

# CHAPTER I

## NECESSITY OF THE RESEARCH WORK

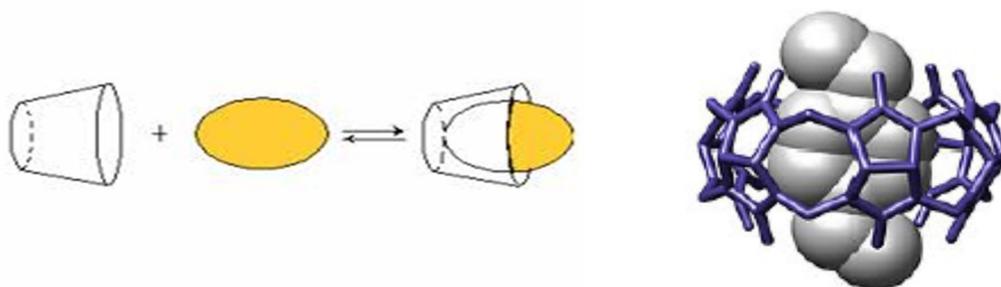
### 1.1. OBJECT, SCOPE AND APPLICATION OF THE RESEARCH WORK

In general, ionic liquids (ILs) are salts with melting point below 100°C. They consist of organic cation along with an organic or inorganic anion. Some of ionic liquids are stable at higher temperatures upto 500K. Because of their unique physicochemical properties, such as miscibility of organic and inorganic materials, low vapour pressures, high thermal stability, ability of good solvent characteristics for organic and inorganic materials. They have normally high solvency power for polar and non polar compounds. Moreover, they have also selective catalytic efficiency, chemical and thermal rigidity; non-flammability and high ionic mobility made them significant interest in wide range of industrial applications. Also, Ionic liquids are considered as a 'designer solvents' and green replacement of volatile organic solvents [1].

A biologically active molecule is one that has an effect on living organism, tissue or cell. For this reason all the drug molecules are biologically active molecules. Basically they are organic molecules having carbon, hydrogen and oxygen and to lesser extent of nitrogen, phosphorus and sulphur. Other elements sometimes incorporate but are much less common. Also they include macromolecules such as polysaccharides, proteins, lipids and nucleic acids as well as small molecules such as natural products etc. Biologically active compounds are widely used as a drug, food or nutrients. These active molecules thus have direct effects on health. These will reduce the many hazards disease, like cancer, cardiovascular disease, etc. Because of these biological activity, diverse and numerous experimental approach are to be considered to understanding of biological significance of bio-active molecules.

The studies on supramolecular chemistry give a broad idea about the formation of 'inclusion complex' between the host and the guest molecules through non-covalent interactions. In molecular inclusion a guest molecule is actually fit inside another host molecule. Thus, most of this interaction has been performed by host-guest interaction. Cyclodextrin, crowns, cucurbitrils, porphyrins, calixarenes etc. are seems to be the host molecules. The guest molecules have suitable polarity

and dimensions. In host-guest chemistry, an inclusion compound is a complex in which one chemical compound ("host") forms a cavity in which molecules of a second "guest" compound are located [2]. Ionic liquids with suitable hydrophobic long chain can also be considered as a guest molecules for inclusion complexes with cyclodextrins.



Release of drugs as of inclusion complex across biological cells and membranes is dependent on physicochemical properties of both drugs and inclusion complex. But direct study of the physicochemical properties in physiological media such as blood, intracellular fluids is difficult to achieve. One of the efficient approaches is the study of molecular interactions in liquids by thermodynamic methods as thermodynamic parameters are suitable for interpreting intermolecular interactions in solution phase. Also the study of thermodynamic properties of drug in appropriate medium can be correlated to its therapeutic effects [3, 4] which are obtained from physicochemical and spectroscopic measurements.

