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Research Article

# Geometric structure and electronic properties of the fluorinated 7-hydroxycoumarin derivative molecule with anti-inflammatory effect: Homo-Lumo, MEP

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***Abstract***

The fluorinated 7-hydroxycoumarin derivative molecule is known for its diverse biological activities, including antimicrobial, antioxidant, antitumor, and anti-inflammatory properties. In our article, the electronic structure and properties of the fluorinated 7-hydroxycoumarin derivative molecule were examined in detail using the Density Functional Theory (DFT) calculation method in the Gaussian program. The B3LYP/LanL2MB basis set was used to investigate the specific molecular properties of the fluorinated 7-hydroxycoumarin derivative. Unlike traditional analyses, this study focused on elucidating HOMO-LUMO energy gaps and Molecular Electrostatic Potentials (MEPs), which provide critical information regarding the potential biological activities of the compound and its suitability for drug design applications. Understanding these molecular features not only helps uncover the mechanisms behind observed biological effects but also paves the way for future advances in medicinal chemistry and pharmaceutical development.

**Keywords:** The fluorinated 7-hydroxycoumarin; DFT; HOMO and LUMO

## Introduction

Coumarin, a naturally occurring compound in plants, is commonly associated with vanilla, cinnamon, and sweet aromas [1]. Coumarin derivatives, including the fluorinated 7-hydroxycoumarin derivative molecule ((E)-6-chloro-3-fluoro-7-hydroxy-4-methyl-2-oxo-2H-chromene-8-carbaldehyde O-ethyl oxime), represent a diverse class of chemical compounds with extensive industrial and medicinal applications [2]. These derivatives exhibit a spectrum of valuable properties:

Firstly, Fragrance: Coumarin derivatives are prized for their pleasant aroma, making them essential components in perfumes, cosmetics, and personal care products [3]. Secondly, Anticoagulant Characteristics: Many derivatives exhibit anticoagulant properties beneficial in medical treatments [4]. However, due to their anticoagulant effects, cautious administration is crucial to avoid potential serious bleeding incidents. Thirdly, Anti-inflammatory and Antioxidant Properties: Specific derivatives also demonstrate significant anti-inflammatory and antioxidant effects, which are pivotal in managing inflammatory disorders and oxidative stress [5-7].

Despite their diverse applications and biological significance, comprehensive theoretical investigations into the molecular structures and spectroscopic properties of the fluorinated 7-hydroxycoumarin derivative molecule using advanced computational methods such as Density Functional Theory (DFT) with the B3LYP/LanL2MB basis set within Gaussian software, remain limited in the literature. This study aims to fill this gap by providing novel insights into the theoretical aspects of this compound's behavior. By conducting detailed theoretical calculations, this research endeavors to elucidate unique structural characteristics and chemical behaviors not extensively explored in existing literature. Such endeavors are pivotal for advancing our understanding of the biological activities and potential pharmacological applications of coumarin derivatives, particularly the fluorinated 7-hydroxycoumarin derivative molecule.

## 2. Computational Details

The geometric structure of the fluorinated 7-hydroxycoumarin derivative molecule was initially visualized using the Gaussian View 5 program [8]. Subsequently, comprehensive theoretical calculations were undertaken to explore various aspects of this compound. Employing the Density Functional Theory (DFT) method, calculations were specifically performed using the B3LYP [9-10] (Becke's Three-Parameter Hybrid Functional) and LanL2MB [11] basis set. This computational approach [12] is particularly suited for predicting molecular structure, energy levels, and diverse chemical properties, especially in systems containing heavy metals and transition metals. The theoretical calculations not only aimed to elucidate the molecular structure of the fluorinated 7-hydroxycoumarin derivative but also to provide insights into its chemical reactivity and confirm experimental findings. By

employing advanced computational tools, this study contributes to a deeper understanding of the compound's structural characteristics and its potential applications in pharmaceutical research and development.

