

ABSTRACT

The research work based on host-guest inclusion complexations and assorted interactions in solution phase of some significant molecules both industrially and biologically. A number of physicochemical and spectroscopic techniques were applied to establish our findings.

The host-guest inclusion complexation actually refers to cyclodextrin molecules as host (we have chosen cyclodextrins) and small or modest size molecules are taken as guest, having biological and industrial value.

The study of inclusion lies on- first the establishment of the inclusion phenomenon i.e. whether the inclusion occurs or not and secondly what changes can be expected after the completion of the overall process of inclusion and also sometimes its execution in biological systems with the help of cell viability or cytotoxicity study between the IC and the pure molecule.

Now in accordance with the title of the thesis, establishment of the formation of inclusion complex is of main concern here as it can cause several modifications in the properties of the guest molecule, which may lead to lessen the toxicity, increase its solubility, stability even it can enhance the bioavailability and decrease the side effects especially for drugs. Drugs that are metabolised before going to the target site, cyclodextrins can be used as carriers for those drugs as CDs are natural, biodegradable and non-toxic.

The research works also includes the study of the interaction of bioactive molecules in solution phase (ternary system). The bioactive molecules that have considerable role in cell functioning were getting into the solution phase to study their interactions through some physicochemical and spectroscopic methods like density measurement, viscosity measurement, refractive index measurement etc. by varying the temperature. The interactions (between solute-solute, solute-solvent and solvent-solvent) that make the changes in the various physicochemical parameters involve hydrogen bonding, ion-ion, hydrophobic-hydrophobic, hydrophobic-hydrophilic, ion-dipole, dipole-dipole etc.

The temperature dependent limiting apparent molar volume gives us the limiting molar expansibility and the value of Hepler constant tells us about the structure making and breaking tendency of solute molecules in solution. The viscosity A and B coefficients deliver a variety of information about the behaviour of solutes or ions.

The characterization of the inclusion complex has been done with numerous spectroscopic techniques; these are NMR (1H, 2D NOESY, ROESY), FTIR, Fluorescence, UV-Vis etc. Other studies were also done for the characterisation of the IC ; PXRD, SEM, ITC and cell viability study.

Indigosulfonic acid dipotassium salt is a derivative of natural dye indigo. It has various applications in different industrial fields. The dye has been incorporated into the cavity of β -CD to reduce its toxicity.

DL-Aminoglutethimide, a drug can cause aromatase inhibition. It possesses the efficiency of inhibiting the synthesis of certain hormones that are responsible for breast cancer and prostate cancers. So it can be used in medical adrenalectomy which is drug induced rather than surgical one. This drug is proved to be an effective medication for the patients having metastatic breast carcinoma. By suppressing estrogen, it inhibits the growth of the hormone-dependent tumors. The inclusion complex of the drug DL-AGT and β -CD is of massive importance in different fields of chemistry.

The guanidine diuretic amiloride hydrochloride has a unique capability of restoring potassium while eliminating sodium with extra fluid from our body. The inclusion phenomena of this drug with α and β -CD have been studied.

Alibendol is an important component of maximum choleric and cholekinetic drugs. It is also an antispasmodic ,helps to relax muscles. In biliary insufficiency, it shows effective results.

Both uracil and gallic acid are the biologically essential molecules. The nucleobase that present in RNA is uracil. Through bonding with phosphates and riboses, it helps in synthesizing many enzymes in our body; thus facilitates cell functioning. On the other hand, gallic acid acts as an antioxidant and present in many plants and fruits. It accumulates a variety of applications.

Summary of work done:

Chapter I: The chapter includes the scope, application and most importantly the objectives of the research work. It consists of the names of the biologically and industrially significant molecules and the reason behind choosing them as the parts of our work.

Chapter II: This chapter contains the review of the earlier works about the host guest inclusion and the phenomena of solution. Detailed description of the theories of investigation of all the interactions in solution including equations and different studies that have been done during the research work are included in this chapter. The studies are NMR, FTIR, fluorescence, ITC, PXRD, UV-Vis, SEM, HRMS, density, viscosity, refractive index etc.

Chapter III: It covers the experimental section i.e. details of the samples and the working principles of the instrument used throughout the research work. The source, purity, application and physical properties of the drugs, dye, bioactive molecules and cyclodextrin molecules have been thoroughly discussed in this chapter. The instrumental details are covered in this particular chapter.

Chapter IV: Here, the solution behaviour of two bioactive molecules uracil and gallic acid has been studied. With the help of different physicochemical parameters like apparent molar volume, limiting apparent volume, viscosity, refractive index data of the two concerned molecules in solution; a definite idea of their interactions in solution have been received. This will be helpful for future researches.

Chapter V: Here in this chapter we have studied the inclusion phenomenon of the drug alibendol with β -CD with the help of different spectroscopic techniques. The host-guest inclusion has been done so that the side effects of the drug can be reduced to some extent. Job's plot (from Uv-visible study) reveals the stoichiometry of complexation as 1:1. Binding constants at three different temperatures supplied information about the interaction between alibendol and β -CD and the cross peaks present in the 2D ROESY spectra is an authentication of the formation of inclusion complex.

Chapter VI: The chapter includes the study of incorporation of a diuretic drug amiloride hydrochloride inside the hydrophobic cavity of α and β -cyclodextrin. Various characterization techniques have been applied for the establishment of the IC e.g. UV-Vis, ^1H NMR, HRMS etc. Theoretical studies showed that the encapsulation of the drug for α -CD is partial and for β -CD is complete and this finding is also satisfied by the values of association constants obtained from Uv-visible study. The antimicrobial activity shown by the complexes formed is commendable than the drug itself.

Chapter VII: The host-guest inclusion complex of DL-Aminoglutethimide and β -CD has been characterised by ^1H NMR, FTIR, SEM, PXRD, UV-vis, molecular docking study. The cell viability study has also been done for the IC, which appeared to be nontoxic in comparison to the drug. The inclusion process will be thoughtful in transforming the drug of low toxicity.

Chapter VIII: The encapsulation of a dye molecule Indigosulfonic acid dipotassium salt with β -CD has been studied with certain spectroscopic and calorimetric studies. These were ^1H NMR, 2D NOESY NMR, SEM, FTIR, UV-vis, Fluorescence and ITC study. The stoichiometry was found to be 1:1 and all the experimental results suggest the occurrence of inclusion within β -CD. The inclusion complex might be effective in reducing the toxicity of the dye.

Chapter IX: This chapter contains concluding remarks of the research works included in the thesis.