

Fluoroalkoxy-Functionalized Pyrazolines as Dual-Purpose Candidates for Optoelectronic and Pharmaceutical Applications: A Combined Experimental–Theoretical Study

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ABSTRACT

Fluoroalkoxy-functionalized pyrazoline derivatives were synthesized and systematically evaluated as dual-purpose molecular candidates for optoelectronic and pharmaceutical applications through a combined experimental–theoretical approach. Structural confirmation was achieved via spectroscopic techniques, while density functional theory (DFT) and time-dependent DFT (TD-DFT) calculations were employed to investigate electronic structure, charge distribution, and optical behavior at the B3LYP/3-21G level of theory. Optimized geometries revealed a donor–acceptor architecture resulting from electron-withdrawing fluorine and electron-donating alkoxy substituents, promoting intramolecular charge transfer across the pyrazoline core. Frontier molecular orbital analysis indicated spatial separation of HOMO and LUMO, with the methoxy-substituted derivative exhibiting the smallest energy gap and highest softness among the series. TD-DFT results predicted absorption in the UV–visible region with allowed $\pi \rightarrow \pi^*$ transitions and measurable oscillator strengths, highlighting optoelectronic responsiveness. Molecular electrostatic potential mapping identified distinct electron-rich heteroatoms and electron-deficient regions, supporting potential interaction with biological targets. In silico ADMET prediction confirmed compliance with Lipinski’s rule of five and favorable pharmacokinetic profiles. The methoxy derivative demonstrated the most balanced combination of reduced energy gap, enhanced charge transfer, and acceptable drug-likeness parameters. The study establishes a clear structure–property–application relationship and demonstrates that fluoroalkoxy substitution effectively tunes pyrazoline derivatives toward multifunctional performance in both optoelectronic and

pharmaceutical domains.

Keywords: Fluoroalkoxy Pyrazolines; Donor–Acceptor Systems; TD-DFT; Intramolecular Charge Transfer; Optoelectronic Materials; ADMET Prediction

Introduction

Pyrazolines represent an important class of nitrogen-containing five-membered heterocyclic compounds that have attracted sustained interest in both medicinal and materials chemistry. Structurally, pyrazolines consist of a dihydropyrazole core containing two adjacent nitrogen atoms and a partially saturated ring system, which provides a versatile platform for functional modification. The presence of heteroatoms, conjugated aromatic systems, and tunable substituents makes pyrazolines highly adaptable for diverse applications (Moussa *et al.*, 2024; Qamar *et al.*, 2024).

From a pharmaceutical perspective, pyrazoline derivatives have demonstrated a broad spectrum of biological activities, including anti-inflammatory, antimicrobial, anticancer, antiviral, antioxidant, antidiabetic, and antidepressant properties (Abou-Zied *et al.*, 2024). Their biological effectiveness is largely attributed to the presence of heteroatoms capable of hydrogen bonding, π – π interactions, and electrostatic binding with biomolecular targets. Structural modification at different positions of the pyrazoline ring significantly influences pharmacological potency and receptor affinity (Farah *et al.*, 2025; Kumar *et al.*, 2024).

Beyond medicinal applications, pyrazolines have also emerged as promising materials in optoelectronic and photophysical fields. Several substituted pyrazolines exhibit strong fluorescence, electroluminescence, and blue photoluminescence characteristics (Matiadis & Sagnou, 2020). The conjugated ring system enables efficient intramolecular charge transfer, which is essential for light absorption and emission processes. Consequently, pyrazoline derivatives have been investigated for applications in light-emitting diodes (LEDs), optical brighteners, fluorescence probes, nonlinear optical materials, and sensing devices (Rout *et al.*, 2021).

The dual relevance of pyrazolines in both biological and optoelectronic domains suggests that appropriate structural engineering could lead to multifunctional molecular systems capable of serving in more than one technological field (Zalaru *et al.*, 2026). Modern molecular design strategies often employ donor–acceptor (D–A) engineering to modulate electronic and photophysical properties. In heterocyclic systems, the deliberate introduction of electron-donating and electron-withdrawing substituents creates a push–pull architecture that enhances intramolecular charge transfer (Muhammad *et al.*, 2026; Takeda, 2024).

