CHAPTER I

NECESSITY OF THE RESEARCH WORK

I.1. OBJECT, SCOPE AND APPLICATION OF THE RESEARCH WORK

Now a days host-gust inclusion complexes and host molecules for regulatory release are very important in pharmaceutical industries and biological fields for civilizing drug delivery science. [1] It focuses on anti-cancer drug release, sensing, gene transfection etc. General Chat Chat Lounge Molecular with the help of automatic nanoparticles capable of trapping and regulating the release of complexes molecules by a range of external stimulus. [2]. Studies of a fast advancing research of supramolecular host – guest complexes in the interaction domain of chemistry, containing a balancing stereo electronic binding (2) take place when encapsulation of a small tiny part of the macro cyclic cavity of a host. Some common host molecules are cyclodextrins, cryptophanes, crown ethers, porphyrins, metallacrowns, calixarenes, cucurbiturils and carcerands, etc. The formation inclusion complexes are applied in supramolecular materials, in enzyme activation, temperature dependence,, photo sensing, changes in pH / redox and competitive binding. Cyclized and bound conformation is of great importance for inclusion complexes (ICs), facilitating the molecular selection of macro cyclic host molecules. Cyclodextrins (CDs) are quite attractive, due to their amphiphilic nature, [3] the combination of CDs and various nano-particles enhances the thermal catalytic properties of the guest by electronically, and macros cyclic hosts as nanosensors, drug delivery vehicles, and recycling agents. Molecular switches, machines, supramolecular CD's There are potential applications for the creation of liquefied polymers, etc. For their applications, chemo sensors, transmembrane channels, molecular-based logic gates and other sophisticated host-guest systems are designed for this purpose.

The family of cyclodextrins is considered as one of the most popular potential hosts for a variety of reasons.

1) It can be formed easily by the decomposition of enzymatic bacteria from starch.

[2] They are cost-effective for industrial purposes .

3) They are non-toxic. Nature is also safe for human consumption .

4) There is a cut cone shaped like CD structure.

5) They form unique structures, keeping their rough and well-defined hydrophobic cavities and hydrophilic rims in primary and secondary –OH groups. Six of them (CD-CD), seven (CD-CD) and eight (CD-CD). Glucopyranose is a unit that binds to tr- (1–4) linkages to form a truncated cone structure. Extraordinary ability of complexes to form complexes of inclusion by guest molecules stabilizes the non-polar part of the guest with its hydrophobic cavity with a polar rim. Being used in various foodstuffs, pharmaceutical industries, pesticides, cosmetics, toilet articles, textile processing and other industries, CDs have been widely applied for encapsulation of various substances. [4] As carriers of solubility, organic availability, protection, stability and guest molecules. Supramolecular and host-guest chemistry, models for studying enzyme activity, molecular recognition encapsulation, intermolecular interactions, and chemical stability. Also, cyclodextrins can be used to reduce irritating gastrointestinal drugs, convert liquid drugs to microcrystalline or formless powders, and prevent the drug - drug and drug - beneficial interactions.

Possible applications for drug control and drug delivery, such as concentration, pH, temperament, etc. Recent ICs are being investigated extensively in the materials and biomedical sciences in recent years [5] The interior is non-polar alkyl group due to the hydrophobic nature and the exterior of the CD cavity is highly hydroxyl groups. Due to their chemical stability, they are suitable and attractive hosts for supramolecular chemistry.

CDs not only have great receptors and chemical stability for molecular recognition but also have great building blocks for functional ingredients. These can be applied to

stimulus-responsive constructs on supramolecular materials.[6]External stimuli, for example, changes in their potential applications such as enzyme activation, light, temperature, nanosensors, drug delivery vehicles and recycling agents can be enhanced by electronic, conductivity, heat, fluorescence and catalytic properties for pH or redox and aggressive binding management. General Chat Lounge considers several difficult problems for Nano particle, due to their applications in the creation of other attractive host-guest systems, such as molecular switches, molecular machines, supramolecular polymers, transmembrane channels, molecule-based logic gates, and chemo sensors. The phenomenon of physical chemistry recognizes that binding is often associated with loss of structural entropy, but overall thermodynamics is still well understood in molecular recognition of its deep importance in biology and treatment. [7] In terms of drug delivery, because of its rigid and precisely defined hydrophobic cavity and hydrophilic outer surfaces, they can act as a host of different molecular receptors for organic and inorganic assembling. Pharmacologically active drugs, in addition to their aqueous solubility, should be lipophilic for passive dispersal in biological membranes. If a drug is hydrophilic, the dissolved drug molecule cannot penetrate the lipophilic biological membrane. Ax Fluid. The use of drug solubilitatile, biological availability, protection, stability and cyclodextrin in assisting drug molecules to form complex carriers.

