CERTIFICATE

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This is to certify that the Thesis, entitled **FT-IR, FT-RAMAN, UV AND NMR ANALYSIS OF CERTAIN ANTIVIRAL COMPOUNDS USING QUANTUM COMPUTATIONAL (DFT) METHODS,** submitted to the Bharathiar University, in partial fulfillment of the requirements for the award of the Degree of Doctor of Philosophy in **PHYSICS** is a record of original research work done by **D. BAKKIYARAJ (R-Ph.D-E-2009-1121)** during the period **2009-2017** of his research in the Research & Development Centre, Bharathiar University, Coimbatore-641046, under my supervision and guidance and the thesis has not formed the basis for the award of any Degree / Diploma / Associateship / Fellowship or other similar title of any candidate of any University.

Date: **Signature of the Guide**

Counter Signed

Director
Research & Development Centre
Bharathiar University

DECLARATION

DECLARATION

I, **D. BAKKIYARAJ** hereby declare that the thesis, entitled "**FT-IR, FT-RAMAN, UV AND NMR ANALYSIS OF CERTAIN ANTIVIRAL COMPOUNDS USING QUANTUM COMPUTATIONAL (DFT) METHODS"** submitted to the Bharathiar University, in partial fulfillment of the requirements for the award of the Degree of Doctor of Philosophy in **PHYSICS** is a record of original and independent research work done by me during **2009-2017** under the Supervision and Guidance of **Dr.S.PERIANDY,** Department of Physics, Kanchi Mamunivar Centre for Post Graduate Studies, Puducherry and it has not formed the basis for the award of any Degree / Diploma / Associateship / Fellowship or other similar title to any candidate in any University.

Date: **Signature of the Scholar**

CERTIFICATE OF GENUINESS OF THE PUBLICATION

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This is to certify that the Ph.D candidate D. Bakkiyaraj working under my supervision has published five research articles in the following refereed journals. The Contents of the publication incorporate part of the results presented in his thesis.

S.No	**Journal Name**	**Vol. No**	**Page No.**	**Year**	**Publisher**
1	Journal of Molecular Structure	Vol.No.1119	490-504	2016	Elsevier
2	Journal of Molecular Structure	Vol.No.1108	33-45	2016	Elsevier
3	Springer Proceedings in Physics	Vol.No.189	599-627	2017	Springer
4	St. Joseph's Journal of Humanities and Science	Vol.No.2,	86-105	2015	St. Joseph's College of Arts & Science, Cuddalore

Signature of the Scholar **Research Supervisor**

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D. Bakkiyaraj

PREFACE

The analytical study of materials with spectroscopic methods combined with advanced computational theories has proven to be most powerful tool in elucidating information about dynamics of the molecules, the molecular structure and characteristics of the organic, inorganic, coordination compounds and polymers. Thus in the present study certain pharmaceutically active antiviral (picornavirus and poxvirus) molecules are chosen for spectroscopic and quantum computational analysis. The thesis is titled as **"FT-IR, FT-RAMAN, UV AND NMR ANALYSIS OF CERTAIN ANTIVIRAL COMPOUNDS USING QUANTUM COMPUTATIONAL (DFT) METHODS"** and it is presented in six chapters. A brief description of the experimental and theoretical aspects of Molecular spectroscopy and quantum computational analysis is presented in first chapter. The next four chapters are dedicated for the individual analysis of four antiviral molecules, comparing with structurally related molecules. The overall comparison and conclusions are discussed in sixth chapter.

The chapter-II deals with the study on adenosine, which is a nucleoside, composed of adenine and d-ribose. Adenosine and its derivatives play many important biological roles in addition to DNA and RNA. Adenosine itself is a neurotransmitter; it functions as energy transfer - as adenosine triphosphate (ATP) and adenosine diphosphate (ADP) - as well as in signal transduction as cyclic adenosine mono phosphate (cAMP). The structural analysis showed that the OH bond length is slightly stretched from the normal value. There is also weak H-N…H hydrogen bond formation between the molecules. All the CH stretching vibrations are observed to be slightly higher than the expected range. The comparison of Mulliken and atomic polar tensor (APT) charge prediction methods implies that the APT method is more akin to the NMR chemical shift variations. Three carbon atoms which are in the neighborhood of nitrogen atoms exhibited unusual chemical shift. The UV transition analysis shows that there are five prominent transitions in the wavelength range 219 to 253 nm., of which most probable transition belongs to $n \rightarrow \pi^*$ transition. Both the unusual NMR shifts and $n \rightarrow \pi^*$ UV transitions are the indicators of the biological active nature or potent of the molecule. The antiviral activity of the compound was

confirmed by the docking of the compound, it gets ported well into the poxvirus protein 5EJ0, at five sites of different amino acids by hydrogen bonding in the range of 2.1-2.3Å.

