CHAPTER I

NECESSITY OF THE RESEARCH WORK

1.1. OBJECT, SCOPE AND APPLICATIONS

Man occupies the highest position in the world of living beings. That is why each and every research work is being continued for the interest of human being that they be alive comfortably. The world of living organisms is broadly divided into three principal groups – animals, plants and microorganism. The scientific study of of the chemical substances is called chemistry. The word Chemistry is derived from the Greek word *chemi (*the black land), the ancient name of Egypt, when science was the "black art". The ancient Greeks learned much about medicine and chemistry from Egyptians.[1] The word *Biochemistry* is derived from a Greek word-bios (meaning life) and chemistry; its true meaning is the Chemistry of Life. Biochemistry is the science which deals with the chemistry of living tissues and the substances that take part in their metabolism. Biochemistry in general deals with the body substances like enzyme, carbohydrates, amino acids, fats or lipids, proteins, hormones, DNA, RNA, pigments etc. It provides information in detail their origin, formation, function, deficiency symptoms etc. It tries to explain life in term of biochemical reactions. One can understand that all the chemical reactions occurring at the molecular level in a living cell or living being. Chemistry has demonstrated that the human body is composed of water principally, of organic matter, and of lime, potassium, Sodium, iron and magnesium, and that these cell-salts enter into the composition, in their proper proportions, of every tissue of the body.

The human body which is a typical Biochemic Body is composed of two kinds of matter : organic and inorganic. The former greatly preponderates, but it does not follow that it is more essential to life than the latter; indeed, could not perform its proper function without the inorganic. These are not mere theories but scientifically proven facts. It has been discovered that the Human Body will

survive for a shorter period of time from the deprivation of inorganic (mineral) salts than of the other (organic) constituents of the diet. It is upon the relative quantities of these two materials that life and health depend. An analysis of the blood shows it to contain organic and inorganic matter which is constantly being built into the human structure. The organic constituents are Carbohydrate (sugar), Lipid (fat), Protein (albuminous substances) etc. Inorganic constituents are water and certain cell salts. The relative quantities in the human organism are about as follows : Water, seven tenths (7/10) i.e. 70%, cell salts, one twentieth (1/20) i.e. 5% and the organic matter the remainder is one fourth, (1/4), i.e. 25% Being so small in quantity, the cell-salts have, until lately, been thought to be of little importance. But now it is known that they are the vital portion of the body, the workers and builders; that water and organic substances are simply inert matter used by these salts in building the cells of the body[2-4].

Much of Chemistry of Life deals with the structures, functions and interactions of biological macromolecules, such as proteins, nucleic acids, carbohydrates and lipids, which provide the structure of cells and carry out many of the functions related with life. The Chemistry which is associated with the cell also depends on the reactions of minor molecules and ions. These molecules or ions may be inorganic e.g. water and metal ions, or organic, e.g. the amino acids, which are applied to synthesize proteins. The experimental results of biochemistry are useful mainly in medicine, nutrition, and agriculture. In medication, biochemists explore the causes and cures of diseases. In nutrition, they investigate how to sustain health wellness and study the effects of nutritional insufficiencies.In case of agriculture, biochemists explore soil and fertilizers, and endeavor to determine ways to develop crop cultivation, crop storage and pest control.

A life active composite is a compound that has an effect on a living organism. These are extra nutritional constituents which is present in very small amount in foods and has effect on living cells. Bioactive compounds can have an influence on health. The effect may be positive or negative. The positive effect means beneficial or good effect and negative effect means adverse or toxic effect. But Biomolecules are also used as essential nutrients. While nutrients are essential to the sustainability of a body, the bioactive compounds are not essential since

the body can function properly without them, or because nutrients fulfil the same function. Similarly mminerals in very small quantities are present in foods in the form of salts and take key role in the formation of body substances like enzyme, carbohydrates, amino acids, fats or lipids, proteins, hormones, DNA, RNA, pigments etc. They are also known as Biochemicals . Optimal level of bio-chemicals in a living organism keep the organism in healthy condition. Either excess or low concentration of bio-chemicals will affect the function of a living organism which leads to a disease state.

