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Electronic Structure and Vibrational Analysis of Quetiapine 2-(2-(4-Dibenzo[b,f][1,4]thiazepine-11-yl-1-piperazinyl)ethoxy)ethanol

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Abstract – Quetiapine is an atypical antipsychotic used for the treatment of schizophrenia, bipolar disorder, and major depressive disorder. Use of quetiapine has been associated with serum aminotransferase elevations and in rare instances with clinically apparent acute liver injury. The structure and the ground state energy of the molecules under investigation has been analyzed employing DFT / B3LYP level. The optimized geometry and their properties such as equilibrium energy, frontier orbital energy, dipole moment and vibrational frequencies have been used to understand the activity ofQuetiapine. The calculated highest occupied molecule orbital or HOMO and the lowest un-occupied molecular orbital or LUMO energies shows that charge transfer within the molecule. The vibrational spectra of IR and Raman have been interpreted with the help of B3LYP level of theory with the 6-31G basis set from the Density function theory.

Keyword: DFT, Vibrational Spectroscopy, HOMO, LUMO, Antipsychotic

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INTRODUCTION

Initially approved by the FDA in 1997, quetiapine is a second-generation atypical antipsychotic used in schizophrenia, major depression, and bipolar disorder. Quetiapine demonstrates a high level of therapeutic efficacy and low risk of adverse effects during long-term treatment. It is well-tolerated and a suitable option for some patients with high sensitivity to other drugs, such as Clozapine and Olanzapine. In addition, it may be used for the management of acute manic or mixed episodes in patients with bipolar disorder, as a monotherapy or combined with other drugs. It may be used to manage depressive episodes in bipolar disorder. In addition to the above indications, quetiapine is used in combination with antidepressant drugs for the treatment of major depression.

The ground state and the empowered state properties of the title molecule have been processed using DFT/B3LYP level of speculations. The thorough examination of geometrical and electronic structure in ground electronic states, dipole minute, may provoke better understanding of the assistant, frightful characteristics of the compound under scrutiny.

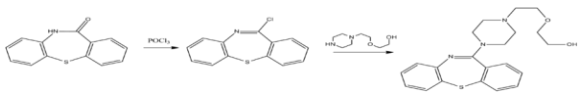
METHOD, MATERIAL AND THEORY

DFT has been very popular for calculations in solid-state physics since the 1970s. Density functional theory (DFT) is a computational quantum mechanical modelling method used in physics, chemistry and materials science to investigate the electronic structure (principally the ground state) of many-body systems, in particular atoms, molecules, and the condensed phases

In the chemistry community, one popular functional is known as B3LYP (from the name Becke for the exchange part and Lee, Yang and Parr for the correlation part). Even more widely used is B3LYP which is a hybrid functional.

The geometries of molecule were optimized using the Gaussian 09 suite of programs . The ground state geometry of quetiapinewere optimized using DFT. The basis set used for all atoms was 6-31G.

The synthesis of quetiapine begins with a dibenzothiazepinone. The lactam is first treated with phosphoryl chloride to produce a dibenzothiazepine. A nucleophilic substitution is used to introduce the sidechain.



Optimized geometrical structure of quetiapine is shown below.

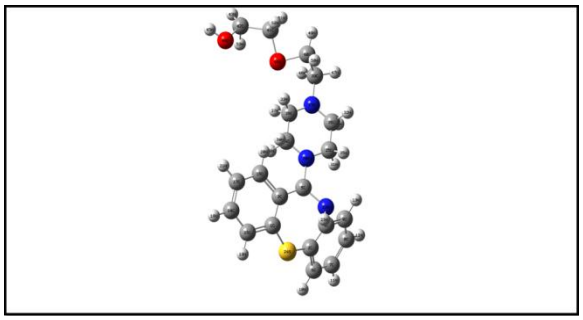


Fig 1

IR and Raman frequency

Vibrational spectroscopic methods use infrared or near infrared (the low energy end of the visible spectrum) to create vibrations (bond stretching or bending) in chemical species. Like visible spectroscopy, the radiation causing the vibration is absorbed and a corresponding peak is created on an Infrared or Raman spectrum. The excitation in Raman spectroscopy results in a transition between electronic states; in IR spectroscopy only a change in vibrational states occurs.