Solution Thermodynamics is an important branch of physical chemistry, the study of which changes in properties, when one substance dissolves in another. The solubility is influenced by both the solvent and the chemical reaction of the solvent has been investigated. Mixing different solvent or solvent with other solvent-solvent mixtures does not give rise to an ideal solution. This deviation from the norm is manifested in many thermodynamic parameters, with apparent molar properties in solid liquid mixtures and by additional properties in liquid –liquid mixture.[8] Physiochemical studies are of utmost importance, modifying the intrinsic properties of raw materials and providing different forces and products. Given the great benefits from these practices, a complete understanding of the properties of raw materials is essential for the success of process design. The last decade has witnessed a surge in investigative

activities related to green chemistry. Most efforts in this direction have focused on replacing widely used volatile organic solvents (VOCs) instead of suitable alternative solvent systems based on minimal chemical waste and environmental pollution, based on several alternative methods based on water reaction medium, ionic liquid, supercritical fluid, microwave,etc have been developed.Ionic Liquid (IL) is a new class of materials that has recently attracted a lot of attention in scientific and industrial studies. Due to the combination of chemical and physical properties they are significantly different from ordinary molecular fluids. ILs are often defined as salts with low melting points, usually below 373 K [1].

In the last decade Ionic liquids have gained worldwide attention as green solvents. In general, an ionic liquid is completely composed of ions and is known as "green solvents" for many reasons that are considered ionic liquids. [9,12]The most important reason is that the ionic liquid has an insignificant vapor pressure, it does not evaporate into the environment. Ionic liquids can be recycled to propose chemical changes in performance. The chemical and physical properties of ionic liquids can, to some extent, be modified by the appropriate selection of the type of anion and cation that makes up ionic liquids, as well as any substituent groups. Biologically active molecules are produced from a biological source, such as microorganisms, organs and tissues of plant or animal origin, human or animal origin of cells or fluids. [10].Biologically active compounds are studied to assess their health effects. This will reduce the risk of many diseases, such as cancer, cardiovascular diseases, etc. The number of bioactive compounds of the biological effects of diversity, several and many experimental approaches increases our understanding of the biological effect on human bodies.

Many bioactive compounds have been widely significant in chemical structure and function. There are chiral amino acids, such as natural ones (the basic components of proteins) and sugars. In biological systems, most of these compounds have the same chirality, the configurations of most amino acids are L- amino acid serves as a buffering agent in antacids, antiperspirants, analgesics, cosmetics and toiletries. It is used as a source of energy for muscle tissue, the brain and the central nervous system, to

strengthen the immune system by producing antibodies. [11] The term 'solution' is mainly used for the special case of a mixture between different components, that is, in a mixture a small amount of solid, liquid or gaseous substance, called solute and dissolves to some extent in a liquid or solid substance of pure quantity, or a mixture itself called solvent.

A solution can be considered, as a large set of molecules bound by non-covalent interactions. In physical systems, such interactions of increasing complexity should start with dimmers, continue through larger groups and end with solutions. In general, the solutions are more complex sets of weakly interacting molecules and the reactivity in the presence of a solvent cannot be reduced to that of non-covalent interactions.

The physical and chemical properties of a liquid solution, the strength of its intermolecular forces and the forces between the molecules are obtained from the same source: the different charges on adjacent molecules that lead to electrostatic attractions are governed by the law of the coulombs.[13] The partial charges acquired by the molecules result in dipole-dipole forces, dipole-induced dipole forces, hydrogen bonds, etc., are known as intermolecular forces. In the liquid phase, intermolecular forces in a solution control and understand the thermodynamics of solvation, characterize and interpret the essential properties of any process performed. These thermodynamic properties are quantities that are an attribute of a complete system or are position functions that are continuous and do not vary rapidly in microscopic distances, except in cases where there are abrupt changes in the boundaries between the phases of the system. Therefore, the studies give a clear idea about the nature of the forces existing within the transport properties of the components of a solution in thermodynamics.

Therefore, the main objective of this research work is to investigate to understand the interactions that prevail in the solutions by studying their transport properties and thermodynamic inclusion complexes.

