Şırnak Üniversitesi Sağlık Bilimleri Dergisi
Şırnak University Journal of Health Sciences
E-ISSN:3149-9856
Yıl/Year: 2026, Cilt/Volume: 1, Sayı/Issue: 1
susbd@sirnak.edu.tr https://dergipark.org.tr/tr/pub/sujhs

Kuersetinin Elektronik ve Doğrusal Olmayan Optik (NLO) Özelliklerinin DFT Tabanlı İncelenmesi ve Lösemi Hedef Proteinlerine (6QGK ve 2O21) Karşı Moleküler Kenetlenme Analizi

DFT-Based Investigation of the Electronic and Nonlinear Optical (NLO) Properties of Quercetin and Molecular Docking Analysis Against Leukemia Target Proteins (6QGK and 2O21)

Mehmet BAĞLAN, mehmetbaglan36@gmail.com, ORCID , ROR

Dr, Kafkas University, Faculty of Science and Letters, Department of Chemistry, 36100, Kars, Türkiye

Makale Bilgisi / Article Information

Atıf (Citation): Bağlan, M. (202). DFT-Based Investigation of the Electronic and Nonlinear Optical (NLO) Properties of Quercetin and Molecular Docking Analysis Against Leukemia Target Proteins (6QGK and 2O21) *Şırnak Üniversitesi Sağlık Bilimeri Dergisi*, *1*(1), 12-23.

Geliş Tarihi *(Submission Date)*	09/07/2026
Kabul Tarihi *(Acceptance Date)*	17.17.2026
Yayın Tarihi *(Publication Date)*	31.07.2026
Makale Türü *(Article Type)*	Araştırma Makalesi *(Research Article)*
Değerlendirme *(Peer-Review)*	Çift Taraflı Körleme / En az İki Dış Hakem *(Double Anonymized / At Least Two External)*
Etik Beyan *(Ethical Statement)*	Bu çalışma, etik kurul izni gerektirmeyen nitelikte olup kullanılan veriler literatür taraması/yayınlanmış kaynaklar üzerinden elde edilmiştir. Çalışmanın hazırlanma sürecinde bilimsel ve etik ilkelere uyulduğu ve yararlanılan tüm çalışmaların kaynakçada belirtildiği beyan olunur. (*This study does not require ethical committee approval, and the data used were obtained from literature reviews/published sources. It is hereby declared that scientific and ethical principles were adhered to during the preparation of this study and that all studies used are cited in the references).* Bu makale, ….. Sempozyumu'nda sözlü olarak sunulan ancak tam metni yayımlanmayan "……." adlı tebliğin içeriği geliştirilerek ve kısmen değiştirilerek üretilmiş hâlidir (*This article is a partially modified and improved version of the paper titled "……" which was presented orally at the …. Symposium but the full text was not published).* Bu çalışma … danışmanlığında … tarihinde sunduğumuz/tamamladığımız … başlıklı yüksek lisans/doktora tezi esas alınarak hazırlanmıştır *(This study is based on the master's / doctoral thesis entitled ……., which we presented / completed on ……. under the supervision of ……..).*
Yapay Zeka Kullanımı (Use of Artificial Intelligence)	Bu çalışmanın hazırlanma sürecinde yapay zeka tabanlı herhangi bir araç veya uygulama kullanılmamıştır. Çalışmanın tüm içeriği, yazar(lar) tarafından bilimsel araştırma yöntemleri ve akademik etik ilkelere uygun şekilde üretilmiştir. *(No artificial intelligence–based tools or applications were used in the preparation of this study. All content of the study was produced by the author(s) in accordance with scientific research methods and academic ethical principles.)*
Benzerlik Taraması *(Plagiarism Checks)*	Evet (Yes) – Ithenticate/Turnitin.
Çıkar Çatışması *(Conflicts of Interest)*	Çıkar çatışması beyan edilmemiştir. *(The author(s) has no conflict of interest to declare).*
Yazar Katkı Oranı *(Author Contribution Rate)*	Yazarların çalışmaya katkıları eşit orandadır. *(Authors contributed equally to the study)*
Etik Beyan Adresi *(Complaints)*	*susbd@sirnak.edu.tr*
Finansman (Grant Support)	Bu araştırmayı desteklemek için dış fon kullanılmamıştır. *(The author(s) acknowledge that they received no external funding in support of this research).*
Telif Hakkı ve Lisans *(Copyright & License)*	Yazarlar dergide yayınlanan çalışmalarının telif hakkına sahiptirler ve çalışmaları CC BY-NC-ND lisansı altında yayımlanmaktadır. *(Authors publishing with the journal retain the copyright to their work licensed under the CC BY-NC-ND).*

Kuersetinin Elektronik ve Doğrusal Olmayan Optik (NLO) Özelliklerinin DFT Tabanlı İncelenmesi ve Lösemi Hedef Proteinlerine (6QGK ve 2O21) Karşı Moleküler Kenetlenme Analizi

