Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2013, 5(5):182-186

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

A theoretical study on absorption spectra of ofloxacin

M. Ramegowda

Research Centre, Post-Graduate Department of Physics, Government College (Autonomous), Mandya, India

---

ABSTRACT

Density functional theory (DFT) and Time dependent density functional theory (TDDFT) calculations have been carried out to study the electronic structure and the UV absorption spectra of ofloxacin. The UV spectra have been investigated with inclusion of solvent effect using the polarizable continuum model (PCM). The B3LYP functional with 6-31G(d,p) basis sets have been used for geometry optimization and also to compute absorption energies. The vertical absorption energies both in gas phase and in ethanol were computed. The absorption maximum both in gas phase and in polar solvent is discussed in terms of electrostatic interaction energy, oscillator strength and dipole moment.

Keywords: DFT; TDDFT; 6-31G(d,p); PCM; Ofloxacin.

INTRODUCTION

Ofloxacin is a synthetic chemotherapeutic antibiotic of the fluoroquinolone drug class considered to be a second-generation fluoroquinolone [1]. Ofloxacin is a racemic mixture, which consists of 50% levofloxacin and 50% of its enantiomer dextrofloxacin [2]. The U.S. Food and Drug Administration (FDA) medical reviewers considered the two drugs to be one and the same and hence interchangeable [3]. As frequent dosing is required to maintain the therapeutic plasma concentration, ofloxacin was chosen as a model drug for the controlled release study [4,5]. Ofloxacin is chemically 9-fluro-2, 3-dihydro-3-methyl-10-(4-methyl-1-piperizinyl)-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxaine-6-carboxylic acid with a molecular formula $C_{18}H_{20}FN_3O_4$ and molecular weight of 361.368 gm/mol [6]. The density functional theory (DFT) [7] with B3LYP [8,9] functional combined with 6-31G(d,p) [10-12] basis set are most useful to optimize the geometries of molecules. The Time-Dependent Density Functional Theory (TDDFT) [13-15] has been used to simulate the electronic absorption spectra of free molecules. The calculated excitation energies are well agreed with experimental data for various compounds. Moreover, the inclusion of solvation effect *via* a PCM [16-19] model tends to change the excitation energies, due to a stabilization of the lowest unoccupied molecular orbitals (LUMO). Thus, the location of the first absorption band and the energy of the highest occupied molecular orbitals (HOMO) were used as parameters to evaluate the absorption maximum (λ_{max}). The absorption maximum is an important parameter of the UV spectrophotometric methods in pharmaceutical formulations especially in quantitative estimation [20-25].

In this work, the absorption maxima of ofloxacin both in gas phase and in polar solvent ethanol are simulated using the DFT/TDDFT method.

COMPUTATIONAL DETAILS

Ofloxacin molecule was modeled using Avogadro [26]. The ground state geometry was optimized using DFT/B3LYP hybrid functional with 6-31G(d,p) basis sets. The effect of solvent (ethanol) was added using the polarizable continuum model (PCM) of solvation. The optimized geometries are utilized to get the frontier molecular orbitals and to carry out the TDDFT studies. λ_{max} of ofloxacin is calculated at the level of TDDFT/6-31G(d,p). All calculations are performed using GAMESS-US software suit [27,28]. Molecular orbitals were plotted using wxMacMolPlt [29] and UV spectra were plotted using Gabedit [30].

RESULTS AND DISCUSSION

The optimized structure of the ofloxacin at S_0 state has non-planar geometries, as can be seen in Fig. 1. N14,C16,C17,N15,C18,C19 heterocyclic ring shows chair configuration. The benzene ring C1-C6 is in plane with the ring comprises of N8, C9, C40 and carbonyl groups. C2,N8,C11,C12,O13,C3 ring is distorted, C11 and C12 atoms are out of plane due to methyl group. A hydrogen bond of 1.677 Å is formed between O39 and H45. Fig. 2 displays the HOMO and LUMO, both of which show π-character. LUMO are localized on benzene ring, carbonyl group, N8 and C9 atoms, whereas HOMO are localized on heterocyclic ring, C1,C3,C4,C5 of benzene ring and O13 atom. This is desirable and leads to the intra-molecular charge separation upon excitation (push-pull effect). The S_1 state of ofloxacin molecule is mainly due to the orbital transition from HOMO to LUMO, which involves the charge transfer from the nitrogen atoms of heterocyclic ring to carbonyl group, N8 and C9 atoms. Thus, S_1 state of the molecule may be an intramolecular charge-transfer (ICT) state.

