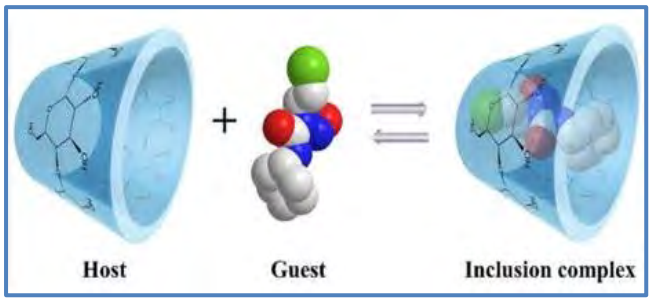
ABSTRACT

As per the title of the thesis, I would like to show my deep insight into the field of Supramolecular Host-Guest Inclusion Complexation and the Amino Acid-Ionic Liquid interaction in aqueous medium. Supramolecular assembly has gained enormous significance these days in drug release due to their excellent bioavailability and remarkable ability to alter various properties of the drug such as its solubility, stability within the body, pharmacokinetics and pharmacodynamics. They also exhibit nontoxic properties, better encapsulation and controlled release.



The spectroscopic contribution confirms the inclusion complexation of various bioactive molecules and their different photophysical properties in aqueous media. The inclusion phenomena can be satisfactorily expressed by UV-visible, ^{1}H-NMR, FTIR, mass spectrometry and fluorescence emission spectroscopic studies. Surface tension, Powder XRD and SEM analysis provides a qualitative idea towards the formation of supramolecular assembly. The thermal stability of such assembly can be explained by TGA and DSC study. Theoretical molecular modelling studies of the supramolecular system confirm the data obtained from the experimental studies.

The study of physicochemical properties of solutions provide significant knowledge on various thermodynamic properties of electrolytes and non-electrolytes, the effects of the variation in ionic constructions, mobility of ions along with their common ions. The genesis of diverse interactions between amino acids-ionic liquid in aqueous phase is usually exposed by measurement of the apparent molar volume (ϕ_v), limiting apparent molar volume (ϕ_v^0), molar refraction (R_M), limiting molar refraction (R_M^0), molar conductance (Λ), viscosity B coefficients obtained from different physicochemical methodologies.

In this study, encapsulation of various biologically active molecules such as, Mephenesin, Riboflavin, 6-Propyl-2-thiouracil, have been investigated. These bioactive

molecules have potential applications in living systems. Pharmacological activity is often considered to describe beneficial effects of bioactive molecules.

Extensive studies on Nile blue and its derivatives have suggested that it could be potentially useful as fluorescent probes in this regard, because of their unique optical properties, excellent thermo and photostability, and low toxicity.

In host–guest chemistry, the application of macrocyclic hosts in molecular recognition, controlled release of a drug and sensing field has received considerable interest. Incorporation of guest molecules in aqueous environment within the cavity of host molecules, e. g., α-cyclodextrin, β-Cyclodextrin or water soluble calixarene, provides the new insight into the molecular recognition (e. g. inclusion or complexation) through non-covalent interactions.

Supramolecular host-guest chemistry gives a broad idea about the formation of inclusion complex between the host and the guest molecules. Hydrophobic cavities of host are capable of binding different guest molecules. In recent years, the whole supramolecular assemble has been vastly studied in many fields such as drug-delivery and analytical chemistry. Among the various host molecules, cyclodextrins and its derivative along with water soluble calixarene seems to be the most promising to form inclusion complexes, especially with various guest molecules with suitable dimension.

Therefore, the primary objective of this thesis is to find out the influence of supramolecular recognition and solution chemistry that are inevitably significant because of their wide range of applications in many fields ranging from pharmaceutical to biomedical sciences.

SUMMARY OF THE WORKS

CHAPTER I

This chapter contains the detail object of the research work, their scope and applications in the contemporary science. It also includes the reason of choosing the bioactive molecules, cyclodextrins, calix[4]arenes, ionic liquid, and the solvent systems. This chapter has a short list of all the methods of investigations used in the research work.