ÖZET

Bu çalışmada, doğal bir flavonoid olan 2-(3,4-dihidroksifenil)-3,5,7-trihidroksi-4H-kromen-4-on (Kuersetin) molekülünün yapısal, elektronik, doğrusal olmayan optik (NLO) ve biyolojik özellikleri, yoğunluk fonksiyoneli teorisi (DFT) ve moleküler modelleme yöntemleri kullanılarak kapsamlı bir şekilde incelenmiştir. Kuantum kimyasal hesaplamalar, B3PW91 ve B3LYP fonksiyonelleri ile 6-31G(d,p) temel seti kullanılarak temel durum geometrisinin optimizasyonu üzerinden gerçekleştirilmiştir. Optimize edilmiş nötr moleküler yapı üzerinden Mulliken atomik yük dağılımları, sınır moleküler orbital (HOMO–LUMO) enerjileri ve küresel reaktivite parametreleri hesaplanarak molekülün elektronik yapısı, yük transfer dinamikleri ve kimyasal kararlılığı değerlendirilmiştir. Moleküler elektrostatik potansiyel (MEP) analizi ile elektrofilik ve nükleofilik saldırılara karşı reaktif merkezler ve potansiyel hidrojen bağı kapasitesi haritalandırılmıştır. Ayrıca, dipol moment, ortalama polarize edilebilirlik ve birinci dereceden hiperpolarize edilebilirlik bileşenleri hesaplanarak molekülün doğrusal olmayan optik (NLO) yanıtları incelenmiştir. Elde edilen bulgular, kuersetinin belirgin bir molekül içi yük transfer karakterine sahip olduğunu ve umut verici bir optoelektronik materyal adayı olabileceğini göstermiştir. Bileşiğin antilösemik aktivite potansiyelini moleküler düzeyde değerlendirmek amacıyla, lösemi patogenezinde kritik öneme sahip hedef proteinler (PDB ID: 6QGK ve 2O21) ile moleküler kenetlenme (docking) çalışmaları yürütülmüştür. Kenetlenme simülasyonları, kuersetinin hedef enzimlerin aktif bölgelerinde kararlı konformasyonlar aldığını; spesifik hidrojen bağları, kovalent etkileşimler ve hidrofobik ağlar (Pi-Sigma, Pi-Alkil) aracılığıyla yüksek bağlanma afinitesi sergilediğini ortaya koymuştur. Elde edilen veriler, kuersetinin hem fonksiyonel optoelektronik uygulamalar hem de hedefe yönelik yeni nesil terapötik ajanların geliştirilmesi açısından yüksek potansiyele sahip bir aday iskele yapı olduğunu göstermektedir.

Anahtar Kelimeler:

Kuersetin, DFT hesaplaması, HOMO-LUMO analizi, NLO, Moleküler doking

DFT-Based Investigation of the Electronic and Nonlinear Optical (NLO) Properties of Quercetin and Molecular Docking Analysis Against Leukemia Target Proteins (6QGK and 2O21)

ABSTRACT

In this study, the structural, electronic, nonlinear optical (NLO), and biological properties of the naturally occurring flavonoid 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one (Quercetin) were comprehensively investigated using density functional theory (DFT) and molecular modeling methods. Quantum chemical calculations were performed through the optimization of the ground state geometry using the B3PW91 and B3LYP functionals and the 6-31G(d,p) basis set. The electronic structure, charge transfer dynamics, and chemical stability of the molecule were evaluated by calculating Mulliken atomic charge distributions, boundary molecular orbital (HOMO–LUMO) energies, and spherical reactivity parameters based on the optimized neutral molecular structure. Molecular electrostatic potential (MEP) analysis was used to map reactive centers and potential hydrogen bonding capacity against electrophilic and nucleophilic attacks. Furthermore, the nonlinear optical (NLO) responses of the molecule were investigated by calculating the dipole moment, mean polarizability, and first-order hyperpolarizability components. The findings showed that quercetin possesses a distinct intramolecular charge transfer character and could be a promising optoelectronic material candidate. To evaluate the antileukemic activity potential of the compound at the molecular level, molecular docking studies were conducted with target proteins (PDB ID: 6QGK and 2O21) that are critical in leukemia pathogenesis. Docking simulations revealed that quercetin assumes stable conformations in the active sites of target enzymes; exhibiting high binding affinity through specific hydrogen bonds, covalent interactions, and hydrophobic networks (Pi-Sigma, Pi-Alkyl). The obtained data indicate that quercetin is a candidate scaffold structure with high potential for both functional optoelectronic applications and the development of next-generation targeted therapeutic agents.

Keywords:

Quercetin, DFT calculation, HOMO-LUMO analysis, NLO, Moleculer dockin

Introduction

Quercetin is a naturally occurring secondary metabolite belonging to the flavonol subgroup of polyphenolic compounds, widely distributed in fruits, vegetables, grains, and nuts (Li et al., 2016). This bioactive compound, frequently found in glycoside form (aglycone structures attached to carbohydrate units such as glucose or rutinose), is present in high concentrations in many plant sources that are essential to human nutrition, such as lettuce, chili peppers, cranberries, onions, black aronia, tomatoes, broccoli, and apples (Kelly, 2011). Literature data indicates that daily dietary intake of quercetin varies between 6–18 mg on average in different populations (Georgiou et al., 2023).

Recent pharmacological and medical research has clearly demonstrated the multifaceted therapeutic effects of quercetin, including antioxidant, anti-inflammatory, cardioprotective, antiviral, and anticancer properties (Aghababaei & Hadidi, 2023). Studies on *in vitro* mechanisms show that, in addition to its ability to directly scavenge free radicals, the compound modulates cellular signaling pathways, suppresses oxidative stress, and regulates apoptotic processes (Sharma et al., 2018). However, some inconsistencies are observed in the results obtained from clinical studies, which are largely attributed to quercetin's poor aqueous solubility, low systemic bioavailability, rapid first-pass metabolism, and inter-individual differences in absorption kinetics (Batiha et al., 2020). Overcoming these limitations and fully elucidating the molecular-level mechanisms of action of the compound, particularly its antileukemic and specific anticancer effects, are critical for rational targeted drug design processes (Khan et al., 2021).

A complete understanding of the pharmacological efficacy of a bioactive molecule and its interaction dynamics with target receptors necessitates the investigation of its molecular geometry, boundary orbitals, reactivity indices, and charge distribution properties at the atomic level (Gören & Yıldıko, 2024). In this context, Density Functional Theory (DFT)-based quantum chemical calculations offer a highly powerful and reliable theoretical approach for determining the electronic structures of molecules, mapping electrophilic/nucleophilic centers, and predicting nonlinear optical (NLO) responses under an external electric field (Bağlan et al., 2023b). In particular, molecular electrostatic potential (MEP) maps and polarizability and hyperpolarizability tensor analyses are fundamental in predicting the weak interaction tendencies of molecules in receptor pockets (Tahiroğlu, Gören, & Bağlan, 2025). Furthermore, high-resolution molecular docking modeling and the detailing of geometric bonding patterns provide strong scientific evidence prior to in vitro processes by rationally elucidating specific amino acid interaction networks at the ligand-receptor interface (Tahiroğlu, Gören, et al., 2025b).

