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Short Communication

DFT BASED INVESTIGATIONS OF ANTIBIOTIC AND ANTIFUNGAL ACTIVITY OF ALLANTOFURANONE AND RELATED γ-LACTONE COMPOUNDS

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ABSTRACT

Herein we report the correlation between the DFT outcomes and the reported antibiotic and antifungal activity of Allantofuranone and related compounds. The structure of Allantofuranone and related compounds containing γ-lactone were optimized by Density Functional Theory (DFT) using B3LYP method with 6-31G (d,p) basis set. The optimized molecular geometry, bond lengths, bond angles and band gap were investigated. The outcomes of the DFT calculations were utilised to formulate all the Quantum chemical parameters of the compounds viz. EA, IP, Electronegativity, hardness (η) and softness (σ). Structural parameters have been compared with the available experimental results, to investigate the structure-activity relationship.

Keywords: DFT, HOMO-LUMO, B3LYP, Allantofuranone, Structure-activity relationship.

1. INTRODUCTION

Plant Fungi adapts to environments though the plant significantly differs in their chemical composition and varying substantiallyduringthe growth of the host. Fungi usuallycope up with both the plantdefense system and competing with other parasites results into a special survival strategy via development ofa highly advanced secondary metabolism. The plant pathogen *Allantophomopsis lycopodina* [1-4] is reported for the leaf lesions effect on lingonberry, Vaccinium vitis-idaea and a fruit-rotpathogen (black rot) on cranberries [5]. The extract of *Allantophomopsis lycopodina* strain IBWF58B-05A contains Allantofuranone which is reported exhibiting strong and selective antibiotic and antifungal activity [6].The compound Allantofuranone is an unusual γ-lactone compound reported exhibiting good biological activities [6].

In this report, we present the study of four γ-lactone containing compounds (Allantofuranone, Xenofuranone A and B, WF 3681) using DFT / B3LYP method. Fig. 1 depicts structures of the compounds used in the current study. We were interested in exploring the frontier orbital energy and structure-activity relationship on the antifungal activities. It is reported that Allantofuranone shows strong antifungal activity, other compounds are though structurally similar but shows no antifungal activity and very weak cytotoxicity [6].

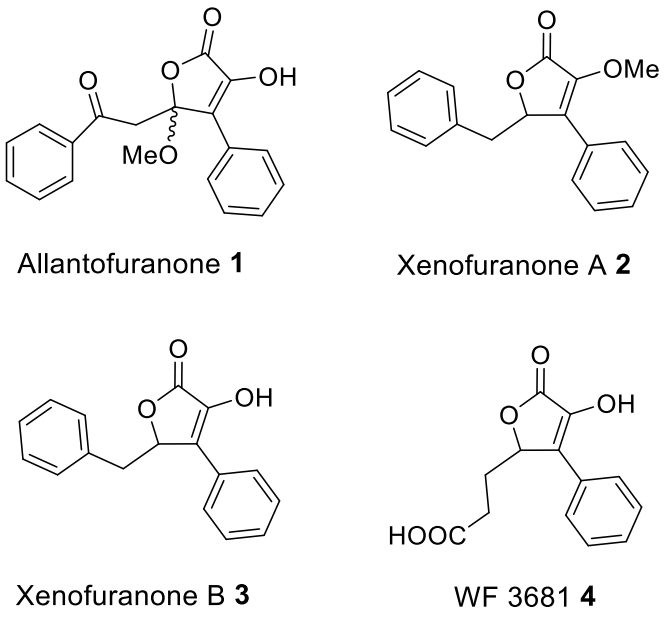

Fig. 1: Structures of the Allantofuranone and related compounds

2. RESULTS AND DISCUSSION

2.1. Comparison of DFT structural parameters with experimental data

The DFT calculations were carried out with B3LYP/6-31G (*d*,*p*) method in GAMESS package [7]. The geometry parameter *viz.* Calculated bond distances and observed bond lengths of compound Allantofuranone are given in table 1. In general, good agreement between the calculated and experimental bond lengths have been observed [6].

2.2. Frontier Orbital Energy Analysis

HOMO and LUMO are reported to act as the most important factor that decides the bioactivity of the organic and other compounds. According to the frontier molecular orbital theory, HOMO has the preference to provide electrons, while LUMO favors to accept electrons first [8]. The energies of HOMO-2 to LUMO +2 orbitals are given table 2. Molecular orbital diagram for the HOMOs and LUMOs are shown in fig. 3. Chem Bio 3D software was used to generate MO diagrams (extended Huckel theory). HOMOs of all the four compounds resides on five membered ring moiety and LUMOs of the three compounds Xenofuranone A, Xenofuranone B and WF 3681 were also observed residing on five membered ring moieties,whereas LUMO of Allantofuranone resides on one of the benzoylrings.