The study of molecular interaction in fluids by thermodynamic methods has drawn attention[14], since thermodynamic parameters are convenient for interpreting intermolecular interaction patterns in mixtures of non-electrolytic solvents that involve both hydrogen bonding and non-hydrogen bonding solvents. . The different sequence of solubility, the difference in solvation power and the possibilities of unknown chemical or electrochemical reactions in aqueous chemistry have open views for chemists and interest in organic solvents transcends the traditional limits of inorganic, physical , organic, analytical and electrochemical [15].

The facts, therefore, encourage us to expand the study of binary or ternary solvent systems with some solvents of industrial importance: polar, weakly polar and non-polar solvents, as well as with some solutes / electrolytes.

The thermodynamic and transport properties are of great importance to characterize the properties and structural aspects of the solutions. The sign and magnitude of the partial molar volume (ϕ_V^0), [16]a thermodynamic quantity, provides information on the nature and magnitude of the ion-solvent interaction, while the experimental slope (Sv*) provides information on ion-ion interactions [16]. In addition, the excess of properties derived from experimental density, viscosity and speed of sound data and the subsequent interpretation of the nature and strength of intermolecular interaction help to test and develop various solution theories. The excess of thermodynamic properties of the mixtures corresponds to the difference between the real property and the property if the system behaves ideally. Therefore, the properties provide important information about the nature and strength of the intermolecular forces that operate between mixed components. Valuable information on the nature and strength of the forces operating in solutions can be obtained from viscosity data. Recently, the use of computer simulation of molecular dynamics has led to a significant improvement towards a successful molecular theory of fluid transport properties and an adequate understanding of molecular movements and interaction patterns in mixtures of non-electrolytic solvents which involve both hydrogen bonding and non-hydrogen bonding solvents .It has been established [17,18].

The refractive index is an important physical property of liquids and liquid mixtures, which affects the solution of different problems in chemical engineering to develop industrial processes. Knowledge of the refractive index of multiple component mixtures provides information on the interactions in these mixtures [9-11], which is essential for many physicochemical calculations, including the correlation of the refractive index with density [19].

The physicochemical properties that imply excess thermodynamic functions are relevant in the realization of engineering applications in industrial separation processes. The importance and use of electrolyte chemistry in non-aqueous and mixed solvents are well recognized. However, studies on the properties of aqueous solutions have provided sufficient information on the thermodynamic properties of different electrolytes and non-electrolytes, the effects of variation in ionic structure, ionic mobility and common ions along with a number of others. properties [20].

The importance and uses of electrolyte chemistry in non-aqueous and mixed solvents have been summarized by [18], Bates [19,20], Parker [21,22], Criss and Salomon [23], Meck [16] , Popovych [17], Franks Mercus [24] and others [25-27]. The solute-solute, solute-solvent and solvent-solvent interactions have been the subject of wide interest and have been explicitly presented in Faraday Trans. of the Chemical Society [28]. Fundamental research on non-aqueous electrolyte solution has catalyzed its wide technical application in many fields. Non-aqueous electrolyte solutions really compete with other ionic conductors, especially at room temperature and at low temperatures, due to their high flexibility based on the choice of numerous solvents, additives and electrolytes with very variable properties. Primary and secondary high-energy batteries, dual-layer wet condensers and super-capacitors, electrode position and electroplating are some devices and processes for which the use of non-aqueous electrolyte solutions has been most successful [29-31]. Other fields in which non-aqueous electrolyte solutions are widely used include electro chromic screens and smart windows, photo electrochemical cells, electronic machining, etching, polishing and electro synthesis. Despite the broad technical applications, our understanding of

these systems at the quantitative level is still unclear. The main reason for this is the absence of detailed information on the nature and strength of molecular interactions and their influence on the structural and dynamic properties of the non-aqueous electrolyte solution.

The physicochemical properties of drugs involve the transport of drugs through biological cells and membranes. But the direct study of physicochemical properties in physiological means such as blood, intracellular fluids is difficult to achieve. One of the well organized approaches is the study of molecular interactions in fluids by thermodynamic methods, since thermodynamic parameters are convenient for interpreting intermolecular interactions in the solution phase. Amino acids are arginine, cysteine, glutamine, tyrosine, glycine, ornithine, etc. In this thesis, the four amino acids studied have biological activity in human bodies. L-Asparagine helps in the biosynthesis of proteins in humans. [32]L-asparagine is also necessary for the improvement of the brain and has a vital role in the preparation of ammonia. Usually, the reaction between asparagine and some reducing carbohydrates or other compounds that use carbonyls produces acrylamide in food after heating to optimum temperature. The products thus formed are present in baked goods such as French fries, potato chips, and toasted bread.