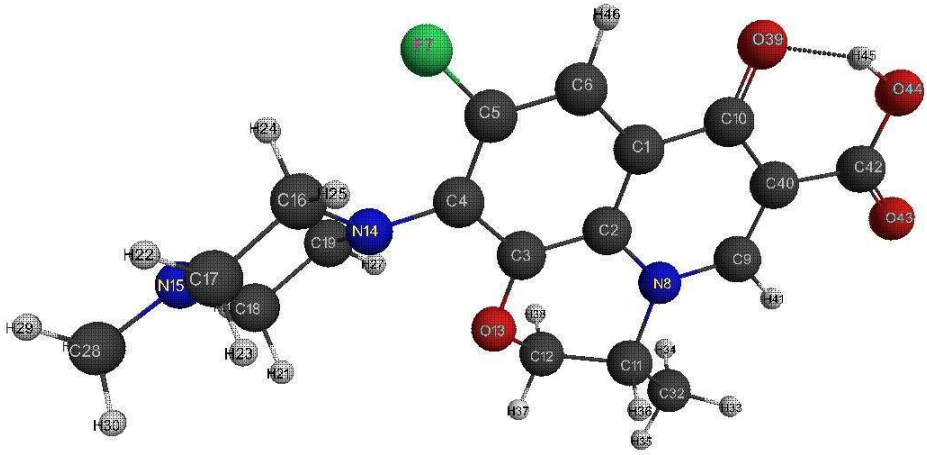

Fig. 1. Optimized structure of ofloxacin (Black-C, Red-O, Blue-N, Green-F and Gray-H)

The dipole moment of the free ofloxacin molecule is 10.199 Debye and it increases to 18.927 Debye in the exited state. The interaction energy between ofloxacin molecules with solvent molecules (fourth column of Table 1) is negative in polar solvent. Due to excitation, the dipole moment of ofloxacin molecule in ethanol is increased by 10.975 Debye (sixth column of Table 1). The change in electronic charge distribution between HOMO and LUMO is also indicative of a large dipole moment and is the possible reason for increase in oscillator strength (seventh column of Table 1) for the HOMO → LUMO transition in ethanol. The large dipole moment of ofloxacin molecule in the excited state is additionally stabilised by polar solvent molecules that leads to the slight decrease in the excitation energy and the corresponding redshift of the spectral maximum.