The main objective of this study is to comparatively investigate the ground-state structural, electronic, and nonlinear optical (NLO) properties of quercetin, a naturally occurring flavonol, using the DFT method with the B3PW91 and B3LYP functionals and the 6-31G(d,p) basis set. Furthermore, to evaluate the antileukemic activity potential of quercetin at the molecular level, its molecular docking behavior towards the active sites of the 6QGK (Bank, 2019) and 2O21 (Bank, 2007) enzyme targets, which play a key role in leukemia pathogenesis, was elucidated in detail through specific bond distances, covalent fixations, and thermodynamic stability parameters.

Although quercetin, DFT programming, and complement docking methods have been studied in detail, most previous series have focused separately on the physicochemical properties of quercetin or its interactions with different biological methods. Therefore, the evaluation of quercetin with electronic comprehensive DFT analyses and its association with leukemia has been adopted based on a theoretical framework summarized by considering complement docking analyses against the 6QGK and 2O21 target proteins. This allows for a greater understanding of the distance between quercetin's electronic properties and potential inhibitory interactions. In our literature search, no integrated disease study was found where quercetin was evaluated with the 6QGK and 2O21 leukemia targets using both DFT and total docking analyses.

1. Materials and Methods

In this study, the biological activity of the quercetin molecule was investigated using theoretical calculations, molecular docking, and pharmacokinetic analyses. All quantum chemical calculations were performed within the framework of Density Functional Theory (DFT) using the Gaussian 09 software package (G.W.T. M.J. Frisch, 2009). The B3PW91 and B3LYP functionals and the 6-31G(d,p) basis set were used for geometry optimization, determination of electronic properties, and calculation of reactivity parameters. For molecular docking studies, the crystal structures of the target proteins were obtained from the Protein Data Bank (PDB) database and prepared using the AutoDock Vina program (Eberhardt et al., 2021). During the protein preparation stage, water molecules were removed, missing hydrogen atoms were added, and appropriate protonation states were assigned. The binding affinity of the quercetin molecule to the active sites of the target proteins and the interaction mechanisms were evaluated using molecular docking analyses. The interaction profiles and visualizations of the obtained protein-ligand complexes were examined using the Discovery Studio Visualizer program (BIOVIA, 2016).

Considering the pKa values of the phenolic hydroxyl groups of quercetin, although it may exhibit a tendency toward partial ionization under physiological pH conditions (pH 7.4), environmental factors such as the molecular environment,

hydrogen bonding interactions, and protein binding sites can influence the protonation equilibrium. Therefore, the neutral form has been widely used as an appropriate starting model in quantum chemical calculations and molecular docking studies, particularly in simulations representing the gas phase and low-polarity binding environments, for evaluating biological interactions.

2. Results and Discussion

2.1. Mulliken Atomic Charges

Mulliken atomic charges provide important information about electronic structure and reactivity by revealing the distribution of electron density among atoms within a molecule (Gören, Bağlan, & Yıldıko, 2024a, 2024b). Atoms carrying a negative charge represent electron-rich (nucleophilic) regions, while atoms carrying a positive charge represent electron-poor (electrophilic) regions (Bağlan et al., 2023a; Gören, Kotan, et al., 2024). Therefore, Mulliken charge analysis is widely used in the evaluation of potential reactive centers, charge transfer, and bond polarization (Gören et al., 2022; Gören, Bağlan, Yıldıko, et al., 2024).

Table 1 shows the Mulliken atomic charges of quercetin using the B3PW91 and B3LYP functionals for a comparative analysis. Overall, a strong agreement is observed between the two methods, with atomic charges exhibiting similar trends in sign and magnitude. This indicates that the electronic charge distribution of the molecule is quite stable against the chosen calculation method. It is noteworthy that negative charges are particularly concentrated on oxygen atoms. Atoms O7, O8, O10, O15, O21, and O22 exhibit significantly high negative Mulliken charges, indicating that these regions are electron-rich and therefore act as hydrogen bond acceptors. Specifically, atom O15 has one of the highest negative charges in both methods (B3PW91: -0.647; B3LYP: -0.635), suggesting that this region is one of the most reactive electron-dense areas of the molecule. The charge distribution among the carbon atoms appears heterogeneous. Some carbon atoms (e.g., C5, C6, C9, C11, C13, C14, C18, and C20) exhibit positive charges, while others, such as C1, C3, C4, C17, and C19, have negative charges. This suggests a pronounced electronic asymmetry in the quercetin skeleton, influenced by π-electron delocalization and aromatic systems. In particular, carbons with higher positive charges, such as C13 and C18, exhibit partial electron deficiency due to their proximity to electron-withdrawing oxygen atoms. All hydrogen atoms carry a positive charge, as expected, confirming their electrophilic character. The fact that some hydrogens, such as H28, H29, H30, and H31, have higher positive charges compared to others indicates that the electron-withdrawing effect around the carbon to which they are attached is stronger. Overall, the small differences between the B3PW91 and B3LYP results reveal that the functionals describe the electronic density distribution similarly but exhibit slight quantitative differences. These findings suggest that the charge distribution in the quercetin molecule is concentrated particularly around oxygen-centered functional groups, and that the chemical reactivity of the molecule is shaped through these regions.

Table 1. Mulliken atomic charges of the Quercetin molecule

ATOMS	B3PW91	B3LYP	ATOMS	B3PW91	B3LYP
C1	-0.169	-0.149	C17	-0.201	-0.164
C2	0.006	0.042	C18	0.345	0.349
C3	-0.146	-0.124	C19	-0.210	-0.170
C4	-0.162	-0.123	C20	0.335	0.316
C5	0.325	0.327	O21	-0.561	-0.552
C6	0.286	0.293	O22	-0.580	-0.570
O7	-0.609	-0.597	H23	0.135	0.098
O8	-0.567	-0.559	H24	0.166	0.130
C9	0.291	0.279	H25	0.142	0.104
O10	-0.571	-0.565	H26	0.343	0.328
C11	0.321	0.303	H27	0.352	0.338
C12	-0.053	0.001	H28	0.145	0.104
C13	0.417	0.399	H29	0.131	0.092
C14	0.253	0.259	H30	0.340	0.326
O15	-0.647	-0.635	H31	0.372	0.355
O16	-0.586	-0.576	H32	0.354	0.339