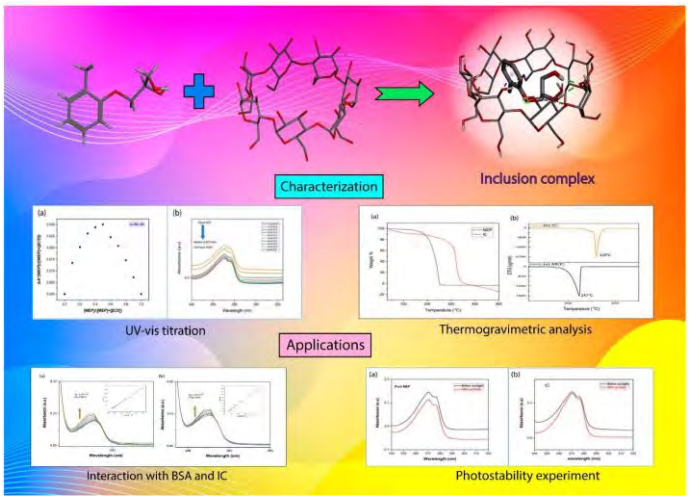
CHAPTER II

This chapter includes the review of the earlier works in this field of research done by various scientist and researchers across the world. This chapter also provides a detail theory of investigations, where the interacting forces among the molecules have been described. Here, the background theory of all the investigating methods, i.e., the theory of ^{1}H-NMR, FTIR spectroscopy, UV-visible spectroscopy, Fluorescence spectroscopy, Mass Spectrometry, Differential Scanning Calorimetry, Thermogravimetric analysis, Scanning Electron microscopy, Powder XRD, Molecular docking study, Antimicrobial study, Cytotoxicity study, DNA and BSA binding study, Surface Tension, Conductivity, Density, Viscosity, Refractive Index have been discussed thoroughly and the significance of their use in the research work described in this thesis have been shown.

CHAPTER III

This chapter contains the experimental section. It covers the name, structure, physical properties, and applications of the biologically active molecules, cyclodextrins, calix[4]arenes, ionic liquid and solvents used in the research work. It also includes the details about the experimental methods, the descriptions and use of the instruments involved in the research work.

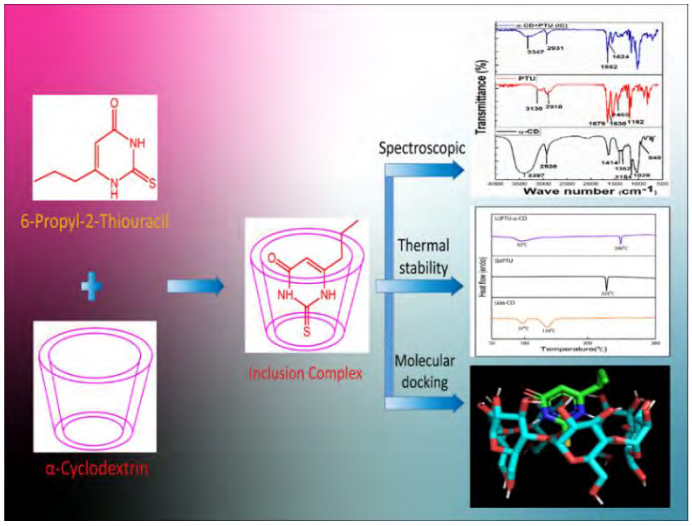
CHAPTER IV



This chapter comprises the experimental study emerged on the encapsulation of polyether compounds such as Mephenesin (MEP) into the nano hydrophobic cage of β-cyclodextrin as host molecule. The commonly known co-precipitation method was followed to prepare inclusion complex (IC) by molar ratio 1:1. Different spectrometric techniques e.g. transform infrared spectroscopy (FTIR), DSC, TGA, DTA, and scanning electron microscope (SEM) indicated molecular interactions between β-CD and MEP. UV-visible titration predicts the binding constant for βCD and MEP in solution state around $2.1\times10^{3}M^{-1}$. The formation of the inclusion complex has been predicted by slight shifts in the FTIR as well as ^{1}H NMR spectrum. Job plot and ESI-MS spectra showed that 1:1 inclusion complex has been formed. Molecular docking study unveils the inclusion mechanism which is well supported with the experimental data. In addition, UV-visible spectroscopic study predicts the binding interaction between Mephenesin with amino acid residues of BSA and DNA.

