CHAPTER IX

CONCLUDING REMARKS

In this thesis I investigated the formation of host guest inclusion complexes of various biomolecules, vitamins, drugs, water pollutant with α and β-cyclodextrins exploring particularly towards their formation, stabilisation, solubility, bioavailability, bio degradability, fire resistivity and HSA assisted controlled release without chemical modification by various dependable methods like ^{1}H NMR, 2D ROESY, FTIR spectroscopy, UV-Visible spectroscopy, Fluorescence spectroscopy, Differential Scanning Calorimetry, Scanning Electron microscopy, Powder X-Ray Diffraction, High Resolution Mass Spectroscopy, Surface tension, Conductivity, which primarily focus on the encapsulation of the guest molecules into the cavity of cyclodextrins. The stoichiometry, association constant and thermodynamic parameters for the inclusion complexes have been determined to communicate a quantitative data regarding the encapsulation of the biomolecules inside into cyclodextrins.

This thesis also includes exploration of food preservatives-ionic liquids interactions in solution phase by means of various physicochemical parameters obtained from density, viscosity, Refractive index and conductivity studies. The antimicrobial activities of the mixture of the solutions were done with some gram-positive and gram-negative bacteria and the food preservatives-ionic liquids interactions were found synergistic towards the microbial activity

The findings are discussed chapter wise as follows –

Chapter IV: The suggestion obtained from surface tension and conductometric study for the formation of 1:1 host-guest inclusion complexes of SNP and PEH with α and β-cyclodextrins are established by UV-vis spectroscopy, spectrofluorimetry, 2D ROESY NMR spectrometry and SEM technique by analyzing surface texture of the solid inclusion complexes. The association constants obtained from all the well-established techniques dictates the stability of inclusion complexes formed and the thermodynamic parameters reveals truth about the feasibility of their formation. Removal of water molecules from the cavity of the CDs to make room for the guest molecule for accommodation while formation of inclusion complex, increases entropy of the process. Dimensional suitability being, one of the major stabilizing factor, the

larger cavity size of β-CD (0.70 nm, diameter) compared to α-CD (0.56 nm, diameter), explains for the greater value of association constants and stability of the inclusion complexes formed with β-CD. The association constants, hence stability of the inclusion complexes of SNP with CDs were found more than that of the PEH. Because, -O-H group of SNP, being oriented to the para position may exert H-bonding interaction with CDs to some greater extent than that of the PEH, in which –OH group, being oriented at the meta – position can't travel the minimum distance for the formation H-bond with the CDs. The hydrophobic and H-bonding interactions thus stabilizes the ICs. The Cytotoxicity and Cell viability also balances for non-toxic behavior of the ICs. Thus, inclusion complexes of the recently emerging two drugs, SNP and PEH (after their banned alternatives) stabilizes SNP and PEH from their chemical modification and conveys a new approach for regulatory release to the targeted site reducing overdoses.

Chapter V: 1:1 host-guest inclusion complexes of THC within the cavity of α and β-CD are well established by the various techniques in solution phase as well as in the solid state. The entire inclusion process is thermodynamically feasible process as obtained from the calculated thermodynamic parameters and evaluated association constants reveal the stability of the formation of ICs. Molecular recognition due to the dimensional suitability is the major stabilizing factor. The positive entropy factor is also responsible for the formation of ICs via non-covalent interactions such as hydrogen bonding and other hydrophobic interactions as more number of water molecules compare to that of THC molecule are released from the cavity of the CDs for making the free suitable space for the incoming THC molecule. Formation of inclusion complexes enhances the photochemical stability of THC, protect it from thermal degradation and retain its property without any kind of chemical transformation. Moreover, the regulatory dischargement of THC molecule at pH 7.4 from the hydrophobic cavity to the polar aqueous media has been clearly explained in the presence of HSA molecule. So, there is a strong probability to show similar kind of binding behavior of THC with HSA in the human body and successfully will be delivered to the targeted area as per required amount of it. Hence the study for the formation of inclusion complex and the regulatory dischargement of THC from the hydrophobic cavity of CDs into the aqueous solution approach a novel way for the versatile uses and formulation in food, medicinal and pharmaceutical industries without any chemical

modification. In conclusion, this article demands far reaching effects by dint of innovative applications in pharmaceutical science.

