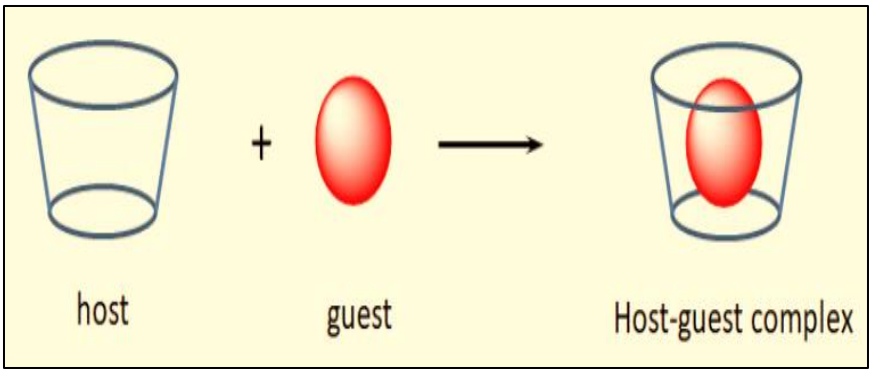
ABSTRACT

Supramolecular assembly have 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, better encapsulation and controlled releasing properties.



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, FT-IR, mass spectrometry and fluorescence spectroscopic studies. Surface tension, PXRD and SEM analysis provides a qualitative idea towards the formation of supramolecular assembly. Thermal stability of such assembly can be illustrated by DSC study. Theoretical molecular modelling studies of the supramolecular system confirm the data obtained from the experimental studies.

In this study, encapsulation of various biologically active molecules such as, Indole-3-methanol, Ticlopidine hydrochloride, Sulisobenzone, L-Valine and L-Aspartic acid have been investigated. These bioactive molecules have potential applications in living systems. Pharmacological activity is often considered to describe beneficial effects of bioactive molecules.

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., cyclodextrins or water soluble calixarene, provides the new insight into the molecular recognition (e. g. inclusion or complexation) through non-covalent interactions.

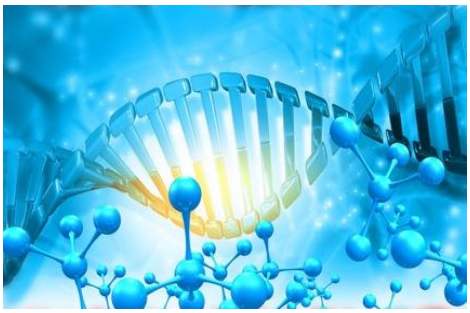
The molecular recognition often influences the pharmacological activity of bioactive guests.

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 ages, the supramolecular assembly has been enormously 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 object of this thesis is to find out the influence of supramolecular recognition that are inevitably significant because of their wide range of advanced applications in many fields ranging from pharmaceutical to biomedical sciences.

Summary of work done

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 and calix[4]arenes. 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 scientists 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., theory of ^{1}H NMR spectroscopy, FT-IR spectroscopy, UV-Visible spectroscopy, Mass spectrometry, Fluorescence spectroscopy, Thermogravimetric analysis, Differential Scanning Calorimetry, Powder X-ray Diffraction, Scanning Electron Microscopy,

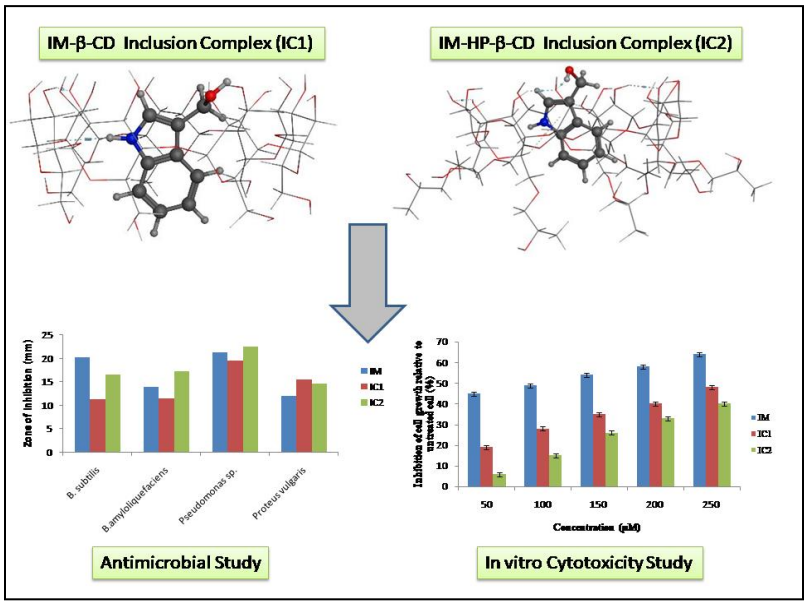
Surface tension study, Molecular docking study, Antibacterial activity study, Cytotoxicity study, Reactive Oxygen Species generation study have been discussed thoroughly and the significance of their use in the research work described in this thesis have been shown.

