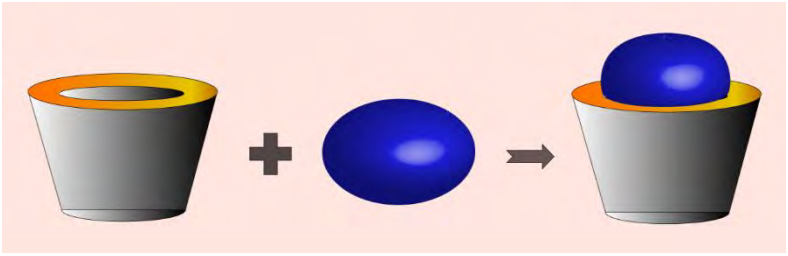
ABSTRACT

Based on the thesis title, my intention is to showcase my extensive expertise in the areas of supramolecular host-guest inclusion complexation and the interaction between amino acids and drugs in aqueous environments. The significance of supramolecular assembly in drug release today lies in its ability to greatly impact various properties of the drug, including solubility, stability within the body, pharmacokinetics, and pharmacodynamics, thereby enhancing its bioavailability. Furthermore, supramolecular assemblies offer favourable characteristics, improved encapsulation, and controlled release.



The utilization of spectroscopy contributes to validating the complexation of numerous bioactive compounds and their distinct photophysical attributes in aqueous settings. Techniques such as UV-visible spectroscopy, ^{1}H-NMR, FT-IR, mass spectrometry, and fluorescence emission spectroscopy effectively illustrate the occurrence of inclusion phenomena. Surface tension analysis, powder X-ray diffraction (XRD), and scanning electron microscopy (SEM) provide a qualitative understanding of the formation of supramolecular assemblies. Thermal stability of such assemblies can be elucidated through thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC). The experimental findings are complemented by theoretical molecular modeling studies of the supramolecular system.

The investigation typically reveals the nature of various interactions between amino acids and drugs in the aqueous phase by measuring apparent molar volume (ϕ_v), limiting apparent molar volume (ϕ_v^0), molar refraction (R_M), limiting molar refraction (R_M^0), and viscosity B coefficients using various physicochemical methods.

This study explores the encapsulation of several biologically active compounds, including 6-Mercaptopurine Monohydrate, 7-(2,3- Dihydroxypropyl)-theophylline, and Chloroquine diphosphate (in solution thermodynamics research), which hold potential applications in living systems. The beneficial effects of bioactive substances are often attributed to their pharmacological activity.

Extensive research suggests that a popular dye Tartrazine and a pollutant Bisphenol A possess exceptional thermal stability, distinctive optical characteristics, and low toxicity, making them promising to be a controlled release complex and comparable hazard free in this context.

The utilization of macrocyclic hosts in molecular recognition, controlled drug release, and sensing has garnered significant interest in the field of host-guest chemistry. By incorporating guest molecules within various host molecules, such as cyclodextrins, in an aqueous environment, a novel understanding of molecular recognition, including inclusion or complexation through non-covalent interactions, is achieved.

Supramolecular host-guest chemistry provides a general understanding of the formation of inclusion complexes between host and guest molecules. Different guest molecules can bind to hydrophobic cavities within the host. Extensive research has been conducted on the overall supramolecular assembly in various domains, including drug delivery and analytical chemistry. Cyclodextrins and their derivatives, along with water-soluble calixarenes, appear to be the most promising host molecules for forming inclusion complexes, particularly when combined with guest molecules of appropriate size.

The primary objective of this thesis is to investigate the impact of supramolecular recognition and solution chemistry, which are crucial in numerous sectors, ranging from pharmacology to biomedical sciences.

SUMMARY OF THE WORKS

CHAPTER I

This chapter outlines the detailed objectives of the research, highlighting their relevance and applications in contemporary science. It delves into the rationale behind selecting significant bioactive molecules, cyclodextrins, drugs, ionic liquids, amino acids and the chosen solvent systems. Additionally, it provides a concise overview of all the investigative methods employed throughout the research.

