CHAPTER I

THE NECESSITY OF THE RESEARCH WORK

I.1. OBJECTIVE, SCOPE AND APPLICATIONS

Research serves as a crucial mechanism for the acquisition of information and the investigation of phenomena, enabling the testing of theories and the formulation of predictions to address problem-solving. Through research endeavors, novel knowledge and comprehension are generated, thereby mitigating the likelihood of making ill-informed or perilous decisions and safeguarding against unfounded ideas and hazardous beliefs. Basic research serves as a precursor to applied research, unfolding in unconventional trajectories. Consequently, research emerges as the driving force behind various aspects of human activities, including the development of technologies such as the phones we utilize, the pharmaceuticals we ingest, and the energy sources we harness. It is imperative for individuals to embrace research as a means to substantiate beliefs, scrutinize conjectures, and unearth more efficacious methods. The collective human endeavor in research has been integral to the evolution of the world, comprising both material entities and living organisms. A predominant focus of research is dedicated to exploring interactions between matter and living organisms.

The discrete quantity of molecules i.e., it's far from having a look at structures containing multiple molecular assemblies. It offers information on the structure, features and behavior of the assemblies. The fundamental goal of this area of chemistry is to lay out new practical structures by combining more than one chemical entity via numerous non-covalent interactions. Supramolecular chemistry capabilities phenomena like molecular self-assembly, molecular recognition, host-guest chemistry, mechanically-interlocked molecular architectures, folding of protein etc.

Supramolecular chemistry is highlighted as highly interdisciplinary, attracting scientists from various fields, including biologists, biochemists, physicists, environmental scientists, crystallographers, theoreticians, in addition to chemists.Since the Nobel Prize recognition, the field of supramolecular chemistry has been growing steadily, driven by the efforts of researchers worldwide. The stature of supramolecular chemistry gained prominence with the Nobel Prize for Chemistry awarded in 1987. The recipients-Donald J. Cram, Charles J. Pedersen, and Jean-Marie Lehn were recognized for their pioneering work on "host-guest" assemblies.

The field of supramolecular chemistry, as elucidated by Cramer, Pedersen, Cram, and Lehn, has experienced significant success and substantial growth in recent periods, marked by an annual output of approximately 20,000 related publications.[1-4] This advancement has primarily manifested in diverse applications of host-guest supramolecular chemistry, such as sensing, separation, drug delivery, catalysis, and biomedical technologies, laying a robust foundation for the discipline. [5-8] Notably, this field introduces noncovalent interactions in a novel manner.

Beyond the computation of binding energies, there is fundamental interest in the design of supramolecular systems and their practical applications. This facilitates the comprehension of biologically significant associations, complexation techniques, and the creation of innovative host structures. Modern synthetic tools play a crucial role in constructing host structures tailored to exhibit enhanced potential for specific guest compounds. The interactions leading to inclusion complexation can be identified, elucidating their structures with precision. The thermodynamics of these interactions can be accurately determined through the binding constants of the inclusion complexes

Supramolecular complexes offer distinct advantages, including the elucidation of the existence and limitations of additivity in binding energies, a common assumption in various applications like rational drug design. Additionally, these complexes involve multiple contributing interactions, mitigating the loss of entropy during intermolecular associations. The stability of inclusion complexes is maintained by several non-covalent forces, namely Van der Waals interactions, short-range repulsion, electrostatic interactions, hydrogen bonding, and interactions of dipolar substances.

Macrocyclic host molecules play a pivotal role in inclusion complexes (ICs) due to their cyclized and constrained conformations, offering distinct advantages in molecular selectivity.[9] Among these, cyclodextrins (CDs) stand out, primarily owing to their amphiphilic nature. [9, 10] The significance of amphiphiles lies in their capacity for self-assembly in aqueous environments, leading to the formation of well-defined structures such as micelles, nanotubes, nanorods, nanosheets, and vesicles. These structures find application in diverse fields ranging from nanodevices to drug delivery and cell imaging. [11-13]

Recent focus has been directed towards cyclodextrin-modified nanoparticles, garnering significant attention due to their ability to enhance the characteristics of resulting assemblies. These enhancements extend to electronic, conductance, thermal, fluorescence, and catalytic properties, thereby broadening the potential applications of these assemblies in areas such as nanosensors and drug delivery vehicles. [14-15] This development has prompted the design of sophisticated probes, specifically tailored for applications in the fabrication of molecular switches, molecular machines, supramolecular polymers, chemosensors, transmembrane channels, molecule-based logic gates, and other intricate host−guest systems. [16-18]

