CHAPTER II

REVIEW OF THE EARLIER WORKS AND THEORY OF INVESTIGATION

II.1. Review of the Earlier Works:

In supramolecular chemistry, host–guest chemistry describes complexes that are composed of two or more molecules or ions that are held together in unique structural relationships by forces other than those of full covalent bonds.[1,2] Host–guest chemistry encompasses the idea of molecular recognition and interactions through non-covalent bonding. Non-covalent bonding is critical in maintaining the 3D structure of large molecules, such as proteins and is involved in many biological processes in which large molecules bind specifically but transiently to one another. Although non-covalent interactions could be roughly divided into those with more electrostatic or dispersive contributions, there are few commonly mentioned types of non-covalent interaction, ionic bonding, hydrogen bonds, van der Waals forces - Keesom force (dipole - dipole) - Debye (dipole - induced dipole), hydrophobic interactions.

Important concepts advanced by supramolecular chemistry include molecular self-assembly, molecular folding, molecular recognition, host–guest chemistry, mechanically-interlocked molecular architectures, and dynamic covalent chemistry. The study of non-covalent interactions is crucial to understanding many biological processes that rely on these forces for structure and function. Biological systems are often the inspiration for supramolecular research. The "host" component can be considered the larger molecule, and it encompasses the smaller, "guest", molecule. In biological systems, the analogous terms of host and guest are commonly referred to as enzyme and substrate respectively.

In order to design synthetic systems that perform specific functions and tasks, it is very important to understand the thermodynamics of binding between host and guest. Chemists are focusing on the energy exchange of different binding interactions and trying to develop scientific experiments to quantify the fundamental origins of these non-covalent interactions by utilizing various techniques such as NMR spectroscopy, UV/visible spectroscopy and isothermal titration calorimetry,.[3] Quantitative analysis of binding constant values provides useful thermodynamic information. The

thermodynamic benefits of host–guest chemistry are derived from the idea that there is a lower overall Gibbs free energy due to the interaction between host and guest molecules. Chemists are exhaustively trying to measure the energy and thermodynamic properties of these non-covalent interactions found throughout supramolecular chemistry; and by doing so hope to gain further insight into the combinatorial outcome of these many, small, non-covalent forces that are used to generate an overall effect on the supramolecular structure. Thus, thermodynamics is an important tool to design, control, and study supramolecular chemistry. Perhaps the most striking example is that of warm-blooded biological systems, which entirely cease to operate outside a very narrow temperature range.

S. Giuffrida et al. described small and stable platinum nanoparticles can be easily obtained in one step through visible light irradiation of a host–guest inclusion complex between â-cyclodextrin and platinum acetylacetonate in a water solution. The exclusive control of the reaction by an external trigger, the removal of the undesired reaction products without any manipulation of the sample, and the absence of ionic repulsions between the metal nanoparticles represent the main remarkable advantages offered by this synthetic methodology.[4]

V. Crupi et al. presented Inclusion complexes of cyclodextrins with nonpolar drugs are a topic of current interest in pharmaceutical science, because they increase the aqueous solubility, chemical stability and bioavailability of poorly water-soluble drugs.[5]

Y. X. Sun et al. describes a facile and targeted gene delivery system was prepared by conjugating β-cyclodextrin modified polyethylenimine (PEI-CD) and adamantyl peptide (AdGRGDS) based on host–guest interaction. With the rational design between PEI-CD and AdGRGDS, the PEI-CD/AdGRGDS gene delivery system showed excellent DNA binding capability and exhibited good ability to compact DNA into uniform spherical nanoparticles.[6]

W. C. E. Schofield et al. presented β-cyclodextrin barrels can be tethered to solid surfaces using the Williamson ether synthesis reaction via an intermediate pulsed plasma deposited poly(4-vinylbenzyl chloride) linker layer. The loading and release of

perfume molecules through hostguest inclusion complex formation with surface tethered β-cyclodextrin.[7]

S. Goswami et al. describes the interaction of a painkiller Isoxicam, belonging to the oxicam group of nonsteroidal anti-inflammatory drugs (NSAIDs) and its copper complex with different cyclodextrins (β-CD, γ-CD, HPβCD, and HPγCD), has been investigated in both solution and the solid state.[8]

M. Gangopadhyay et al. describes that a newly synthesized triphenylamine derivative shows significant differences in inclusion complex formation with two different macrocyclic hosts, cucurbit[7]uril and β-cyclodextrin.[9]

D. Patra et al. presented a supramolecular approach to the fabrication of self-powered micropumps based on "host-guest" molecular recognition between R- and β-cyclodextrin and transazobenzene. Both hydrogels and surface coatings based on host-guest partners were used as scaffolds to devise the micropumps. These soft micropumps are dual stimuli-responsive and can be actuated either by light or by introducing guest molecules. Furthermore, the micropumps can be recharged through reversible hostguest interaction.[10]

Z. Du et al. describes about the controlled self-assembly of multiple-responsive SAP based on a selective host–guest inclusion of β-cyclodextrin with a modified poly(ethylene glycol) consisting of a ferrocene end group, a C_{11} alkyl chain, an azobenzene block, and a poly(ethylene glycol)methyl ether chain.[11]

M. Gupta et al. presented a supramolecular strategy to improve the fluorescence intensity of coumarin dye through its interaction with the relatively new host cucurbit[7]uril (CB[7]). The virtually nonfluorescent coumarin was converted into a highly fluorescent entity in water upon addition of the nonfluorescent host CB[7].[12]

II.2. Theory of Investigations:

II.2.1. Hydrophobic Interactions:

The tendency that leads nonpolar substances to undergo aggregation in an aqueous solution ignoring water molecules is termed as hydrophobic effect. Simply, it means "water-hating", and describes the segregation of water and nonpolar substances, which maximizes hydrogen bonding interaction between molecules of water, as a result water - nonpolar molecules contact area get reduced. Thermodynamically, the change in free energy of water molecules surrounding a solute is the hydrophobic effect. A positive free energy change of the surrounding solvent designates hydrophobicity, whereas a negative free energy change entails hydrophilicity.

