aqueous phase, the more will be the driving force for the forward transfer from the phase A to phase N and hence PC is greater.

High polar molecules have little tendency to leave the aqueous phase and hence PC will be smaller.

Non polar molecules have high PC values'

Eg : Narcotics and general anesthetics show greater affinity for lipids

Compound	**lipid/water PC**
Ethanol	0.03
Morphine	0.40
Barbitone	1.40
Phenobarbitone	5.90

Measurement of Partition Coefficient:

Since PC are difficult to measure in living systems, they are determined invitro using 1-octanol as lipid phase and phosphate buffer of pH7.4 as the aqueous phase.

This permits standardized measurements of partition coefficients.

Log P vs. Activity graph predicts the distribution of the compound in a biological system.Greater the P, greater is the absorption of drug through membrane.