CHAPTER II

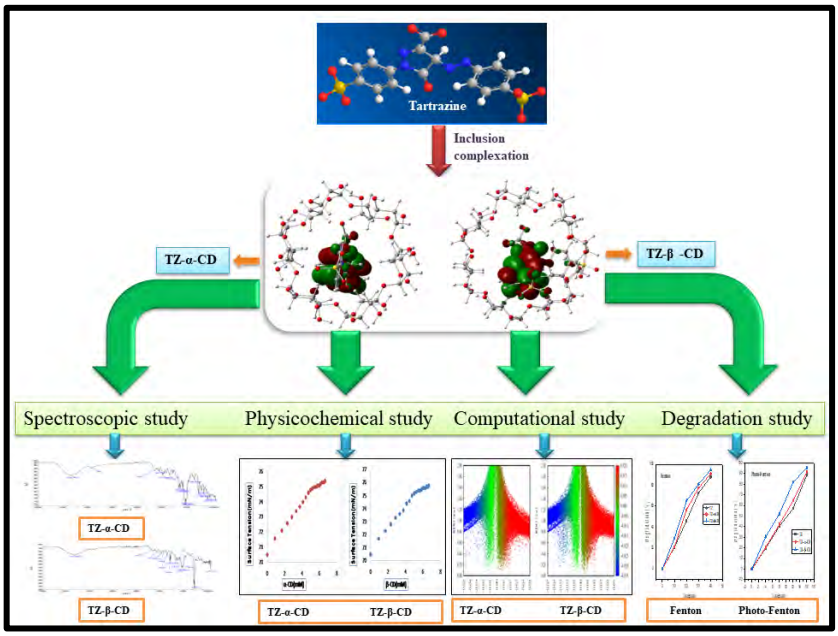
This chapter offers a comprehensive review of previous work in this research domain, conducted by scientists and researchers worldwide. It presents an in-depth theoretical framework of the investigations, detailing the intermolecular forces at play. The background theory of various investigative methods, including ^{1}H-NMR, FTIR spectroscopy, UV-visible spectroscopy, Differential Scanning Calorimetry, Thermogravimetric Analysis, Scanning Electron Microscopy, Powder XRD, Molecular Docking Study, DFT, Antimicrobial Study, Cytotoxicity Study, Anti-oxidant study, Binding Study, Surface Tension, Conductivity, Density, Viscosity, and Refractive Index, is thoroughly discussed. The significance of these methods in the context of the research is also highlighted.

CHAPTER III

This chapter focuses on the experimental aspects of the research. It details the names, structures, physical properties, and applications of the biologically active significant molecules, cyclodextrins, dyes, and solvents utilized. It also encompasses a comprehensive description of the experimental methods and the instruments used, providing insights into their roles in the research work.

CHAPTER IV

This chapter presents the experimental investigation into the encapsulation of azo pyrazolone orange dye commonly named as Tartrazine (TZ) or Acid Yellow 23, within the nano hydrophobic cavity of α and β-cyclodextrin as the host molecule. To determine the saturation concentration and stoichiometry of the inclusion complexes, two reliable physicochemical methods-conductance and surface tension were employed. UV-Vis spectroscopy confirmed the 1:1 stoichiometry of the inclusion complexes and assessed the stability constants and thermodynamic parameters with high precision, demonstrating the feasibility of the inclusion process. The mechanism of inclusion was elucidated through ^{1}H NMR and FTIR spectroscopy, while SEM analysis revealed the surface structures. The formation of inclusion complexes was supported by hydrophobic interactions, hydrogen bonding, electrostatic forces, and structural effects. This study predicts the release behavior of Tartrazine in the presence of CT-DNA without any chemical modifications. Furthermore, the degradation of the inclusion complexes via Fenton and Photo-Fenton processes showed significant environmental implications. Density Functional Theory was utilized to evaluate optimized geometries, adsorption energies, Non-Covalent Interaction (NCI) regions, and electrostatic potential maps (ESP), thereby corroborating the experimental findings.