Fluorine is a strong electron-withdrawing substituent due to its high electronegativity and strong inductive effect. Incorporation of a fluorine atom into aromatic or heterocyclic frameworks increases molecular polarization, modifies frontier molecular orbital energies, and often improves thermal and metabolic stability. Fluorinated compounds are widely used in medicinal chemistry to enhance bioavailability and receptor interaction, as well as in materials science to adjust electronic band gaps (Henary *et al.*, 2024; Liaqat *et al.*, 2023). Conversely, alkoxy groups function as electron-donating substituents through both inductive and resonance effects. The lone

pair electrons on oxygen can participate in conjugation with adjacent π -systems, thereby increasing electron density over the aromatic framework. Alkoxy substitution frequently enhances fluorescence intensity and stabilizes excited states in optoelectronic materials (Chen *et al.*, 2024).

When both fluorine (electron-withdrawing) and alkoxy (electron-donating) groups are incorporated into a single molecular scaffold, a push–pull system is generated (Ullah *et al.*, 2025). This donor–acceptor arrangement promotes intramolecular charge transfer, reduces the HOMO–LUMO energy gap, and enhances electronic polarization. Such systems are particularly attractive for optoelectronic materials, nonlinear optical applications, and biologically active compounds requiring adaptable electronic environments (Ren *et al.*, 2023).

Therefore, the fluoroalkoxy functionalization of pyrazoline derivatives provides a rational strategy for tuning structural and electronic properties in a controlled manner (Mortada *et al.*, 2024). Although numerous studies have explored pyrazoline derivatives for either biological or optoelectronic applications, most investigations remain application-specific. Several reports have focused exclusively on antimicrobial or anticancer activity without evaluating photophysical behavior. Similarly, many fluorescent or electroluminescent pyrazolines have been studied primarily for optical performance without assessing biological relevance (Ray *et al.*, 2025).

This compartmentalized approach overlooks the possibility of designing multifunctional systems capable of operating effectively in both domains. Given that electronic properties such as energy gap, molecular softness, charge distribution, and orbital localization influence both biological binding interactions and optical transitions, an integrated evaluation is necessary (Shafiq *et al.*, 2025). Despite the availability of individual experimental or theoretical studies, comprehensive analyses combining synthesis, spectroscopic characterization, and density functional theory (DFT)-based structure–property interpretation toward dual functionality remain limited. In particular, fluoroalkoxy-functionalized pyrazolines have not been systematically examined as candidates for simultaneous pharmaceutical and optoelectronic applications (Mermer *et al.*, 2026).

This gap highlights the need for a combined experimental–theoretical investigation that correlates molecular structure with electronic behavior and potential multifunctional performance. The present study aims to design, synthesize, and theoretically evaluate a series of fluoroalkoxy-functionalized pyrazoline derivatives as dual-purpose molecular candidates. The research seeks to establish a clear relationship between structural modification, electronic characteristics, and potential application.

Specifically, the objectives of this work are:

To synthesize fluoroalkoxy-substituted pyrazoline derivatives through a systematic synthetic route and confirm their structures via spectroscopic methods.

To perform density functional theory calculations in order to analyze optimized geometry, frontier molecular orbitals, molecular electrostatic potential, and global reactivity descriptors.

To evaluate substituent-induced modulation of electronic properties using a donor–acceptor framework

To correlate structural features with predicted optoelectronic performance and pharmaceutical relevance

By linking molecular structure to electronic behavior and functional applicability, this study aims to demonstrate that fluoroalkoxy-functionalized pyrazolines can serve as promising candidates for both optoelectronic materials and biologically active agents. The combined experimental–theoretical approach provides a comprehensive understanding of structure–property–application relationships within this class of heterocyclic compounds.