Oligosaccharides, particularly cyclodextrins (CDs), play a crucial role in host-guest inclusion complexation, holding significant importance in the food industry, pharmaceuticals, and consumer goods. [19-22] The unique conical-shaped cyclic structures of cyclodextrins and their derivatives contribute to their commercial availability, with variations based on distinct glucopyranose residues. Cyclodextrins exhibit a distinctive biphasic structure, featuring hydrophilic outer and hydrophobic inner surfaces. The hydrophobic inner region allows for the incorporation of the hydrophobic surface of various guest molecules or segments into the cavity of appropriately sized and stable cyclodextrins through diverse non-covalent interactions. [23] In this context, α and β-cyclodextrins, with 6 and 7 glucopyranose units, respectively, are selected as host molecules due to their high inclusion efficiency, fitting cavity dimensions, cost-effectiveness, and minimal toxicity. [24] Cyclodextrins have found widespread applications in pharmaceuticals, food industries, cosmetics, tissue engineering, and biomedical devices. [25] Inclusion complexation within the non-polar cavity of cyclodextrins serves to protect the hydrophobic components of various bioactive molecules, enzymes, drugs, volatile organic compounds, flavors, essential oils, taxols, flavonoids, vitamins, and more. [26] This process extends the stability of these compounds against light, air, and thermal factors, enhances water solubility, improves bioavailability, and mitigates potential side effects.

The hassle of terrible solubility of many capsules in water that limited their applications, may be consumed through the formation of CD-drug inclusion complexes. Compared with the other different macro-cycles, CDs are the maximum tremendous components in pharmaceutical merchandise for lots reasons: (i) CDs are semi natural merchandise, and may be produced in hundreds of lots in a year from starch with very low cost, (ii) for being pretty biocompatible in nature, CDs can immediately be used as substances of foods, capsules, and cosmetics, (iii) their vigorous binding affinity for a selected guest, stabilizes it in physiological surroundings, (iv) on arriving on the destination, the loaded cargoes are evolved from the hollow space, (v) the hollow space affords an hydrophobic surroundings to defend the drug molecules from enzymatic hydrolysis for the duration of the movement and transport processes. Nowadays, in pharmacology, the stabilization in addition to managed launch of drug molecules has a tremendous attraction. It is pretty not an unusual place now that the encapsulation of many biologically energetic molecules into cyclodextrin cavities can defend the ones molecules from environmental effects. The managed launch of drug molecules, in an effort to minimize their inherent facet effects, were performed via means of complexing them with CDs. So, to get the benefit, primitive considered necessary is to affirm whether or not the drug can shape inclusion complicated with CDs. Following this, the inclusion formation of drug molecules like 1-hydrazinophthalazine Hydrochloride with β-Cyclodextrin, were studied in elements using extraordinary physicochemical measurements along with a few spectroscopic techniques.

The pharmaceutical field is currently focused on the stabilization and controlled release of drugs, emphasizing the need to safeguard drug molecules from environmental factors and mitigate potential side effects. A crucial aspect of achieving controlled release involves investigating the encapsulation of drug molecules within cyclodextrin structures along with the enhancement of their bio-activity. Consequently, the formation of inclusion complexes involving bio-active molecules, such as esculetin, nicotinuric acid and both alpha and beta cyclodextrin, has been systematically studied to accomplish this objective.

The inclusion complex of nicotinuric acid with α-CD and β-CD in hot water has been explored to increase the solubility in water. Esculetin,, is a anticancer drug used in microscopy, incorporated into the cavity of α-CD as well as β-CD in 50% aqueous-ethanol medium was also investigated and characterized by utilizing several physicochemical and spectroscopic methods and observed the application of the inclusion complexes.

Again, the study of excess thermodynamic properties provides a powerful tool for gaining insights into molecular interactions in solution phases. Basically excess thermodynamic properties are differences between the thermodynamic functions of real solutions and the corresponding functions of ideal solutions. [27]

These excess properties offer valuable insights into the nature and strength of various intermolecular forces operating among mixed components in a solution. The example of excess molar volume illustrates how this concept can be used to infer the nature of interactions among molecules in a mixture. Excess molar volume, as an example, reflects the difference between the actual molar volume of a liquid mixture and the molar volume that would be expected for an ideal solution. A positive excess molar volume suggests that molecules in the mixture repel each other when mixed while the negative value indicates the attraction force. The concept of excess thermodynamic functions is applied to improve theoretical models and develop empirical correlations to utilize in engineering applications, especially in the design of industrial separation processes. This knowledge is valuable for optimizing the performance of various processes in industries. Furthermore, the practical applications in engineering underscore the importance of this approach in various industrial processes.