Figure 1: Thiamine hydrochloride(Vitamin B1)

Research, from the commencement of the age, is the tool for probing and rising new systems and events which are previously present to be ready with the environment. This research work is the attention to the consequence of solvent systems and the investigations on different interactions dominant in solid and liquid phases. The significance of solution in natural measures is eminent. In a word Chemistry is worthless without solution. This was summarised by the alchemists, "Corpora non agunt nisi soluta,"or in the equally concise, "Menstrua non agunt nisifluida." These interpretations are a bit too broad in that period what was well-known about solutions.

Interaction in chemistry is the main factor for a variety of systems to exist. The word interaction signifies both the striking or repulsive forces molecules or non-bonded atoms. Molecular interactions are important in different areas of protein folding, designing drug and drug liberation systems, material science, sensors,

nano-technology, separation science and mainly significant source of life. These types of interactions are accepted as non-covalent interactions [8-11]

The molecule is produced by the involvement of a set of atoms which are bound powerfully sufficient to overcome different effects when it interacts with the environment in which it is exposed. But the interactions are not particularly the bonds or they are not as strong as covalent bonds. Several processes such as melting of ice, boiling of water, unfolding of proteins and RNA, disassembling of membrane, vaporization the covalent bonds are not broken but remain unchanged. Such procedures do not get completed by means of chemical reactions rather these processes involve changes in molecular interactions. A paired non-bonded atoms when interact, the change of enthalpy of that interaction is 1-10 k Cal/mol, which is significantly less than a covalent bond. It should be noted that though non-covalent interactions are feeble individually, the energies molecular sense are appreciably high. One tool is the boiling point of a particular compound which can provide qualitative indications about the strength of the interactions in the molecule. Molecules with high boiling points are measured to cover strong molecular interactions. For example water is boiled at 373.15K but nitrogen is in gaseous form in normal temperature. Though, this variation is mostly owing to the interactions playing the main role in both the systems. The forces of interaction among the interacting molecules in water are larger than those in nitrogen.

Molecular interactions can be better understood by studying a variety of excess thermodynamic properties. The surplus thermodynamic properties of the mixtures communicate to differentiate between real property and the property if the system behaves ideally. Thus, these properties afford important information about the nature and strength of intermolecular forces operating amongst mixed components. Also, physicochemical properties connecting surplus thermodynamic functions have significance in carrying out engineering applications in the process industries and in the design of industrial separation processes. Information of these surplus thermodynamic functions can also be

used for the progress of empirical correlations and development of new theoretical models.

A variety of molecular interactions are (a) Van der waals forces of interactions (b) Short range of repulsion (c) Electrostatic force of interactions (d) Interactions of Hydrogen Bonding (e) Interactions of Dipolar substances. Dipolar interactions are also of different types such as: (i) Dipole-dipole interactions or Keesom Interactions (ii) Dipole-induced dipole interactions (iii) Ion-Dipole Interactions (iv) Variable Dipoles interaction, which are Dispersive interactions and London Forces.

Both the Physical and Chemical properties of a solution are th effects of strengths of their intermolecular forces of interactions and the forces amongst molecules occur from the same source unstable charges on adjacent molecules that tend to be electrostatic forces of attractions and originated by coulombs law. Incorporation of partial charges in molecules consequences in dipole-dipole forces, hydrogen bonding, dipole-induced dipole forces etc. and these are jointly named as intermolecular forces of interactions. In a solution the intermolecular forces control their thermodynamic properties and the understanding of the solvation thermodynamics is compulsory for the categorization and elucidation of any process finished in the liquid phase. All these thermodynamic properties are thermodynamics quantities which are either an feature of the whole system or are functions of situation which is constant and do not vary rapid in excess of nano distances, excluding in the positions where, there are sudden changes at borders between diverse phases of the system. Hence, the thermodynamic investigations together with the transportation properties of a solution would result a clear idea about the nature of the interactions existing within the constituents of a solution[12-15].