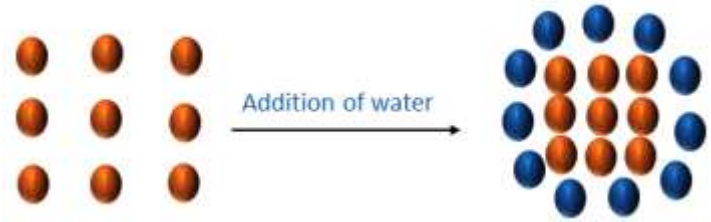

Figure 1: Hydrophobic interaction brings the interacting molecules closer

The hydrophobic effect controls various biological functions like, cell membrane and vesicle formation, insertion of membrane proteins into the nonpolar lipid environment, protein folding and protein-small molecule associations. Applying the concept of hydrophobicity sometimes, we can make two non-interacting molecules to undergo reactions by means of reducing the inter-molecular distance adding water to the system.

II.2.2. Van der Waals Forces:

According to van der Waals, van der Waals force is a distance-dependent interaction between atoms or molecules. These attractions are not like that of covalent bond resulting from a chemical electronic bond. The van der Waals force are relatively weak and quickly vanishes as the distances between interacting molecules gone large. The magnitude of van der Waals force depends on the surface area of the molecule and the magnitude of the force increases with increasing surface area.

Van der Waals force shows an ultimate part in fields as diverse as supramolecular chemistry, polymer science, structural biology, surface science and

nanotechnology. It also explains many properties of organic compounds and the formation of molecular solids, as well as the driving force that causes a solute molecule to undergo solvolysis in polar and non-polar media. The term van der Waals force is sometimes includes all intermolecular forces as well as the London dispersion force between instantaneously induced dipoles.

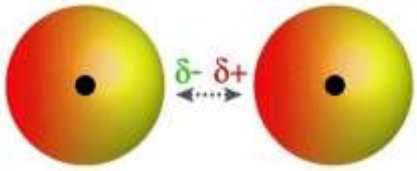

Figure 2: Van der Waals forces acting between molecules

The distance between atoms at which the force becomes repulsive rather than attractive as the atoms approach one another is termed as the van der Waals contact distance; the mutual repulsion between the atoms' electron clouds develops this phenomenon.

II.2.3. Hydrogen bonds:

A hydrogen bond is a partial intermolecular bonding interaction between a lone pair on an electron rich donor atom, particularly the elements nitrogen (N), oxygen (O) or fluorine (F) and hydrogen (H) atom.

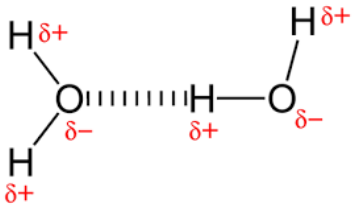

Figure 3: Hydrogen bonding in water molecules

There are two distinct types of Hydrogen bonds, intermolecular Hydrogen bond, bonding interaction between two separate molecule and intramolecular Hydrogen bond, bonding interaction between parts of same molecule. The bonding energy may vary from 1 to 40 kcal/mol and Depends on their geometry, the nature of the donor and acceptor atoms which constitute the bond and environment. This makes them to some extent stronger than a van der Waals interaction, but remains weaker than fully covalent or ionic bonds. This type of bond is found to occur in inorganic molecules such

as water and in organic molecules like DNA and proteins. Hydrogen bonding between the water molecules enhances the boiling point of water to 100 ^{0}c and makes difference in boiling point from other group 16 hydrides. Intramolecular hydrogen bonding is also responsible for the secondary and tertiary structures of proteins and nucleic acids. It also plays a vital role in the structure of polymers, both synthetic and natural.

II.2.4. Electrostatic Forces:

Electrostatic force governed from the Coulomb's law and it is defined as the as the amount of force between two stationary, electrically charged particles. The electrical force imparting between two charged bodies at rest is conventionally called electrostatic force or Coulomb force. Coulomb's law always describes the quantity of electrostatic force between stationary charges.

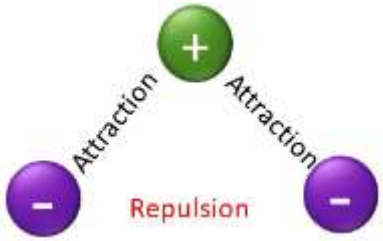

Figure 4: Electrostatic force working between charged species

The magnitude of the electrostatic force is directly proportional to the product of the magnitudes of charges and inversely proportional to the square of the distance between them and works along the direction of bond. The same charges repels each other whereas the opposite charges attracts each other.

II.2.5. Ion-Dipolar Attractions:

An electrostatic interaction between a charged ion and a dipolar molecule is termed as the ion-dipolar interaction. It is basically, an attractive force that is generally found to govern in solutions, exclusively ionic compounds when undergoes dissolution in polar liquids. A cation or an anion attracts the counter part of a polar molecule. Ion-dipole attractions become stronger with the increase in charge on the ion or as the magnitude of the dipole of the polar molecule increases. These interactions becomes very important issues in many chemical circumstances.

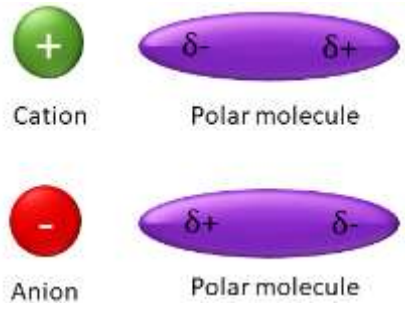

Figure 5: Ion–Dipolar attraction between the ion and polar molecules

II.2.6. Dipole-Dipole Attractions:

Dipole-dipole forces can be define as the attractive forces between the positive end of one polar molecule and the negative end of another polar molecule. Dipole-dipole forces have strengths that ranges from 5 kJ to 20 kJ per mole. Being weaker than ionic or covalent bonds in strength have a substantial effect only when the molecules involved are close together.

