# ABSTRACT

Bioactive compounds are found in mainly plants kingdom, fruits, vegetables, whole grains and various oil seeds. These compounds are secondary metabolites and provide the good health benefits from ancient times. Therefore, both laboratory and industrial synthetic chemists around the globe became extremely interested in the synthesis of these valuable compounds. Biomimics is a very popular protocol for the synthesis of pharmaceutically important compounds where transition metal complexes have been employed to produce the value-added products day by day. Due to the economic and environmental sustainability the metal-free, additive-free synthetic method has become a promising alternative which gained great interest in the recent decades.

**Chapter I:** This is an introductory chapter of my thesis. Here, the importance of the transition metal complex and bioactive compounds are discussed along with the objectives of the present study.

**Chapter II:** This chapter deals with the the synthesis, structural description, bio-mimics of phenazine oxidase activity and *in-vitro* antibacterial as well as antiproliferative activity of mononuclear aurum(III) complex, $[Au(bpy)Cl_2]NO_3$ (Complex **1**) [bpy = 2,2'-bipyridine]. The crystal structure analysis of Complex **1** reveals that Au(III) centre adopts a nearly perfect square planar geometry and theoretical calculations agree well with the structural features. Examination of the catalytic fate for Au(III) complex towards oxidative coupling of o-phenylenediamine (OPD) in acetonitrile displays a good catalytic activity with a high turnover number, $k_{cat} = 6.75\times10^2$ $h^{-1}$. The cytotoxic effect of **complex 1** against the human lung cancer cell line (A549) is assessed through changes in morphologies observed in different fluorescent staining methods as well as MTT assay. The experimental outcomes ensure that most of the cell destruction of A549 occurs by apoptosis mode. The antibacterial activity of **complex 1** against pathogenic bacteria is examined through the nature of variation in mitochondrial trans-membrane potential and depolarization pattern which suggests that destruction of mitochondrial membrane drives the development of antibacterial properties.

**Chapter III:** In this chapter, we demonstrate the synthesis, structural characterization, computational studies and bio-mimics of the phenazine oxidase activity of a newly designed cobalt(III) complex, $[Co(dpa)(dpa\text{-}H^+)(N_3)_2]Cl_2$ (**complex 2**) [dpa = 2,2'-

dipyridylamine] under an aerobic condition. The crystal structure analysis reveals that the cobalt(III) centre adopts an octahedral geometry and the complex forms a beautiful supramolecular frameworks through non-covalent interactions. The cobalt(III) catalyst turns out to be a promising catalyst for the oxidative coupling of *o*-phenylenediamine (OPD) in oxygen-saturated methanol with an excellent turnover number, $k_{cat} = 7.85\times10^3$ $h^{-1}$. Spectrophotometric, electrochemical, mass spectrometry and computational analysis ensure that the course of catalysis undergoes through a catalyst-substrate complexation, facilitating the development of cobalt-iminobenzoquinone species in the solution. The computational calculations employing the density functional theory (DFT) throw a light on the mechanistic insights of the phenazine oxidase mimics. ETS-NOCV plots of the reactive intermediates portray the coordination-driven depletion of electron density from the nitrogens of OPD to the cobalt centre leading to the enhancement of electrophilic character on para-positioned C-atoms with respect to N-atoms of OPD, thereby catalysing the nucleophilic attack by second OPD to produce the oxidation product, 2,3-diaminophenazine (DAP). Interestingly, we are able to isolate the oxidation product of the OPD oxidation reaction as a hydrated chloride salt, $DAPH^+Cl^-\cdot 3H_2O$ (**2**). The crystal engineering perspectives of **2** attribute the intriguing fate of the secondary chlorides to the stabilization of the oxidation product in the crystalline phase.