Fig 2 and 3 show the calculated IR and Raman spectra of quetiapine. These calculations were done by using DFT/6-31G.

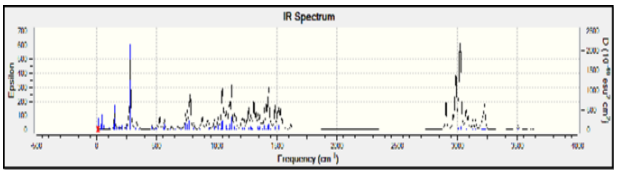


Fig2

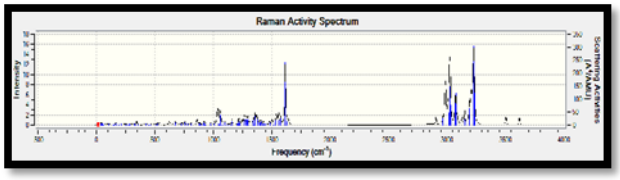


Fig 3

Depolarization spectra-

In Raman spectroscopy, the depolarization ratio is the intensity ratio between the perpendicular component and the parallel component of Raman scattered light. The Raman scattered light is emitted by the stimulation of the electric field of the incident light. Therefore, the direction of the vibration of the electric field, or polarization direction, of the scattered light might be expected to be the same as that of the incident light.The optimised spectra of p-depolarization and u-depolarization is shown in the fig-4 and fig-5

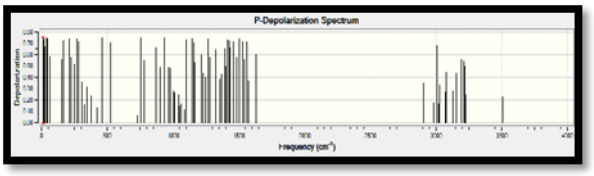


Fig 4

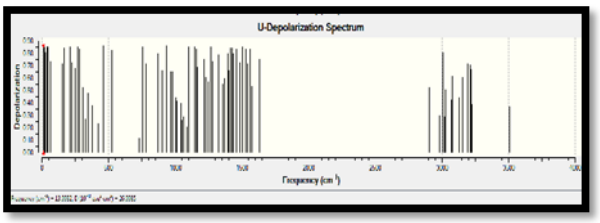


Fig 5

Theoretically computed ground state optimized parameters

Parameters	Quetiapine (B3LYP/6-31G)
Energy	-1528.33810857 a.u.
Dipole moment (in Debye)	6.6588 Debye

Electronic Properties

The most important orbitals in a molecule are the frontier molecular orbitals, called highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO).These orbitals determine the way the molecule interacts with other species. HOMO-LUMO orbitals are also called frontier orbitals as they lie at the outermost boundaries of the electrons of the molecules. The frontier orbital gap helps the chemical reactivity and kinetic stability of the molecule. A molecule with a small frontier orbital gap is generally associated with a high chemical reactivity, low kinetic stability and is also termed as soft molecule. The difference in energy between these two frontier orbitals can be used to predict the strength and stability of transition metal complexes, as well as the colors they produce in solution.

The HOMO and LUMO energy calculated by B3LYP /6-31G method –

HOMO Energy	-0. 18919a.u.
LUMO Energy	-0.12953 a.u.
ENERGY GAP	0.05966 a.u.