Published in the Journal of Molecular Liquids, 344, (2021) 117977

CHAPTER V

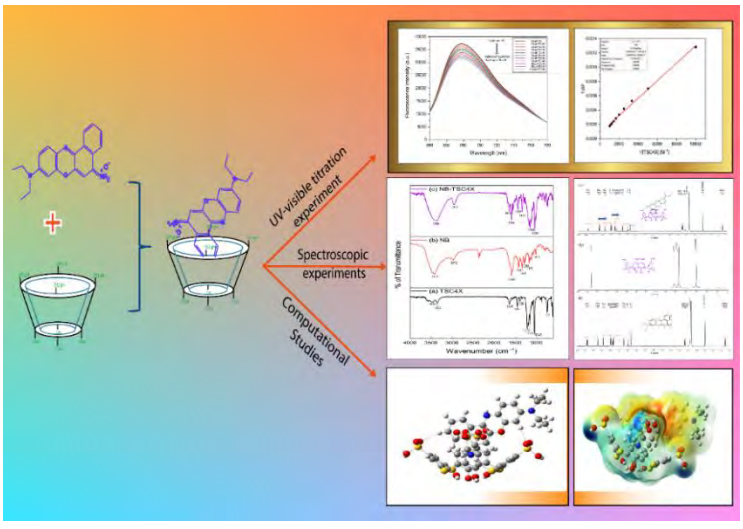


This chapter consists of the formation of inclusion complex (IC) of an antithyroid drug 6-propyl-2-thiouracil (PTU) with α-cyclodextrin (α-CD) and to analyse its aqueous solubility, photostability, binding with Calf thymus DNA (CT-DNA), antibacterial and cytotoxic activities. The PTU-α-CD complex was synthesized by following the co-

precipitation method with a molar ratio of 1:1. The formed complex was characterized by employing several spectroscopic techniques such as ^{1}H NMR, FTIR, DSC, TGA, powder XRD and SEM indicated the successful encapsulation of drug PTU into the nano cage of α-CD. The enhancement of thermal stability of PTU after complexation was shown by TGA and DSC analysis. Job's plot confirmed the 1:1 molar ratio of guest (PTU) and host (α -CD) during the formation of IC and the molecular association constant as predicted between PTU and α-CD using UV-vis titration method was found to be 3297.57±0.15 M^{-1}. The most desired orientation of the PTU molecule within the non-polar binding pocket of α -CD cavity was speculated by molecular modelling study. The PTU- α -CD complex showed better in vitro antimicrobial activity results as compared to pure drug PTU. The aqueous solubility and photostability of PTU were greatly improved owing to the formation of the PTU- α -CD complex as shown using UV-vis spectroscopy. The PTU- α -CD complex (IC_{50} = 2.12 μM) also displayed noteworthy in vitro cytotoxic activity than pure PTU (IC_{50} = 6.44 μM) towards human kidney cancer cell line (ACHN) whereas (IC_{50} = 3.63 μM) and (IC_{50} =2.09) μM) for PTU- α -CD and drug respectively in a normal kidney cell line (HEK-293). This research also predicts the release of PTU in presence of CT-DNA without any chemical alteration. Finally, these outcomes disclose that the complexation of PTU with α -CD could enhance the stability of PTU and display various applications associated with it.

Published in the Journal of Molecular Liquids, 380, (2023)121708

CHAPTER VI

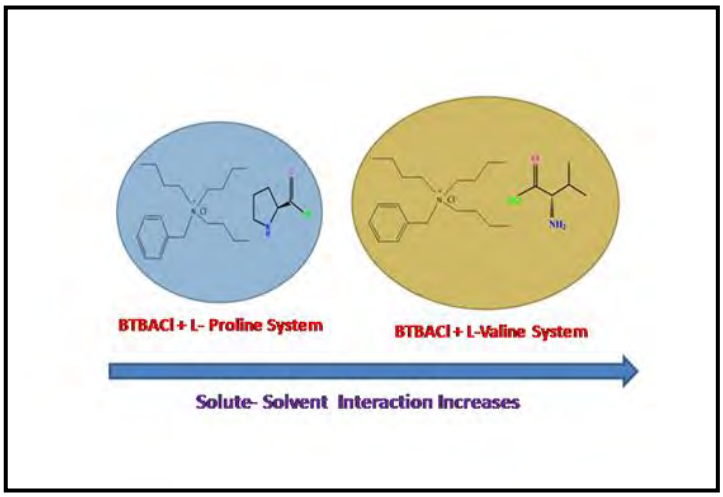


This chapter incorporates the construction of a supramolecular encapsulated complex between Nile blue (NB) and *p*-sulfonatothiacalix[4]arene (TSC4X). The developed inclusion complex (NB-TSC4X) was established by fluorescence spectroscopy, TGA, FTIR, ^{1}H-NMR, and DFT studies. Benesi-Hildebrand calculation showed a linear plot that indicated a 1:1 stoichiometric ratio

having fairly high stability constant of 2720 M^{-1} in the solution phase. DFT analysis helps us to find out the optimized structure of the inclusion complex. Finally, the binding interaction of inclusion complex with bovine serum albumin (BSA) was evaluated. In brief, this work uncloses a new strategy to enhance the performance of fluorescent dye.

