CHAPTER – 1
INTRODUCTION

In the past, the compounds with expected biological activity have been tested by the use of animal models (example rat) for human diseases. The experimental method of structure determination (crystallography) together with computational approach (molecular modeling) is inevitable recently. Organic compounds that are used to prevent or cure diseases in humans, animals and plants are drugs. They act by interfering with the biological process. The significant organic compounds in the present work include biologically active compounds (gemfibrozil, sulfonamides) and raw materials used in industry (nitrophenol derivatives, ethyl centralite). In the recent years, a lot of importance has been given for the synthesis of structurally novel organic compounds and their structural elucidation. Fibrate, sulfonamides, phenol and urea derivatives are of recent scientific interest owing to its properties and applications in diverse fields. Since research on these compounds in the field of vibrational spectroscopy is scant serious attempt has been made to expose its complete vibrational properties.

1.1 Aims and objectives

The aim of the present investigation is the vibrational spectroscopic analysis of certain organic molecules with some pharmaceutical and industrial importance. The special interest on the chosen molecules stems from the wide range of pharmaceutical and industrial applications exhibited by the compounds, including anti-cholesterol, anti-bacterial and intermediate compound in the synthesis of pesticide, gunshot residue in forensic analysis. The main objective of this work is to

investigate the electronic properties like electron delocalization, phenyl-N conjugation, intramolecular charge transfer (ICT) and effect of hydrogen bonding using vibrational, UV-visible spectroscopic techniques and computational tools. And these properties are used to probe if there is any physical basis for the enhancement of the bioactivity and stability of the molecules.

1.2 Review of literature

Literature based guidance is essential for any scientific research which correlates the current research with the research in the past. The combination of experimental and theoretical studies on the organic compounds of pharmaceutical and industrial significance can be found on the literature. Vibrational spectroscopic study supported by density functional theory is proved to be an effective tool to interpret the physiochemical properties of organic molecules.

Over the past several years there have been enormous vibrational spectroscopic studies with the aid of density functional theory on complex organic compounds [1-7]. In the 4-chloro-3, 5-dinitrobenzoic acid (CDNBA) molecule, the dimer is formed by O–H···O hydrogen bond through carboxylic group. The deviation between calculated and observed NO_2 symmetric stretching vibration is due to the appreciable effect of hydrogen bonding in the NO_2 symmetric stretching vibration. M. Karabacak *et al.* [8] studied the intra-molecular charge transfer of $\pi \rightarrow \pi^*$ type electronic transition in CDNBA by UV-vis spectral analysis. S. Muthu, E. I. Paulraj *et al.* [9] had studied the molecular structure and vibrational spectra of 4-amino-3(4-chlorophenyl) butanoic acid. Vibrational spectra and *ab initio* calculations of 2-methoxy-benzaldehyde dimer reported by P. J. A. Ribeiro-Claro *et al.* [10] reveals

that the blue shift of C–H stretching mode is due to the C–H···O contacts. Further it is understood that the carbonyl stretching mode is splitted into the higher wavenumber for free carbonyl group and at the lower wavenumber component for hydrogen bonded carbonyl group. Investigations on the anomalous spectral behavior of 3-fluoroisonicotinic acid [11] provide the down-shifted O–H stretching mode due to O–H···N bonding. The inter-molecular interactions has also been analyzed by performing natural bond orbital calculations and it provided evidence for the existence of O–H···N and weak C–H···O interactions in dimer. M. Karabacak *et al.* [12] had studied the monomeric and dimeric structure of 2- and 6-bromonicotinic acid using the B3LYP/6-311++G(d, p) method. The effect of intermolecular hydrogen bonding in the vibrational spectra has been studied and it is concluded that the chosen DFT method is reliable for prediction of vibrational spectra. Ferulic acid [13], a phenolic compound is investigated because of its diverse pharmacological effects. In the Ferulic acid, the charge transfer within the molecule is studied by frontier molecular orbital analysis. It is concluded that the molecule might have microscopic nonlinear optical behavior.

Phenol derivatives are molecules of intense theoretical interest due to their relatively small size. Nitrophenol derivatives are used as the intermediate compound in the synthesis of pesticides. Infrared and Raman spectra of organometallic derivatives of nitrophenols are examined by L. M. Epstein *et al.* [14]. The detailed investigation on the vibrational analysis of 3-nitrophenol-1,3,5-triazine-2,4,6-triamine (2/1) confirmed the presence of intermolecular hydrogen bonding in the crystal and the influences of triazine and phenyl rings to the vibrational frequencies have been discussed [15]. A. J. Abkowicz-Bienko *et al.* reported that BLYP/6-31G(d,p) method

is reliable for prediction of the infrared spectra of phenol derivatives [16]. Vibrational analysis of 2-nitrophenol reported by A. Kovacs *et al.* [17] showed that the hydroxyl and nitro group vibrations reflect the effect of the strong intramolecular hydrogen bonding.