## 3. Results and Discussion

### *3.1. Geometric Structure*

The synthesis and spectral properties of the fluorinated 7-hydroxycoumarin derivative molecule ((E)-6-chloro-3-fluoro-7-hydroxy-4-methyl-2-oxo-2H-chromene-8-carbaldehyde O-ethyl oxime) have been previously reported by Qing-Qing Wang et al. [13]. Utilizing data from the Cambridge Crystallographic Data Centre (CCDC) with the code CCDC 2043279, the X-ray single crystal structure of the synthesized coumarin derivative provided a basis for theoretical geometric calculations. Density Functional Theory (DFT) calculations were performed using the GAUSSIAN 09 software, employing the LANL2MB basis set in conjunction with the B3LYP methodology. The stable conformation was refined through the DFT/B3LYP/LanL2MB(d,p) approach, as illustrated in Figure 1. These calculations were instrumental in elucidating the intricate geometric arrangement and chemical bonding within the molecule. DFT is widely recognized for its ability to reveal electron behaviors and molecular properties, making it indispensable for understanding the structural complexities of the coumarin derivative. The insights gleaned from these calculations not only advance our comprehension of molecular structures but also ensure alignment between experimental observations and theoretical predictions in relevant scientific disciplines.

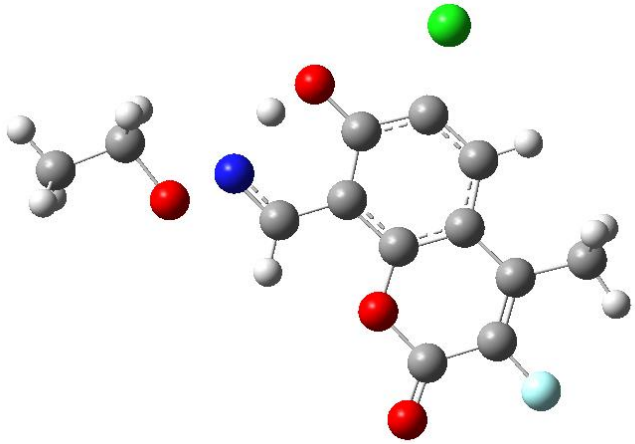

**Figure 1:** The optimized geometry of the fluorinated 7-hydroxycoumarin derivative molecule calculated using the B3LYP/LANL2MB method.

### 3.2. Electronic Properties

Molecular orbitals, pivotal in understanding the electronic structure and behavior of chemical compounds, can now be quantitatively assessed thanks to the advancements in modern quantum chemical computation methods, notably utilizing sophisticated techniques like Density Functional Theory (DFT). In the scope of this research, the $E_{HOMO}$ (Highest Occupied Molecular Orbital) and $E_{LUMO}$ (Lowest Unoccupied Molecular Orbital) energy values for the fluorinated 7-hydroxycoumarin derivative molecule were meticulously determined through the application of the DFT method. $E_{HOMO}$ and $E_{LUMO}$ serve as the fundamental orbital structures dictating the course of chemical reactions. The HOMO energy signifies the molecule's propensity to donate electrons (π donor), while the LUMO energy characterizes its capability to accept electrons (π acceptor). Utilizing the LANL2MB set and B3LYP methods, the electronic structural parameters were rigorously calculated. The computed $E_{HOMO}$ and $E_{LUMO}$ energies served as the foundation for deriving crucial parameters such as energy gap (ΔE), electron affinity (A), ionization potential (I), electronegativity (χ), chemical softness (S), and chemical hardness (η). These parameters, grounded in the distribution of electron density, offer profound insights into the compound's chemical behavior and reactivity. The comprehensive analysis of these electronic properties contributes significantly to our understanding of the compound's molecular behavior and its potential applications in various chemical processes and industries.

| | **B3LYP /LANL2MB** |
|---|---|
| $E_{HOMO}$ (eV) | -3.67656 |
| $E_{LUMO}$ (eV) | 0.484094 |
| $\Delta E = E_{LUMO}-E_{HOMO}$ (eV) | 4.160654 |
| I (eV) | 3.67656 |
| A (eV) | -0.484094 |
| χ (eV) | 1.596233 |
| η (eV) | 2.080327 |
| S ($eV^{-1}$) | 0.135997 |
| $E_{TOTAL}$ (a.u) | -959.88966 |