In Solution Chemistry the technique for appropriate thoughtful of a choice of phenomena relating to the molecular interactions produces the root of elucidating quantitatively the consequence of the solvent and the various interactions of ions in solvents. Estimation of ion-solvent interactions can be measured thermodynamically and from the account of partial molar volumes,

limiting ionic conductivity as well as viscosity *B*-coefficient studies. Approximate single-ion values make us capable to purify our models of ion-solvent interactions. Important values of ion-solvent interactions would hold the chemists to choose solvents that will progress (a) the solubility of minerals in discharging operations (b) the rates of chemical reactions, or (c) reverse the route of equilibrium reactions. At present the importance and uses of chemistry of electrolytes in mixed solvents are well established[16,17].

Even if an extensive collection of data on different solution of electrolyte and non-electrolyte in water are obtainable, the structure of water and different types of interactions that water goes throughout with electrolytes are so far properly under stood. However, the studies on physicochemical properties of solutions have provided adequate materials on the thermodynamic properties of various electrolytes and non-electrolytes, the effects of the difference in ionic constructions, mobility of ions and common ions along with a host of other properties [18].

The properties of solutes in non-aqueous and solvent mixtures with a view to inspect solute-solute and solute-solvent interactions under various conditions the physicochemical properties have given a lot of information. However, different structures of solubility, differences in solvation power and the probabilities of electrochemical reactions unidentified in aqueous chemistry have opened landscapes for physical chemists and notice in these organic solvents exceeds the conventional boundaries of organic, inorganic, analytical, physical and electrochemistry [19].

The investigation on non-aqueous electrolytic solutions has exposed their wide uses in diversified fields. The solution of electrolyte in non-aqueous solvents are in fact disagreeing with other conducting ion, principally at ambient and at important low temperatures, due to their high flexibility basing upon the choice of plentiful solvents, additives and electrolytes with widely unstable characteristics.

The Supramolecular Chemistry deals with a extensive idea about the improvement of inclusion complex between the host and the guest molecules.

Most of the interactions performed during the construction of inclusion complex are well known as host-guest interaction. There are various host molecules being used in the recent age, but cyclodextrin seems to be the most approving to produce inclusion complexes with a lots of guest molecules having appropriate polarity and dimensions. In Host-Guest Chemistry, an inclusion complex is the one in which one molecule (the "Host") already has a hollow space where another molecule ("Guest") located having suitable chemical properties and dimensions [12, 14, 15,].

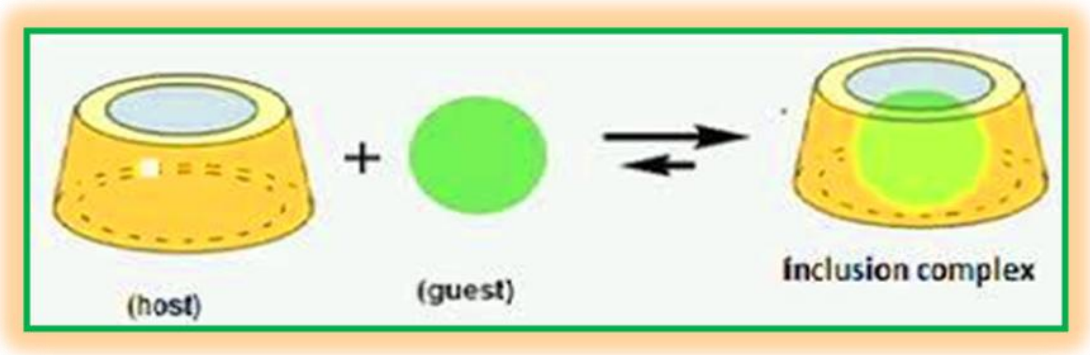

Figure 2: Host- Guest Inclusion Complex.