Centralites in gunshot residues are important in forensic science due to their limited contamination from environmental sources. The vibrational spectra of ethyl centralite and methyl centralite [18] were studied based on DFT simulation and the centralites particles on coverslips were detected by applying Raman imaging. H. M. Badawi *et al.* [19] found that symmetrically substituted 1,3-diphenylurea and 1,3-diphenylacetone have near planar *cis-cis* and *gauche-gauche* conformation respectively. Investigation on 1-phenyl-3-(1,2,3-thiadiazol-5-yl)urea [20], a substituted phenylurea by HF/6-31G(d,p) shows that the molecule has large NLO property compared to urea. The electronic transition from phenyl ring to thiadiazol through bridge is confirmed by UV-Vis spectral analysis. From the analysis made by L. Sinha *et al.* [21] it is found that electron cloud movement through conjugation from electron donor group to electron acceptor group results in simultaneous IR and Raman activity. According to C. Ravikumar *et al.* [22] the methyl C–H stretching modes is blue shifted due to back-donation of charge from lone pair oxygen atoms to antibonding C–H bonds. It is also identified that red shifting of NH_2 stretching wavenumbers is due to the formation of intra and inter molecular N–H···O hydrogen bonds. The intensity of C–O stretching modes is enhanced owing to increased conjugation with the ring π–system.

Sulfonamides were the most widely used synthetic antibiotics which inhibit the biosynthesis of folic acid compounds in bacteria *Escherichia coli* [23]. P. A. Ajibade *et al.* indicated that two cobalt complexes of sulfadiazine have similar structure by synthesizing the complexes. The presence of water in the coordination sphere of the complex has been confirmed by IR spectra [24]. Sulfonamide compounds are biologically important materials administered to patients with bacterial infection. Sulfadiazine is a sulfonamide used as an antibacterial agent. The investigation of sulfadiazine by G. Ogruc-Ildiz *et al.* [25] by both experimental and computational vibrational spectra confirmed the presence of three conformers in room temperature. Sulfasalazine is an antibacterial drug which treats inflammatory bowel disease and rheumatoid arthritis. The charge transfer reaction between sulfasalazine and different types of acceptors was investigated by M. S. Refat *et al.* [26]. In this study, charge-transfer complexes were characterized through electronic, IR, H-NMR and mass spectra. Vibrational spectral studies of 2-hydroxy-4-methyl-3-nitropyridine and 2-hydroxy-4-methyl-5-nitropyridine supported by density functional theory done by V. Balachandran *et al.* [27] reveals the effects of methyl, hydroxyl and nitro group substitution to the pyridine ring. Investigations on molecular structure and vibrational spectra of four azobenzene containing materials [28] showed that the simultaneous strong IR and Raman activity of some normal modes are the prerequisite for a good nonlinear optical material. K. Chaitanya [29] investigated the molecular structure, vibrational frequencies of 2,4-dicarboxylic acid and the hyperpolarizability calculation shows that the compound is the best material for NLO applications.

1.3 Scope of the present work

The most vital task in the world today is to discover new drugs for the new diseases. Developing drugs directly without any computational support is very expensive. Spectroscopic and quantum chemical computation of chosen organic compounds provides the information about the molecular structure, intra, intermolecular interactions, charge transfer, delocalization, conjugation etc. Molecular modeling provides information of the structures of molecules and properties that are dependent upon those three-dimensional structures.

Structure elucidation and complete vibrational assignment of certain pharmaceutical compounds including fibrate derivative, sulfonamide derivatives and industrial compounds including nitrophenol derivatives, centralite compound have been performed in this study. The present thesis is concerned with the spectroscopic and quantum chemical computational analysis of some of the following important organic molecules with applications in various fields.

- Gemfibrozil or 5-(2,5-dimethylphenoxy)-2,2-dimethyl pentanoic acid
- Sulfasalazine or 5-{4-[(2-pyridylamino)sulfonyl]phenyldiazenyl}salicylic acid
- Sulfamerazine or 4-Amino-N-(4-methyl-2-pyrimidinyl) benzenesulfonamide
- 2-methyl-4-nitrophenol (PNOC) and 3-methyl-4-nitrophenol (PNMC)
- Ethyl Centralite or 1, 3-diethyl-1, 3-diphenylurea

1.4 Suggestions for future work

Current research is focused on modeling of organic compounds and spectroscopic studies depending on the molecular structure. The functional groups in the compounds under study can be changed and the corresponding change in the

activities of the new compound can be studied in the future as the extension of this work. In future, attempts will be made to design novel organic compounds and the electronic properties can be studied with the computational tools used in the present work. Further quantitative structure-activity relationship (QSAR) analysis can be done to provide the activity of the new molecules from the known activity and reactivity of a series of compounds.