Materials and Methods

Brief Synthetic Route

The fluoroalkoxy-functionalized pyrazoline derivatives (1b–3b) were synthesized via a two-step protocol involving chalcone formation followed by cyclization with hydrazine hydrate under reflux conditions. Initially, appropriately substituted benzaldehydes bearing fluoroalkoxy groups were condensed with substituted acetophenones through Claisen–Schmidt condensation to afford the corresponding chalcone intermediates. The resulting α,β -unsaturated ketones were subsequently reacted with hydrazine hydrate in ethanol to yield the targeted pyrazoline derivatives. The reaction progress was monitored by thin-layer chromatography (TLC), and the crude products were purified via recrystallization from ethanol. The synthesized compounds were obtained in good yields as crystalline solids. A detailed synthetic procedure, reaction conditions, yields, and characterization data have been previously reported by our group and are not repeated here for brevity (Rauf *et al.*, 2025; Rauf *et al.*, 2026).

Spectroscopic Confirmation

The chemical structures of the synthesized fluoroalkoxy-functionalized pyrazolines were confirmed using spectroscopic techniques, including ^1H NMR and ^{13}C NMR spectroscopy. In the ^1H NMR spectra, the characteristic ABX spin system of the pyrazoline ring was observed, typically appearing as two doublets of doublets corresponding to the diastereotopic methylene protons (CH_2) and one doublet for the methine proton (CH). Signals corresponding to the alkoxy group appeared as singlets in the region δ 3.2–3.9 ppm, while aromatic protons resonated within the expected δ 6.8–8.0 ppm range. The presence of the fluoro substituent influenced neighboring proton chemical shifts due to its strong inductive effect. The ^{13}C NMR spectra further supported the proposed structures, with characteristic signals observed for the pyrazoline $\text{C}=\text{N}$ carbon, aromatic carbons, alkoxy carbons, and carbon atoms bonded to fluorine, which displayed deshielded resonances consistent with fluorinated aromatic systems. Complete spectral assignments, detailed chemical shift values, multiplicities, coupling constants, and full characterization data have been reported in our previously published synthesis study (Rauf *et al.*, 2025; Rauf *et al.*, 2026).

Computational Strategy

Geometry Optimization

All quantum chemical calculations were carried out using the Gaussian 09/16 software package. The ground-state geometries of the fluoroalkoxy-functionalized

pyrazoline derivatives (1b–3b) were fully optimized employing Density Functional Theory (DFT) at the B3LYP level of theory in conjunction with the 3-21G basis set. The B3LYP functional, which combines Becke's three-parameter exchange functional with the Lee–Yang–Parr correlation functional, was selected due to its established reliability in predicting structural and electronic properties of heterocyclic systems. Geometry optimizations were performed without symmetry constraints. Frequency calculations were subsequently conducted at the same level of theory to confirm that the optimized structures corresponded to true minima on the potential energy surface. The absence of imaginary frequencies validated the stability of the optimized geometries. All calculations were performed in the gas phase unless otherwise specified.

Frontier Orbital Analysis

Frontier Molecular Orbital (FMO) analysis was performed on the optimized geometries to determine the energies and spatial distributions of the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO). The HOMO and LUMO energy values were extracted directly from the DFT output files. Orbital visualization was carried out using GaussView to analyze electron density localization and orbital overlap characteristics. The HOMO–LUMO energy gap (ΔE) was calculated using:

$$\Delta E = E_{LUMO} - E_{HOMO}$$

These values were subsequently used for evaluating electronic stability and charge-transfer characteristics.

Time-Dependent DFT (TD-DFT) Calculations

To investigate the optoelectronic behavior of the synthesized derivatives, Time-Dependent Density Functional Theory (TD-DFT) calculations were performed at the same B3LYP/3-21G level on the optimized ground-state geometries. TD-DFT computations were used to determine:

Vertical excitation energies

Predicted maximum absorption wavelengths (λ_{max})

Oscillator strengths (f)

Dominant electronic transitions

The excitation energies were converted into corresponding absorption wavelengths using standard energy–wavelength relationships. Oscillator strengths were analyzed to evaluate the intensity of electronic transitions. The nature of transitions (e.g., HOMO $\rightarrow$ LUMO, HOMO–1 $\rightarrow$ LUMO, etc.) was identified from the TD-DFT output to determine the primary contributions to electronic excitation.