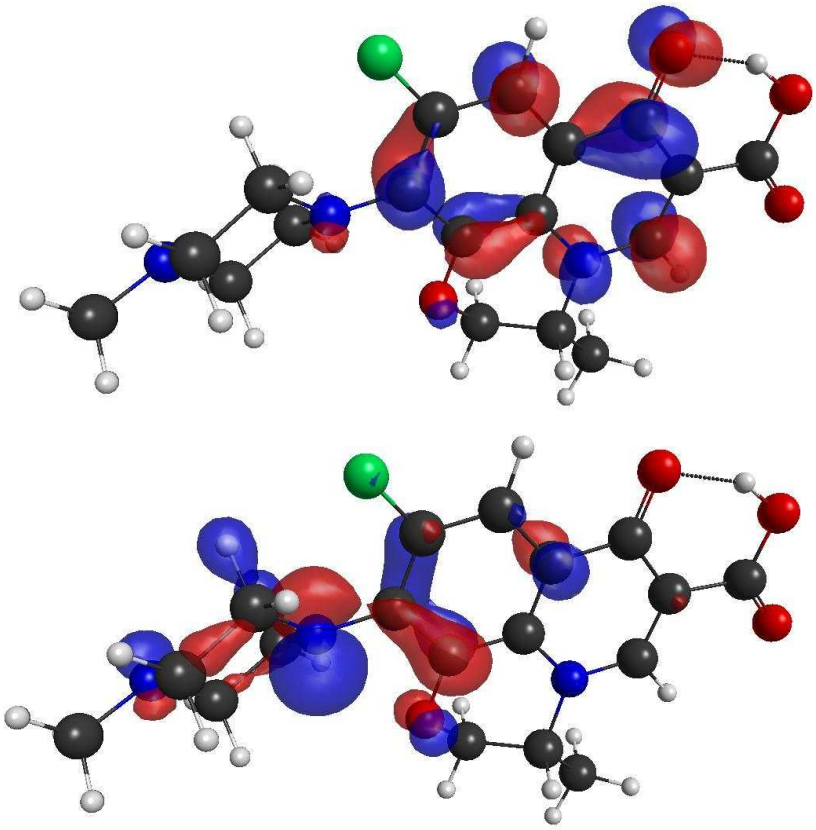

Fig. 2. The Molecular orbitals of ofloxacin. LUMO (top) and HOMO (bottom)

Table 1. λ_{max} corresponding to HOMO→LUMO transition, electrostatic interaction energy (E_{int}), dipole moment (D_D) of ofloxacin at S_0 and S_1 states, and oscillator strength (f)

Isolated state/ Solvent	λ_{max} (nm)	H→L (eV)	E_{int} (kCal/mol)	D_D at S_0 (Debye)	D_D at S_1 (Debye)	f
Isolated state	295.06	4.202	-	10.199	18.927	0.067
Ethanol	305.38	4.060	-16.20	12.989	23.964	0.180

The computational UV absorption spectra of ofloxacin in gas phase and in polar solvent are shown in the Fig. 3. Spectra show a similar profile in gas phase as well as in solvent and also it present intense band in polar solvent than in gas phase. The spectra show absorption energies corresponding to the λ_{max} of 295.06 in gas phase and 305.38 nm in ethanol which is in good agreement with the experimentally determined value 299.40 [31].

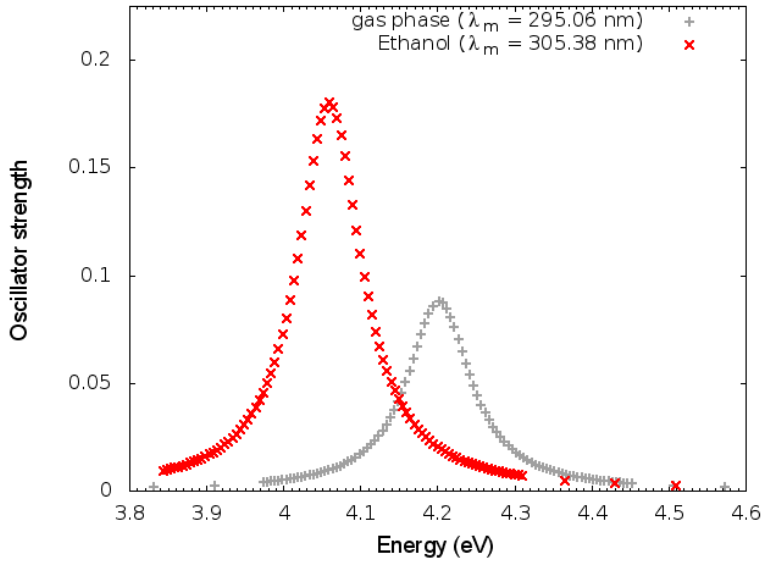

Fig. 3. Calculated UV absorption spectra of ofloxacin

CONCLUSION

In this study geometry optimization and UV absorption energy of ofloxacin in isolated state and in polar solvent ethanol has been carried out using DFT/TDDFT *via* the PCM model for solvation. From the results, some parameters such as excitation energy, oscillator strength, electrostatic interaction energy, dipole moment of ofloxacin have been chosen to evaluate λ_{max}. Absorption energy calculation shows redshift for λ_{max} in the presence of polar solvent. The absorption intensity of ofloxacin molecule in isolated state is considerably low as compared with the absorption intensity in polar solvent.