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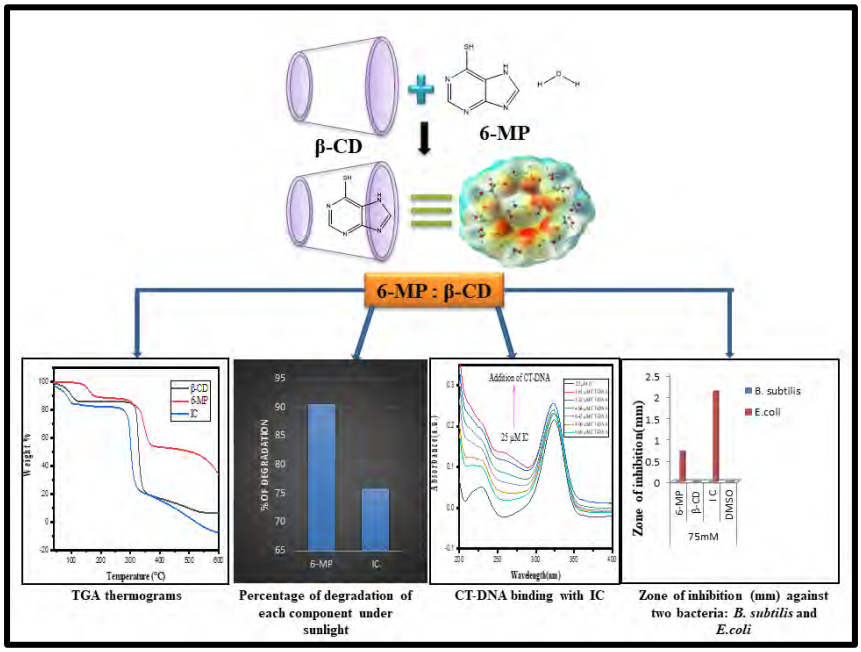
CHAPTER V

This chapter involves of the host-guest interaction and the cytotoxic and antibacterial properties of the vital anti-cancer drug, 6-Mercaptopurine monohydrate (6-MP), with β-Cyclodextrin (β-

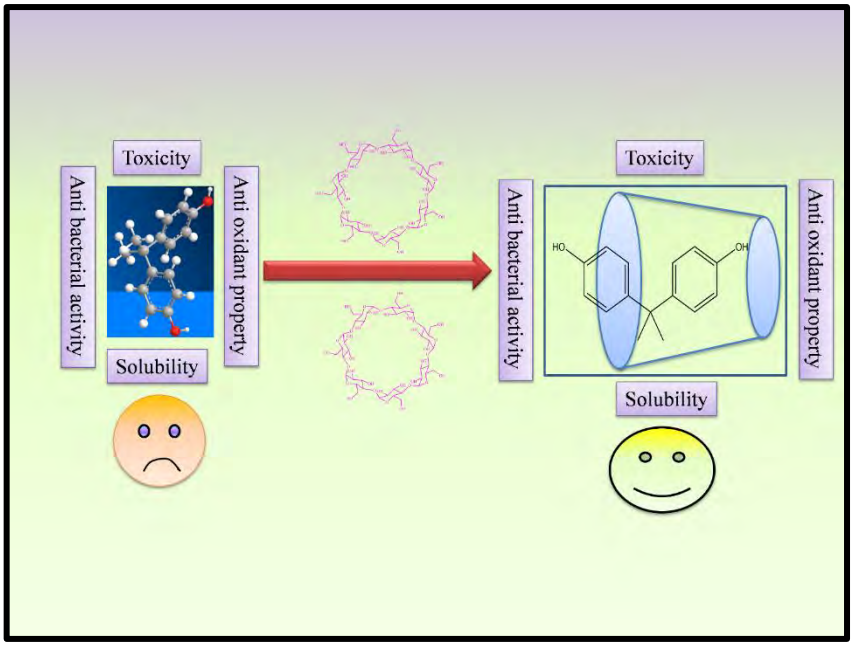
CD) were meticulously investigated using the co-evaporation approach. UV-Vis spectroscopy confirmed the 1:1 stoichiometry of the inclusion complex (IC) and assessed the feasibility of the inclusion process. Advanced spectrometric techniques, including FTIR, NMR, and XRD, elucidated the molecular interaction mechanisms between β-CD and 6-MP, further supported by Density Functional Theory (DFT) to validate the experimental results. Thermal analysis through TGA and DSC demonstrated enhanced thermal stability of 6-MP post-encapsulation. The encapsulation also imparted greater photostability to 6-MP due to the protective effect of β-CD. This study predicts the release behavior of 6-MP in the presence of CT-DNA without chemical modification. The *in vitro* antibacterial assessment revealed that the IC exhibited superior efficacy compared to pure 6-MP. Additionally, the *in vitro* cytotoxic activity against the human kidney cancer cell line (ACHN) was significantly improved for the IC (IC_{50} = 4.18 µM) compared to pure 6-MP (IC_{50} = 5.49 µM). These findings indicate that incorporating 6-MP with β-CD enhances its stability and effectively improves its solubility, cytotoxic, and antibacterial properties.