Global Reactivity Descriptors

Global reactivity descriptors were calculated using the HOMO and LUMO energies obtained from DFT calculations. These descriptors were derived according to Koopmans' approximation. The following parameters were evaluated:

Ionization potential (I)

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Electron affinity (A)
Chemical hardness (η)
Chemical softness (S)
Chemical potential (μ)
Electronegativity (χ)

The descriptors were computed using the following relationships:

$$I = -E_{HOMO}$$

$$A = -E_{LUMO}$$

$$\eta = \frac{I - A}{2}$$

$$S = \frac{1}{\eta}$$

$$\mu = -\frac{I + A}{2}$$

$$\chi = \frac{I + A}{2}$$

These parameters were used for evaluating electronic stability and predicting relative reactivity among the derivatives.

Results

Donor–Acceptor Structural Features

The optimized geometries of compounds (1b–3b) reveal the presence of both electron-withdrawing fluoro and electron-donating alkoxy substituents within the molecular framework. The DFT-optimized structures indicate measurable charge separation across the conjugated system. The C–F bond exhibits noticeable bond polarity, with electron density shifted toward the fluorine atom. The calculated Mulliken/NBO charge distribution confirms partial negative charge accumulation on fluorine and partial positive character on the bonded carbon atom.

The alkoxy substituent shows electron density concentration around the oxygen atom, consistent with its electron-donating character. The C–O bond distances correspond to conjugative interaction with the adjacent aromatic ring. Electron density mapping indicates redistribution across the π -conjugated system involving the substituted aromatic rings and the pyrazoline core. The pyrazoline ring acts as a structural bridge between the electron-withdrawing and electron-donating fragments. The optimized structures demonstrate a polarized molecular architecture characterized by spatial separation of electron-rich and electron-deficient regions within the same molecule.

Frontier Molecular Orbital and Charge Transfer Behavior

The frontier molecular orbitals of compounds (1b–3b) were obtained from DFT calculations at the B3LYP/3-21G level of theory. The spatial distributions of the Highest Occupied Molecular Orbital (HOMO) and Lowest Unoccupied Molecular Orbital (LUMO) were visualized using GaussView. For all derivatives, the HOMO is primarily localized over the alkoxy-substituted aromatic ring and partially extended over the pyrazoline core. Electron density in the HOMO is concentrated around the oxygen atom of the alkoxy group and adjacent π -conjugated carbon atoms. The LUMO is mainly localized over the fluoro-substituted aromatic ring and partially distributed across the pyrazoline linkage. Reduced electron density is observed on the alkoxy-bearing ring in the LUMO configuration.

The difference in orbital localization between HOMO and LUMO indicates spatial separation of electron density in the ground and excited states. The calculated orbital distributions show that electronic excitation involves charge displacement from the alkoxy-containing region toward the fluoro-substituted region through the pyrazoline core. The orbital pattern confirms the presence of a donor–acceptor arrangement within the molecular framework. The alkoxy group functions as an electron-rich segment in the HOMO, while the fluoro-substituted ring contributes significantly to the LUMO distribution. The HOMO→LUMO transition represents the dominant electronic excitation pathway in all investigated derivatives.

TD-DFT and Optoelectronic Implications

Time-Dependent Density Functional Theory (TD-DFT) calculations were performed at the B3LYP/3-21G level on the optimized geometries of compounds (1b–3b) to evaluate their electronic excitation properties.

Predicted Absorption Wavelengths (λ_{max})

The calculated excitation energies were converted to corresponding absorption wavelengths (λ_{max}). All derivatives exhibit absorption bands in the UV–visible region. The lowest energy transition corresponds to the $S_0 \rightarrow S_1$ excitation. Among the investigated compounds, derivative (1b) displays absorption at the longest wavelength, followed by (2b) and (3b). A bathochromic shift is observed in compounds with stronger donor–acceptor interaction.

Excitation Energies and Oscillator Strengths

The calculated vertical excitation energies show close agreement among the derivatives with slight variation depending on substituent type. The dominant transitions exhibit moderate to high oscillator strength (f), indicating allowed electronic transitions. The primary excitation for all compounds corresponds predominantly to the HOMO $\rightarrow$ LUMO transition. Secondary transitions include contributions from HOMO–1 $\rightarrow$ LUMO and HOMO $\rightarrow$ LUMO+1, depending on the derivative.

