Quadrant II – Transcript and Related Materials

Programme: T. Y. B. Sc

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Paper Title: Essentials in Pharmaceutical Chemistry

Unit: 2

Module Name: Effect of solubility, partition coefficient and ionization constant

Module No: 04

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Notes

Physicochemical chemical properties

These are due to specific nature of the structures of the drugs which favour absorption and distribution to increase the drug concentration and specific orientation on the receptor site.
A chain of events is created which leads to observed drug effect.

(i) Solubility:

Solubility is a measure of the degree of attraction of drugs by lipidic hydrophobic regions of the macromolecules of the biological system.
Solubility is related to the transport of the drug from exobiophase to the receptor site, and interaction between drug's hydrophobic region and the receptors.
Passage of the drug across the membrane of oral cavity, gastrointestinal epithelium, through the skin, and into the bile, central nervous system, tissue cells and kidney is related to lipid solubility of the drug molecule.
The solubility of the drug varies with different media between two extremes, like polar solvent (e. g., water), and non-polar solvent (e.g. lipids).
Polar groups (hydrophilic or lipophobic groups) of the drug molecule induce water solubility and other aqueous fluid solubility.
Presence of unsaturation -CH=CH- and -C≡CH- makes the drug hydrophobic.
Presence of ionic or non-ionic groups in the drug molecule makes it water soluble or dispersible. Hence the chemical nature of the drug molecule decides the solubility and the concentration of the drug on the receptor site.

(ii) Partition Coefficient:

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

Narcotics and general anesthetics show greater affinity for lipid. They fix primarily to nervous system cells rich in lipid and thus exhibit higher biological action.

Oil/gas partition coefficient is a measure of the minimal alveolar concentration of several anesthetics necessary to produce standard analgesic effect.

When anesthetics reach relative saturation in some lipid structures situated in the brain, anesthesia is induced.

(iii) Ionisation Constant:

Most drugs are weak electrolytes, i. e, either weak acids or weak bases and exist in either ionized or unionised form depending on pH of the biological medium.

Unionised drug molecules are lipid soluble and hence possess high penetration capacity through biological membrane barriers. Comparatively, ionized form of the drug molecule has less penetration capacity.

Normally drugs pass through cell membranes in undissociated forms and act in dissociated form as ions.

Transport of the drug across the cell membrane is by

(i) simple diffusion

(ii) leakage through small holes in the cell membranes

(iii) specified cellular transport mechanism.

The diffusion of lipid soluble unionized form continues till the concentration of the unionized form is equal on each side of the membrane. The degree of ionization remains unchanged except where there is a difference in pH, e.g., gastric juice and blood which are separated by the lumen of the stomach. Transport of drug from blood to gastric juice is simple diffusion whereas transport across a membrane with lipid characteristics is absorption.

Absorption of the weakly acidic drug is less than weakly basic drug with the rise in pH of the medium.