A 'liquid system' is a homogeneous mixture of two or more substances, consisting of ions or molecules, i.e. when a small amount of substance, called solute (solid, liquid or gas), dissolves to a certain limit in a liquid or solid substance (pure, or a mixture itself) called the solvent. In a liquid system the solute is dispersed uniformly throughout the solvent and substances must have similar intermolecular forces to form solutions. The force of attraction of solid and liquid (solute molecules) with various solvent systems are different. When a solute particle is poured into a solvent, the solute particles dissolve with the surrounding solvent molecules. For the solid or liquid solute, the interactions between the solute-solvent is so strong that the individual solute molecules. The relative force of attraction of the solute for the solvent is a key factor in determining their solubility [5].

By an IUPAC definition, Solvation Consequences is an interaction of a solute with the solvent, which leads to stabilization of the solute species in the solution. Solvation consequences, also is the process of attraction and association of

molecules in a solvent with molecules or ions of a solute. The solvation consequences are closely akin to ionic solvations can be studied from different angles using almost all the available thermodynamic and physicochemical techniques. The solvation consequences also studied from different type of interaction as ion-solvent, electrostatic, ion-dipole, dipole-dipole, van der Waal, hydrophobic interactions, etc. and that can be investigated using the experimental measurable properties such as, surface tension, conductance, density, viscosity, refractive index, spectroscopy and various derived parameters factors associated with solvation.

Physicochemical properties are of growing interest of solvent-solvent [6, 7] and solute-solvent [8, 9] systems. The physicochemical properties play a crucial role in interpreting the intermolecular interactions among mixtures and efforts in recent years have been directed at an understanding of such properties at microscopic and macroscopic levels. To understand the mechanism of such interactions thermodynamic, volumetric and transport studies on binary and ternary solvent systems are extremely helpful. The excess thermodynamic properties of the various assorted compounds represent the difference between actual property and the property of the system if the system is ideal. Thus these properties provide important information about the nature and strength of intermolecular forces operating among mixtures. Also physicochemical properties involving excess thermodynamic functions have relevance in carrying out engineering and industrial applications.

The studied thermophysical, thermodynamic, transport, optical and spectroscopic properties are of great significance in characterizing the properties and structural aspects of solutions. The nature of intermolecular interactions can be exposed from the analysis of the derived properties through the thermophysical and spectroscopic investigations.

Volumetric properties like apparent molar volume are of also immense significance in measured the properties and feature of solutions. The facts therefore encourage us to extent the density study of binary or ternary solvent systems with some industrially important solvents: polar, weakly polar and non polar solvents as well as with some solutes, bio-molecules, ionic liquids and complex mixtures. The sign and magnitude of partial molar volume ( $\phi_v^0$ ), a thermodynamic quantity, provides information about the nature and magnitude of ion-solvent interaction

while the experimental slope ( $S_v^*$ ) provides information about ion-ion interactions. Besides, the derivative parameters derived from experimental density and viscosity measurements and subsequent interpretation of the nature and strength of intermolecular interaction occurring in the diverse systems help in testing and improvement of various theories of solution systems. Thus the properties afford important information about the nature and strength of intermolecular forces functioning among mixtures also [10].

Valuable information relating to the nature and strength of forces of electrolytes/non-electrolytes effective in solutions can be obtained from viscosity measurements. In current times the use of computer simulation of molecular dynamics has led to major progress in the direction of a successful molecular theory of transport properties in liquids and an appropriate understanding of molecular motions and interaction patterns in non-electrolytic solvent mixtures involving both hydrogen bonding and non-hydrogen bonding solvents has been recognized [11,12].

The refractive index is also an essential optical property of liquids and liquid systems. Knowledge of refractive index of various liquid systems provides vital information concerning the molecular interactions occurring in the solutions which is essential for many thermophysical parameters [13, 14]. The refractive index results also help to determine the various volumetric properties [15].

UV-Vis, FTIR and NMR techniques are used to measure qualitatively and quantitatively the ion-solvent, ion-ion and molecular interactions in different ion-association and host-guest complex systems [16].

## **1.2. SELECTION OF SOLVENTS, SOLUTES AND BIOLOGICALLY ACTIVE MOLECULES**

Distilled water, acetonitrile, methanol, methoxy ethanol, ethoxy ethanol, propoxy ethanol, solution of ionic liquid, solution of 18-Crown-6, dibenzo-18-Crown-6 and solution of cyclodextrin along with water, considered as a universal solvent, have been selected as main solvent in this research work because these solvents are industrially and biologically very important and by mixing these solvents we could obtain a wide variation of viscosities and dielectric constants giving us an optimum environment for the study.