**Chapter IV:** This chapter highlights the phenazine scaffolds which are the versatile secondary metabolites of bacterial origin. It functions in the biological control of plant pathogens and contributes to the producing strains' ecological fitness and pathogenicity. In light of the excellent therapeutic properties of phenazine, we have synthesized a hydrated 2,3-diaminophenazinium chloride ($DAPH^+Cl^-\cdot 3H_2O$) through direct catalytic oxidation of o-phenylenediamine with a cobalt(III) complex, $[Co(dpa)(dpa\text{-}H^+)(N_3)_2]Cl_2$ (**complex 2**) [dpa = 2,2'-dipyridylamine] in ethanol under aerobic condition. The crystal structure, molecular complexity and supramolecular aspects of $DAPH^+Cl^-$ were confirmed and elucidated with different spectroscopic methods and single crystal X-ray structural analysis. Crystal engineering study on $DAPH^+Cl^-$ exhibits a fascinating formation of $(H_2O)_2\ldots Cl^-\ldots(H_2O)$ cluster and energy framework analysis defines the role of chloride ions in the stabilization of $DAPH^+Cl^-$. The bactericidal efficiency of the compound has been testified against a few clinical bacteria like *Streptococcus pneumoniae, Escherichia coli,* and *K. pneumoniae* using the disc diffusion method and the results of the high inhibition zone suggest its excellent antibacterial properties. The phenazinium chloride exhibits a significant percentage of cell viability and a

considerable inhibition property against SARS-CoV-2 at non-cytotoxic concentration compared to remdesivir. Molecular docking studies estimate a good binding propensity of $DAPH^+Cl^-$ with non-structural proteins (nsp2 and nsp7-nsp-8) and the main protease ($M^{pro}$) of SARS-CoV-2. The molecular dynamics (MD) simulation studies attribute the conformationally stable structures of the $DAPH^+Cl^-$ bound $M^{pro}$ and nsp2, nsp7-nsp8 complexes as evident from the considerable binding energy values, –19.2±0.3, –25.7±0.1, and –24.5±0.7 kcal/mol, respectively.

**Chapter V:** This chapter addresses a metal-free methodology for the synthesis of 1,2-disubstituted and 2-substituted benzimidazoleswith high to excellent yields has been developed. The course of synthesis involves easy work-up, straightforward purification, inexpensive reaction setup, and wide substrate scope under extremely mild and operationally simple conditions which makes the synthetic strategy more lucrative, practical and reliable. The serious challenge to carry out these reactions in a pure aqueous medium has been achieved at 75 °C in the presence of air bubbles. The applicability of this operationally simple and metal-free synthetic approach for the gram-scale synthesis of benzimidazole derivatives with good yield (~74%) further strengthens its potentiality for synthesis at an industrial scale.

**Chapter VI:** Here, we report the solvent-free green synthesis of two Schiff bases, (E)-2-((2-hydroxy-3-methoxybenzylidene)amino)-4-methylphenol ($\mathbf{H_2L^1}$) and (E)-2-((2-hydroxybenzylidene) amino)-4-methylphenol ($\mathbf{H_2L^2}$), and their inclusion complexes with β-cyclodextrin (β-CD). The encapsulation phenomenon, structural characteristics and hydrolytic stabilities of the $\mathbf{H_2L^1}$, $\mathbf{H_2L^2}$ and their inclusion complexes are determined with a suite of spectroscopic, analytical and crystallographic analyses. Dose and time-dependent cytotoxicity study of $\mathbf{H_2L^1}$-β-CD and $\mathbf{H_2L^2}$-β-CD against two breast cancer cell lines, Michigan Cancer Foundation-7 (MCF-7) and Metastatic mammary adenocarcinoma1 (MDA-MB-231), exhibit excellent inhibitory activity with significant non-cytotoxic concentrations and ensure a multifold elevation of bio-potency than the parent Schiff base compounds. The annexin-V assay determines the efficacy of these inclusion complexes to trigger apoptosis, suggesting that $\mathbf{H_2L^2}$-β-CD possesses better efficacy as an anti-cancer drug. To the best of our knowledge, we, for the first time, report the inclusion of nanocrystalline Schiff bases into β-CD for multifold enrichment of bio-potency.

**Chapter VII:** Finally, this chapter has defined the conclusion outlook and the future range of the research endeavour.

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