**Table 1:** Molecular orbital energy calculations for the fluorinated 7-hydroxycoumarin derivative molecule

LUMO, an abbreviation for Lowest Unoccupied Molecular Orbital, signifies the orbital with the lowest energy level that lacks electrons. Conversely, HOMO, which stands for Highest Occupied Molecular Orbital, refers to the orbital with the highest energy level containing electrons. $E_{LUMO}$ denotes the energy associated with the lowest unoccupied molecular orbital, whereas $E_{HOMO}$ represents the energy associated with the highest occupied molecular orbital. In the context of the coumarin derivative compound, the electronic transitions of specifically chosen frontier molecular orbitals (LUMO, HOMO) are visually depicted in Figure 2. These frontier orbitals play a critical role in understanding the compound's electronic structure and its potential reactivity in chemical processes. By analyzing the electronic transitions between these orbitals, valuable insights can be gained into the compound's optical and chemical properties, facilitating further exploration of its applications in various fields.

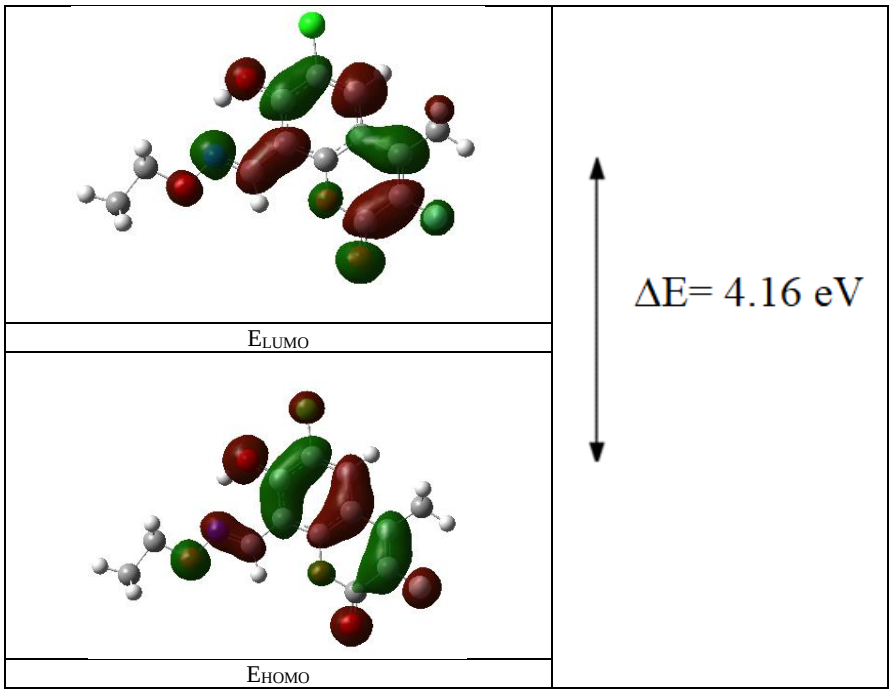


**Figure 2:** 3D orbital energies of the coumarin derivative compound.

When analyzing the depictions of the HOMO-LUMO orbitals, it is evident that this research validates previous experimental findings. According to the electrostatic potential mapping, electron density increases along the green-red axis, indicating areas depicted in red are electron-rich. Additionally, the positioning of the HOMO orbitals serves as an indicator of reactivity. Reactions typically occur between the HOMO and LUMO orbitals; hence, atoms where the HOMO-LUMO orbitals reside are more prone to undergo reactions. This observation underscores the importance of comprehending the electronic structure and spatial distribution of molecular orbitals in predicting and interpreting chemical reactivity.

### 3.3. Molecular Electrostatic Potential Surfaces (MEPS)

Molecular electrostatic potential (MEP) is a useful method for explaining the reactivity of molecular behaviors, structural activity, and hydrogen bonding. The three-dimensional molecular electrostatic potential maps of the optimized structures of the fluorinated 7-hydroxycoumarin derivative molecule using the B3LYP/LanL2MB method are shown in Figure 3.

