ABSTRACT

Knowledge of the physicochemical properties of potential chemical compounds is a primary concern of the alternative assessment process for two reasons. First and foremost, the inherent hazards of the chemical taken into consideration, such as its capacity to interfere with normal biological phenomena, physical hazards and environmental fate such as degradation, persistence can be determined by its intrinsic physicochemical properties and the system with which it is interacting. In cases of organic and inorganic chemicals, these intrinsic properties are determined by molecular structure. These properties are determined on the basis of their sizes, composition and morphology. Secondly, physicochemical properties which are a measure of physical hazards could also be used to abolisht specific chemicals because of their toxicity and prioritize compounds which are proved beneficial for the screening of human and ecotoxicological effects.

Contrarily, the study of Inclusion Complexes has become a matter of utmost importance because of their widespread applications in arenas of bio sensing and bio imaging, drug delivery and regenerative medicine.

The advantages that provide these inclusion complexes in the pharmaceutical industry are:

- The increase or decrease of the solubility and the dissolution rate of the complex in relation to the active substance depending on the nature of the guest and host molecules;
- A better bioavailability of the drug;
- The change of reactivity of the active substance after the protection of some functional groups;
- Extended the life of the drug (improved physical and chemical stability);
- The reduction of the contraindications;
- The correction of odour and flavour.

Inclusion complexes can be defined as a special group of compounds known as ‘non-classical’ complex, which is prepared under the effect of mechanical factors and has molecules of host and guest as its components. compounds molecules without formation of any specific chemical bond (the weak Van der Waals attractive forces, hydrogen bonding interactions and polar interactions) between guest and host; the essential criterion is simply that the enclosed molecule or “guest” be of a suitable. size and shape to fit into a cavity within a solid structure

formed by “host” molecules . This principle of formation allows some particular coordinated and saturated molecules to form thermodynamically more stable. supramolecular crystalline phases without forming any solid chemical bonds , van der Waal’s interaction, hydrogen bonding and hydrophobic interaction play pivotal roles during such association phenomenon.

The host molecules are the compounds having the sufficiently large cavities to incorporate the other components (the guest molecules) and the guest molecules are those compounds which get encapsulated into those cavities by the means of non covalent interactions. The preparation of the inclusion complexes depends on the size and shape of the guest molecules, as well as the dimensions of cavities formed from the aggregates of the host molecules. On the basis of the nature of the cavity of the host molecule, there can be a cage and canal inclusion complexes.

Choice of solutes and solvents

Chemicals used in Solution Chemistry

(i) D(-) Fructose

(ii) D(+) Galactose

(iii)**Ionic liquid:**1-butyl-1-methylpyrrolidinium chloride

Guest Molecules

(ii)Drug molecule

- Azelaic acid
- Dopamine hydrochloride
- Sulphanilamide
- Aspartic acid
- Glutamic acid

Host Molecules

- α-Cyclodextrin
- β-Cyclodextrin
- Dicyclohexano-18-crown-6 (DC18C6)
- 18-crown-6 (18C6)
- Dibenzo-18-crown-6 (DB18C6)

Solvents

Water has been used as the main solvent in most of the cases and non-aqueous solvent like absolute ethanol and acetonitrile have also been used.

Methods of Investigation

1. Density measurement

The density (ρ) was evaluated by using vibrating U-tube Anton Paar digital density meter (DMA 4500 M) having a precision of ±0.00005g.cm^{-3} .

2. Viscosity measurement

The viscosity measurement was done using a Brookfield DVIII Ultra Programmable Rheometer with fitted spindle size of 42. The instrument was calibrated by using distilled water and aqueous $CaCl_2$ solutions.

3. Refractive index

Refractive index measurement was done by using Mettler Toledo digital refractometer. The light emitting diode (LED) having wavelength 589.3 nm was the source of light.

4. Conductance

Conductivities of the solutions were measured by Mettler Toledo Seven Multi conductivity meter having uncertainty 1.0 μSm^{-1}. The conductivity cell was calibrated using 0.01 M aqueous KCl solution.

