ABSTRACT

My research work deals with the interaction of different imperative molecules like amino acid ,Ionic liquid with diverse liquid medium and formation of host –guest inclusion complexes of the oligosaccharide cyclodextrin with vital guest molecules namely amino acids, drug molecules in various environments with the help of different spectroscopes and physicochemical investigation.

Host-Guest Chemistry

Host-guest chemistry has diverse application in the field of modern biochemistry as it covers the area of complexes formed by two or more molecules joined together by forces other than covalent bonds. It is very difficult to explain the 3D structure of large biomolecules by non covalent bonding; rather it is involved in biological processes in which molecules bind specifically but transiently to another molecule. Inclusion complex formation is one type of host–guest chemistry. Common host molecules are cyclodextrin, crown ether, cucurbit, porphyrins etc. while amino acids, vitamins, ionic liquids, drugs etc can act as guest molecules. The guest molecules are encapsulated in the cavity of host molecules and bound by some non-covalent interactions such as hydrogen bonding, van der Waals force and hydrophobic interactions. The thermodynamic driving force for the formation of host-guest inclusion complex is the lowering of Gibb's free energy of the system. Contrarily, the study of Inclusion Complexes has become a matter of utmost importance because of their extensive applications in areas of bio sensing and bio imaging, drug delivery and regenerative medicine.

The advantages that provide these inclusion complexes in the pharmaceutical industry are:

(1) The increase or decrease of the solubility and the dissolution rate of the complex in relation to the active substance depending on the nature of the guest and host molecules;

(2) The change of reactivity of the active substance after the protection of some functional groups.

(3) A better bioavailability of the drug.

(4) The correction of dour and flavor.

(5) Extended the life of the drug (improved physical and chemical stability).

(6) The reduction of the contraindications.

Inclusion complexes can be defined as a special group of compounds known as 'non-classical complex, which is prepared under the effect of mechanical factors and has molecules of host and guest as its components, compounds molecules without formation of any specific chemical bond (the weak Van der Waals attractive forces, hydrogen bonding interactions and polar interactions) between guest and host; the essential criterion is simply that the enclosed molecule or "guest" be of a suitable, size and shape to fit into a cavity within a solid structure.

Cyclodextrin as Host Molecule

Cyclodextrins are cyclic, nonreducing oligosaccharides in which the glucopyranose units are linked α-1, 4 glycosidic bonds. The unique characteristic of its structure is that it adopts a cylindrical shape providing a somewhat hydrophobic central cavity and a hydrophilic outer surface. Naturally occurring α, β and γ cyclodextrins consist of six, seven, and eight D-glucose units, respectively. Topand bottom cavity diameters typically measure 4.7 and 5.3 ˚ A for α-CD, 6.0 and 6.5˚A forβ-CD, and 7.5 and 8.3˚A for γ-CD, respectively. CDs are water-soluble molecules with rigid and well defined molecular structures. The hydrophobic central cavity of cyclodextrin is suitable for forming inclusion complexes with a large variety of organic molecules in solutions and in solid state. Inclusion complexes of CDs are being formulated and studied for varied purposes such as dissolution rate enhancement, solubility of the poorly water soluble drugs, evaporation of guest molecules that are highly volatile stability of the system and even as drug carriers.

Chemicals used in Solution Chemistry

(i) Solvents

- Water
- N,N-Dimethyl formamide(DMF)
- Tetra hydrofuran(THF)
- 1,4, Dioxane(DO)

(ii) Amino Acids

- L Valine
- Asparagine
- Glutamine
- Cystine
- 3-(2-Napthyl)-D-Alanine(guest molecules)

(iii) lonic liquid

1-Ethyl-3Methyl imidazolium Tosylate.

(iv) Drug molecules

• Sodium Valproate (guest molecules)

• Acetaminophen

(v) Salts

- NaCl
- KCl
- LiCl

(vi) Host Molecules

• α-Cyclodextrin

•β-Cyclodextrin

Chapter IV: The apparent molar volume (ϕ_V), viscosity B-coefficient and molar refraction (R_M) have been determined of L-valine in aqueous solution of LiCl, NaCl and KCl at 298 K, 303 K and 308 K from density (ρ), viscosity (η) and refractive index (n_D) measurements respectively. The limiting apparent molar volumes (ϕ_V^0) and experimental slopes (S_V^*) derived from the Masson equation have been interpreted in terms of solute–solvent and solute–solute interactions respectively. The viscosity data were analysed using the Jones–Dole equation and the derived parameter B has also been interpreted in terms of solute–solvent interactions in the solutions. Molar refraction (R_M) has been calculated using the Lorentz–Lorenz equation.