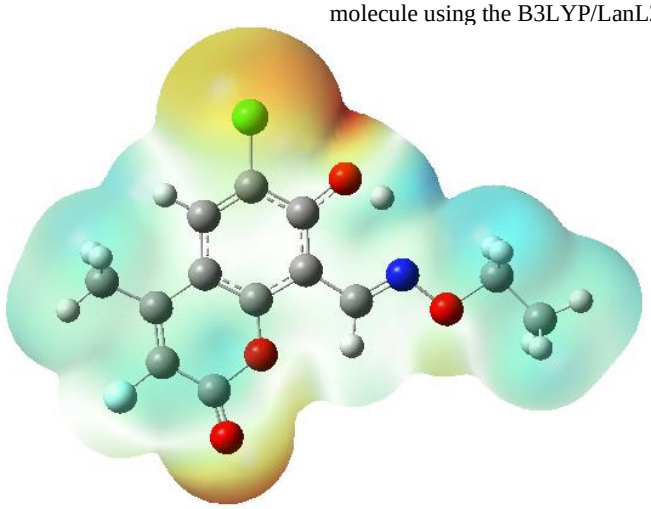

**Figure 3:** Molecular electrostatic surface map of the fluorinated 7-hydroxycoumarin derivative molecule.

At every point of the molecule, electron density exhibits a homogeneous distribution. The electrostatic potential (MEP) map determines the molecular size, shape, and electrostatic potential value. In a neutral molecule, regions where electron density increases are depicted in red on the MEP map, while areas of decreased electron density are shown in blue. Upon shape analysis, it is observed that in the neutral form, areas with the highest electron density generally concentrate around oxygen atoms, while the lowest density regions are observed at N-H bonding points.

The MEP map serves as a multifaceted indicator elucidating intrinsic molecular properties and structural attributes that govern chemical reactivity. Through the spatial distribution of electron density, the MEP map offers nuanced insights into the molecule's interaction capacity and propensity to engage in chemical reactions. Regions of electron-rich density not only signify areas more prone to molecular interactions but also hint at potential roles in catalyzing reactions. Moreover, the intricate interplay between molecular size, shape, and electrostatic potential delineates the molecule's biological or pharmacological activity, underscoring the MEP map's pivotal

role as an indispensable tool in guiding molecular design strategies and facilitating drug discovery endeavors within the scientific community.

## 4. Conclusions

Coumarin derivatives are well-known for their pivotal role in plant defense mechanisms, showcasing diverse biological activities such as antimicrobial, antioxidant, antitumor, and anti-inflammatory properties. These compounds have garnered significant attention in pharmaceutical research as promising candidates for developing novel therapeutics. Particularly intriguing are the molecular interactions and affinity towards target proteins exhibited by coumarin derivatives, which are focal points in current medical research. Computational techniques, including Gaussian-based Density Functional Theory (DFT) calculations with the B3LYP/LanL2MB basis set, offer a robust approach to unraveling the intricate biological, chemical, and physical characteristics of coumarin derivatives. In this study, we conducted a detailed theoretical exploration of the electronic properties, including the Highest Occupied Molecular Orbital (HOMO), Lowest Unoccupied Molecular Orbital (LUMO), and Molecular Electrostatic Potential (MEP), of our specific coumarin derivative compound. This comprehensive analysis serves as a cornerstone in understanding the compound's complex electronic characteristics and its potential pharmacological implications. In conclusion, the fluorinated 7-hydroxycoumarin derivative molecule emerges as a promising candidate in pharmaceutical research due to its diverse biological activities and potential therapeutic applications. Our study, employing Gaussian-based DFT calculations with the B3LYP/LanL2MB basis set, has provided valuable insights into its electronic properties, thereby enhancing our understanding of its pharmacological implications and highlighting its potential in drug development. Future research aimed at further elucidating its electronic interactions and exploring novel therapeutic applications will be crucial for fully harnessing the pharmacological benefits of the fluorinated 7-hydroxycoumarin derivative molecule.

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