5. IR Spectroscopy

FT-IR spectroscopic study was performed by Perkin Elmer FT-IR Spectrometer 8300 (SHIMADZU) using KBr pellet method for solid sample with scanning range 400-4000 cm^{-1}.

6. UV-VIS Spectroscopy

Agilent 8453 spectrophotometer was used to measure the UV spectral pattern.

7. Raman Spectroscopy

The Raman spectroscopic study was done in ENSpectr R532 using 532 nm laser.

8. 1H NMR Spectroscopy

For 1H and 2D ROESY NMR analysis, spectra were recorded at 600 MHz and 400MHz BRUKER AVANCE .

9. Mass Spectrometry

The Mass Spectroscopic analysis was performed using Agilent Accurate-MassQ-TOFLC/MS6520.

10. Scanning Electron Microscope Study

Scanning Electron Micrographs were recorded using JEOL JSM-IT100.

Summary of the work done

CHAPTER-I

Consists of the objective, utility and applications of the research work, chemicals used and methods of investigation.

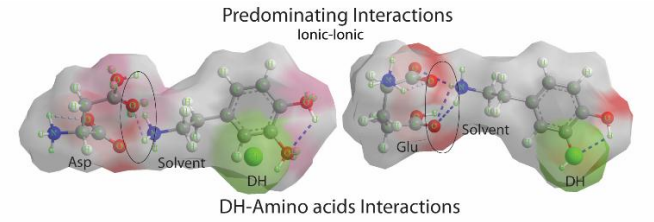
CHAPTER-II

This chapter consists of the general INTRODUCTION part of the thesis. A brief review of 'Host-Guest Inclusion Phenomena" has been given. Various derived parameters dependent on density, viscosity, association constant (derived from UV-Visible spectroscopy and Fluorescence spectroscopy), SEM analysis, HRMS Study, conductance study and refractive index measurement and their importance in Host-guest inclusion chemistry and solution chemistry has been discussed.

CHAPTER-III

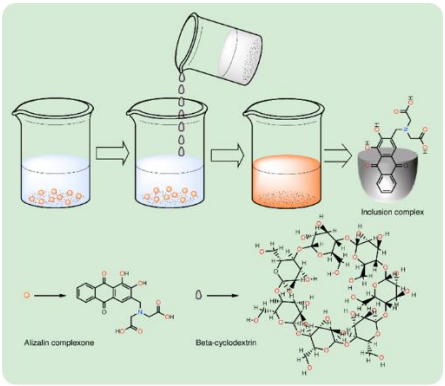
It is based on the experimental section which predominantly includes structure, source, mass purity and utility of the solvent and fundamental properties of the components (ionic liquids and drug molecules) used throughout my research work. It also includes instrumentational details, procedure, working principle and related equations.

CHAPTER-IV



In this chapter, Interactions of Aspartic acid and glutamic acid are investigated in aqueous Dopamine Hydrochloride with the help of density, viscosity, conductance, NMR spectroscopy and Raman spectroscopy. The experimental observation concluded that Glutamic acid shows more extensive interaction than Aspartic acid in aqueous Dopamine Hydrochloride, which is reflected in the values of apparent molar volume, A and B coefficient, chemical shift values, conductance pattern and changes in the frequency pattern of Raman spectroscopy.

CHAPTER-V



In this chapter, an industrially important dye Alizarin complexone has been incorporated inside the cavity of β-cyclodextrin and the inclusion complex formed was characterised by 1H NMR, 2D ROESY, UV-Visible Spectroscopy, Fluorescence Spectroscopy, HRMS and SEM study. Such inclusion phenomena protects the dye molecule from external hazards like enviromental degradation, oxidation, photolytic cleavage and can be used to remove the dye present in savage water.