Table 1: Comparative selected structure parameters of the compound Allantofuranone

Distances (Å)/ Angles (°)	Allantofuranone	
	Expt	DFT
O1-C13	1.400	1.403
O1-C14	1.447	1.430
O2-C10	1.228	1.221
O3-C16	1.354	1.353
O4-C23	1.354	1.342
O5-C16	1.218	1.211
C6-C8	1.478	1.464
C6-C13	1.525	1.533
C6-C23	1.341	1.348
C7-C8	1.399	1.410
C7-C12	1.399	1.394
C8-C17	1.400	1.411
C9-C10	1.503	1.500
C9-C18	1.398	1.403
C9-C22	1.397	1.404
C10-C11	1.513	1.527
C11-C13	1.526	1.533

Table 2: Energy levels (a.u.) of MOs for compound Allantofuranone, Xenofuranone A and Xenofuranone B and WF 3681 calculated in their ground state in the gas phase

Compound	HOMO-2	HOMO-1	HOMO	LUMO	LUMO+1	LUMO+2
Allantofuranone	-0.2546	-0.2513	-0.2161	-0.0579	-0.053	-0.0097
Xenofuranone A	-0.2430	-0.2402	-0.2295	-0.0419	-0.0173	-0.0047
Xenofuranone B	-0.2448	-0.2408	-0.2336	-0.0456	-0.0227	-0.0060
WF 3681	-0.2664	-0.2632	-0.2312	-0.0460	-0.0200	0.0002

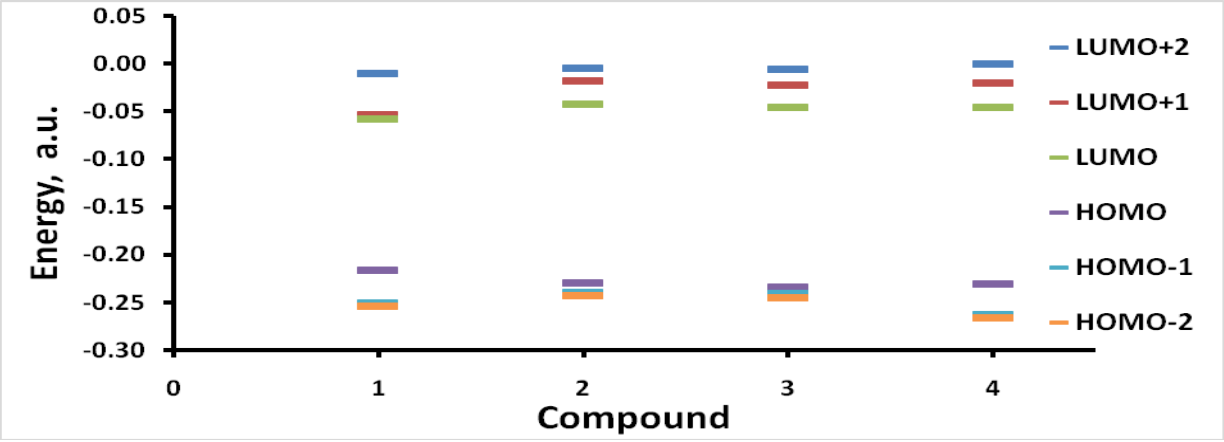

Fig. 2: Energy levels of MO diagram for compounds Allantofuranone, Xenofuranone A and Xenofuranone B and WF 3681 calculated in their ground state in the gas phase

The quantum chemical parameters of four γ-lactone containing compounds were calculated using the above equations. The obtained values of IP, EA, hardness, softness, and electronegativity associated with HOMO and LUMO energies are formulated in table 3.

The quantum chemical parameters were calculated as described by Cakmak et. al.[9] IP and EA can be obtained using HOMO and LUMO energies, these were calculated according to the Janak's Theorem [10].

$IP = -E_{HOMO}$, $EA = -E_{LUMO}$

Distortion of chemical species or opposition to electron cloud polarization is formulated as Hardness (η) of the compound [11]. The concepts of Hardness and softness were utilized to study the behaviour of the Chemical entity. The molecules are said to be hard if they possess large energy gap while, the molecules are said to be soft if they possess small energy gap. Thus, soft molecules are more polarizable than the hard molecules. $\eta = (IP-EA)/2$

Table 3: Quantum chemical parameters of compounds Allantofuranone, Xenofuranone A and Xenofuranone B and WF 3681calculated at B3LYP/6-31G(d,p)

	E_{HOMO} (eV)	E_{LUMO} (eV)	ΔE (eV)	IP= $-E_{HOMO}$	EA= $-E_{LUMO}$	η= (I-A)/2	σ= 1/η	χ= (I+A)/2	Log p
Allantofuranone	-5.880	-1.576	4.30	5.880	1.576	2.152	0.465	3.728	3.695
Xenofuranone A	-6.245	-1.140	5.10	6.245	1.140	2.552	0.392	3.693	2.774
Xenofuranone B	-6.357	-1.241	5.12	6.357	1.241	2.558	0.391	3.799	2.412
WF 3681	-6.291	-1.252	5.04	6.291	1.252	2.520	0.397	3.771	1.101