Ionic liquids, Bio-logically active molecules (dopamine hydrochloride, tyramine hydrochloride, epinephrine hydrochloride, parlidoxime), were considered

as solutes. The study of these solutes is of great interest because of their wide use as solvents solubilising agents in pharmaceutical, cosmetics and medicinal industries.

### 1.3. METHODS OF STUDY

The existence of free ions, solvated ions, and ion-pairs in aqueous and non-aqueous media depends upon the concentrations of the solvent systems. Hence the study of various interactions and equilibrium of ions in different concentration regions are of immense importance to the technologist and theoretician as most of the chemical processes occurs in these systems.

It is of interest to employ different experimental techniques to get a better insight into the phenomena of solvation and different interactions prevailing in solution. I have, therefore, employed various methods, namely conductometry, surface chemistry (surface tension), viscometry, densitometry, refractometry, UV-Visible, FTIR and NMR spectroscopic technique to explore the problem of solvation consequences and inclusion phenomena.

### 1.4. DERIVED PARAMETERS AND THEIR CONSEQUENCE

The limiting molar conductance ( $\Lambda_0$ ), gives a fundamental idea about the ion-solvent interaction the solution. More the magnitude of conductance of the solution less is the ion-solvent interaction. Another parameter obtained from the conductance study i.e. association constant ( $K_A$ ) gives an idea about the solvation of the ions or ion association by the solvent molecules.

The surface tension measurements were performed by platinum ring detachment method using a Tensiometer (K9, KRÜSS; Germany) at the experimental Kelvin. The accuracy of the measurement was within  $\pm 0.1$  mN·m<sup>-1</sup>. Temperature of the system has been reserved by circulating auto-thermostated water bath through a double-wall glass vessel containing the solution.

Apparent molar volume ( $\phi_V^0$ ) is obtained from experimental density results. The sign and magnitude of apparent molar volume ( $\phi_V^0$ ) gives information about the nature and magnitude of ion-solvent interaction while the experimental slope ( $S_V^*$ ) signifies about ion-ion interactions.

Viscosity  $B$ -coefficients and  $A$ -coefficients also provide the valuable information about the ion-solvent interaction, estimated from experimental viscosity data.

The refractive index is an optical property of the binary and ternary solution which used to measure the compactness of the studied liquid systems.

FTIR spectroscopy is used to confirm the interaction and inclusion occurring in the liquid systems. The total internal energy of a molecule in a first approximation is the sum of rotational, vibrational and electronic energy levels. Infrared spectroscopy is the study of interactions between matter and electromagnetic fields in the IR region. In this spectral region, the electromagnetic waves mainly couple with the molecular vibrations; i.e., a molecule can be excited to a higher vibrational state by absorbing IR radiation. The probability of a particular IR frequency being absorbed depends on the actual interaction between this frequency and the molecule. IR spectroscopy is therefore a very potent method which provides fingerprint information about the chemical composition.

UV-visible spectroscopy or ultraviolet-visible spectrophotometry termed as absorption spectroscopy or reflectance spectroscopy in the ultraviolet-visible region. This means it uses light in the visible and near-UV and near-infrared [NIR] regions. Interacting molecules undergo electronic transitions in this region. Molecules containing  $\pi$ -electrons or non-bonding electrons can absorb the energy in the form of ultraviolet or visible light to excite these electrons to higher anti-bonding molecular orbitals. The more easily excited the electrons (i.e. lower energy gap between the HOMO and the LUMO), the longer the wavelength of light it can absorb. The wavelengths of absorption peaks can be correlated with the types of bonds in a given molecule and are valuable in determining the interacting functional groups within a molecule or complexed molecules.

Nuclear Magnetic Resonance (NMR) spectroscopy is also applied to study the inclusion mechanism of the molecules. Proton NMR spectroscopy and 2D-NMR is used to confirm the insertion path and stoichiometry of inclusion in liquid environments.