Published in RSC Advances, 22(48), (2022) 30936-30951

CHAPTER VI

In this chapter, in an effort to enhance the bioavailability of the non-biodegradable pollutant Bisphenol A (BPA), inclusion complexation procedures were employed to develop improved formulations of BPA. This study focused on forming an inclusion complex (IC) of β-Cyclodextrin (β-CD) with BPA to assess its impact on water solubility, antioxidant and antibacterial activity, toxicity, and thermal stability. UV-Vis spectroscopy, along with NMR, FTIR, and XRD, revealed the molecular interaction mechanisms between β-CD and BPA,

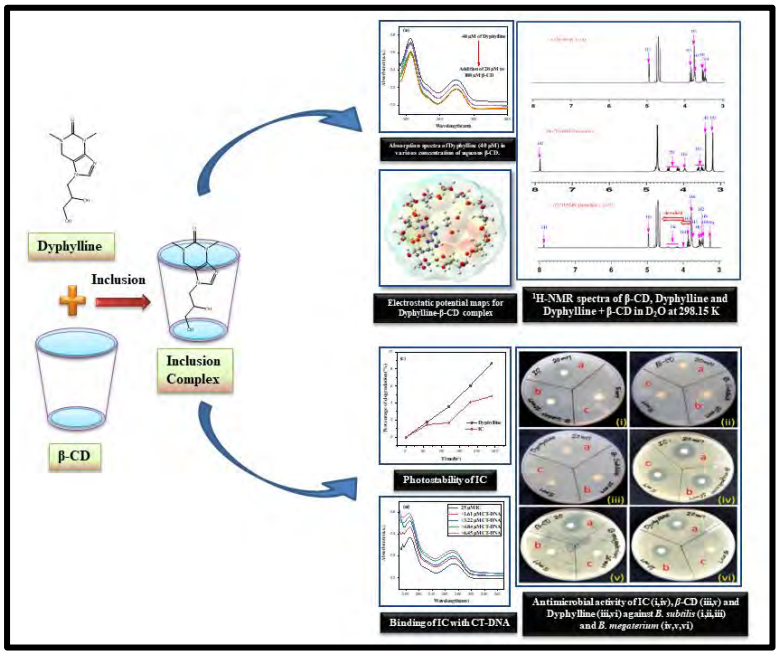


further substantiated by molecular modeling. Thermal analysis via TGA and DSC showed that encapsulation significantly enhanced BPA's thermal stability. This research also explores the predicted release behavior of BPA in the presence of CT-DNA. In vitro antibacterial tests indicated that the IC exhibited superior performance compared to pure BPA. *In silico* studies revealed a notable reduction in the toxicity levels of the IC compared to pure BPA. Consequently, β-CD-encapsulated BPA demonstrates reduced toxicity through increased antioxidant activity. Moreover, its enhanced antibacterial properties suggest potential therapeutic applications. This innovative approach to formulating BPA with controlled release and protective characteristics offers a promising strategy to mitigate its harmful effects while boosting its efficacy.

