Journal of Molecular Structure 1156 (2018) 172–181

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: http://www.elsevier.com/locate/molstruc

Computational study of some fluoroquinolones: Structural, spectral and docking investigations

Koray Sayin*, Duran Karakaş, Sultan Erkan Kariper, Tuba Alagöz Sayin

Department of Chemistry, Faculty of Science, Cumhuriyet University, 58140 Sivas, Turkey

ARTICLE INFO

Article history:
Received 4 May 2017
Received in revised form
5 June 2017
Accepted 21 November 2017
Available online 22 November 2017

Keywords:
Fluoroquinolones
Antibiotics
Modelling studies
Spectral analysis
Docking

ABSTRACT

Quantum chemical calculations are performed over norfloxacin, tosufloxacin and levofloxacin. The most stable structures for each molecule are determined by thermodynamic parameters. Then the best level for calculations is determined by benchmark analysis. M062X/6-31 + G(d) level is used in calculations. IR, UV-VIS and NMR spectrum are calculated and examined in detail. Some quantum chemical parameters are calculated and the tendency of activity is recommended. Additionally, molecular docking calculations are performed between related compounds and a protein (ID: 2J9N).

1. Introduction

Research on antibiotics has been around for a long time [1–6] and the number of these studies is increasing day by day. Research of new antibiotic molecules attracts the interest of researchers. Fluoroquinolone is the member of quinolone which is broad-spectrum synthetic antibiotic drugs family. These antibiotics act as natural molecules in the cell and show their antimicrobial effect by preventing bacterial DNA. Additionally, fluoroquinolones are known as a chemotherapeutic agent. Investigations on quinolones have been started with synthesizing of nalidixic acid in 1962 by Lesher et al. [7]. These antibiotics are both beneficial and harmful to living organisms [8,9].

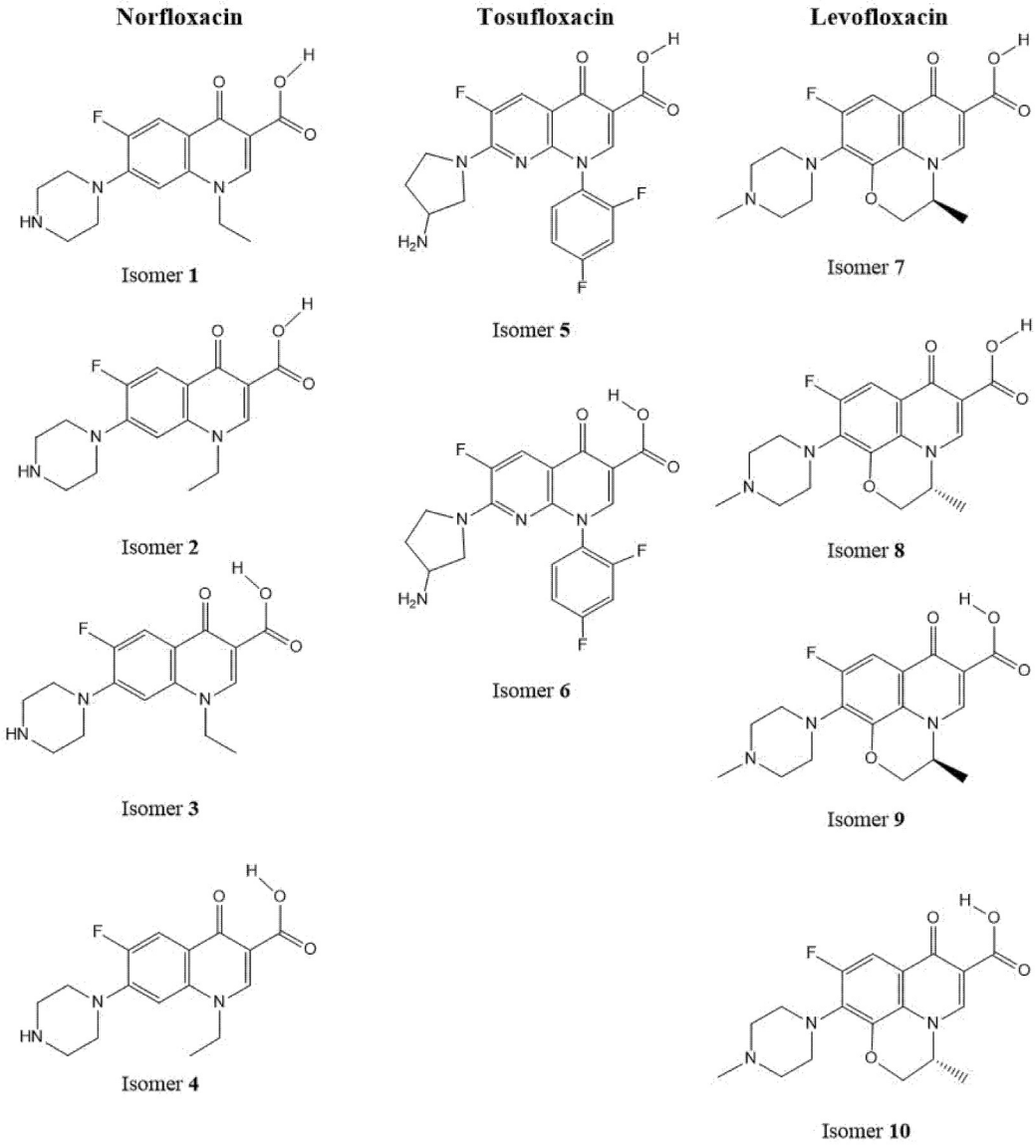
There are restricted quantum chemical investigations over the quinolones [10–18]. Some quantum chemical investigations have been performed on fluoroquinolone derivatives recently. In these study, benchmark analyses have not been done and a single level has been used in these studies. In this study, three different methods and five different basis sets are used to determine the best level for norfloxacin, tosufloxacin and levofloxacin. Some isomers for mentioned fluoroquinolones is drawn and the most stable structure for each fluoroquinolone is determined by using thermodynamic parameters, total energy (E_{Total}), enthalpy (H) and Gibbs free energy (G). Additionally, structural and spectral (IR, UV-VIS and NMR) analyses are done at the same level of theory for the most stable structure. Molecular electrostatic potential (MEP) maps, MEP contours, molecular orbital energy diagram (MOED) and contour diagram of some molecular orbitals are investigated. Additionally, some quantum chemical parameters are calculated to investigate the biological reactivity. These parameters are energy of the highest occupied molecular orbital (E_{HOMO}), energy of the lowest unoccupied molecular orbital (E_{LUMO}), energy gap between LUMO and HOMO (E_{GAP}), absolute hardness (η), absolute softness (σ), absolute electronegativity (χ), chemical potential (CP), electrophilicity index (ω), nucleophilicity index (N), additional electronic charges (ΔNmax), global softness (S). Koopmans theorem is taken into consideration in the calculation of these parameters. In addition to this analysis, molecular docking is performed between mentioned antibiotics and appropriate protein (ID: 2J9N) are taken from Protein Data Bank (http://www.rcsb.org/pdb/home/home.do). The interaction between related protein and mentioned molecules are calculated and examined in detail.