CHAPTER-VI

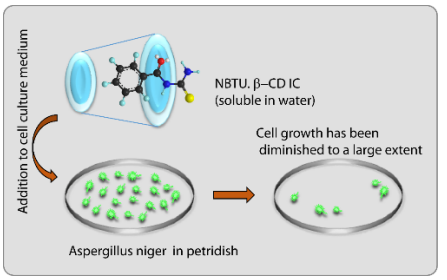
Dictates about the interaction between 1-butyl-1-methylpyrrolidinium chloride [bmp]Cl in different concentrations of aqueous solution of D(-)fructose and D(+) galactose at different temperatures ranging from 293.15-303.15K. The limiting molal conductivities, association constants of the above systems have been calculated. The limiting apparent molal volume, experimental slope and the limiting partial molal transfer volumes, were also derived. The

values of B-coefficient, Gibbs free energy (ΔG^0), enthalpy (ΔH^0) and entropy (ΔS^0) of ion-pair formation indicates greater extent of interaction for [bmp]Cl in D(+)galactose solution rather than in D(-)fructose solution and such process was found to be endothermic in nature.

CHAPTER-VII

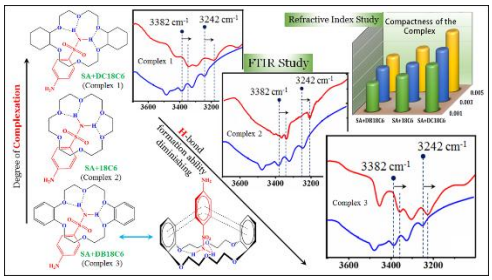
Explains the phenomena of inclusion complex formation between CD and Azelaic acid and it has been investigated by UV-Visible, NMR spectroscopic method,HRMS study and SEM study along with density functional theory. The β-CD inclusion complex got stabilized by the intermolecular hydrogen bonding and DFT data reveals that. Data obtained from Enthalpy and Gibbs free energy of formation in aqueous solution indicate that the formation of β-CD inclusion complex is spontaneous, and hence Azelaic acid forms more stable. inclusion complex with β-cyclodextrin in the aqueous medium compared to the α-cyclodextrin, this fact has also been supported by the value of association constant and other spectroscopic measurements.

CHAPTER-VIII



The inclusion complexes of N-Benzoylthiourea with β-cyclodextrin (β-CD) was prepared, the resultant complex was characterised by FTIR, UV-Visible Spectroscopy, proton nuclear magnetic resonance spectroscopy (1H NMR), fluorescence spectroscopy, 2D ROESY, HRMS, SEM study . The stoichiometry was established using a Job plot method of continuous variation and it was found to be 1:1. The inclusion procedure was clarified by applying 2D ROESY study. The stability of the inclusion complex was confirmed by the means of the values of ΔH^0, ΔG^0, ΔS^0 and association constants derived from UV-Visible spectroscopy and Fluorescence Spectroscopy. The 1:1 stoichiometry was visually demonestrated by HRMS study. Our results showed that less polar part of the guest molecule that is aromatic ring was deeply inserted into the cavity of β-CD. By complexation with β-CD, both the water and thermal of NBTU were prominently improved and NBTU.β-CD complex showed antifungal activity against *Aspergillus niger* (fungal pathogen).

CHAPTER-IX



In this chapter, we have discussed complexation of sulfanilamide with 18-crown-6, Dicyclohexano-18-crown-6, Dibenzo-18-crown-6 using 1H NMR, IR and UV-visible spectra in solution state. The interaction phenomena between crown ethers with sulfanilamide have been described with the help of by density, viscosity, refractive index measurements, which indicate a greater extent of complexation in case of dicyclohexano-18-crown-6. The stoichiometry was determined by Job method and the 1:1 stoichiometry was found for all the complexes. The Benesi-Hildebrand method was employed to evaluate the association constant of the IC. The ΔG^0 of the inclusion complex process was found negative, which indicates spontaneity of the the process. Hydrogen bonding was considered as one of the key factors for such complexation and π–π interactions also have a minor contribution towards complexation of dibenzo-18-crown-6.

Chapter-X

This chapter contains Concluding Remarks.