The strength of the inclusion complex lies first and foremost on the hydrophobic non-covalent interactions. Generally molecules with hydrophobic nature or only the hydrophobic moiety of a polar molecule are encapsulated inside into the hydrophobic cavity of CD releasing the aqua molecules from the void, which is favoured due to repulsions between the non polar guest and the water polar molecule and the incompatibility of water molecule inside the hole. This process leads to the total or partial amalgamation of the guest molecule, rising solubility of the guest in the aqueous and polar solvents. However, on further dilution of the inclusion complex in a larger volume, the phenomenon gets reverted and the guest species becomes free in solution. This unusual characteristic of the inclusion complexes exposes the huge field of application.

1.2.Objectives of the Research Work

*The main object of the research work is to study the molecular interactions of some life active molecules in diversified solvent systems and gather the detailed information about the nature and extend of various interactions.

*To study the interactions of life active molecules in physiological fluid media by physicochemical and spectroscopic techniques.

* To examine of the transportation property, ion solvation and solubility of some electrolytes in aqueous, non- aqueous mixed solvent systems.

*To probe the interactions of a number of industrially important chemicals in diversified solvent system.

*To search the molecular interactions by physicochemical and thermodynamical paproperties of the drug molecule in our suitable laboratory system as a model experiment and compare it in our biological fluid system.

*To survey the different types of hydrophobic-hydrophobic and hydrophilic-hydrophilic interactions occurring between host and guest molecule in case of inclusion complexes.

* Investigation of interactions of life active substances with ionic liquids by physicochemical examinations.

* The objective of this research work is to study the interactions in a variety of chemical systems and collection of thorough information about the nature and the strength of different interactions.

* The investigation of different type of chemical systems in solution and in solid phase helped to understand different types of interactions that play the key role during the formation of inclusion complexes.

*The revision of host-guest chemistry helps to complicate the engagement of the inclusion complexes in the field of chemical science.

*The understanding of the transportation properties of a variety of significant compounds, salts, the interactions of bioactive molecules, ionic liquids, drug molecules in green solvents and industrially significant solvents along with the study of thermodynamic properties help to typify molecular interactions in solutions.

1.3. METHOD OF INVESTIGATION

To have a enhanced understanding into the phenomena of diversified interactions in solvation and inclusion complex formations of various experimental methods in solution and in solid phase have been engaged. Therefore, different significant methodologies that have been used are densitometric, viscometric, conductometric, refractometric techniques to explore the solvation and inclusion phenomena.

The use of different spectroscopic investigation can be highly defined a variety of interactions in a broad sense. The exact characteristic properties of different molecules are seen in various spectroscopic studies in aqueous and mixed solvents. The spectroscopic studies like UV-Vis, Proton-NMR, 2D-ROESY, FT-IR spectroscopic and EMI-Mass, HR-Mass, and Maldi -Mass spectrometric study have been engaged to elucidate a variety of interactions.

Thermodynamic properties, such as partial molar volumes from density measurements, are usually the suitable parameters for understanding solute-solvent or ion-solvent and solute-solute or ion-ion interactions in solution. The sign and magnitude of limiting apparent molar volume (ϕ_V^0) also delivers evidence about the nature and extent of ion-solvent interaction while the experimental slope (S_v^*) offers the evidences of ion-ion interactions [13].Viscosity B-coefficient obtained from the viscosity values indicates the extent of ion-solvent interaction in a solution.

In most of the cases the transport properties are interpreted by means of the data obtained from conductance study, especially at infinite dilution. The conductance data collected as a function of concentration can be used to study the ion-association or molecular association solving appropriate equations.