2.2. HOMO-LUMO Analysis

According to molecular orbital (MO) theory, the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) are called frontier molecular orbitals (FMOs) (Agbektas et al., 2026; Gören, Bağlan, Tahiroğlu, et al., 2024). These orbitals provide important information about the molecule's electronic structure, chemical stability, and reactivity (Bağlan, Gören, Tahiroğlu, et al., 2026; Bağlan et al., 2022). HOMO represents the tendency to donate electrons, while LUMO represents the capacity to accept electrons. The HOMO–LUMO energy difference (ΔE) is one of the fundamental indicators of a molecule's reactivity and stability. Density Functional Theory (DFT) calculations allow for the determination of global reactivity parameters such as chemical potential (μ), chemical hardness (η), and electrophilicity index (ω) from HOMO and LUMO energy values. These parameters play a crucial role in evaluating the electron exchange tendencies and reactive centers of molecules, and DFT-based analyses are widely used in organic

synthesis, drug design, and functional material development studies (Bağlan, Gören, Kotan, et al., 2026; GÖREN, BAĞLAN, YILDIKO, et al., 2024).

Table 2 presents the HOMO–LUMO energies (Figure 1 and Figure 2) calculated for the quercetin molecule using the B3PW91 and B3LYP density functional theory (DFT) methods, along with the resulting spherical chemical reactivity parameters. The close proximity of the results obtained from both functionals demonstrates the reliability of the calculations and indicates that the electronic structure of the molecule is not significantly affected by the functional used. The HOMO energies were calculated as −6.7752 and −6.6514 eV for the B3PW91 and B3LYP methods, respectively, while the LUMO energies were calculated as −0.2759 and −0.2202 eV. The lower HOMO energy obtained with the B3PW91 method indicates that the tendency to donate electrons is somewhat lower than that of B3LYP. The HOMO–LUMO energy gap (ΔE) is 6.4993 and 6.4312 eV, respectively, and the lower ΔE value obtained with the B3LYP method shows a slight increase in the chemical reactivity of the molecule, but the high ΔE values in both methods reveal that quercetin has high electronic stability. The ionization potential (I) and electron affinity (A) values were found to be consistent with the HOMO and LUMO energies, respectively. The low electron affinity values indicate that the molecule's tendency to accept electrons is limited. The chemical hardness (η) values were calculated as 3.2497 and 3.2156 eV for B3PW91 and B3LYP, respectively, and the chemical softness (s) values were calculated as 0.1539 and 0.1555 eV^{-1}. These results demonstrate that quercetin exhibits high hardness, low polarizability, and good structural stability. The negative chemical potential (μ) values (−3.5256 and −3.4358 eV) support the electronic stability of the molecule, while the electronegativity (χ) values indicate a moderate tendency to accept electrons. The electrophilicity index (ω) was calculated as 1.9125 and 1.8354 eV for the B3PW91 and B3LYP methods, respectively, with the B3PW91 method predicting quercetin as a slightly more electron-accepting electrophile. Overall, only minor differences were observed between the global reactivity parameters obtained from both methods, and it was determined that the quercetin molecule possesses high electronic stability, moderate chemical reactivity, and balanced electron-donating and electron-accepting properties. These findings are consistent with the high antioxidant and free radical scavenging properties of quercetin reported in the literature.

$$\Delta E = |EHOMO - ELUMO| \quad (1)$$

$$\eta = (I - A)/2 \quad (2)$$

$$s = I/2\eta \quad (3)$$

$$\mu = \frac{(I+A)}{2} \quad (4)$$

$$\chi = (1 + A)/2 \quad (5)$$

$$\omega = \mu^2/2\eta \quad (6)$$

Table 2. The HOMO and LUMO quantum chemical characteristics determined by applying the B3PW91 and B3LYP techniques for the Quercetin molecule

	E_{HOMO}	E_{LUMO}	E_{HOMO-1}	E_{LUMO-1}	ΔE	I	*A*	*η*	*s*	*μ*	*χ*	ω
B3PW91	-6.7752	-0.2759	-7.0836	0.2024	6.4993	6.7752	0.2759	3.2497	0.1539	-3.5256	3.5256	1.9125
B3LYP	-6.6514	-0.2202	-6.9654	0.2384	6.4312	6.6514	0.2202	3.2156	0.1555	-3.4358	3.4358	1.8354

ΔE→Energy Gap, I→Ionization Potential($-E_{HOMO}$), *A*→Electron Affinity($-E_{LUMO}$), *η*→Chemical hardness, *s*→Chemical softness, *μ*→Chemical Potential, *χ*→Electronegativity, ω→Electrophilicity in

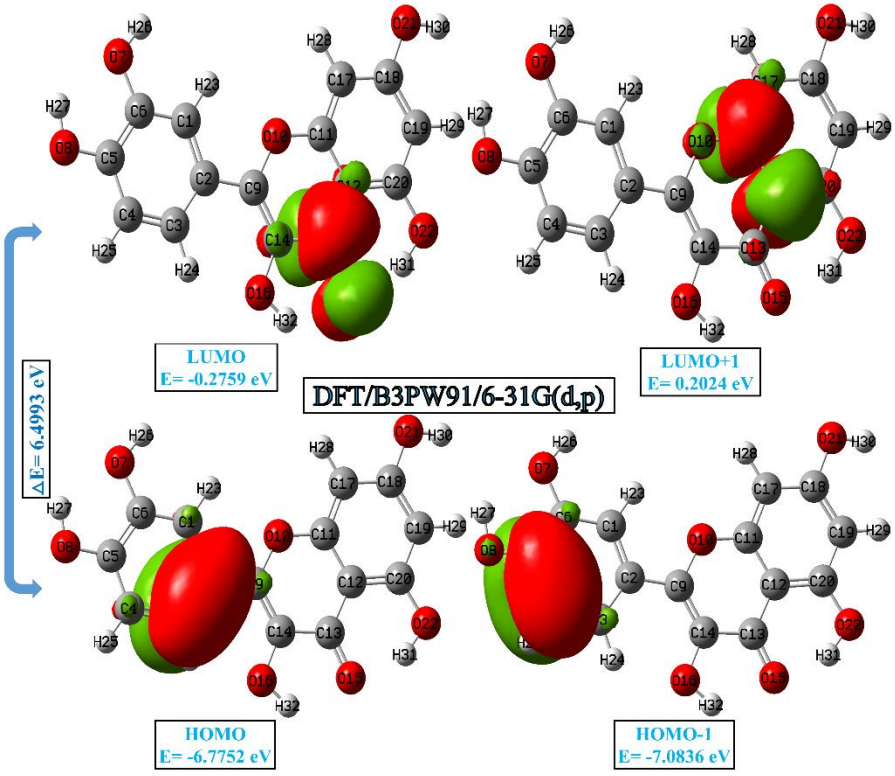

Figure 1. Boundary molecular orbitals of the Quercetin molecule according to the B3PW91 level