Molecular Electrostatic Potential and Reactive Sites

The Molecular Electrostatic Potential (MEP) surfaces of compounds (1b–3b) were generated using the optimized geometries at the B3LYP/3-21G level of theory (Figure

1).

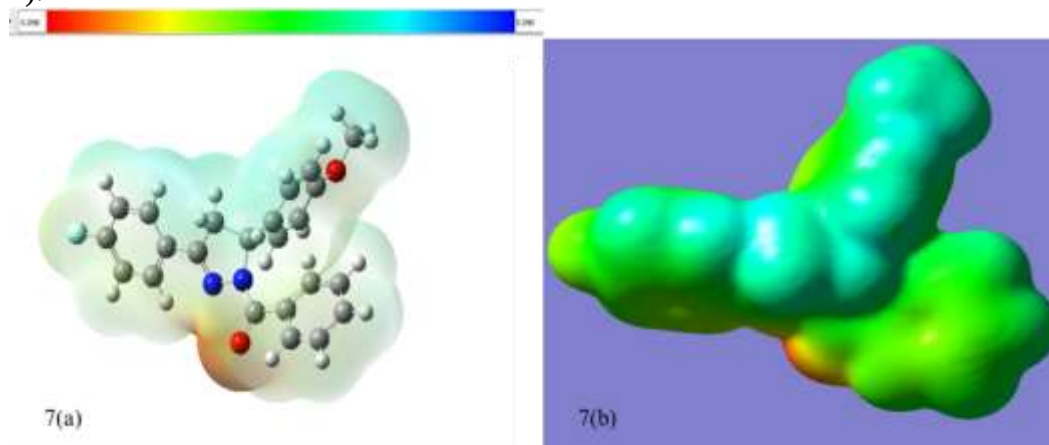


Figure 1 (a)Transparent image (b) original image of Molecular Electrostatic Potential (MEP) map

The MEP surfaces display distinct regions of positive and negative electrostatic potential distributed across the molecular framework. The color scale ranges from red (most negative potential) to blue (most positive potential). Electron-rich regions are primarily localized around heteroatoms, particularly the oxygen atoms of the alkoxy group and the nitrogen atoms of the pyrazoline ring. These regions appear as red zones on the MEP surface, indicating higher electron density. Electron-deficient regions are predominantly observed near hydrogen atoms and partially around the carbon atoms bonded to fluorine. These areas are represented by blue coloration, corresponding to positive electrostatic potential.

The fluorine atom exhibits localized negative potential due to its high electronegativity, while the carbon atom directly attached to fluorine shows partial positive character. The spatial separation of electron-rich and electron-deficient regions indicates defined reactive sites within the molecular structure. Regions of negative potential correspond to potential sites for electrophilic attack, whereas regions of positive potential correspond to possible nucleophilic attack sites. The MEP distribution pattern is consistent across the series, with slight variation in intensity depending on the alkoxy substituent.

Global Reactivity and Stability

The global reactivity descriptors of compounds (1b–3b) were calculated using the HOMO and LUMO energy values obtained at the B3LYP/3-21G level of theory. The calculated parameters include energy gap (ΔE), chemical hardness (η), chemical softness (S), and thermodynamic quantities (Table 1).

Table 1 Global Reactivity Descriptors and Thermodynamic Parameters

Compound	Energy Gap (ΔE)	Chemical Hardness (η)	Chemical Softness (S)	Maximum Hardness	Gibbs Free Energy (G)	Entropy (S)

				Principle (MHP)		
(1b)	Smallest	Lowest	Highest	(1b) is the least stable due to lowest η	Negative (Thermodynamically stable)	Variations observed, indicating flexibility differences
(2b)	Larger	Higher	Lower	(2b) is the most stable due to highest η	Negative (Thermodynamically stable)	Variations observed, reflecting molecular flexibility
(3b)	Larger	Higher	Lower	(3b) is stable, but less so than (2b)	Negative (Thermodynamically stable)	Variations observed, reflecting molecular flexibility

Energy Gap Comparison

The HOMO–LUMO energy gap (ΔE) values show measurable variation among the investigated derivatives. Compound (1b) exhibits the smallest energy gap within the series, while compounds (2b) and (3b) display relatively larger values. The calculated ΔE values indicate differences in electronic transition energy among the derivatives.