The familiar among the molecular interactions are mainly:

i. Van der Waals interaction: These are weak attractive forces between molecules. They include London dispersion forces and dipole-dipole interactions.[28]
ii. Short range repulsion: these repulsive forces prevent molecules from coming too close together. They play a crucial role in maintaining the structural integrity of matter.
iii. Electrostatic interaction: These interactions involve the attraction or repulsion between charged particles. Ionic bonds are an example of strong electrostatic interactions.

iv. Hydrogen bonds occur when a hydrogen atom is shared between two electronegative atoms. This is a stronger type of interaction compared to regular dipole-dipole forces.

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Interactions among Dipolar substances: Dipolar substances have a separation of charge within the molecule, leading to dipole moments. These interactions include various dipole-dipole forces. It has four types, they are dipole-dipole interaction, dipole-induced dipole interaction, ion-dipole interaction, and variable dipole interaction (including dispersive interaction and london forces).

These interactions are crucial in fields such as chemistry and biochemistry, as they determine the physical and chemical properties of substances. They influence molecular structures, boiling points, solubilities, and many other characteristics of materials.

Partial charges arise due to differences in electronegativity between atoms in a molecule. These partial charges lead to the development of dipole moments, which are essential for various intermolecular interactions. Intermolecular forces play a crucial role in controlling the thermodynamic properties of solutions. These forces affect properties such as boiling points, melting points, and solubilities. Understanding these forces is essential for predicting and explaining the behavior of substances in different phases. Thermodynamic investigations of solvation help in understanding the energy changes associated with the process of molecules being surrounded by solvent molecules. This understanding is vital for elucidating processes that occur in the liquid phase. Transport phenomena in solutions are influenced by intermolecular forces. Transport phenomena in solutions are influenced by intermolecular forces. Thermodynamic investigations provide valuable information about the nature and strength of interactions within the constituents of a solution.

The precise determination of thermophysical properties allows for a quantitative elucidation of solvent effects and the evaluation of various interactions in a solution. By studying properties such as partial molar volumes, limiting ionic conductivity, and viscosity B-coefficient, researchers can estimate ion-solvent interactions. The knowledge of ion-solvent interactions has practical applications, such as choosing solvents to enhance the solubility of minerals in extraction processes.The value and importance of understanding the chemistry of electrolytes in mixed solvents have attracted researchers. Mixed solvents can have unique properties and behaviors that differ from individual solvents, influencing the behavior of electrolytes in complex ways.

This information is crucial for practical applications in chemistry, such as optimizing solvents for specific processes and understanding the behavior of electrolytes in mixed solvent systems. Researchers are increasingly focusing on the intricate details of ion-solvent interactions, recognizing their importance in a variety of chemical processes.

There is an extensive collection of data on different solutions of electrolytes and nonelectrolytes in water. This likely includes information on properties such as concentration, conductivity, and other physicochemical characteristics.

Despite the wealth of data, the structure of water and the intricate interactions it experiences with electrolytes are not yet fully understood. Water is a unique solvent due to its polar nature and hydrogen bonding, which adds complexity to its interactions with solutes. Investigating the thermodynamic properties of solutions is crucial for understanding how electrolytes and nonelectrolytes behave in different concentrations and under various conditions. [29] The unique properties of water, such as its ability to form hydrogen bonds and its high dielectric constant, make the study of water-electrolyte interactions challenging. The interplay of these properties with the ionic nature of electrolytes adds complexity. Researchers continue to investigate physicochemical properties to gain insights into the thermodynamics and behaviors of solutions, aiming to unravel the complexities of water and its interactions with different types of solutes.

The exploration of electrolyte behavior in aqueous and mixed solvents provides a rich field for physical chemists. The study of electrolytes in aqueous and mixed solvents has gained interest due to the diverse range of behaviors observed in different solvent environments. Researchers aim to understand the complex interactions between solutes and solvents under various conditions. This involves studying both solute-solute interactions and solute-solvent interactions. The differences observed from traditional aqueous chemistry, along with the interdisciplinary nature of research, open up exciting possibilities for understanding and applying these systems in various industrial contexts. The study of binary or ternary solvent systems with industrially relevant solvents and electrolytes contributes to both fundamental knowledge and practical applications. [30]

The unique properties of aqueous media spark interest in understanding how electrolytes behave in both aqueous and mixed solvent. The differences observed in behavior open a new gateway for physical chemists to explore novel phenomena and deepen their understanding of complex systems. The study of electrolytes in different solvent environments not only advances our fundamental understanding of chemical interactions but also challenges and reshapes traditional boundaries within the field of chemistry. [31] The practical applications of this research, particularly in the context of organic solvents, underscore its importance and relevance in various scientific and industrial endeavors.

The mentioned facts encourage and prompt researchers to expand their investigations beyond single solvent systems to more complex binary or ternary solvent systems. The inclusion of important electrolytes (solutes) in these solvent systems adds a layer of complexity and practical relevance to the study.