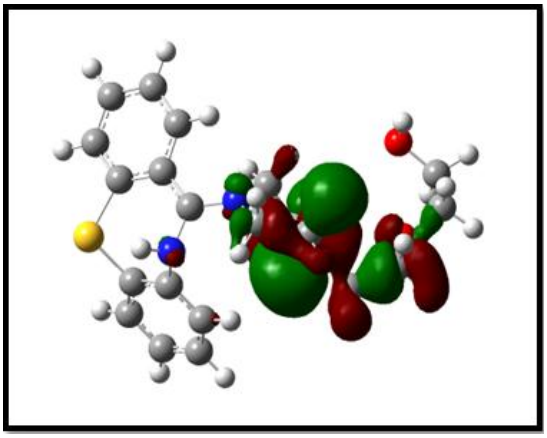


Fig 6

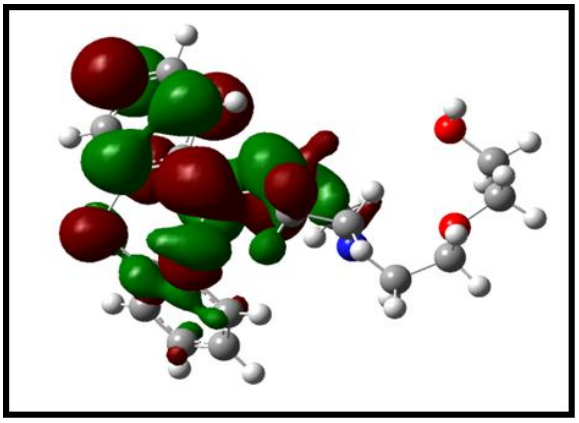
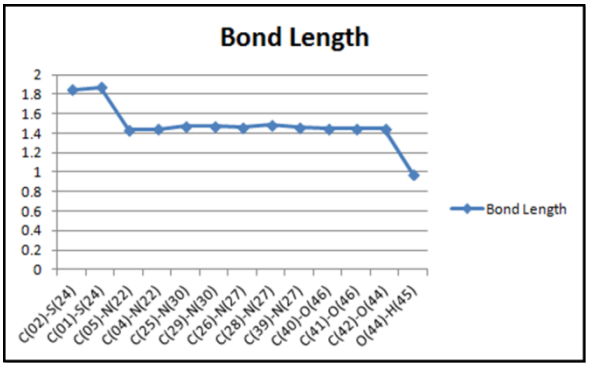


Fig 7

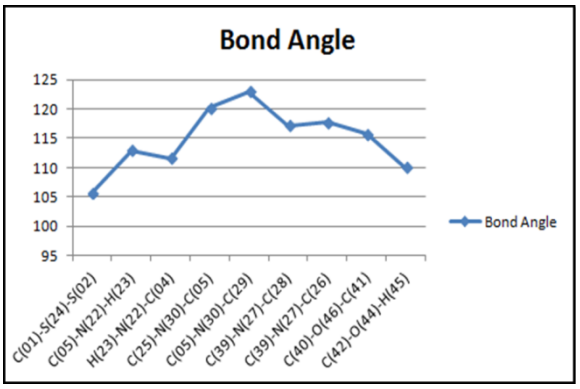
Bond length and bond angle

The optimized structural parameters such as bond length and bond angle were determined at B3LYP level theory with 6-31G basis set and are presented in Table and graph is given below-

Atom	Bond Length
C(02)-S(24)	1.84694
C(01)-S(24)	1.87192
C(05)-N(22)	1.43489
C(04)-N(22)	1.44325
C(25)-N(30)	1.47734
C(29)-N(30)	1.47318
C(26)-N(27)	1.46247
C(28)-N(27)	1.48528
C(39)-N(27)	1.45963
C(40)-O(46)	1.45311
C(41)-O(46)	1.44396
C(42)-O(44)	1.45262
O(44)-H(45)	0.9792



Atom	Bond Angle
C(01)-S(24)-S(02)	105.749
C(05)-N(22)-H(23)	112.914
H(23)-N(22)-C(04)	111.588
C(25)-N(30)-C(05)	120.144
C(05)-N(30)-C(29)	122.93
C(39)-N(27)-C(28)	117.155
C(39)-N(27)-C(26)	117.789
C(40)-O(46)-C(41)	115.676
C(42)-O(44)-H(45)	110.069



CONCLUSION

Simulation work of Quetiapine is in the process. Simulation report of Quetiapinewe will reported very soon.

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