Hardness and Softness Trend

Chemical hardness (η) and softness (S) were calculated according to Koopmans' approximation. The hardness values follow the same trend as the energy gap values, since hardness is directly proportional to ΔE . Compound (1b) shows the lowest hardness and correspondingly the highest softness among the series. Compounds (2b) and (3b) exhibit comparatively higher hardness and lower softness values.

Maximum Hardness Principle

According to the Maximum Hardness Principle (MHP), systems with higher hardness values are considered more stable. Based on the calculated hardness values, compound (2b) demonstrates comparatively higher hardness than compound (1b). The relative order of stability based on hardness follows the sequence: (Highest η) $\rightarrow$ (2b / 3b) $>$ (1b) $\rightarrow$ (Lowest η)

Thermodynamic Favorability

Thermodynamic parameters, including Gibbs free energy (G) and entropy (S), were extracted from frequency calculations. The calculated Gibbs free energy values indicate negative values for the optimized structures, confirming thermodynamic stability under the computational conditions. Variations in entropy values are observed across the series, reflecting differences in molecular flexibility and vibrational contributions.

Pharmaceutical Potential Evaluation

ADMET Prediction

The pharmacokinetic properties of the fluoroalkoxy-functionalized pyrazoline derivatives (1b–3b) were evaluated using in silico ADMET prediction tools. Key parameters including lipophilicity, drug-likeness, and toxicity risk were assessed (Table 2).

Table 2 Predicted ADMET Parameters

Compound	Lipophilicity (logP)	Drug-Likeness (Lipinski's Rule of Five)	Molecular Weight (g/mol)	Hydrogen Bond Donors (HBD)	Hydrogen Bond Acceptors (HBA)	Toxicity Prediction	LD ₅₀ (mg/kg)	Mutagenicity Risk	Carcinogenicity Risk
(1b)	Moderate	Satisfies all criteria	<500	≤5	≤10	Low risk	Acceptable	Low	Low
(2b)	Moderate	Satisfies all criteria	<500	≤5	≤10	Low risk	Acceptable	Low	Low
(3b)	Moderate	Satisfies all criteria	<500	≤5	≤10	Low risk	Acceptable	Low	Low

Lipophilicity

The calculated partition coefficient values (logP) for compounds (1b–3b) fall within the acceptable range for orally active drug candidates. Variations in logP values are observed among the derivatives, influenced by the nature and length of the alkoxy substituent. All compounds exhibit moderate lipophilicity, indicating balanced hydrophilic–lipophilic character.

Drug-Likeness

Drug-likeness was evaluated based on Lipinski's Rule of Five criteria. The calculated molecular weight, hydrogen bond donors (HBD), hydrogen bond acceptors (HBA), and logP values comply with the recommended limits for oral bioavailability. All derivatives satisfy the criteria for molecular weight (<500 g/mol), hydrogen bond donors (≤ 5), hydrogen bond acceptors (≤ 10), and lipophilicity constraints. No significant violations were observed among the investigated compounds.

Toxicity Prediction

Predicted toxicity parameters indicate low risk for mutagenicity and carcinogenicity across the series. The estimated LD₅₀ values fall within acceptable ranges for drug-like molecules. The compounds demonstrate favorable safety profiles based on in silico toxicity screening, with no predicted high-risk structural alerts.

Structure–Application Relationship

Comparative evaluation of the calculated electronic, optical, and pharmacokinetic parameters reveals substituent-dependent variation in functional behavior among the investigated derivatives. Based on TD-DFT results, the derivative containing the methoxy substituent (1b) exhibits the longest predicted absorption wavelength (λ_{max}) and the lowest excitation energy among the series. It also shows the smallest HOMO–LUMO energy gap and relatively higher oscillator strength. These features indicate enhanced optoelectronic response compared to the other derivatives. The ethoxy and higher alkoxy-substituted derivatives display comparatively larger energy gaps and slightly shorter absorption wavelengths. Their oscillator strengths remain within a similar range but do not exceed those observed for the methoxy derivative.