**Communicated*

CHAPTER VII

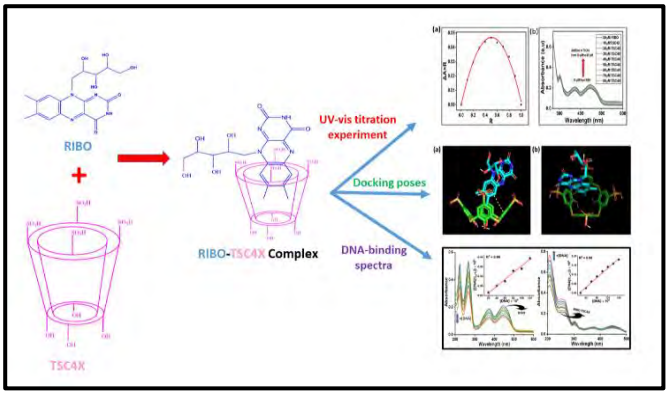


This chapter includes the solute–solvent interaction between ionic liquids (ILs) and amino acids (AA) in aqueous media plays a significant role for the optimization of a number of important biotechnological processes. L-Valine and L-Proline (two solute molecules) interact with an ionic liquid (Benzyltributylammonium chloride) in aqueous medium. Based on the different parameters such as apparent molar volume, viscosity B-coefficient, molar refraction, molar conductance, surface tension at different temperatures and different concentrations from density, viscosity, refractive index, conductance, surface tension measurements have been used to explain the molecular level interactions which was supported by NMR and UV-vis studies. Using Masson equation, the experimental slopes and the limiting apparent molar volumes are obtained which explain the solute-solute and solute-solvent interactions. Hepler's technique and dB/dT values have been used to examine the structure-making and structure-breaking nature of the solutes in the solvents. Viscosity parameters, A and B obtained from Jones-Doles equation explained the solute-solute and solute-solvent interactions in the solution. Lorentz-Lorenz equation has used to calculate the molar refraction. The specific conductance and surface tension also explained the interaction properties. Further the findings have been supported by NMR study of the solutions and also considerable amount of theoretical analysis has been done which was in good agreement with the experimental result. The behavior of many other bio-molecules can be explained by considering

amino acids as model and the mechanism has been extended to elucidate the behavior of other (biological) systems. In our findings we were emphasized on the nature of solute–solvent interactions and the presence of structural effect on the solvent in solution to analyze the molecular-level interactions prevalent in the systems.

Published in Fluid Phase Equilibria, 557, (2022) 113415

CHAPTER VIII



This chapter includes the synthesis of a new encapsulated complex denoted as RIBO-TSC4X, that was derived from an important vitamin Riboflavin (RIBO) & p-sulfonatothiacalix[4]arene(TSC4X). The synthesized complex RIBO-TSC4X was then characterized by utilizing several spectroscopic techniques such as ^{1}H-NMR, FT-IR, PXRD, SEM, and TGA. Job's plot has been employed to show the encapsulation of RIBO (guest) with TSC4X (host) having a 1:1 molar ratio. The molecular association constant of the complex entity (RIBO-TSC4X) was found to be 3116.29±0.17 M^{-1}, suggesting the formation of a stable complex. The augment in aqueous solubility of the RIBO-TSC4X complex compared to pure RIBO was investigated by UV-vis spectroscopy & it was viewed that the newly synthesized complex has almost 30 times enhanced solubility over pure RIBO. The enhancement of thermal stability upto 440^{0} C for the RIBO-TSC4X complex was examined by TG analysis. This research also forecasts RIBO's release behaviour in the presence of CT-DNA, and at the same time, BSA binding study was also carried out. The Synthesized RIBO-TSC4X complex exhibited comparatively better free radical scavenging activity, thereby minimizing oxidative injury of the cell as evident from a series of antioxidant and anti-lipid peroxidation assay. Furthermore, the RIBO-TSC4X complex showed peroxidase-like biomimetic activity, which is very useful for several enzyme catalyst reactions.

Published in ACS Omega, 8,7, (2023) 6778-6790

CHAPTER IX

This chapter includes the concluding remarks about the research works done in this thesis.