CHAPTER 8

SUMMARY AND CONCLUSIONS

Spectroscopic studies of certain fungicide compounds have been performed using the emerging experimental spectroscopic techniques to correlate with quantum chemical interpretation of their structure activity relationship. Fungicides are either chemicals or biological agents that inhibit the growth of fungi or fungal spores. The experimental techniques includes FT-IR, FT-Raman, UV-visible, NMR and fungicidal activity. The structural elucidation and complete vibrational assignment of fungicide compounds such as anilazine, benalaxyl, benomyl, clotrimazole, flutolanil and mepronil are performed using experimental and theoretical techniques. The quantum chemical computation has been carried out for related compounds to identify the structural relationship to fungicidal activities and compared with experimental data. A brief summary of the work carried out is given as follows.

Anilazine is a nonsystemic fungicide used for controlling fungal diseases, which attack lawn, turf, cereals, coffee and wide varieties of vegetables and other crops. The FT-IR, FT-Raman, UV-visible and NMR spectroscopic analysis of anilazine have been performed. The quantum chemical methods performed on anilazine has been correlated with it's related compound N-(4,6-dichloro-1,3,5-triazine-2-yl)aniline with the aid of density functional theory using B3LYP/6-311G(d,p) basis set. The optimized geometrical parameters, vibrational assignments and normal mode frequencies have been performed. The vibrational spectral analysis is performed with the help of normal coordinate analysis. The Hirshfeld surface analysis helps to identify the intermolecular interactions within the crystal. The

lowering of HOMO-LUMO energy gap further supports the charge transfer interaction. The molecular docking study reveals the inhibitory activity against the receptors and possess the highest potential affinity into the binding site of the molecules. The lowest binding energy of 6STD PDB with the anilazine is more effective and shows more fungicidal activity. The triazine ring acts as the active binding site of the anilazine. The inhibitions of fungal strains are measured with two antifungal pathogens *Aspergillus niger* and *Candida albicans*. From the above studies it is conlude that anilazine is suitable for fungicidal activity.

Phenylamide fungicides are a class of systemic fungicides including benalaxyl, metalaxyl and furalaxyl that show excellent protective, curative and eradicative antifungal activity and exclusively control diseases caused by peronosporales. The FT-IR, FT-Raman, UV-visible and NMR spectral analysis on benalaxyl are performed with the aid of density functional theory in order to predict the structural, electronic and spectroscopic properties. The spectroscopic analysis on benalaxyl along with quantum chemical computation on metalaxyl and furalaxyl are performed. The vibrational spectral analysis has been performed with the help of vibrational energy distribution analysis. Natural population analysis is performed and it provides evidence for involvement of electron present in the N_{18} atom. Natural bond orbital analysis is also performed and it explains about intramolecular interaction and hyperconjugative interaction. The potential energy surface scan analysis explains the stable conformer of the compound. The highest value of electrophilicity index explains fungicidal activity of the compound under study. The phenyl amide part acts as the active binding site of the title compound. The antifungal activity results of the viability assay have proved that benalaxyl possess excellent antifungal nature.

Benomyl is a systemic fungicide applied to cereals, fruits, vegetables, vines and also used for handling of crops. The spectroscopic analysis, optimized parameters and molecular dynamic simulation on benomyl and its related compounds ethyl N-[-piperidin--yl methyl)benzimidazol-2-yl)carbamte, ethyl N-[-pyrrolid-1-yl methyl) benzimidazol-2-yl)carbamate have been performed. For benomyl experimental spectra have been taken by FT-IR, FT-Raman, UV-visible and NMR spectroscopic techniques. The vibrational spectral analysis has been performed with the help of normal coordinate analysis. The resulting wavenumbers are scaled by using wavenumber linear scaling method. The stability and the chemical reactivity of the compounds are examined by HOMO-LUMO and NBO analysis. The stable conformer of benomyl has been identified. For identifying the fungicidal activity of benomyl, β-tubulin synthesis mode of action type PDBs are collected and verified with the help of molecular docking.The stability of the benomyl is also investigated by molecular dynamic simulation techniques to evaluate the binding stability with different target proteins. The benomyl exhibits high fungicidal activity due to the influence of benzimidazole bioactive region. In antifungal activity test, considerable activity is observed in *Aspergillus niger* and *Candida albicans.*

Clotrimazole is a synthetic imidazole derivative with broad spectrum antifungal activity. The structural activity of the clotrimazole is theoretically correlated with triphenyl imidazole dervative compounds like 1-trityl-1H-imidazole, 1-(diphenyl-(2-(trifluoro methyl)phenyl]methyl]imidazole and 1-[(2-methylphenyl)-diphenylmethyl]imidazole.The most stable complex form of coltrimazole-water complex has been studied. The FT-IR, FT-Raman, UV-visible and NMR techniques are performed. The lowering of HOMO-LUMO energy gap and highest value of

electrophilicity index explains the highly active nature of clotrimazole. Lanosterol 14α-demethylase is an essential enzyme required for bio synthesis of ergosterol, a primary sterol molecule in fungal cell membrane. In moelcular docking study, clotrimazole forms a stable complex with the proteins, as evident from the highest binding energy. The imidazole ring shows the active binding site of the clotrimazole compound. The RMSD, RMSF and radius of gyration are analyzed and it is found that clotrimazole has higher stability than other chosen ligands. Thus the above results conclude that clotrimazole behave as good antifungal compound.

Flutolanil and Mepronil are phenyl benzamide fungicides primarily developed for the control of rice sheath blight caused by Rhizoctonia solani. The structural activity, spectroscopic analysis, chemical reactivity, biological activity and molecular dynamics simulation of phenyl benazamide fungicides flutolanil and mepronil based on monomer and dimer model with the aid of combination of experimental and computational methods are performed. In dimer model, the intermolecular interactions N_{17}-H_{18}...O_{43} and C_{27}-H_{28}...O_{43} strengthen the stability of the compounds. The highest stabilization energy of flutolanil exhibits to perform highest fungicidal activity. The stable conformer of flutolanil and mepronil has been identified by potential energy surface scan analysis. Flutolanil shows lowest binding score towards the protein 17β-hydroxy steroid dehydrogenase. The RMSD, RMSF and radius of gyration are performed. The above results conclude that flutolanil is more fungicidal active nature than mepronil.

In the last few years, fungicides play an important role in modern agriculture through the control of fungal diseases to acheive high productivity with low cost. The

current research is focused on the analysis of spectroscopic properties of certain fungicides by using FTIR, FT-Raman, UV-visible and NMR experimental techniques with quantum chemical computational tecniques. The study reveals the structural activity of the compounds. This study emphasise, how spectral study provide information about intermolecular interaction, intramolecular interaction, hyperconjugative interaction, delocalization, steric repulsion,charge transfer and mesomeric effect. The present study explains the vibrational contribution of various modes of six fungicide compounds. The most stable fungicide compounds are compared with other related compounds by computational methods. Finally and most essentailly the molecular docking study helps to identify the binding site and the bioactive region of the six fungicide compounds. From this work, to identified the active binding site of the fungicide compounds. Thus the spectroscopic techniques and the density functional theory studies along with the structure activity relationship can be made powerful tools in structure based fungicide design process.