L-Cystine is the oxidized dimmer of the amino acid cysteine and has the formula $[SCH_2CH\ (NH_2)\ CO_2H]_2$. It is a white solid, that is, slightly soluble in water. It fulfills two biological functions: a location of redox reactions and a mechanical bond that allows proteins to retain their three-dimensional structure. Cysteine is an amino acid that is the building block of protein. (Scheme 1) It is a powerful antioxidant. It is also used to metabolize lipids, stimulating the immune system. In the body,[33] cysteine is also used to produce the amino acid touring, as well as coenzyme A, biotin and heparin. Cysteine is a component of beta karatin and has been shown to preserve skin elasticity. It also protects the lining of the digestive system. L-Valine is a branched-chain amino acid (such as L-isoleucine and L-leucine), which is important for supplying energy to the muscles. Branched chain amino acids improve energy, increase endurance and aid

in the recovery and repair of muscle tissue.[34] As a branched chain amino acid, L-valine is important for optimal growth in infants and children and nitrogen balance in adults. Branched chain preparations are used in sports nutrition and healthy foods.

Asparagine amino acids form long chains by hydrogen bonding interactions with the peptide skeleton, these amino acid residues are commonly found at the beginning of alpha helices as asx turns and asx motifs, and on similar rotation motifs, or as rings amide, in beta sheets Its main function is to limit hydrogen bond communications that can also be fulfilled by the polypeptide skeleton. [32] The glutamines that have an additional methylene group, have a greater entropy due to conformation and, therefore, are less able to limit themselves. Asparagine are also useful for providing free sites for N-linked glycosylation, the modification of the protein chain with the accumulation of carbohydrate chains. [16] In the human body, aspartate is most often synthesized through naturally, a carbohydrate side chain can be summarized exclusively in an asparagine residue if it is bordered on the C side by X-serine or X-threonine, here X is any amino acid with the exception of proline. Three ionic liquids used for research experiments have vast applications as green solvents. Ionic liquids (IL) that have a combination of organic-organic and organic-inorganic cations / anions are of great interest in the current chemical field. Their intrinsic physicochemical properties make them "design solvents" or "green solvent", such as the favorable solubility of organic and inorganic compounds, negligible vapor pressures, low melting points, high thermal stability, solvated many organic, inorganic and polymeric materials , adjustable polarity, selective catalytic effects, chemical stability. In addition, along with these exceptional properties. The 1-ethyl-3-methylimidazolium tosylate is also an imidazolium-based ionic liquid, of molecular formula C13H18N2O3S, which contains ethyl, methyl groups with two active nitrogen atoms in the imidazole or five-membered ring, exists as a liquid phase melted with a melting point lower than 313K. 1-Ethyl-3-methylimidazolium tosylate is liquid at room temperature. This ionic liquid has vast applications in chemical reactions, synthesis, cellulose processing, reprocessing of nuclear fuel, waste recycling, metallic air batteries, etc. They are considered ecological solvents since they do not produce any environmental risk. Due

to their distinctive properties, they attract more and more attention in many fields, such as organic chemistry, electrochemistry, catalysis, physical chemistry and applied supramolecular chemistry. It is used as recyclable solvents for organic reactions and separation processes, lubricating fluids, heat transfer fluids for biomass processing and electrically conductive liquids as an electrochemical device in the field of electrochemistry. ILs are used as heat transfer materials to process biomass and transport liquids electrically as an electrochemical tool in electrochemistry. ILs based on imidazolium cations are prominent commercially available, highly thermally stable bio-applications. ILs that have large anions are also susceptible to additional interactions with polar solvents. Sodium valproate (SV) is an anticonvulsant medication that is used in epilepsy and bipolar disorder [33]. It is also used for neuropathic pain and migraine prophylaxis. SV is an extremely hygroscopic and completely ionized solid to form a highly active mode of administration . Consideration of clinically high doses for use, that is why the drug has a high side effect known as a black box warning for hepatotoxicity, pancreatitis and fetal abnormalities . The search leads to reduction.], Supramolecular and host-host chemistry, models to study enzymatic activity, molecular recognition and molecular encapsulation, study intermolecular interactions and chemical stabilization [8]. In addition, cyclodextrins can be used to reduce gastrointestinal irritation by drugs [9], convert liquid drugs to microcrystalline or amorphous powder and prevent drug-drug and drug-receptor interactions [10].

