DFT Study of 3-[2-(4-chloro-phenyl)-2-oxo-ethyl]-5-(2,4-dichloro-thiazole-5-yl-methylenyl)thiazolidine-2,4-dione as antifungal agent

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Abstract- The molecular structure of 3-[2-(4-chloro-phenyl)-2-oxo-ethyl]-5-(2,4-dichloro-thiazole-5-yl-methylenyl)thiazolidine-2,4-dione as an antifungal agent against Candida albicans in the ground state was optimized by density functional using Becke's three-parameter hybrid method with the Lee, Yang, and Parr correlation functional method with 3-21G(d,p) basis sets. The calculated geometric parameters were compared with obtained experimental results.

Index Terms- Thiazolidine-2,4-dione; DFT; Antifungal agent

1 INTRODUCTION

1,3-Thiazolidines are the new class of antimicrobial agents with activity against broad spectrum of Gram-positive pathogens including *Staphylococci*, *Streptococci* and *Enterococci* [1].

moieties at different positions of the thiazolidine ring increased the antimicrobial effect [2, 3].

Organic compounds having thiazoles of different pharmacodynamic nuclei are found to possess potent antibacterial and antifungal activities [4, 5].

In the past 10 years there has been a major progression in the development of antifungal compounds, however there are still weaknesses in the range and scope of current antifungal chemotherapy [6]. New developments have contained the modification of substantial drug molecules to improve activity and eliminate toxicity.

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Therefore, we are also trying to screen the antifungal activity beside antibacterial to be able to luckily discover a new lead compounds.

Density Functional Theory (DFT) has used for geometry optimisation in theoretical drug design [7]. Recently, the methods based on DFT have come by steadily in popularity. The best DFT methods accomplish meaningfully greater accuracy than Hartree-Fock theory at only a modest enhance in cost. They do so by including some of the effects of electron correlation much less expensively than traditional correlated methods.

DFT methods compute electron correlation via general functionals of the electron density. Density Functional Theory, functional partition the electronic energy into several components which are calculated individually: the kinetic energy, the electron-nuclear interaction, the Coulomb repulsion, and an exchange-correlation term accounting for the remnant of the electron-electron interaction which is itself splited into separate exchange and correlation components in most truth DFT formulations.

The aim of this work was to calculate the molecular in the ground state of 3-[2-(4-chloro-phenyl)-2-oxo-ethyl]-5-(2,4-dichloro-thiazole-5-yl-methylenyl)-thiazolidine-2,4-dione (Fig. 1), which was two-fold dilution better antifungal activity against *Candida albicans* ATCC 10145 than standard drug, miconazole [8], by using Becke`s three-parameter hybrid method with the Lee, Yang, and Parr correlation functional (B3LYP) methods with 3-21G(d,p) basis set [9,10]. The calculated geometric parameters were compared with obtained experimental results in Ref. 8.

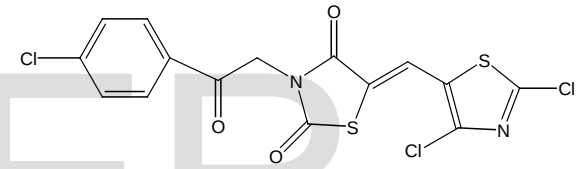

Fig. 1

2 CALCULATION

The molecular structure of 3-[2-(4-chloro-phenyl)-2-oxo-ethyl]-5-(2,4-dichloro-thiazole-5-yl-methylenyl) thiazolidine-2,4-dione in the ground state was optimized by density functional using Becke's three-parameter hybrid method with the Lee, Yang, and Parr correlation functional method with 3-21G(d,p)

basis sets. The single point calculations for effect modeling were performed in order to describe environmental influence on the properties of the molecule. This calculation was done by using Gaussian O3W program package [11]. The assignment of the calculated wavenumbers was assisted by the animation option of GaussView 3.0 graphical interface for Gaussian programs [12].

3 RESULTS AND DISCUSSION

In this study, the molecular geometry in the ground state of 3-[2-(4-chloro-phenyl)-2-oxo-ethyl]-5-(2,4-dichloro-thiazole-5-yl-methylenyl)-thiazolidine-2,4-dione (Fig. 1), which was found to be two-fold dilution better antifungal activity against *Candida albicans* ATCC 10145 than standard drug, miconazole [8], has been calculated by using B3LYP/3-21G(d,p) method. Moreover, the DFT data of the title molecule has been compared to its X-ray crystal structure (Fig. 2) [8], which was drawn in ORTEP [13]. Selected bond lengths, angles and torsion angle of the X-ray structure is presented in Table 1 in accordance with the atom numbering scheme given in Fig. 2.

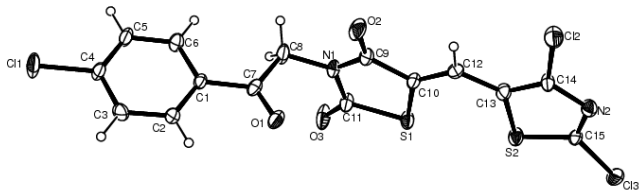

Fig. 2. An ORTEP3 view of the X-ray title compound showing the atom numbering scheme with %30 probability displacement ellipsoids.