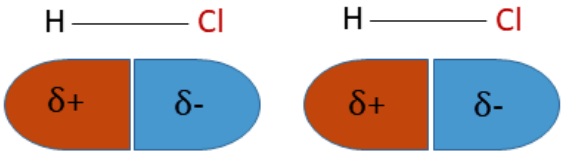

Figure 6: Dipole-Dipole attraction between the polar molecules

II.2.7. Solute-Solvent Interactions:

Chemistry of a solution is the study of a homogeneous mixture composed of two or more substances. The little quantity of substance that undergo dissolution to the another substance present in large quantity is termed as the solute and the substance presenting in large quantity determines the ultimate phase of the solution is known as the solvent. In the preparation of a solution, the solute-solvent interaction is one of the most accountable factors in solution chemistry. A profound solute-solvent interaction allows a solute, to undergo dissolution in a particular solvent molecule. Concentration of a solution is one of the important parameters, which is a measure of the amount of solute present in a given amount of solution or solvent. When the solvent is water then it is termed as the aqueous solution.

II.2.8. ^{1}H NMR Spectroscopy:

Among all of the spectroscopic techniques, Nuclear magnetic resonance spectroscopy, i.e. NMR spectroscopy is the most reliable method to characterize an organic molecule. It gives us information about the local magnetic environment around the atomic nuclei distinguishing number of total hydrogen atoms with magnetically different environment. Beside this, it also enriched us with the information that number of hydrogen atoms present in all the magnetically different environment.

The sample is placed in a magnetic field and the NMR signal is produced by excitation of the nuclei sample with radio waves into nuclear magnetic resonance, which is detected with sensitive radio receivers. The intramolecular magnetic field around an atom in a molecule changes the resonance frequency, thus giving access to details of the electronic structure of a molecule and its individual functional groups. As the fields are unique or highly characteristic to individual compounds, in modern organic chemistry practice, NMR spectroscopy is the definitive method to identify monomolecular organic compounds. Similarly, biochemists use NMR to identify proteins and other complex molecules. Besides identification, NMR spectroscopy provides detailed information about the structure, reaction state, dynamics and chemical environment of molecules. The most common types of NMR are proton and carbon-13 NMR spectroscopy, but it is applicable to the sample that contains nuclei possessing spin.

Long timescale of NMR does not allows for observing fast phenomena, therefore produces an averaged spectrum. Samples having a large extent of impurities unable show on an NMR spectrum. So, higher external magnetic field strength may be used for higher sensitivity.

Integrals and integration

With the help of software we can analyse peak intensity and the number of protons of different types. Integrating the peak area, we can easily measure the signal intensity and hence the number of hydrogen atoms presents in that area i.e. the number of protons is only proportional to the intensity or the integral, of the NMR signal in the very simplest NMR experiments. In case of carbon-13 NMR spectra, the integral of the signals also depends on the scalar and dipolar coupling constants and the relaxation

rate of the nucleus. But, lack of information about that, difficulties remains to have integrals of complicated systems.

Chemical Shift

Depending upon the nature of magnetic environments, protons with different magnetic environments registers their signals at different positions in ^{1}H NMR spectrum. Although strength of the external magnetic field may alter the position of the signals in the spectrum. A reference signal is usually used to report a NMR signal, usually that of TMS (tetramethylsilane). Electron density around a nucleus also generate a local magnetic field and as opposition to the external magnetic field shielding the nucleus from the external magnetic field. Then it undergoes upfield shifting in the ^{1}H NMR spectrum. Now, an electronegative atom nearby to proton atoms withdraws electron density from the proton and experiences the external magnetic field more resulting downfield shift of that proton in the ^{1}H NMR spectrum. The chemical shifts for heavier nuclei are strongly influenced by other factors including excited states.

In this research work, the interacting protons from both the host and guest molecules undergo shifting while the formation of inclusion complexes, suggesting diamagnetic or paramagnetic shielding host and guest protons.

II.2.9. 2D ROESY:

When two protons originating from same or different molecules somehow come closer in 0.4 nm range through space even if they are non-bonded will show a correlation through space registering an off diagonal cross peak in 2D ROESY spectrum. Thus, it provides vital information about the special proximity between two molecules through space. It can also detect chemical and conformational exchange. A ROESY spectrum exhibits a diagonal and cross peaks signals. The diagonals consist of the 1D spectrum. The cross peaks obtained owing to the presence of protons those are close to each other. So, 2D ROESY spectroscopy provides vital confirmation about the spatial closeness of the interacting atoms of the host and the guest by observing the intermolecular dipolar cross-correlations.

Consistent with the structure of α and β-CD, inclusion complexation inside into cyclodextrin cavity can be shown by the appearance of NOE cross-peaks between the protons of cyclodextrin and the protons of the aromatic guest identifying their spatial

proximity. To prove this, 2D ROESY spectra of the inclusion complexes with α and β-CD in D2O, were recorded, which shows significant correlation of aromatic protons of guest molecule with the H_3 and H_5 protons of α and β-CD, establishing the aromatic ring was encapsulated inside both the cyclodextrin cavities.

II.2.10. FTIR Spectroscopy:

Infrared (IR) spectroscopy, however, provides a direct way of observing these functional groups because it detects the stretching and bending of bonds rather than any property of the atoms themselves. It is particularly good at detecting the stretching of unsymmetrical bonds of the kind found in functional groups such as OH, C=O, NH_2, NO_2 etc. and for this reason IR spectroscopy complements NMR beautifully as a method for structural analysis.