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 and solvents used in the research work. It also includes the details about the experimental methods and the description and use of the instruments involved in the research work.

Chapter IV

This chapter consists of the molecular encapsulation of indole-3-methanol within the nanocage of β-cyclodextrin and hydroxypropyl-β-cyclodextrin. The work has been explored by spectroscopic, physicochemical and calorimetric methods. Job plots have been drawn by

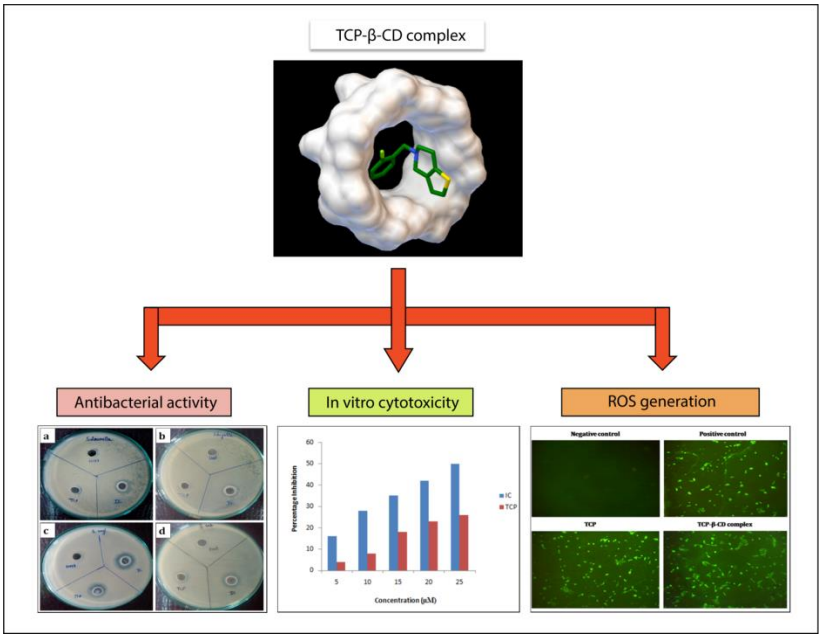


UV-Visible spectroscopy to confirm the 1:1 stoichiometry of the host-guest assembly, which was further supported by surface tension study and mass spectrometric analysis. Association constants for the inclusion complexes have been calculated by UV-Visible spectroscopy and Fluorescence spectroscopy using Benesi–Hildebrand method. Thermodynamic parameters have been estimated with the help of van't Hoff equation, which demonstrate that the overall inclusion processes are thermodynamically favourable. ^{1}H NMR and FT-IR studies provided quantitative

information on the possible inclusion mode of inclusion complexes. Thermal stability of indole-3-methanol on complexation with cyclodextrins has been studied by DSC analysis. Molecular docking study presented useful insight on the encapsulation mode of indole-3-methanol molecule into the cavity of cyclodextrins. The surface morphology of the inclusion complexes was studied by SEM. Finally, the antimicrobial activity and cytotoxicity of the inclusion complexes were examined and compared with pure indole-3-methanol.

Chapter V

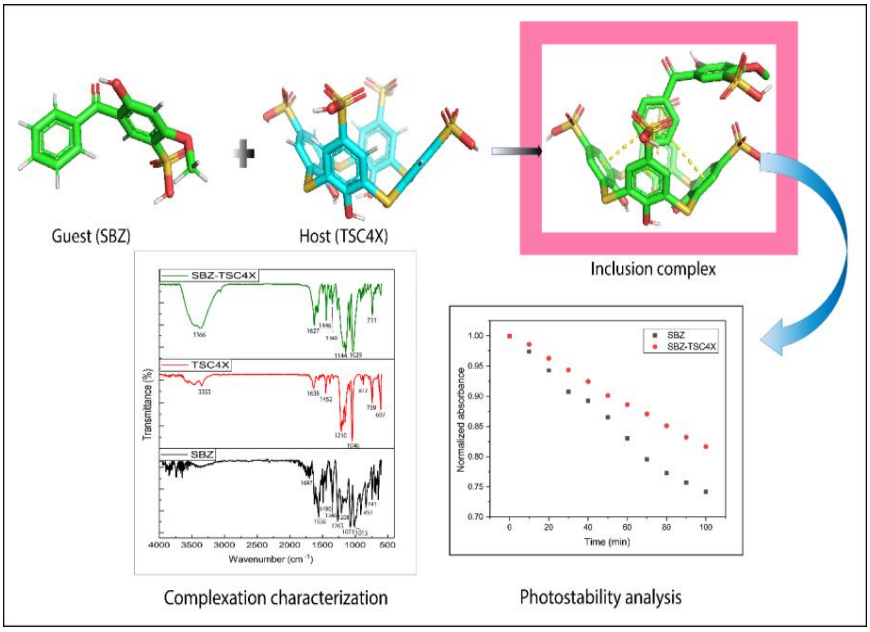
This chapter comprises the exploration of the formation of stable host-guest inclusion complex of ticlopidine with β-cyclodextrin, and investigation of its bioactivity. The complex was characterized by various physicochemical as well as spectroscopic techniques. Job plot, surface tension study and mass spectrometric analysis confirm the 1:1 host-guest inclusion complexes. Binding constant has been calculated by using Benesi–Hildebrand method, and the Gibb's free energy of binding has been derived from the binding constant value which indicates that the inclusion process is spontaneous. The mechanism of inclusion was drawn by ^{1}H NMR and FT-IR spectroscopic analysis. PXRD and SEM analysis have been performed to confirm the inclusion complex formation. The improvement in the thermal stability of ticlopidine after complexation was studied by thermogravimetric analysis. Molecular docking study speculated the most preferred orientation of ticlopidine molecule within the binding pocket of β-cyclodextrin cavity. The antibacterial activity and cytotoxic activity of the inclusion complex were evaluated and compared with free ticlopidine. Furthermore, the induction of intracellular reactive oxygen species generation in ACHN cells by ticlopidine and its inclusion complex has been studied,