The optimized structure parameters of 3-[2-(4-chloro-phenyl)-2-oxo-ethyl]-5-(2,4-dichloro-thiazole-5-yl-methylenyl)thiazolidine-2,4-dione was listed in Table 2 in accordance with the atom numbering as shown in Fig. 3. The largest difference between experimental and calculated DFT bond length and angle was about 0.0025 Å and 2.774 º for the 3-21G(d,p) basis set (Table 2). As a result, our calculation DFT method correlated well for the bond length and angle when we compared with the experimental data.

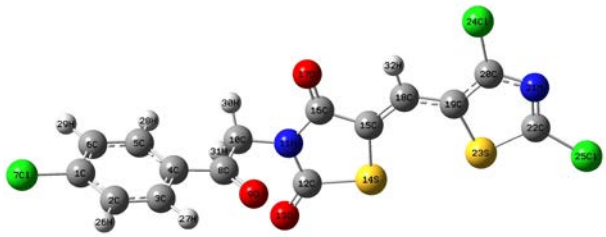

Fig. 3: 3D-Structure of the title compound calculated at B3LYP/3-21G(d,p)

The experimental C13—S2—C15 bond angle of 88.5(3)° and the calculated C(22)-S(23)-C(19) bond angle of 88.7869 have almost the same value with the values given in a survey of the Cambridge Structural Database [14] for 1,3-thiazole rings [90.79(5)°].

The experimental C9—C10—C12—C13 torsion angle [178.6(7)°] indicated existence of cis-configuration. According to DFT study, C(19)-C(18)-C(15)-C(16) torsion angle has been found to be a pretty closed number [179.9332 º] compared with experimental one.

Table 1. Experimental selected bond lengths (Å), bond and torsion angles (°) of the title compound

S1—C10	1.743(7)	S2—C15	1.711(7)
S1—C11	1.796(7)	S2—C13	1.736(7)
N1—C9	1.371(9)	Cl3—C15	1.718(6)
N1—C11	1.386(8)	Cl2—C14	1.710(7)
O3—C11	1.185(8)	N2—C15	1.289(8)
C9—C10	1.478(9)	N2—C14	1.352(8)
O2—C9	1.221(8)	C14—C13	1.375(9)
N1—C8	1.464(8)	C12—C10	1.344(10)
C7—O1	1.211(8)	C12—C13	1.431(8)
C10—S1—C11	91.4(3)	C15—S2—C13	88.5(3)
C9—N1—C11	117.7(6)	N2—C14—C13	19.0(6)
N1—C9—C10	110.2(6)	C15—N2—C14	107.5(6)
C9—C10—S1	111.1(5)	C14—C13—S2	107.0(5)
N1—C11—S1	109.2(5)	N2—C15—S2	118.1(5)
C13—C12—C10—C9	178.6(7)		

Table 2. Optimized geometrical parameters of 3-[2-(4-chloro-phenyl)-2-oxo-ethyl]-5-(2,4-dichloro-thiazole-5-yl-methylenyl)- thiazolidine-2,4-dione, atom labeling is according to Figure 3 and differences between experimental and calculated DFT.

Parameters	Calculated B3LYP/3-21G(d,p)	Δ*	Parameters	Calculated B3LYP/3-21G(d,p)	Δ*
Bond lenghts (Å)					
S(14)-C(10)	1.7557	0.0127	S(23)-C(22)	1.7494	0.0384
S(14)-C(12)	1.8263	0.0430	S(23)-C(19)	1.7591	0.0231
N(11)-C(16)	1.3972	0.0262	Cl(25)-C(22)	1.7224	0.0044
N(11)-C(12)	1.3905	0.0045	Cl(24)-C(20)	1.7280	0.0180
O(13)-C(12)	1.2192	0.0342	N(21)-C(22)	1.3069	0.0179
C(16)-C(15)	1.4862	0.0082	N(21)-N(20)	1.3747	0.0227
O(17)-C(16)	1.2335	0.0125	C(19)-C(20)	1.3878	0.0128
N(11)-C(10)	1.4588	0.0052	C(18)-C(15)	1.3501	0.0061
C(8)-O(9)	1.2351	0.0241	C(18)-C(19)	1.4285	0.0025
Bond angles (°)					
C(15)-S(14)-C(12)	91.3840	0.0160	C(22)-S(23)-C(19)	88.7869	0.2869
C(16)-N(11)-C(12)	118.2579	0.5579	N(21)-C(20)-C(19)	116.8507	2.1493
N(11)-C(16)-C(15)	109.7238	0.4762	C(22)-N(21)-C(20)	110.2740	2.7740
C(16)-C(15)-S(14)	111.7626	0.6626	C(20)-C(19)-S(23)	108.3091	1.3091
N(11)-C(12)-S(14)	108.8042	0.3958	N(21)-C(22)-S(23)	115.7792	2.3208
Torsion angle (°)					
C(19)-C(18)-C(15)-C(16)	179.9332	1.3332			

Abbreviation: Δ*; The difference between experimental and calculated DFT bond length and angle.

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