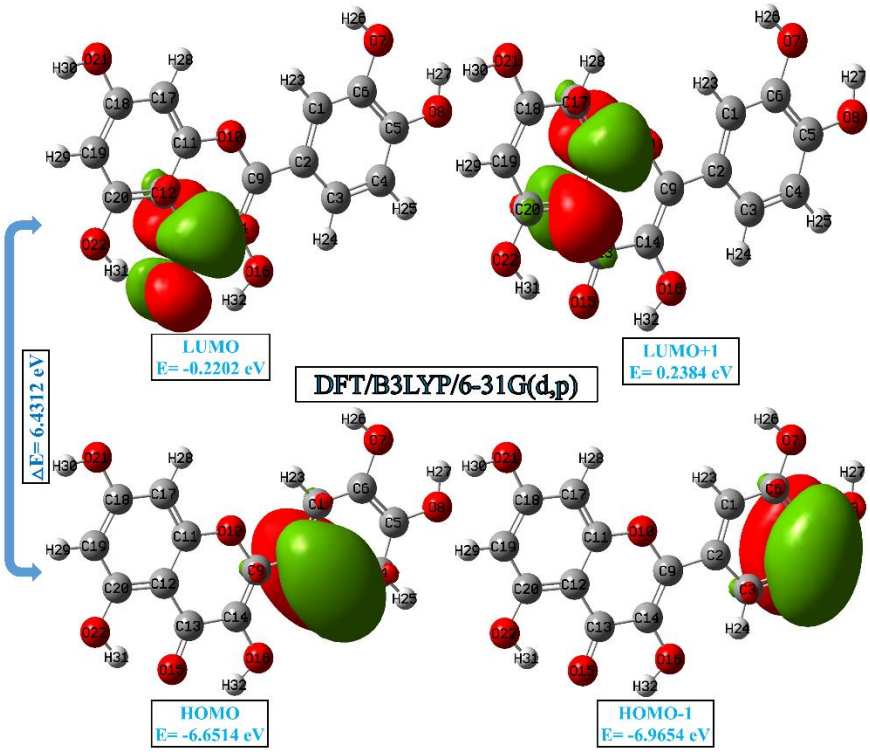

Figure 2. Boundary molecular orbitals of the Quercetin molecule according to the B3LYP level

2.3. Molecular Electrostatic Potential (MEP)

Molecular Electrostatic Potential (MEP) is a method that reveals the charge distribution on a molecule's surface and provides important information for evaluating the molecule's chemical reactivity (Kotan et al., 2025). MEP maps allow for the identification of regions susceptible to electrophilic and nucleophilic attacks, as well as the prediction of weak interactions such as hydrogen bonding (Tahiroğlu et al., 2024). On MEP surfaces, red represents electron-rich regions with high negative electrostatic potential, blue represents electron-poor regions with dominant positive electrostatic potential, and green represents neutral regions with approximately zero electrostatic potential (Gören et al., 2025). This distribution contributes to the identification of possible interaction sites of the molecule, providing qualitative information about its chemical behavior and reactivity (Kartal et al., 2026).

Figure 3 shows the Molecular Electrostatic Potential (MEP) surfaces of the quercetin molecule calculated using the B3PW91 and B3LYP theoretical methods. MEP maps show the electron density distribution on the molecule and possible electrophilic/nucleophilic attack sites. In the MEP color scale, red regions represent negative electrostatic potential, i.e., electron-rich areas susceptible to electrophilic attack; blue regions represent positive electrostatic potential, i.e., electron-poor areas susceptible to nucleophilic attack. Green colors indicate intermediate potential values. In both theoretical methods, the most negative potential regions are concentrated around oxygen atoms. In particular, oxygen atoms in hydroxyl groups (O15, O16, O21, O22) and carbonyl-like oxygen centers form distinct red regions, indicating that they are the main electrophilic interaction centers of the molecule. This supports the proton-accepting character of quercetin and its hydrogen bonding capacity. Positive potential regions are located around hydrogen atoms and especially near hydroxyl protons, and these regions can be considered as areas where the molecule can interact with nucleophilic species. The predominance of green tones on the aromatic ring system indicates that the electron density is delocalized throughout the molecule. The electrostatic potential values for the B3PW91 method ranged from −8.014 to +8.014 a.u., while for the B3LYP method, this range was calculated as −7.604 to +7.604 a.u. The fact that both methods yielded similar distributions indicates that the electrostatic properties of quercetin are largely independent of the theoretical method. However, the B3PW91 method exhibits a wider potential range, revealing slightly more pronounced charge separation.