Benzil Dioxime is studied in Chapter –III, Oxime compounds are used as antidotes for nerve agents and as chelating agents to find the metals like cobalt and nickel in the vegetable food materials. Oxime-ethers frequently exhibit satisfactory insecticidal, fungicidal and herbicidal activities. The geometrical analysis confirms the earlier studies and the non deviant characters of the molecule between theoretical and experimental data. The vibrational analysis reveals that the nitrogen and oxygen atoms are found to play vital role in the vibrational modes of the molecule. CN in-plane and out of plane bending modes are found influenced by NO and CC vibrations and NO stretching are mixed with CC vibrations. The polarity of the molecule exhibits well with the nature of the conjugation of the molecule. The *ipso* carbon atoms are found to be highly positive compared to all other carbon atoms in the molecule which are basically negative. The NMR chemical shifts for these two carbon atoms at the point of substitution in the two rings have same values 132 and 136 ppm both in experimental and theoretical studies respectively. The chemical shifts of both carbon atoms attached to nitrogen atom are 155 ppm. Among many UV transitions predicted the two transitions are correlated with NBO analysis corresponding to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions. The antiviral activity of the compound was confirmed by the docking of the compound, the ligand is docked well into the picornavirus, protein 1C8M, at four sites of different amino acids by hydrogen bonding in the range of 2.1-2.7Å.

The study on adenine is presented in chapter -IV, which is a purine derivative (neucleobase) and it is an important component in all biological systems. It is present in the deoxyribonucleic acid (DNA), where it pairs with nucleobase cytosine. Adenine is also known as 6-aminopurine which possesses the structure of the pyrimidyl pyrine. It functions as a chemical component of RNA and DNA in the proton synthesis. The theoretical and experimental data obtained are compared and analyzed; and deviant characters of the molecule are well discussed and analyzed. In the structural analysis the identification of the CC & CN single and double bond

could not achieved because the bond lengths inside the purine ring do not vary much from one another. It implies that the conjugation of the electron is observed like that of benzene ring. The charge analysis and chemical shift analysis predicted positive charges and higher chemical shift values for carbon atoms attached to Nitrogen atoms. The UV analysis predicts five strong transitions in the range of 227 to 264 nm, of which three transition belong to $n\rightarrow\pi^*$ and two to $\pi\rightarrow\pi^*$ predictions. There are several mixing vibrations are found in the regions of NH and CC which are influenced by CN band, and found below the expected range in the bending vibrations. The protein activity of the molecule has been predicted by the PASS (Prediction of Activity Spectra for Substance) online tool with the value 0.787 activity with poxvirus, protein 2W0S, the molecule as a ligand is docked in the protein selected at three sites with hydrogen bonding with bond length range 2.0-2.2Å

The chapter V deals with acetazolamide. This compound is used clinically for the treatment of glaucoma and it is prescribed as drug to cure the intraocular pressure in a human eyes. The physical and chemical properties of the molecule have undergone theoretical and experimental studies and data are compared and analyzed. The geometrical investigation reveals a variation of ~0.1Å in C1=N4 and C2=N5 double bonds. The C-S bond length inside the ring is found shortened due to the conjugation inside the ring. The NBO analysis predicted all the six most probable transitions are $n\rightarrow\pi^*$ transitions in the range of 284 - 304 nm. The hyperpolarizability and dipole moment of the compound are 849.2949 $x10^{-33}$ esu and 5.5539 Debye respectively, which is three times higher than the reference (urea) values, thus the compound can make a good NLO material. The compound gets easily docked into the poxvirus, protein 5EJ0, at six sites of the amino acids having hydrogen bonds in the range 1.8 - 2.3 Å.

Chapter VI is dedicated to overall discussions and conclusions. Some of the common findings of the all the four molecules are:

The structural analysis is carried out for all these molecules for their minimum energy conformers, bond lengths and bond angles are analysed in comparison with the experimental values from the structurally related molecules. There is a considerable change in these structural

parameters due to substitutional groups which make the molecules biologically active. The vibrational analysis is carried out with experimentally recorded frequencies in comparison with the theoretically computed frequencies and also with frequencies observed in structurally similar molecules. Reasonable changes have been noticed in some of the vibrational frequencies due to the substitutional groups which also reflect the biological active nature of the molecules.

The NBO, UV and HOMO - LUMO analysis helps to find out the complete donor and acceptor molecular orbitals, the probable electronic transitions, with stabilization energy and oscillator strength or absorption coefficients for all these transitions. The identification of charge distribution and the potential variation at different part of these molecule and their mapping helps to identify the various reaction prone sited in the molecules. The computation of dipole moment, polarizability and hyperpolarizability helps to identify the NLO characters of the molecules. The thermodynamical parameter analysis helps to find out the overall energy levels for different configurations, the contribution of vibrational and rotational energy levels to these parameters and the temperature dependence of them, for all these molecules.

The Mulliken and APT charge distribution among the atoms and the NMR chemical shift analysis helps to predict the chemical environment of the molecules. The experimental NMR spectra and their comparison with the computed values throw much light on the background theory of the methods and basis sets and also on the dynamical nature of the molecules, with their extreme sensitiveness toward every substitution made in these molecules. The docking of the molecules help to find out the antiviral nature of the molecules; the proteins to which they get docked and also the numbers of amino acid sites where they are prone to get attached reveal the true nature of the molecule.