I.2 CHOICE OF SOLVENTS AND SOLUTES USED:

Mainly used as solvent like Dimethyl formamide, Tetra hydro furan,1,4 di oxane, and universal solvent like water and different salt like sodium chloride Potassium chloride Lithium chloride, N-acetyl para amino phenol, Asparagine, Glutamine, And ionic liquid like 1-ethyl-3 methyl imidazolium tosylate .

Study on Ion Pair and Triple Ion Formation of an Ionic Liquid,[(EMIM) (TOS)] in Different Solvents with the Manifestation of Solvation Consequence,

Physico-Chemical Studies of a Biologically Active Molecule (L-Valine) Predominant in Aqueous Alkali Halide Solutions with the Manifestation of Solvation Consequences.

Choice of Host and Guest Molecules:

For host guest inclusion complexes, I used cyclodextrine as a host molecules,like α-Cyclodextrine, β- cyclodextrine and guest mlecules are 3-(2 Nepthyal) Danaline, Lcystine, sodium valporate drug .

Investigation of Inclusion Complexes of Sodium Valproate Inside into α and β-Cyclodextrins, Host-Guest Inclusion Complexation of 3-(2-Napthyl)-D-Alanine with α and β-Cyclodextrins Explored

I.3. METHODS OF INVESTIGATION

The host guest inclusion complexes and tharmodynamicly existence of free ions, solvated ions, ion-pairs and triple-ions in aqueous and non-aqueous media depends upon the concentrations of the solution. 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. We have, therefore, employed five important methods, namely, densitometry, viscometry, conductometry, refractometry, UV-Visible , NMR spectroscopic technique,DSC AND SEM to investigate the problem of solvation phenomena.

Thermodynamic properties, like partial molar volumes obtained from density measurements, are generally convenient parameters for interpreting solute-solvent and solute-solute interactions in solution.

The change in viscosity by the addition of electrolyte solutions is attributed to inter-ionic and ion-solvent effects. The viscosity *B*-coefficients are also separated into ionic components by the 'reference electrolyte' method and from the temperature

dependence of ionic values, a satisfactory interpretation of ion-solvent interactions such as the effects of solvation, structure-breaking or structure-making, polarization, etc. may be given.

The transport properties in most cases are studied using the conductance data, especially the conductance at infinite dilution. Conductance data obtained as a function of concentration can be used to study the ion-association with the help of appropriate equations.

The optical property, refractive index is an useful tool to understand the interaction occurring in the solution systems.

The surface tension experiments were done by platinum ring detachment mehod using a Tensiometer (K9, KRŰSS; Germany) at the experimental temperature. The accuracy of the measurement was within ±0.1mN.m^{-1}. Temperature of the system has been maintained by circulating auto-thermostated water through a double-wall glass vessel containing solution.

The pH values of the experimental solutions were measured by a Mettler Toledo Seven Multi pH meter. The measurement of pH of the solution state is very useful to understand the molecular form of solute and solvent and the type of interactions occurring in solution.

Nuclear Magnetic Resonance (NMR) spectroscopy is used to study the structure of molecules, the kinetics or dynamics of molecules and the composition of mixtures of biological or synthetic solutions or composites.

UV-visible spectroscopy refers to absorption spectroscopy or reflectance spectroscopy in Ultraviolet-visible region. This means it uses light in the visible and ultraviolet region. In this region of electromagnetic spectrum, molecules undergo electronic transitions. Molecules containing π-electrons or non-bonding electrons (n-electrons) can absorb the energy in the form of ultraviolet or visible light to excite these electrons to higher antibonding 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 wavelength of absorption peaks can be correlated with the types of bonds in a given molecule and are valuable in determining the functional groups (specially conjugation) within a molecule.

Differential scanning calorimetric (DSC) study:

From the DSC study, various kind of information such as crystallization, thermal stability, melting etc. can be obtained of chemical compounds in their solid states. The peaks of guest molecule in the thermogram may be completely diminished or shifted to the different temperatures due to the formation of inclusion complexes with the respective host supramolecules [ ].

A scanning electron microscope (SEM):

produce image of sample by scanning of surface by a focused beam of electrones. Specimens are observed in high vacuum condition. The electrone intareact with atom in the sample produce different signals which informed topography of surface and composition of sample. Secondary electron emitted by atom exited by electron beam are dected, the number of secondary electron that can be detected. SEM can achieves resolution better thane 1 nanometer.