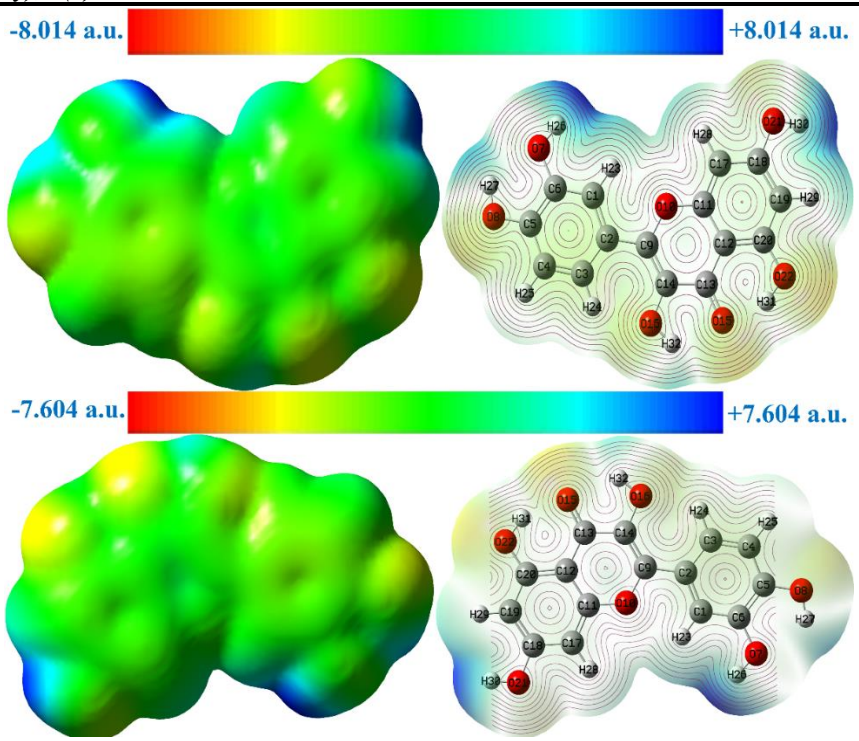

Figure 3. Molecular electrostatic potential surface of the Quercetin molecule using B3PW91 and B3LYP methods

2.4. Non-Linear Optical Properties (NLO)

Nonlinear optical (NLO) properties play a significant role in optoelectronic and photonic applications. These properties are related to the optical responses of molecules under the influence of electromagnetic fields and are characterized by changes in the phase, amplitude, and frequency of light (Tahiroğlu, Gören, et al., 2025a). Theoretical evaluation of NLO behavior utilizes molecular parameters such as mean polarizability (⟨α⟩), polarizability anisotropy (Δα), first-order hyperpolarizability (β_{tot}), second-order hyperpolarizability (γ), and dipole moment (μ). These parameters are calculated using tensor components obtained from quantum chemical calculations and are considered fundamental criteria in evaluating the nonlinear optical potentials of molecules (Janjua et al., 2014).

Table 3 shows the dipole moment, polarizability, and first-order hyperpolarizability (β) values calculated for the quercetin molecule using the B3PW91 and B3LYP methods. The results show that both functionals describe the electronic properties of the molecule in a very similar way. When the dipole moment components are examined, it is seen that the largest contribution in both methods comes from the μy component. The total dipole moment values were calculated as 4.1818 D and 4.0997 D for the B3PW91 and B3LYP methods, respectively. These results reveal that the quercetin molecule exhibits a distinct polar character and that the electron density is predominantly distributed in the y-direction. In addition, the B3PW91 method yielded a slightly higher dipole moment value compared to the B3LYP functional. When the polarizability components are evaluated, it was determined that the αzz component has the highest value in both theoretical levels. The average polarizability values were calculated as 117.9466 au and 118.9323 au for the B3PW91 and B3LYP methods, respectively. The B3LYP method predicts a slightly higher polarizability value than B3PW91. This indicates that the electron cloud of the quercetin molecule can be easily deformed under the influence of an external electric field, exhibiting high electronic flexibility. When examining the first-order hyperpolarizability tensor components, the most dominant contributions are found to be from the βxxy and βxxx components. For the B3PW91 method, βxxy=113.3921 au and βxxx=96.0431 au were calculated, while for the B3LYP method, βxxy=111.7110 au and βxxx=96.7538 au were calculated. In contrast, the relatively small values of the components related to the z-axis suggest that the charge transfer mechanism primarily occurs in the x-y plane of the molecule. The total hyperpolarizability values were found to be 1.296×10^{-30} esu (B3PW91) and 1.280×10^{-30} esu (B3LYP), respectively. The fact that these values are quite close to each other indicates that the functionals used consistently and reliably describe the nonlinear optical behavior of the quercetin molecule. The high hyperpolarizability values obtained suggest that the quercetin molecule could be a potential NLO material for use in nonlinear optical applications.

$$\mu = \left(\mu_x^2 + \mu_y^2 + \mu_z^2\right)^{\frac{1}{2}} \quad (7)$$

$$\alpha(\text{au}) = \frac{1}{3}(\alpha xx + \alpha yy + \alpha zz) \quad (8)$$

$$\beta_{Total} = (\beta^2 x + \beta^2 y + \beta^2 z)^{1/2} \quad (9)$$

$$= [(\beta xxx + \beta xyy + \beta xzz)^2 + (\beta yyy + \beta yxx + yzz)^2 + (\beta zzz + \beta zxx + \beta zyy)^2]^{\frac{1}{2}} \quad (10)$$

Table 3. The dipole moments (Debye), polarizability (au), components, and total value of the Quercetin molecule are computed using B3PW91 and B3LYP methods

Parameters	B3PW91	B3LYP	Parameters	B3PW91	B3LYP

β_{XXX}	96.0431	96.7538	μ_x	0.3155	0.3650
β_{YYY}	23.0571	22.1449	μ_y	4.1699	4.0834
β_{ZZZ}	-0.0001	-0.0053	μ_z	-0.0004	0.0000
β_{XYY}	-33.0070	-32.4195	$\mu_{(D)}$	4.1818	4.0997
β_{XXY}	113.3921	111.7110	α_{XX}	-115.5416	-117.2747
β_{XXZ}	0.0040	0.0033	α_{YY}	-112.4332	-113.8800
β_{XZZ}	2.1818	2.2046	α_{ZZ}	-125.8649	-125.6423
β_{YZZ}	-1.3984	-1.4061	α_{XY}	3.1377	3.2071
β_{YYZ}	-0.0094	-0.0061	α_{XZ}	-0.0119	-0.0013
β_{XYZ}	-0.0280	0.0029	α_{YZ}	0.0059	-0.0014
β(esu)	1.296×10^{-30}	1.280×10^{-30}	**α(au)**	117.9466	118.9323

2.5. Molecular Docking Analysis

In current structure-based drug design (SPD) studies, molecular docking analyses, which are among the leading in silico methods, play a critical role. This computational approach is widely used to predict how a potential ligand fits into the active site of a target protein or enzyme in three-dimensional space, the thermodynamically most stable binding conformation, and the affinity score of the complex (Dogan & Goren, 2026; Noureddine et al., 2021). It is well known in the literature that elucidating hydrogen bonds, van der Waals forces, covalent bonds, and hydrophobic interaction networks formed with specific amino acids at the ligand-receptor interface provides highly reliable data for understanding the mechanisms of action of next-generation therapeutic agents (Boy et al., 2026; Ramalingam et al., 2021). In this context, high-resolution static docking analyses and detailed examination of geometric bonding patterns provide a sufficient and scientifically convincing level of evidence for the identification of targeted inhibitors. In line with this theoretical framework, molecular docking studies were conducted on Quercetin against the active sites of 6QGK and 2O21 enzymes, which play a key role in leukemia pathogenesis, in order to elucidate the molecular mechanisms of action of naturally occurring compounds with antileukemic activity potential. The obtained theoretical binding affinities (kcal/mol) and ligand-receptor interaction scores are summarized in Table 4.