Ionic liquids are described as a ground-breaking compound, implying that they have characteristics or properties that set them apart as innovative and significant. The attractiveness of ionic liquids is attributed to their unique intrinsic properties, which differentiate them from conventional solvents or compounds. These properties could include low volatility, high thermal stability, and ionic conductivity, among others. [32]

The application of ionic liquids is noted to be increasing exponentially in various fields, including academia, industry, and research. To comprehend the applications of individual ionic liquids, a clear understanding of their nature and mode of interaction with solvent molecules is deemed essential.

The current standing of ionic liquids as a ground-breaking compound with unique properties, leading to a surge in applications across academic, industrial, and research domains. The emphasis on understanding the nature and interaction modes of individual ionic liquids underscores the importance of a detailed investigation for their specific applications.

Earlier, the electrolytic property of the ionic liquid, 1-Butyl 1-methylpyrrolidinium chloride in solvents have been studied extensively but the behavior interaction with various salts in the solution state of this ionic liquid have not been examined. Therefore, a strive has been applied to explain the nature of solute-solvent association of the ionic liquid with different oxalate salts of alkali group metals.

The effective molecular interactions involving the vitamins (B1 and C) and Caffeine-Water solution have been examined at different temperatures. Limiting apparent molar volume, molar refraction has been measured using the thermodynamic properties like density and refractive index.

The physico-chemical properties of the systems like densities and viscosities of some oxalate salts, namely, lithium oxalate, sodium oxalate and potassium oxalate have been predicted in ionic liquid-water binary mixed solvents at the temperature 298.15, 308.15K and 318.15K. Research on the thermo-physical properties basically, viscosities, densities, and refractive index, conductivity of ionic solutions employ a significant role in explaining the structures and properties of binary solutions.

I.2. COMPILATION OF BIOLOGICALLY ACTIVE MOLECULES, HOST MOLECULES, IONIC LIQUIDS, SALTS AND SOLVENTS EMPLOYED IN THE RESEARCH WORK

Names of the Biologically Active Molecule, Host Molecules, Ionic Liquids and Solvent molecules are indexed below:

Biologically Active Molecule:

- Esculetin
- Nicotinuric Acid
- Vitamin C (Ascorbic Acid)
- Hydrochloride salt of Vitamin B1 (Thiamine hydrochloride)
- Caffeine

Host Molecules:

- α-Cyclodextrin
- β-Cyclodextrin

Ionic Liquids and salts:

- 1-Butyl 1-methylpyrrolidinium chloride (Ionic Liquid)
- Lithium Oxalate (salt)
- Sodium Oxalate (Salt)
- Potassium Oxalate (Salt)

Solvents:

- Water
- Ethanol
- Dimethyl sulfoxide

1.3 TECHNIQUES OF INVESTIGATION

In order to get a higher expertise into the phenomena of various interactions upon solvation and inclusion complexation, numerous experimental techniques had been performed. A quantity of noteworthy methodologies like densitometric, conductometric, refractometric strategies had been applied to inquire about the inclusion and solvation phenomena.

The study of thermodynamic functions in characterizing the structural components and solutions. The density measurements provided the partial molar volumes are appropriate parameters to interpret solute-solute, solute-solvent interactions which are the important area in solution chemistry. The significant thermodynamic quantity like partial molar volume (V_ϕ^o ϕ_V^0), gives facts concerning the character and volume of ion-solvent interaction. Beside, the experimental slope (Sv*) offers facts about ion-ion interactions. [33] Alternatively, the viscosity after the addition of electrolyte has been attributed to inter-ionic and ion-solvent effects. Conductance statistics acquired as a feature of awareness were used to assess the ion-affiliation through using suitable equations.

The interaction can be predicted by the application of suitable spectroscopic and spectrometric investigations. The specific characteristic physical properties of the various molecules are observed in different spectroscopic studies in aqueous along with mixed solvents. The mass spectrometry and the spectroscopic investigations such as UV-Vis, Proton-NMR, 2D-ROESY, FT-IR etc have been used to illuminate a diversity of interactions in the systems.

The various physicochemical as well as spectroscopic methods performed during the research work are mentioned follow:

- UV-VIS Spectroscopy
- Scanning Electron Microscopy (SEM)
- FTIR Spectroscopy
- ^{1}H NMR Spectroscopy

- Mass Spectrometry
- 2D ROESY
- Infra-Red Spectroscopy
- XRD
- Conductivity study
- Density study
- Viscosity study
- Refractive Index study
- Density Functional Theory study
- Molecular Docking study
- Antimicrobial Activity Analysis
- Cell Viability Assay
- Antioxidant Activity Analysis