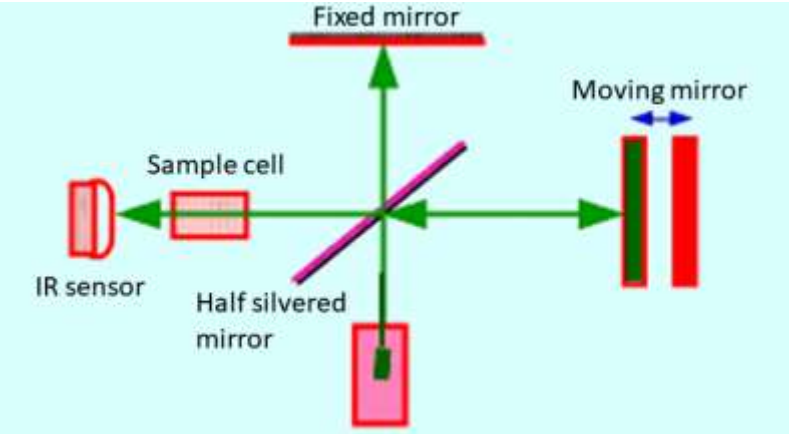

Figure 7: Diagrammatic representation of working principle of FTIR

The bonds between the two atoms are considered as a spring, which undergoes vibration like a simple harmonic oscillator. The frequency of vibration depends on the strength of the bond (force constant K) and the masses of the atoms, m_1, m_2 which are held together by the bond. According to the Hook's law frequency of vibration can be expressed as follows-

$$\bar{\nu} = \frac{1}{2\pi c}\sqrt{\frac{K}{\mu}} \qquad \text{(II.1)}$$

Where, μ is the reduced mass of the molecular system and can be expressed as follows-

$$\mu = \frac{m_1 m_2}{m_1 + m_2} \qquad \text{(II.2)}$$

The force constant K signifies the bond strength.

Preparation of Samples:

We recorded all the FTIR spectra in the solid state by preparing a palette of a minute quantity of sample mixing with a large quantity of dried KBr.

Elucidation of the Infrared spectroscopic data of the ICs as well as the pure Host and Guest molecules also reveals the veracity about the way by which the ICs are formed and supports the circumstances of host – guest interaction.

II.2.11. UV-Visible Spectroscopy:

Molecules containing various electronic energy levels can undergo transition from the lower energy state to the higher energy level showing a broad peak in the UV-Visible spectrum. Different energy levels, in terms of bonding and non-bonding electrons can absorb energy in the form of ultraviolet or visible light to excite these electrons to higher anti-bonding molecular orbitals. Lower the energy gap between the HOMO and the LUMO more easily the molecule get excited in the longer the wavelength of light. The possible four types of transitions are π–π*, n–π*, σ–σ* having the order of energy gap σ–σ* > n–σ* > π–π* > n–π*

According to the Lambert-Beers law, UV-Visible spectrometer shows absorbance of a sample and records the spectrum.

$A = \log(I_0/I) = \varepsilon c l$, for a given wavelength

A = Absorbance

I_0 = Intensity of incident light

I = Intensity of the light leaving sample

ε = Molar absorptivity

c = Molar concentration of solution containing sample

l = Length of cuvette containing sample

In this thesis, the UV-Visible spectroscopic data were fitted to the Benesi-Hildebrand equation for the calculation of the binding constants of the inclusion complexes formed by the cyclodextrin host with various guest molecules. The stoichiometries of the inclusion complexes were also determined with the data obtainable from the UV-Visible spectroscopy.

II.2.12. Fluorescence Spectroscopy:

Fluorescence spectra is an emission spectra originating by the transition from the higher energy levels to the lower energy level. Molecules having different electronic energy levels simultaneously have vibrational energy levels and can show fluorescence spectra. In fluorescence, a photon first excited the species from its ground electronic state to one of the various vibrational states in the excited electronic state. The excited molecule then undergoes deactivation through collisions with other molecules. it causes the excited molecule to lose vibrational energy until it reaches the lowest vibrational state from the excited electronic state according to the Jablonski diagram. Finally, the molecules drops down to one of the various vibrational levels of the ground electronic state again as a result photons gets emitted the process showing fluorescence. Since the vibrational energy levels of the ground electronic state have different energies, the energies of the emitted photons will have different energies by which we can determine the structure of the different vibrational levels.

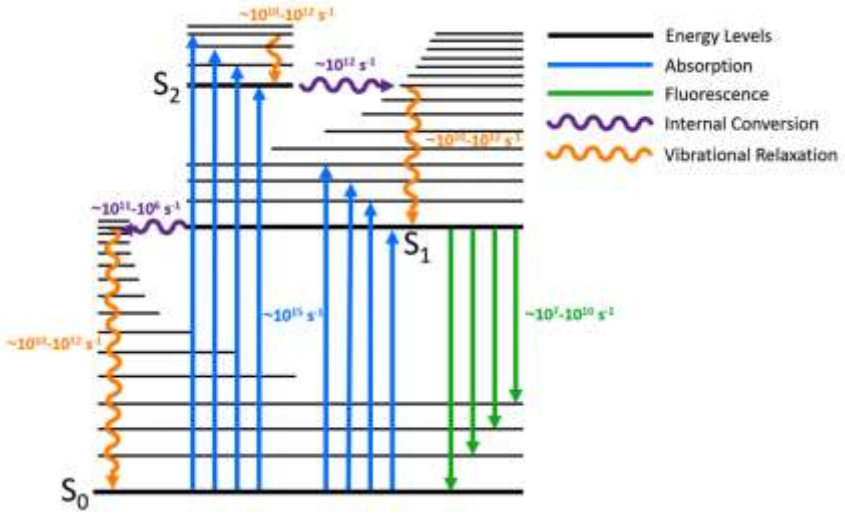

Figure 8: Jablonski Diagram

Fluorescence Spectroscopic measurement was employed for the further verification of the association constants obtained from the UV-Visible spectroscopic measurements.

Data obtained here with were fed to the modified Benesi-Hildebrand as well as the Stern-Volmer equation for the determination of association constants of the inclusion complexes and the guest – HSA binding interactions.

II.2.13. Differential Scanning Calorimetry (DSC):

DSC is a significant instrument by which we can analyse the heat change in a sample with the variation of temperature. Sometimes it helps us to observe the presence of impurities or change in crystal structure by studying the change in melting point registering a peak other than the melting temperature in the DSC thermograms. Various thermodynamic parameter can also obtained from this saying about the thermal stability of the sample under experiment.