Table 4. Molecular docking interactions scores with PDBID: 6QGK, PDBID: 2O21 enzymes of Quercetin compound

Compound	**Docking Score**	
	(PDB: 6QGK)	(PDB: 2O21)
Qurcetin	-7.70	-8.50

When the docking results were examined, it was determined that the Quercetin compound showed a significant binding affinity to both leukemia target molecules. The docking score of -8.50 kcal/mol exhibited by the compound against the PDB:2O21 enzyme, compared to the score of -7.70 kcal/mol exhibited against the PDB:6QGK enzyme, indicates a higher binding affinity and a more thermodynamically stable conformation. Visual data generated using Discovery Studio Visualizer software to detail the orientations of the Quercetin compound in the active pockets of the target proteins, the three-dimensional (3D) binding modes, and the two-dimensional (2D) ligand-amino acid interaction networks are presented in Figures 4 and 5. The parameters supporting these visual analyses and quantitatively revealing the nature of the interactions (bond types and bond lengths) are listed in Table 5.

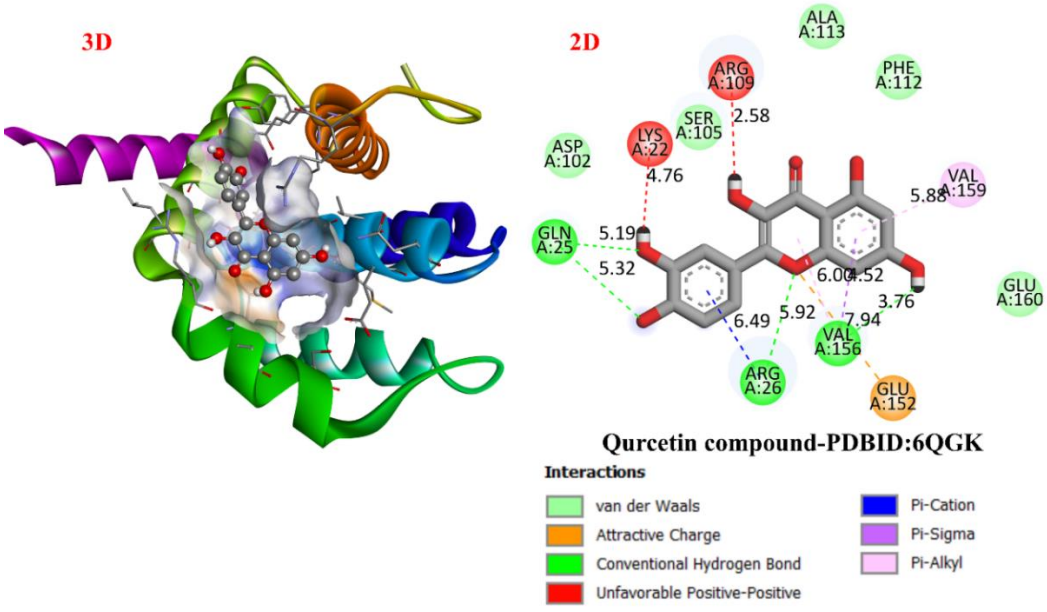

Figure 4. 2D and 3D images of the Quercetin compound and PDB: 6QGK enzyme

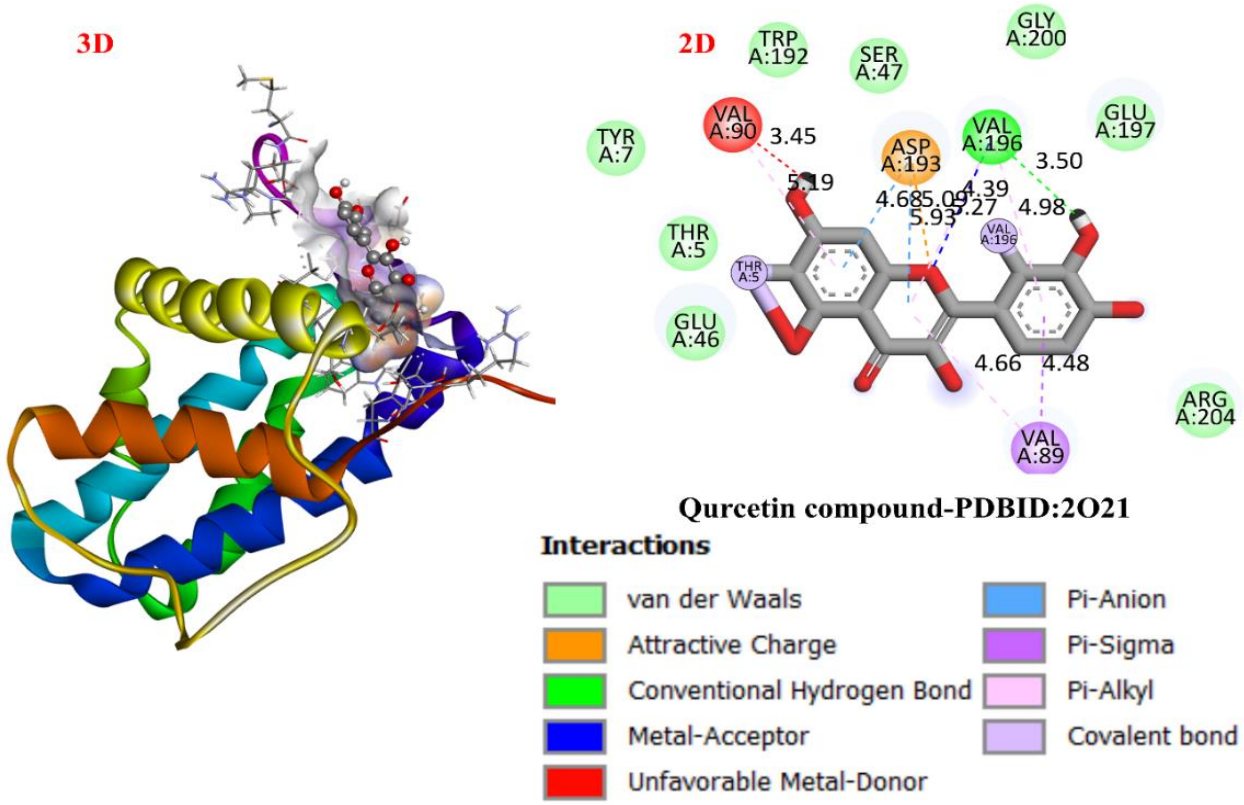

Figure 5. 2D and 3D images of the Quercetin compound and PDB: 2O21 enzyme

Table 5. The interaction parameters between Quercetin compound and 6QGK, 2O21 enzyms

Type of Bond	Quercetin PDB: 6QGK	Bond Length (Å)	Quercetin PDB: 2O21	Bond Length (Å)
Van der Waals Interactions	ASP-102	-	TYR-7	-
	SER-105	-	THR-5	-
	ALA-113	-	GLU-46	-
	PHE-112	-	ARG-204	-
	GLU-160	-	GLU-197	-
Attractive Charge	GLU-152	7.94	ASP-193	5.93
Conventional Hydrogen Bonds	GLN-25	5.19, 5.32	VAL-196	3.50
	ARG-26	5.92	-	-
	VAL-156	3.76	-	-
Un-favorable Positive-Positive	LYS-22	4.76	-	-
	ARG-109	2.58	-	-
Pi-Cation	ARG-26	6.49	-	-
Pi-Sigma	VAL-156	4.52	VAL-89	4.48
Pi-Alkyl	VAL-156	6.00	VAL-90	5.99
	VAL-159	5.88	VAL-89	4.66
	-	-	VAL-196	4.39, 4.98
Metal Acceptor	-	-	VAL-196	5.27
Unfavorable Metal-Donor	-	-	VAL-90	3.45
Pi-Anion	-	-	ASP-193	4.68
Potential Covalent Bond	-	-	THR-5	-
			VAL-96	-

According to the data in Figure 4 and Table 5, the Quercetin compound stably binds to the active site of the 6QGK enzyme. This binding is stabilized by conventional hydrogen bonds established with amino acid residues GLN-25 (5.19 Å, 5.32 Å), ARG-26 (5.92 Å), and VAL-156 (3.76 Å). Furthermore, the ligand's aromatic ring system forms a Pi-Cation interaction (6.49 Å) with the ARG-26 residue, a Pi-Sigma interaction (4.52 Å) with VAL-156, and hydrophobic Pi-Alkyl bonds (6.00 Å and 5.88 Å, respectively) via residues VAL-156 and VAL-159. The binding mode in the active pocket is further supported by the widespread Van der Waals interactions established with residues ASP-102, SER-105, ALA-113, PHE-112, and GLU-160. However, it is assessed that unfavorable positive-positive electrostatic repulsions occurring with residues LYS-22 (4.76 Å) and ARG-109 (2.58 Å) within the pocket negatively affect the total energy of the system, causing the docking score to remain at -7.70 kcal/mol.