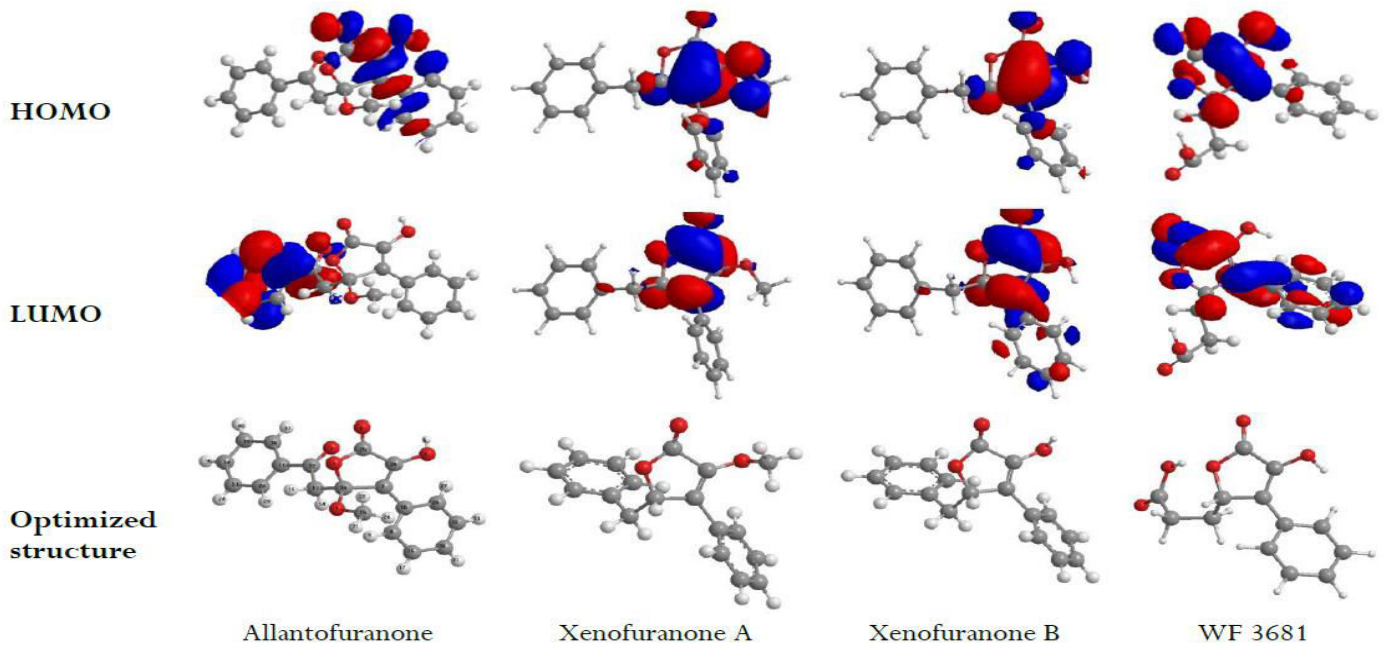

Fig. 3: Molecular orbital diagram for the HOMOs, LUMOs and optimized structures of the four compounds Allantofuranone, Xenofuranone A, Xenofuranone B and WF 3681

The softness of the molecules is calculated by taking inverse of global hardness [12]. $\sigma = 1/\eta$

Ability of the molecules to attract the electron is termed as Electronegativity (χ) and was calculated using the following equation. $\chi = -(E_{HOMO} + E_{LUMO})/2$

It is clear from table 3 that the HOMO - LUMO energy gap of Allantofuranone is small compared to other compounds. Further it is also observed that lower the value of LUMO energy, more is the activity. This is in accordance with the literature which reported the strongest antifungal activity for Allantofuranone.

Here it is observed that the activity correlates very well with the computed values of all the quantum chemical parameters viz. EA, IP, Electronegativity, band gap,

hardness (η) and softness (σ). From theLop p calculations it is observed that Allantofuranone is more lipophilic in nature. Higher values of Lop p are indicative of stronger antifungal as well as antibiotic activity.

3. CONCLUSIONS

The DFT calculations of compounds Allantofuranone, Xenofuranone A, Xenofuranone B and WF 3681 revealed small HOMO-LUMO gap, lower value of LUMO, more lipophilic character and rich topography of Allantofuranone are prerequisite for antifungal activity. Here we highlight the electronic characteristics responsible for the strong biological activity, which separates Allantofuranone from other structurally similar compounds. Overall, we observed good correlation between biological activity and computed values of all the quantum chemical parameters viz. EA, IP, Electronegativity, band gap, hardness (η) and softness (σ).

Conflict of interest

None declared

4. REFERENCES

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