There are two types of DSC, Heat Flux Type and Power Compensation Type. Heat Flux DSC includes the sample and reference holder, the heat sink, the heat resistor and the heater. The heater is supplies heat to the sample and the reference through heat sink and heat resistor. There is a proportional relationship between heat flow the heat difference of heat sink and holders. Heat sink has the greater heat capacity than the sample. Heat sink compensate the endothermic or exothermic phenomena of sample. It helps to keep constant temperature difference between the sample and the reference. The difference the amount of heat supplied to the sample and the reference is proportional to the temperature difference of both holders. Calibration of the standard material, allows measuring unknown sample quantitatively.

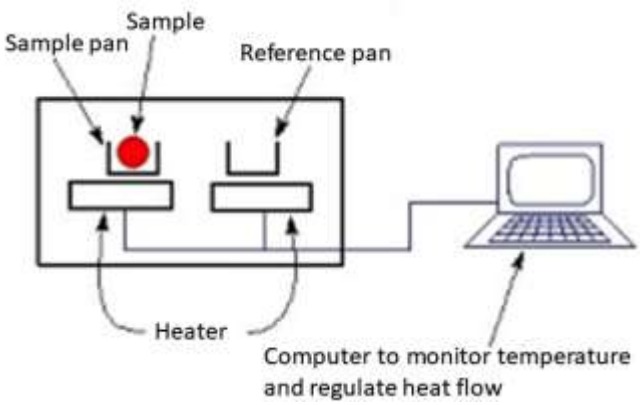

Figure 9: Diagrammatic representation of working principle of DSC

In this thesis, we gather both the qualitative and quantitative insight about the physicochemical state of the drug while encapsulated into the cavity of CDs. Generally,

the shifting of an endothermic peak to a different temperature or absence of an endothermic peak for the pure guest molecule in the inclusion complexes are found in DSC thermograms which indicates a change in melting point, crystal lattice or sublimation point due to inclusion complexation.

II.2.14. Powder X-Ray Diffraction (PXRD):

PXRD is a quick analytical method mostly used for phase identification of a crystalline material and can provide information on unit cell dimensions. The material which, is analysed, be finely ground, homogenized and average bulk composition is determined.

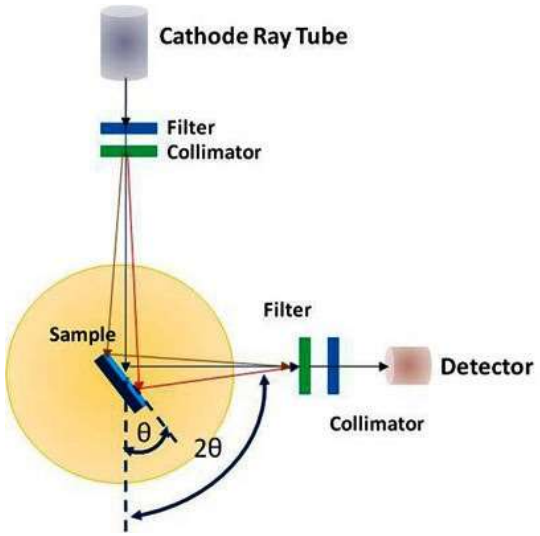

Figure 10: Diagrammatic representation of working principle of PXRD

It was revealed that, crystalline materials functions as three-dimensional diffraction grating for X- ray and the spacing of planes in crystal lattice comparable to wavelength of X-Ray. XRD is now a general practice for the determination of atomic spacing and crystal structures. Diffractions arise whilst light is scattered by a periodic array with long-range order, producing constructive interference at specific angle. The wavelengths of X-ray are related to the distance between two atoms; monitoring this principle crystalline character of a substance can be explained. The interactions of the incident rays with the sample makes constructive interference whilst satisfy the condition of the Bragg's Law-

$$n\lambda = 2d\sin\theta \qquad \text{(II.3)}$$

Where, n = Order of diffraction, d = inter-planar spacing, Θ = Glancing angle, λ = Wavelength of X-Ray used.

X-rays produced from the X-ray tube have been directed at the sample and diffracted X-rays are then recognized, processed and counted. Data were recorded throughout a range of 2θ angles.

II.2.15. Scanning Electron Microscopy (SEM):

In the Scanning Electron Microscope (SEM) a focused beam of high-energy electrons is used to produce a high-energy resolution image of the sample. After getting accelerated primary electrons hit the sample forming secondary electrons (SE).