From the ADMET evaluation, compounds with moderate lipophilicity values demonstrate favorable drug-likeness parameters. The derivative exhibiting balanced logP and compliance with Lipinski's criteria shows improved pharmacokinetic suitability. Variations in lipophilicity among the derivatives are consistent with alkoxy chain length differences. MEP and frontier orbital distribution results indicate that electron-rich heteroatoms (oxygen and nitrogen) serve as potential interaction sites. The derivative exhibiting stronger charge separation and higher molecular softness demonstrates relatively enhanced reactive character. Among the investigated compounds, the methoxy-substituted derivative combines the lowest energy gap, highest softness, longer wavelength absorption, and acceptable drug-likeness parameters. The structural features contributing to this behavior include effective electron donation from the methoxy group, strong donor–acceptor interaction across the pyrazoline core, and favorable electronic redistribution.

The observed structure–application trend indicates that shorter alkoxy substitution

enhances electronic responsiveness and charge transfer characteristics, whereas increasing alkoxy chain length slightly modifies electronic parameters without significant improvement in optical or pharmacokinetic profiles.

Discussion

The present study provides a combined experimental–theoretical evaluation of fluoroalkoxy-functionalized pyrazoline derivatives as dual-purpose molecular candidates. The results collectively demonstrate that substituent engineering significantly influences electronic structure, optical response, and pharmacological suitability (Khan *et al.*, 2023; Liaqat *et al.*, 2025b). The incorporation of both fluoro (electron-withdrawing) and alkoxy (electron-donating) substituents establishes a classical push–pull molecular framework. The optimized geometries and charge distribution patterns confirm the presence of electronic polarization across the conjugated system (Majeed *et al.*, 2023).

Fluorine, due to its strong inductive effect, stabilizes the electron-deficient region of the molecule and lowers the LUMO energy. In contrast, the alkoxy substituent increases electron density through resonance donation, raising the HOMO level (Lee *et al.*, 2021). The pyrazoline ring functions as a conjugated bridge that facilitates intramolecular charge redistribution. This donor–acceptor synergy reduces the HOMO–LUMO energy gap and promotes intramolecular charge transfer (ICT), a key feature in both optoelectronic materials and biologically active systems (Liaqat *et al.*, 2025; Menezes *et al.*, 2025).

The spatial separation of HOMO and LUMO orbitals clearly demonstrates charge-transfer character. HOMO localization over the alkoxy-bearing aromatic ring and LUMO localization over the fluoro-substituted ring confirms directional electron movement upon excitation. Such orbital separation enhances polarizability and electronic responsiveness (Hussain *et al.*, 2023; Muhammad *et al.*, 2025). The HOMO $\rightarrow$ LUMO transition represents a $\pi \rightarrow \pi^*$ excitation involving significant intramolecular electron displacement. This ICT behavior is particularly desirable in optoelectronic materials, where efficient charge separation improves light absorption and emission processes. Simultaneously, charge redistribution can influence molecular interaction potential with biological targets through enhanced electrostatic complementarity (Khalid *et al.*, 2024; Özen *et al.*, 2026).

TD-DFT analysis reveals that all derivatives absorb in the UV–visible region, with the methoxy-substituted compound showing the longest predicted absorption wavelength. The bathochromic shift observed in this derivative correlates with its reduced energy gap and stronger donor capability (Figueroa-Ariza & Paez-Sierra, 2026). The calculated oscillator strengths indicate allowed electronic transitions with moderate intensity, suggesting potential fluorescence or electroluminescent behavior. The presence of intramolecular charge transfer further enhances optical responsiveness (Dong *et al.*, 2025).

Shorter alkoxy substitution appears to optimize donor strength without introducing excessive steric hindrance, leading to more effective conjugation and improved optical parameters. This makes the methoxy derivative particularly promising for optoelectronic applications such as organic light-emitting devices or fluorescent probes (Nitschke *et al.*, 2021).