which demonstrate that the complexation with β-cyclodextrin leads to increased apoptotic activity of ticlopidine.

Chapter VI

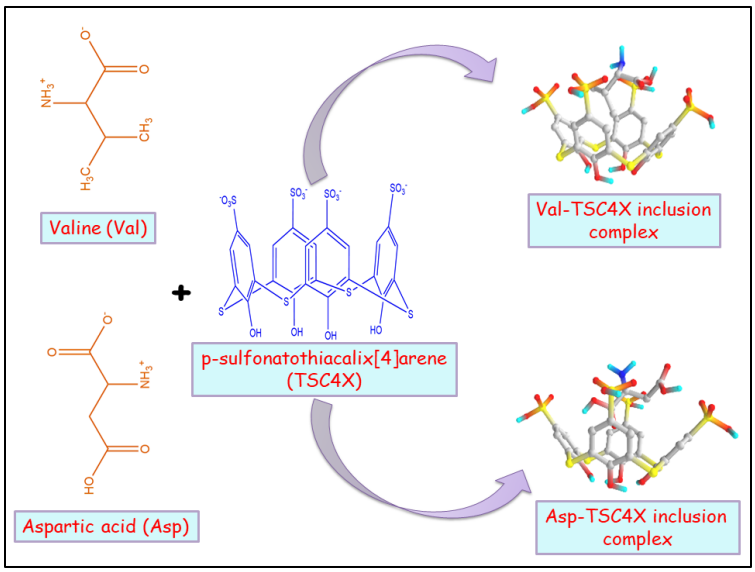
This chapter includes the study of the molecular recognition of sulisobenzone by *p*-sulfonatothiacalix[4]arene. Various physicochemical techniques have been employed to establish the outcome of the work. New inclusion system of sulisobenzone with *p*-sulfonatothiacalix[4]arene was fabricated, and its binding behaviour both in solution and solid states has been investigated. The 1:1 stoichiometry of the inclusion complex was confirmed by Job plot and mass spectrometry. Association constant and Gibb's free energy of binding have been evaluated for the formed inclusion complex by UV-Visible spectroscopy. DSC experiment was employed to evaluate thermal stability of the inclusion complex. The molecular interactions have been explained and critically discussed with the help of FT-IR and ^{1}H NMR spectroscopic studies. The improvement in the aqueous solubility and photostability of sulisobenzone after complexation was studied by UV-Visible spectroscopy. The molecular docking study depicted the most feasible conformation of inclusion complex with lowest binding energy.



Chapter VII

This chapter incorporates the supramolecular complexations of two natural amino acids, viz., L-Valine and L-Aspartic acid, with *p*-sulfonatothiacalix[4]arene to form inclusion complexes in aqueous medium which are highly suitable for diverse applications in modern

bio-medical sciences. The interactions at molecular level have been explained and decisively discussed by means of ^{1}H NMR spectroscopic studies, while mass spectrometric analysis confirm that the inclusion complexes have been formed with 1:1 stoichiometry. NMR titrations have been performed by ^{1}H NMR spectroscopy to determine the binding constants of the inclusion complexes using Benesi–Hildebrand method, and the estimation of free energy of binding from the binding constant value determines thermodynamic feasibility of the inclusion process. PXRD and SEM analysis revealed the formation of inclusion complexes. Thermal stability of the inclusion complexes was verified by DSC analysis. Molecular docking study presented the most stable binding orientation of L-Valine and L-Aspartic acid within the cavity of *p*-sulfonatothiacalix[4]arene.



Chapter VIII

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