Chapter V: Cystine is the oxidized dimer of the amino acid cysteine and has the formula $[SCH_2CH(NH_2)CO_2H]_2$. It is a white solid i.e. faintly soluble in water. It serves two biological functions: a location of redox reactions and a mechanical linkage that allows proteins to retain their 3-D structure. The host-guest interaction of an amino acid (L-Cystine) as a guest with α and β cyclodextrins have been investigated which have significant applications in the field of medical science. FTIR study corroborates the formation of inclusion complexes. The host-guest interaction has been explained on the basis of H-bonding, Van der Waals force and exceptional structure of cyclodextrin. SEM studies show the change in morphology and SEM EDS indicate the change in the elemental composition upon inclusion complexation. DLS experiments show the change in hydrodynamic diameter upon insertion of the amino acid inside the hydrophobic core of cyclodextrins. The thermogram for IC-2 is more flattened compared to that for the IC-1 which indicates more complexation of cys with β-CD rather than with α-CD.

Chapter VI: The host –guest interaction of an amino acid (L-cysteine) as guest with α and β cyclodextrines have been investigated which have significant applications in in the field of medicine such as controlled drug delivery. The ^1H NMR study confirms the formation of inclusion complex while surface tension and conductivity studies support the formation inclusion complex with 1:1 stoichiometry. The host-guest interaction has been explained on the basis of hydrogen bonding, Vanderwaal's force and exceptional structure of cyclodextrin.

Chapter VII: Solution behaviour of 1-ethyl-3-methyl imidazolium tosylate (IL) and some industrially important solvents (dimethylformamide, tetrahydrofuran and 1,4-dioxane) have been studied by electrolytic conductivity, density (ρ) and viscosity (η) study. The limiting molar conductivities (Λ_0), association constants (K_A), and the distance of closest approach (R) of the ions have been measured using the Fuoss and Fuoss-Krass theory. The observed molar conductivities were explained by the formation of ion pairs and triple ions. Ion–solvent interactions have been interpreted in terms of apparent molar volumes and viscosity B-coefficients. Tetrabutylammonium tetraphenylborate [Bu_4NBPh_4] was measured as "reference electrolyte" to estimate the limiting ionic conductivity ($\lambda_0^{\pm}$) of the ions along with the numerical appraisal of ion-pair formation constant.

Chapter VIII: The apparent molar volume (ϕ_V), viscosity B-coefficient , molar refraction (R_M)and specific coductance determined of Acetaminophen solution in different amino acid supplemented with the density (ρ), viscosity (η) and refractive index (n_D) and conductance data at different temperature 298.15 K, 303.15 K and 308.15 K respectively at different mass fractions. The limiting apparent molar volumes (ϕ_V^0) and experimental slopes (S_V^*) derived from the Masson equation ($\phi_V = \phi_V^0 + S_V^* \sqrt{m}$), have been interpreted in terms of solute–solvent and solute–solute interactions respectively. The structure making or structure breaking ability of Asparagine and glutamine has been discussed in terms of the sign of $(\delta^2\phi_V^0/\delta T^2)_P$ .The viscosity data were analyzed using the Jones–Dole equation ($(\eta/\eta_0 - 1)/\sqrt{m} = A + B\sqrt{m}$) and the derived parameter B has also been interpreted in terms of solute–solvent interactions in the solutions. An increase in the transform volume of solute with increasing acetaminophen concentration has been explained by Friedman–Krishnan co sphere model. From the application of transition state of theory have also been calculated and explained activation parameters of viscous flow for the solutions studied. Molar refraction ($R_M = \left\{\left(\frac{n_D^2 - 1}{n_D^2 + 2}\right)\right\}\frac{m}{\rho}$) has been calculated using the Lorentz–Lorenz equation. Molecular interaction of two amino acid in acetaminophen

solution in aqueous medium have been investigated by molar conductivity at three different temperature.

Chapter IX: Molecular assemblies in α and β-cyclodextrin with most important anticonvulsant drug sodium valporate in aqueous medium and solid phases have been explored by reliable spectroscopic and physicochemical techniques as potentially important controlled drug delivery systems. Host–guest inclusion complexes of 1:1 stoichiometry have been determined by surface tension, conductivity studies and inclusion phenomena was confirmed by ^{1}H NMR, FT-IR studies. The results indicated a higher degree of encapsulation in the case of α-cyclodextrin than that in β-cyclodextrin. The formation of the inclusion complexes was elucidated by hydrophobic effects, structural effects, electrostatic forces and H-bonding interactions.