Published in Environmental Science and Pollution Research, 30(15), (2023) 43300-43319

CHAPTER VII

The chapter includes the formation of an inclusion complex in an aqueous medium using Dyphylline as the guest and β-cyclodextrin (β-CD) as the host has been successfully established, offering promising applications in modern biomedical sciences. ^{1}H-NMR confirmed the formation of the inclusion complex, while surface tension and conductivity measurements demonstrated a 1:1 stoichiometry. Thermodynamic parameters derived from density, viscosity, and refractive index measurements provided insights into the nature of the complex. This study also predicts the release behavior of dyphylline in the presence of CT-DNA without any chemical modifications. The resulting inclusion complex exhibited enhanced

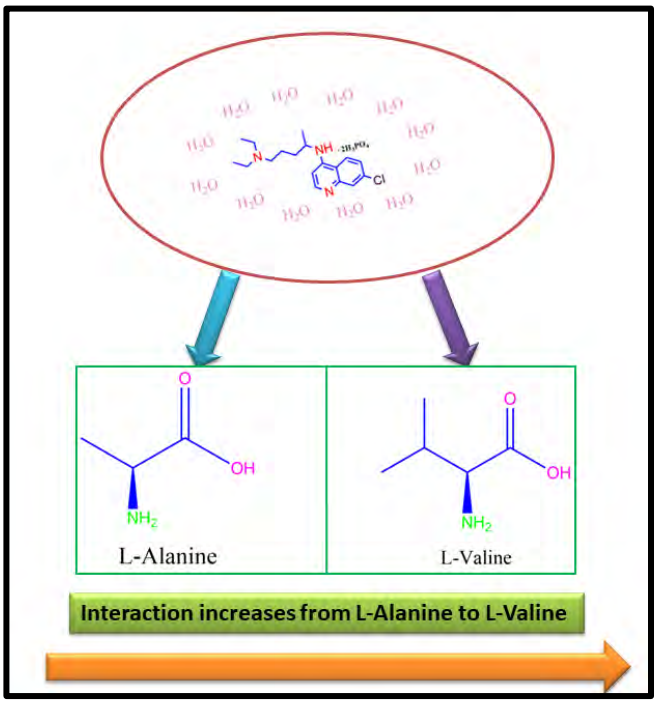


photostability, as β-CD effectively protected the dyphylline. Furthermore, the antibacterial activity of dyphylline was significantly enhanced upon complexation, showing increased toxicity against Gram-negative bacteria, particularly *Escherichia coli*, compared to Gram-positive bacteria. The encapsulation mode of dyphylline within the β-CD cavity was further investigated using Density Functional Theory (DFT) to validate the initial findings.

Published in ACS Omega, 7(30), (2022) 26211-26225

CHAPTER VIII

This chapter delves into the solute-solvent interactions between drug and amino acids (AAs) in aqueous media, which are crucial for optimizing various biotechnological processes. A comprehensive analysis was conducted on the interactions between L-Alanine/L-Valine and Chloroquine diphosphate (CDP) in aqueous solutions. Key physicochemical parameters, including density, viscosity, refractive index, conductivity (at three different temperatures), and surface tension (at 298.15 K) at atmospheric pressure, were evaluated to elucidate potential intermolecular interactions in the ternary system (Drug + Water + Amino acid). Apparent molar volume, limiting



apparent molar volume, viscosity *B*-coefficient, molar refraction, and limiting molar refraction indicate that solute-solvent interactions are significantly influenced by solute concentration and temperature. Both amino acids demonstrated structure-breaking activities in aqueous Chloroquine diphosphate. The Gibbs free energy change of the system, indicating spontaneity, was measured. ^{1}H NMR spectroscopy revealed notable shifts in the aromatic protons of Chloroquine diphosphate and the protons of amino acids, suggesting strong hydrophobic-hydrophobic interactions, which align with theoretical predictions. The interactions between L-Valine and the drug were found to be more dominant compared to those between L-Alanine and the drug, as supported by both experimental and theoretical findings. The experimental and correlated results provide a foundation for developing models of drug-amino acid mixtures.

Published in the Journal of Molecular Liquids, 341, (2021) 116933

CHAPTER IX

This chapter presents the concluding remarks summarizing the research conducted in this thesis.

CHAPTER X

This chapter contains the bibliography and references for all preceding chapters.