2. Calculation method

All computational processes were done by Gaussian program [19–21]. Input files of related compounds were prepared by using ChemDraw Professional 15.1 [22] and GausView 5.0.8 programs.

* Corresponding author.
E-mail addresses: krysayin@gmail.com, ksayin@cumhuriyet.edu.tr (K. Sayin).

https://doi.org/10.1016/j.molstruc.2017.11.091
0022-2860/



Scheme 1. Schematic diagram of studied isomers.

Calculations were performed by using Gaussian IA32W-G09RevA.02 and Gaussian AS64L-G09RevD.01 programs. Firstly, the whole molecules were optimized by using universal force field (UFF) method. Then, all compounds were reoptimized by using HF, B3LYP and M062X methods with STO-3G, 6-31G, 6-31G(d,p), 6-31 + G(d) and 6-311 + G(2d,p) basis sets in the gas phase. Experimental and calculated vibrational frequencies were compared with each other in each level. So, the best method and basis set was found via these analyses. Structural parameters, UV-VIS and NMR spectrum were investigated and examined in detail. Some quantum chemical parameters which are energy of the highest occupied molecular orbital (E_{HOMO}), energy of the lowest unoccupied molecular orbital (E_{LUMO}), energy gap between LUMO and HOMO (E_{GAP}), absolute hardness (η), absolute softness (σ), absolute electronegativity (χ), chemical potential (CP), electrophilicity index (ω), nucleophilicity index (N), additional electronic charges (ΔN_{max}) and global softness (S), were calculated by using Eq. (1)–(11) [23,24,32].

$$I = -E_{HOMO} \tag{1}$$

$$A = -E_{LUMO} \tag{2}$$

$$E_{GAP} = E_{LUMO} - E_{HOMO} \tag{3}$$

$$\eta = \frac{I - A}{2} = \frac{E_{LUMO} - E_{HOMO}}{2} \tag{4}$$

$$\sigma = \frac{1}{\eta} \tag{5}$$

$$\chi = \frac{|I + A|}{2} = \frac{|-E_{HOMO} - E_{LUMO}|}{2} \tag{6}$$