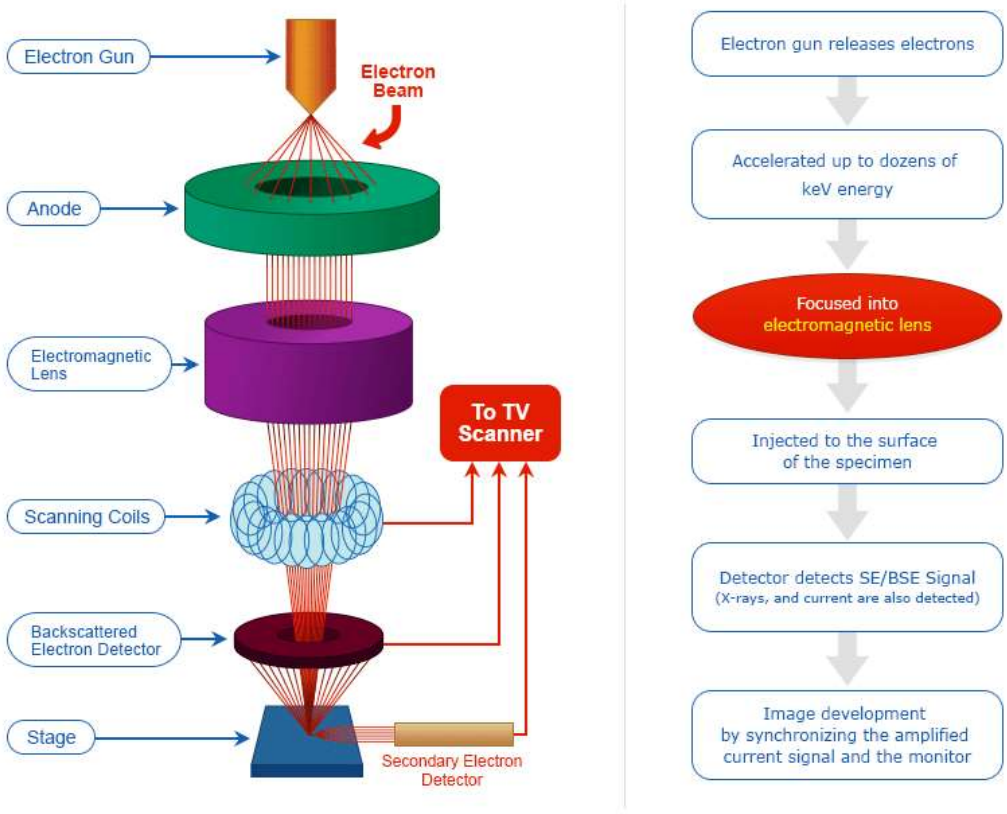

Figure 11: Diagrammatic representation of working principle of SEM

A positively charged electron detector composes these secondary electrons, which in turns provide 3D image of the sample. The signals developing from electron-sample interactions make known information concerning the sample along with the external morphology, crystalline structure, chemical composition and orientations of substances making up the sample. SEM scanning can image areas ranging from about 1cm to 5 microns width. The SEM is also able to perform analyses of chosen point of locations on the sample.

II.2.16. Mass Spectrometry:

Mass spectrometry, the most accurate analytical method, is used in different fields to establish the elemental composition. Here, molecules are bombarded with a beam of energised electrons to split and ionize the fragments. Specific kind of ions has a definite mass to charge ratio (i.e. m/z ratio). The m/z ratio is equal to the molecular mass for most of the ions as the ions mostly contain single charge. A parent ion or a molecular ion is formed when single electron is removed from the molecule.

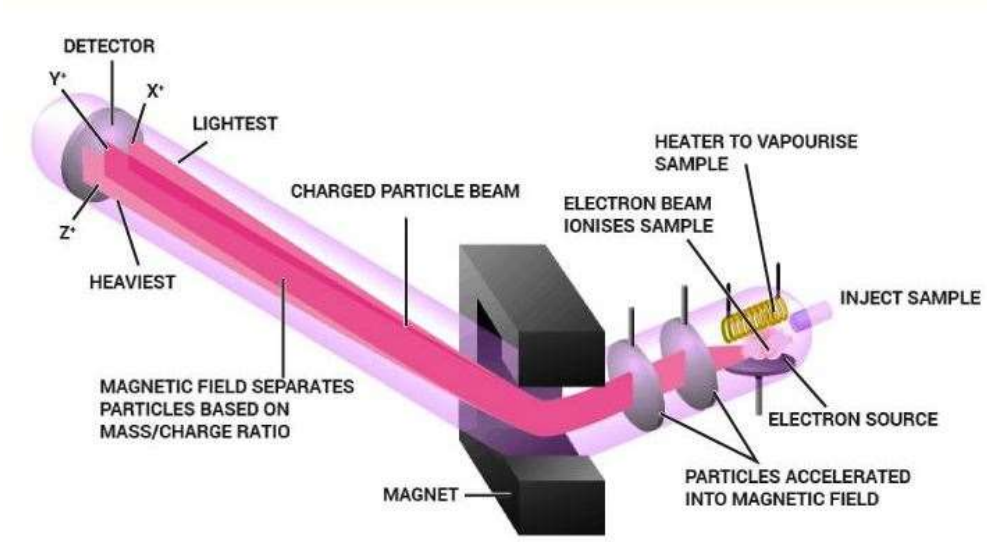

Figure 12: Diagrammatic representation of working principle of HRMS

$$M + e^- \text{ ----------> } M^+ + 2e^-$$

In case of the parent ion the m/z value is the molecular mass of the compound. Sometimes, the parent ion peak becomes the base peak that can be easily recognized but in most of the cases, molecular ion peak does not appear as base and is often of insignificant abundance. In the process of inclusion complexation there is no bond formation or breaking and hence the m/z ratio of inclusion complex should be equal to the sum of the masses of host and the guest molecules or it may add with proton or certain impurities such as sodium. Thus From the mass spectrometric analysis formation of the inclusion complex can be confirmed. The stoichiometry of inclusion complex can also be discussed.

II.2.17. Density measurements:

The volumetric information includes 'Density' as a function of weight, volume and mole fraction and excess volumes of mixing. It is a well-recognized method to the analyse molecular interactions in fluids. Depending upon the nature of solvent molar volume of the solute molecules changes. So, calculating apparent molar volume of a solution system, we can track about the nature of interaction taking place between solute and solvent in solution. The volumetric information may have immense importance in this regard.

Apparent molar volumes

Apparent molar volume of a substance in solution can be defined as the sum of the geometric volume of the two solute molecules while undergo solvation through solute-solvent interaction with the co-solvent. Density data can be used for the calculation of molar volume of a pure substance. However, the volume contributed to a solvent by the addition of one mole of an ion is difficult to determine. This is so because, upon entry into the solvent, the ions change the volume of the solution due to a breakup of the solvent structure near the ions and the compression of the solvent under the influence of the ion's electric field, i.e., electrostriction. Electrostriction takes place when there are electric fields of the order of 109-1010 V m^{-1}, the compression of ions and molecules is likely to be significant. The effective volume of an ion in solution, the partial molar volume, can be determined from a directly obtainable quantity- apparent molar volume (ϕ_v). The apparent molar volumes, (ϕ_v), of the solutes can be calculated by using the following relation.

$$\phi_v = \frac{M}{\rho} - \frac{1000(\rho - \rho_0)}{m\rho\rho_0} \qquad \text{(II.4)}$$

Where, M is the molar mass of the solute; m is the molality of the solution; ρ and ρ0 represents the densities of the solution and solvent respectively.