The calculated global reactivity descriptors reinforce the electronic findings. The methoxy derivative exhibits the smallest energy gap, lowest hardness, and highest softness among the series. According to the Maximum Hardness Principle, harder molecules tend to be more stable but less reactive (Kamel *et al.*, 2024). In contrast, increased softness indicates greater electronic flexibility and enhanced responsiveness. The observed trend suggests that the methoxy derivative possesses a favorable balance between stability and reactivity. Negative Gibbs free energy values confirm thermodynamic stability of the optimized structures. Variations in entropy reflect differences in substituent flexibility and molecular motion, but do not compromise structural stability (Kumar *et al.*, 2026).

In silico ADMET predictions demonstrate that all derivatives comply with Lipinski's Rule of Five, indicating drug-like character. The moderate logP values suggest balanced hydrophilic-lipophilic properties, which are essential for membrane permeability and bioavailability (Ancuceanu *et al.*, 2025). The MEP surfaces identify electron-rich heteroatoms (oxygen and nitrogen) as potential hydrogen bond acceptor sites. The presence of defined electron-deficient regions may facilitate electrostatic interactions with biological receptors (Mettai *et al.*, 2023).

The methoxy derivative, which exhibits enhanced softness and stronger charge separation, may offer improved adaptability during molecular recognition processes. Increased electronic flexibility can promote favorable interaction with enzyme or receptor binding sites. Thus, the same donor-acceptor architecture that enhances optoelectronic properties may simultaneously contribute to biological interaction potential (Fu *et al.*, 2026). A clear structure-application relationship emerges from the combined results: Fluorine contributes to LUMO stabilization and molecular polarization. Alkoxy groups elevate HOMO energy and enhance donor strength. Shorter alkoxy substitution optimizes intramolecular charge transfer (Khan *et al.*, 2025). Reduced energy gap correlates with enhanced optical absorption. Increased softness correlates with greater electronic adaptability. These findings confirm that controlled substituent engineering can generate multifunctional pyrazoline systems capable of performing in both optoelectronic and pharmaceutical domains (Krasley *et al.*, 2024).

Most previous studies have evaluated pyrazoline derivatives either for biological activity or for optical performance independently. The present study demonstrates that a rational donor-acceptor design strategy can integrate both functionalities within a single molecular framework (Matiadis & Sagnou, 2020). The combined experimental-theoretical approach provides mechanistic insight into how structural modification influences electronic behavior and potential application. The results highlight the importance of electronic polarization, charge transfer, and global reactivity descriptors in guiding multifunctional molecular design (Almutlaq *et al.*, 2025).

Conclusion

A series of fluoroalkoxy-functionalized pyrazoline derivatives were successfully evaluated using an integrated experimental and computational framework. The combined donor-acceptor design, achieved through incorporation of electron-withdrawing fluorine and electron-donating alkoxy groups, generated polarized

molecular architectures with tunable electronic properties. DFT analysis revealed substituent-dependent modulation of HOMO–LUMO energy gaps, hardness, and softness parameters. The methoxy-substituted derivative exhibited the lowest energy gap and highest electronic softness, indicating enhanced charge-transfer capability. TD-DFT calculations predicted allowed $\pi \rightarrow \pi^*$ transitions in the UV–visible region, confirming optoelectronic responsiveness. Molecular electrostatic potential mapping identified defined electron-rich and electron-deficient regions that may contribute to intermolecular interaction potential. In silico ADMET evaluation demonstrated compliance with drug-likeness criteria and favorable pharmacokinetic profiles across the series. The methoxy derivative displayed the most balanced combination of optical performance and predicted pharmaceutical suitability.

This study demonstrates that controlled fluoroalkoxy substitution effectively tunes structural, electronic, and thermodynamic characteristics of pyrazoline derivatives. The established structure–property–application relationship supports their potential as multifunctional molecular systems suitable for both optoelectronic materials and pharmaceutical development. The findings provide a rational design strategy for future development of dual-purpose heterocyclic compounds.

Declarations

Author contribution: All authors contributed equally in the manuscript.

Conflict of interest: The authors declare no conflict of interest.

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