MEDICINAL CHEMISTRY-I – BP402T

UNIT: 1

CLASS: 2

TOPIC: HYDROGEN BONDING

HYDROGEN BONDING:

Hydrogen bonding is a special type of dipole-dipole interaction between the hydrogen atom in a polar bond such as N-H, O-H, F-H and an electronegative atom O,Nor F atom.

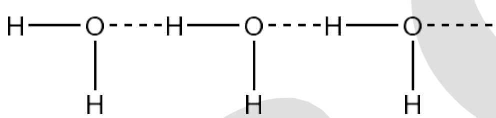
This interaction is written as A-H   B-H, A&B represent O,N and F.

A-H is one molecule or part of a molecule and B is part of another molecule

The dotted line represents the hydrogen bond.

These three atoms lie along the straight line, but the angle AHB or AHA can deviate as much as 30^{o} from linearity.

Eg. H2O, NH3, NH3-HF



Generally the hydrogen bonding is classified into two types

A) Intermolecular hydrogen bonding

B) Intramolecular hydrogen bonding

A) Inter molecular hydrogen bonding:

In this type, H-bonding occurs between two or more than two molecules of the same compound and results in the formation of polymeric aggregates.

Eg. NH3, H2O

H-N------H-N-------H-N-------H-N

Intermolecular hydrogen bonding increases the boiling point of the compound and also its solubility in water.

The increase in solubility is due to association of several molecules of the compound.

As a result the effective molecular weight of the compound increases and hence more energy is required to dissociate the molecules for vaporization.

The molecules that are able to develop intermolecular H-bonding improve their solubility by the formation of intermolecular hydrogen bonding with water.

Eg: Ethanol shows higher B.P and higher solubility in water than dimethyl ether even though both have the same molecular weights.

	Mol.wt	**B.P**
1. Ethanol	46	78C
2. Dimethyl ether	46	-25C
3. Diethyl ether	74	61
4. 1-butanol	74	118C

Intra molecular Hydrogen Bonding:

- In this type, hydrogen bonding occurs within the two atoms of the same molecule
- This type of H-bonding is commonly known as chelation and frequently occurs in organic compounds.
- Sometimes intramolecular hydrogen bonding develops a six or five membered ring.

  Eg: o-chloro phenol and o- nitro phenol

Consequences:

1. Decrease in boiling point of the compound.
2. Decrease in its solubility in water.

Because of the chelation between the o- substituted groups that restricts the possibility if intermolecular H-bonding with water.

Chelation is not possible in m- and p- positions,

Eg:o-nitro phenol , m-nitro phenol and p-nitro phenol has m.p 215C, 279C,279C respectively.

Effects of Hydrogen bonding:

- Almost all physical properties are affected by hydrogen bonding.
- The properties that predominantly alter are B.P, M.P, water solubility, strength of acids, spectroscopic properties, surface tension,viscocity, biological products and drug receptor interactions.
- In addition to the physical properties, chemical properties like acid character, base character, properties of carbonyl group are also affected.

1. **Boiling and Melting points:**

   a) Intermolecular hydrogen bonding increases the boiling point of the compound due to the association of several molecules of the same compound as a result of increased intermolecular forces.

   b) Intramolecular H-bonding decreases the boiling point of the compound because of the chelation between the groups of the same molecule that results in restriction of the possibility of intermolecular H-bonding, thereby preventing association of the molecules.

2. **Water solubility:**

Solubility of a substance increases tremendously when hydrogen bonding is possible between the solvent and the solute.

Eg: methanol and ethanol are highly soluble in water due to H-bonding between the molecules.

The high solubility of polyhydric phenols and sugars are due to the availability of a greater number of –OH groups for H-bonding.

3. **Strength of acids**:

Any structural feature that contributes for the greater stability of anion in comparison to free acid will shift the ionization equilibrium to the right.

Thus if the anion of the acid were stabilized due to intramolecular H-bonding, there would be a marked increase in the strength of the acid.

Eg: the ionization constant of salicylic acid is higher than the other two isomers and is 17 times more acidic than benzoic acid.

4. **Spectroscopic properties**:

The hydrogen bonding shifts the position of bands in infra red and NMR spectra of organic compounds.

Eg: IR spectra of ethanol in vapour phase shows absorption band at 3700 cm-1 due to free hydroxyl group. In solution this band is completely replaced by a broad band around 3500cm-1 which is characteristic of hydrogen bonded hydroxyl groups.

5. **On surface tension and viscocity**:

The compounds which possess hydrogen bonding are found to have higher Surface Tension and Viscocity.

Eg: glycerol, glycol, sugar syrup, phosphoric acid, etc.,

6. **Biological products:**

The three dimensional structures of proteins and nucleic acids is due to H-bonds. In α-helices, H-bonds extend from the H- atoms of polar N-H units in peptide group to oxygen of polar carbonyl units.

- N—H-----------0=C-

7. **Drug receptor interactions:**

H-bonding is also a secondary binding force in drug receptor interactions.

3. SURFACE ACTIVITY:

A surfactant is briefly defined as a material that can greatly reduce the surface tension of water when used in very low concentrations.

This molecule is made up of water soluble (lipophobic/hydrophilic) and a water insoluble

(lipophilic/hydrophobic) component.

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Hydrophobe hydrophile

- The hydrophobe is usually the equivalent of an 8 to 18 C-hydrocarbon and can also be aliphatic or aromatic or a mixture of both.
- The sources of hydrophobes are normally natural fats and oils, petrolelum fractions, relatively short synthetic polymers or relatively high molecular weight synthetic alcohols.
- The hydrophilic groups give the primary classification to surfactants and are anionic, cationic and nonionic in nature.
- The anionic hydrophiles include carboxylates,, sulfates, sulfonates, phosphates.
- The cationic hydrophiles include amines.
- The nonionic hydrophiles associate with water at the ether oxygens of a PEG chain.
- In each case, the hydrophilic end of the surfactant is strongly attracted to the water molecules and the force of attraction between the hydrophobe and water is only slight.
- As a result, the surfactant molecules align themselves at the surface and internally so that the hydrophilic end is towards water and the hydrophobe is squeezed away from the water.
- This internal group of surfactant molecules is referred to as micelle(m).
- Because of this characteristic behavior of surfactants to orient at surfaces and to form micelles, all surfactants perform basic functions—foaming agents, emulsifiers,dispersants which suspend respectively a gas, an immisible liquid or solid in water or some other liquids.

Applications:

1. The bactericidal activity of cationic quaternary ammonium compounds such as benzalkonium chloride, cetrimide, cetyl pyridinium chloride etc, is explained through surface activity.
2. The anthelminthic activity of hexyl resorcinols.
3. Steroidal harmones and barbiturates have surface active properties.
4. Phenol and cresol act as disinfectants by denaturing the proteins of biological membranes.