Chapter VI: In this novel study the inclusion complexation of a non-biodegradable pollutant (HBCDD) with β-CD and HP-β-CD were synthesized and characterized to retain its fire resistance property and to convert it into bio-degradable molecule. Various spectroscopic and thermal studies have been performed to establish this fact. The stoichiometry of the two complexes has been found as 1:1 molar ratio of host and guest molecules. Surface texture properties of the inclusion complexes were studied by SEM and the presence of bromine in the complexes were evidenced by EDXS. The melting point analysis indicates that the inclusion complexes are more stable than HBCDD and hence ICs are preferred to HBCDD. The aqueous solubility of the inclusion complexes demonstrates that the inclusion complexes are more bio-available to the microorganism and thus evidently inclusion complexation of HBCDD converts it into biodegradable material making them eco-friendly in nature and minimizes the environmental pollution.

Chapter VII: All the experiments suggest the successful formation of inclusion complex with 2:1 stoichiometry. The association constants of the inclusion complexes of ALVC formed with β-cyclodextrin were found greater than that of the inclusion complexes formed with the α-cyclodextrin and hence more stable, this is may be due to the better fitness of the guest molecule into the larger hydrophobic cavity of β-cyclodextrin compared to the α-cyclodextrin. The ready availability of the association constants enables us to calculate the thermodynamic parameters of the inclusion process which makes the thermodynamic background of the process and recognise it as a thermodynamically feasible process. When the guest molecule gets encapsulated into the hydrophobic cavity of cyclodextrin molecule, the water molecules removed from the hydrophobic cavity of cyclodextrin molecule increases the entropy of the process. Thus, the hydrophobic-hydrophobic interaction and entropy factor would become the driving forces for the formation of inclusion complexes. The binding constant of ALVC to the HSA become appreciable showing an affinity of HSA towards the drug molecule. Thus, it is expected that, the drug molecule gets released from the inclusion complex and binds successfully with the HSA which then get transported to the targeted site

promoting regulatory release consequently reduces overdoses without any chemical modification.

Chapter VIII: The motive to reduce unnecessarily-excessive use of food preservative in the preservation of food is reached, since antimicrobial activity of SBz and Scyt studied herewith, in all possible combination with the BTEACl and BTMACl reveal synergistic to kill micro-organisms and found to act properly below their reported MICs. The physico-chemical methodologies, describes the mode of interaction between the FPs and ILs in solution. Calculation of apparent molar volume, limiting apparent molar volume, molar refraction, limiting molar refraction and viscosity B coefficient makes possible to identify the interaction as predominant solute – solvent interaction. The values of $(\delta\phi_E^0/\delta T)_P$ and (dB/dT) have been calculated to provide the information that, the solute – solvent interaction is structure making. Association constants, optimisation energy and free energy changes for the molecular assembly grown in solution assorted by structure making solute – solvent interaction dictate their stability in solution and consequently, the order of synergism between them. Thus, solution chemistry for all the possible combinations explores the chemistry behind the synergism. This makes one easy to choose a mixture of compounds such that their combination would arise synergistic. Nevertheless, the synergistic combination of food preservatives reduces the level of hazardous food preservative, which is used to stop spoilage of foods produced worldwide and makes the world health, safe. So, the study of microbial activity along with solution chemistry would be a great interest in the field of food chemistry for their preservation.

My research may be justified by the following novel outcomes -

- All the studies supports successfully the formation of inclusion complexes.
- Van der waals forces gives the stability to the inclusion complexes. Sometimes H-bonding interaction gives the extra stability to the inclusion complexes.
- Enhances solubility, bio-avalability, fire returdacy and biodegradability of the inclusion complexes.
- HSA assists the guest molecules to come out form the inclusion complexes.
- Food preservatives-ionic liquids interactions were found synergistic towards antimicrobial effect.