REFERENCES

[1] A Arunachalam; BS Rathinaraj; Subramanian; PK Choudhury; AK Reddy; Fareedullah. *J. Appl. Biol. Pharm. Tech.*, **2010**, 1(1), 61-67.
[2] http://www.wvnd.uscourts.gov/Opinions/orthoorder.pdf
[3] RW Johnson (April 24, 2007). USA: FDA. Retrieved July 22, **2009**.
[4] R Davis; HM Bryson. *Drugs*, **1994**, 47(4), 677–700.
[5] http://www.drugbank.ca/drugs/DB01165
[6] en.wikipedia.org/wiki/Ofloxacin
[7] RG Parr; W Yang. Density-Functional Theory of Atoms and Molecules. New York: Oxford University Press **1989**.
[8] K Kim; KD Jordan. *J. Phy. Chem.*, **1994**, 98(40), 10089–10094.
[9] PJ Stephens; FJ Devlin; CF Chabalowski; MJ Frisch. *J. Phys. Chem.*, **1994**, 98(45), 11623–11627.
[10] KL Schuchardt; BT Didier; T Elsethagen; L Sun; V Gurumoorthi; J Chase; J Li; TL Windus. *J. Cheminf.*, **2007**, 47(3), 1045-1052.
[11] D Feller. *J. Comp. Chem.*, **1996**, 17(13), 1571-1586.
[12] https://bse.pnl.gov/bse/portal.
[13] A Dreuw; MH Gordon. *Chem. Rev.*, **2005**, 105, 4009-4037.
[14] P Elliott; F Furche; K Burke. *Rev. Comp. Chem.*, **2009**, 26, 91-166.
[15] S Hirata; MH Gordon. *Chem. Phys. Lett.*, **1999**, 314, 291-299.
[16] H Li; CS Pomelli; JH Jensen. *Theo. Chem. Accs.*, **2003**, 109, 71-84.
[17] H Li; JH Jensen. *J. Comp. Chem.*, **2004**, 25, 1449-1462.
[18] Y Wang; H Li; *J. Chem. Phys.*, **2010**, 133, 034108.
[19] M Cossi; G Scalmani; N Rega; V Barone. *J. Chem. Phys.*, **2002**, 117, 43-54.
[20] G Gomes; HRN Salgado. *Acta Farmacéutica Bonaerense*, **2005**, 24(3), 406-8.

[21] K Divya; B Narayana. *J. Chem. Pharm. Res*., **2012**, 4(9), 4352-4358.
[22] V Dongala; P Tigulla. *J. Chem. Pharm. Res*., **2013**, 5(4), 340-346.
[23] S Sahoo; CK Chakraborti; PK Behera. *Int. J. PharmTech Res*., **2012**, 4(1), 382-391.
[24] PK Murthy; KB Naidu; NV Naidu. *J. Chem. Pharm. Res*., **2012**, 4(1), 96-99.
[25] G Abirami; T Vetrichelvan; M Bhavyasri. *Int. J. PharmTech Res*., **2012**, 4(2), 623-629.
[26] MD Hanwell; DE Curtis; DC Lonie; T Vandermeersch; E Zurek; GR Hutchison. *J. Cheminf.*, **2012**, 4, 17.
[27] MW Schmidt; KK Baldridge; JA Boatz; ST Elbert; MS Gordon; JH Jensen; S Koseki; N Matsunaga; KA Nguyen; SJ Su; TL Windus; M Dupuis; JA Montgomery. *J. Comp. Chem.*, **1993**, 14, 1347-1363.
[28] MS Gordon; MW Schmidt. Advances in electronic structure theory: GAMESS a decade later Chapter 41, pp 1167-1189, in Theory and Applications of Computational Chemistry, the first forty years CE Dykstra; G Frenking; KS Kim; GE Scuseria. Editors (Elsevier, Amsterdam, **2005**).
[29] BM Bode; MS Gordon. *J. Mol. Graph. Mod*., **1998**, 16, 133-138.
[30] AR Allouche. *J. Comp, Chem*., **2011**, 32(1), 174-182.
[31] A Mohammed; Al-Omar; Ofloxacin. In G Harry. Brittain editor: Profiles of Drug substances, Excipients, and Related Methodology, Vol. 34. Burlington: Academic Press, **2009**, pp. 265-298.