1.4. SCOPE AND APPLICATIONS

In Supramolecular Chemistry i.e. specifically the Host-Guest Chemistry the development of the inclusion complexes by means of non-covalent interactions offer the root of exceptional methodologies in medicines and also support to understand the interactions occurring in living systems. The formation of the inclusion complexes with cyclodextrins improve bioavailability from solid and semi-solid formulations, enhances stability and reduces adverse effects, masks unpleasant odour and taste. The categorization of physical and structural properties is of specific consequence for these host-guest complexes, which are the basis of the most cyclodextrins' applications in fields of medicines, catalysis, food chemistry, separation of science, sensor technology etc. Pharmacological use of cyclodextrin for drug protecting or aiming now requires physical characterisations of the applied complexes. For understanding of reactivity and selectivity in case of organic reactions so far and also to understand the association behaviour of this unique host system, the present work has been carried out by physicochemical categorization of cyclodextrin-inclusion complexes by use of different analytical methodologies[20,21].

To discover the nature, constructions and interactions in the host-guest inclusion complexes of consecutive surface active imidazolium and pyridinium based ionic liquids with ∝-Cyclodextrin, β- Cyclodextrin and HP-β-Cyclodextrin the outcome of size, shape and structural consequences have been considered qualitatively and quantitatively using different physicochemical methodologies such as Surface Tension, Density, Viscosity, Conductance and Proton-NMR, 2D-ROSEYNMR UV-Visible, IR-Spectroscopy, P-XRD and different Mass spectroscopic techniques.

The transportation of drug molecules crossing living cells and membranes depends essentially on the physical and chemical properties of drug molecules. But the study of the physicochemical activities in physiological media like intracellular fluids, blood, is highly difficult. One of the well-ordered methods is the study of the dealing interactions in fluids using thermodynamic methods as thermodynamic parameters are suitable for understanding intermolecular

interactions in fluid phase. Moreover, the understanding the thermodynamic properties of drug molecules in appropriate medium can be interrelated to its therapeutic effects.

The stabilisation and the controlled release of the drugs now days, are of great concern in pharmacology. To guard drug molecules from environmental effects and to reduce the side effects for their controlled release it is vital to investigate whether they can be encapsulated into the cyclodextrin molecule. Thus to complete such aim, the inclusion complex formation of drug molecules such as Theophylline, Allopurinol and Vitamin B1 with alpha and beta cyclodextrin have been studied to achieve the goal in detail based on the physicochemical measurements including some spectroscopic techniques and the factors affecting the inclusion process are described[22-24].

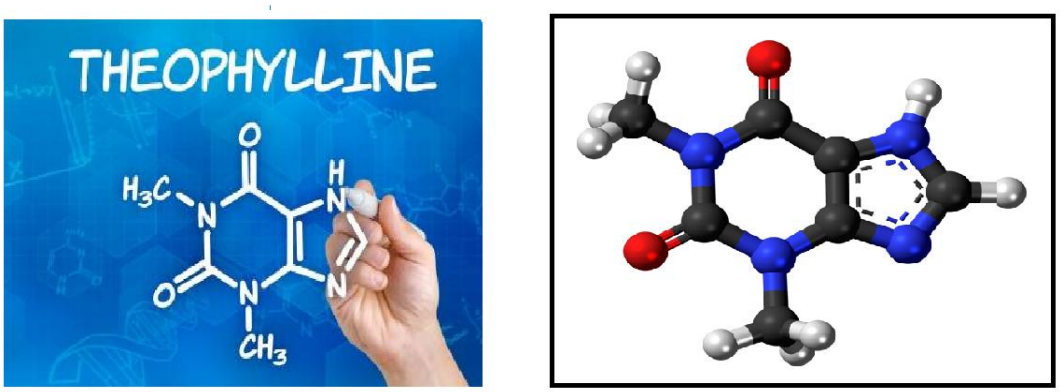

Figure 3: Drug Molecule Theophylline & It's 3D form

Study of the life active molecules in various solvents experience their changed properties due to various interactions in solution. Study of such interactions in solution systems is very useful in medicinal chemistry.

1.5. REFERENCES

References of CHAPTER I are given in BIBLIOGRAPHY (Page No.270-271)