Limiting apparent molar volumes

Apparent molar volume at infinite dilution is termed as the limiting molar apparent volume (ϕ_v^0). Least squares fitting of linear plots of (ϕ_v) against the square root of

molar concentrations ($m^{1/2}$) using the Masson equation gives the values of limiting molar apparent volume (ϕ_v^0) and experimental slopes (S_v^*).

$$\phi_v = \phi_v^0 + S_v^*.\sqrt{m} \qquad \text{(II.5)}$$

Generally, the values of limiting molar apparent volume (ϕ_v^0) are always positive in all the cases and signifies the solute-solvent interaction taking place in the solution. On the other hand experimental slopes (S_v^*) suggests the solute-solute interaction in solution. Greatness the values between limiting molar apparent volume (ϕ_v^0) and experimental slopes (S_v^*) suggests the respective interaction in the solution as the profound interaction.

In this research work, I have found that, values of the experimental slope, (S_v^*) assigning the extent of ion-ion interaction in the solution has negative values indicating the presence of less ion-ion interaction in the medium. Quantitative comparison shows, greater the magnitude of (ϕ_v^0) than (S_v^*) recommends the ion-solvent interactions dominants over ion-ion interactions.

Structure making/structure breaking interaction

The solute – solvent interaction studied so far may be of two types, structure breaking or synergistic structure making interaction. The way developed by Hepler is helpful to analyse the nature of the solute – solvent interaction taking place in the solution phase.

In this connection, the limiting apparent molar volumes of solutions were calculated and the data obtained were fitted with the following polynomial equation-

$$\phi_v^0 = a_o + a_1 T + a_2 T^2 \qquad \text{(II.6)}$$

Where, a_0, a_1 and a_2 are the empirical coefficients depending on the nature of solute, mass fraction (W) of co-solvent. T represents temperature in Kelvin scale.

First derivative of equation ( ) gives the values of limiting apparent molar expansibilities (ϕ_E^0) which have been calculated for various temperatures.

$$\phi_E^0 = (\delta\phi_v^0/\delta T)_P = a_1 + 2a_2T \qquad \text{(II.7)}$$

Positive values of limiting apparent molar expansibilities (ϕ_E^0) suggests the absence of caging or packing effect in the solutions.

According to Hepler, values of $(\delta\phi_E^0/\delta T)_P$ in the expression given below, determines whether, it is structure breaker or structure maker interaction

$$(\delta\phi_E^0/\delta T)_P = (\delta^2\phi_v^0/\delta T^2)_P = 2a_2 \qquad \text{(II.8)}$$

Generally, positive or small negative values of strongly suggests structure making rather than structure breaking interaction. In this research work, I got structure making type of interaction in all the cases.

II.2.18. Refractive Index Measurements:

Optical data (refractive index) of electrolyte mixtures provide interesting information related to molecular interactions and structure of the solutions, as well as complementary data on practical procedures, such as concentration measurement or estimation of other properties.

Index of Refraction (n_D) for a substance is defined as the ratio of the speed of light in a vacuum to the speed of light in another medium.

$$\text{Refractive Index } (\text{n}_\text{D}) \text{ of substance } = \frac{\text{Speed of light in vacuum}}{\text{Speed of light in substance}}$$

Light changes its speed when it crosses a boundary from one medium into another, its path of travel also changes that is refraction occurred. The relationship between speed of light in the two mediums (V_A and V_B), the angles of incidence ($\sin\theta_A$), refraction ($\sin\theta_B$) and the refractive indexes of the two mediums (n_A and n_B) is shown below-

$$\frac{V_A}{V_B} = \frac{\sin\theta_A}{\sin\theta_B} = \frac{n_B}{n_A} \qquad \text{(II.9)}$$

Refractive index can be determined without measuring the speed of light of a sample. It is possible to establish the refractive index of the sample moderately accurately as a substitute, by measuring the angle of refraction, and knowing the index of refraction of the layer, which is in get in touch with the sample.

The refractive index of mixing can be correlated by the application of a composition-dependent polynomial equation. Molar refractivity, was obtained from the Lorentz- Lorenz relation by using n_D, experimental data according to the following expression-

$$R_M = \frac{(n_D^2 - 1)}{(n_D^2 + 2)}\left(\frac{M}{\rho}\right) \qquad \text{(II.10)}$$

Where, R_M, n_D, M and ρ represents molar refraction, refractive index, molar mass and density of solution respectively.

The limiting molar refraction, ( ) listed in Table S can be calculated using the following equation-

$$R_M = R_M^0 + R_S\sqrt{m} \qquad \text{(II.11)}$$

Where, 'm' is the molality of solution and is the limiting molar refraction that signifies solute – solvent interaction. Therefore, this measurement operates as an expensive tool for studying the molecular interaction in solution.

II.2.19. Viscosity measurement:

The viscosity relationships of electrolytic solutions are multifarious. Because ion-ion and ion-solvent interactions are occurring in the solution and separation of the related forces is a difficult task. But, from careful analysis, vivid and valid conclusions can be drawn regarding the structure and the nature of the solvation of the particular system. As viscosity is a measure of the friction between adjacent, relatively moving parallel planes of the liquid, anything that increases or decreases the interaction between the planes will raise or lower the friction resulting increase or decrease the viscosity. Therefore, monitoring the viscosities of the solution, simultaneously we deals with various interactions between solute and solvents taking place in solution.

Viscosity A- and B- coefficients

If a large sphere is placed in the liquid, the planes will be keyed together in increasing the viscosity. Similarly, increase in the average degree of hydrogen bonding between the planes will increase the friction between the planes, thereby viscosity. An ion with a large rigid co-sphere for a structure-promoting ion will behave as a rigid sphere placed in the liquid and increase the inter-planar friction. Similarly, an ion increasing the degree of hydrogen bonding or the degree of correlation among the adjacent solvent molecules will increase the viscosity. Conversely, ions destroying correlation would decrease the viscosity. In 1905, Grüneisen performed the first systematic measurement of viscosities of a number of electrolytic solutions over a wide range of concentrations. He noted non-linearity and negative curvature in the viscosity concentration curves irrespective of low or high concentrations. In 1929, Jones and Dole suggested an empirical equation quantitatively correlating the relative viscosities of the electrolytes with molar concentrations (c)-

$$\frac{\eta}{\eta_o} = \eta_r = 1 + A\sqrt{c} + Bc \qquad \text{(II.12)}$$

The above equation can be rearranged as-

$$\frac{\eta_r - 1}{\sqrt{c}} = A + B\sqrt{c} \qquad \text{(II.13)}$$

Where, A and B are constants specific to ion-ion and ion-solvent interactions. The equation is applicable equally to aqueous and non-aqueous solvent systems where there is no ionic association and has been used extensively. The term A√c, originally ascribed to Grüneisen effect, arose from the long-range columbic forces between the ions. The significance of the term had since then been realized due to the development Debye-Hückel theory of inter-ionic attractions in 1923. The A -coefficient depends on the ion-ion interactions, can be calculated from interionic attraction theory and is given by the Falkenhagen Vernon equation-

$$A_{Theo} = \frac{0.2577\Lambda_o}{\eta_o(\varepsilon T)^{0.5}\lambda_+^o\lambda_-^o}\left[1 - 0.6863\left(\frac{\lambda_+^o\lambda_-^o}{\Lambda_o}\right)^2\right] \qquad \text{(II.14)}$$

Where, the symbols have their usual significance.

The plots of $(\eta/\eta_0 -1)/\sqrt{c}$ against $\sqrt{c}$ for the electrolytes should give the value of A- and B-coefficient. But, sometimes, the values come out to be negative or considerably scatter and also deviation from linearity occur. Thus, instead of determining A - coefficient from the plots or by the least square method, the A - coefficient are generally calculated using Falkenhagen-Vernon equation. A-coefficient should be zero for non-electrolytes. According to Jones and Dole, the A - coefficient probably represents the stiffening effect on the solution of the electric forces between the ions, which tend to maintain a space-lattice structure.

The viscosity B - coefficient may be either positive or negative, that represents the ion-solvent interaction parameter. The B – coefficients are obtained as slopes of the straight lines using the least square method and intercepts equal to the A values.

The factors influencing viscosity B - coefficients

(1) The effect of ionic solvation and the action of the field of the ion in producing long-range order in solvent molecules, increases η or B - value.

(2) The destruction of the three-dimensional structure of solvent molecules (i.e., structure breaking effect decreases η values.

(3) High molal volume and low dielectric constant, which yield high B-values for similar solvents.

(4) Reduced B-values are obtained when the primary solution of ions is sterically hindered in high molal volume solvents or if either ion of a binary electrolyte cannot be specifically solvated.

Temperature dependence of viscosity B-coefficient

Regularity in the behaviour of B and dB/dT, has been observed in both aqueous and non-aqueous solvents and useful generalizations have been made by Kaminsky. He observed that (i) within a group of the periodic table the B -ion values decrease as the crystal ionic radii increase, (ii) within a group of periodic system, the temperature co-

efficient of B_{Ion} values increase as the ionic radius. The results can be summarized as follows-

(i) A and dA /dT >0

(ii) $B_{Ion} < 0$ and $dB_{Ion} / dT > 0$, characteristic of the structure breaking ions.

(iii) $B_{Ion} > 0$ and $dB_{Ion} / dT < 0$, characteristic of the structure making ions.

First derivative of viscosity B-coefficient over temperature is an upgradation of viscosity B coefficient in predicting the nature of solute – solvent interaction as structure maker or structure breaker. The value of dB/dT is a measure of activation energy required for the viscous flow in solution. This is the reason, why the measure of dB/dT is indicative towards the structure making or structure breaking ability than sign or magnitude of the B-coefficient. The negative small positive value of dB/dT signifies structure-making (kosmotropic) whereas the larger positive value identifies it as structure-breaking (chaotropic).

II.2.20. Conductivity measurement:

Conductivity (or specific conductance) of an electrolyte solution is a measure of its ability to conduct electricity. The SI unit of conductivity is Siemens per meter (S/m). Conductivity measurements are used routinely in many industrial and environmental applications as a fast, inexpensive and reliable way of measuring the ionic content in a solution. For example, the measurement of product conductivity is a typical way to monitor and continuously trend the performance of water purification systems.

Conductimetric study is also another approach, which makes us able to conclude about the supramolecular Host-guest interaction between the guest and CDs and their stoichiometric ratio in the ICs. However, guest molecules studied in regarding this thesis are organic compound, aqueous solution of guest molecules shows appreciable conductivity. Gradual increase in concentration of CDs leads to the decrease in conductivity (κ), of the aqueous guest solutions. The fruit full explanation for this observation comes through the decrease in the mobility of the conducting species in the solution due to molecular encapsulation of guest into the hydrophobic

cavity of the CDs. After a certain point there is no change in conductivity was observed generating a single break point behind that supports the 1:1 stoichiometries of the inclusion complexes.

II.2.21. Surface Tension measurement:

The attractive force exerted upon the surface molecules of a liquid by the molecules beneath that tends to draw the surface molecules into the bulk of the liquid and makes the liquid assume the shape having the least surface area.

The guest molecules used in this research work, having a hydrophobic part, aqueous solutions of the guest molecules shows an appreciable surface activity lowering the surface tension value less than pure water. On the addition of aqueous cyclodextrin solution surface tension of the solution rises, this is due to the migration of the guest molecules from the surface to the bulk of the solution by means of encapsulation of the guest molecules into the cavity of cyclodextrin. After reaching a certain concentration of cyclodextrin, no change in surface tension was observed showing a single break point in the surface tension vs concentration of cyclodextrin plot, suggesting the 1:1 stoichiometry of the inclusion complexes. Thus, the study of surface tension supports the inclusion phenomenon and the stoichiometry of the inclusion complexes.