The docking architecture of the quercetin compound with the PDB:2O21 enzyme (Figure 5) reveals a very strong and stable binding profile. This high affinity directly stems from the unique geometric bond sequence that the compound forms with the amino acids in the active pocket. The ligand formed a very short and strong conventional hydrogen bond (3.50 Å) with residue VAL-196. In addition to the hydrogen bond network, it was determined that the functional groups of the ligand form direct potential covalent bonds with the THR-5 and VAL-96 residues. This covalent fixation in the active

site maximizes the conformational stability of Quercetin in the enzyme pocket. Furthermore, the aromatic centers of the structure conduct Pi-Sigma (4.48 Å) interactions with the VAL-89 residue; and multiple Pi-Alkyl (5.99 Å, 4.66 Å, 4.39 Å and 4.98 Å, respectively) interactions with the VAL-90, VAL-89 and VAL-196 residues. Both Attractive Charge (5.93 Å) and Pi-Anion (4.68 Å) interactions established with the ASP-193 residue contribute to electrostatic stability. The residues TYR-7, THR-5, GLU-46, ARG-204, and GLU-197 extending outwards from the active pocket surround the ligand by forming Van der Waals forces. Although a weak, unfavorable metal-donor interaction (3.45 Å) is observed at the VAL-90 position, Quercetin exhibited a highly superior antileukemic inhibitor candidate performance of -8.50 kcal/mol against the 2O21 enzyme due to the predominance of covalent bonds and strong hydrophobic/steric interactions. In conclusion, these specific geometric bond patterns, hydrogen bond distances, and covalent interaction parameters theoretically confirm that the Quercetin compound possesses a strong inhibitory potential with high conformational stability on these two target enzymes associated with leukemia, especially on the PDB:2O21 structure.

Conclusion

In this study, the structural, electronic, nonlinear optical (NLO), and bioactive properties of quercetin, a naturally occurring flavonoid in its neutral protonation state (net charge = 0), were comprehensively investigated using Density Functional Theory (DFT) calculations and molecular docking simulations. The theoretical results obtained using the B3PW91 and B3LYP functionals with the 6-31G(d,p) basis set showed a high level of consistency, confirming the reliability of the calculated molecular properties. The HOMO-LUMO energy gap (ΔE) and global reactivity descriptors revealed that quercetin possesses a stable electronic structure with balanced chemical reactivity. Mulliken charge distribution and molecular electrostatic potential (MEP) analyses demonstrated that oxygen atoms and hydroxyl groups, particularly O15, O21, and O22, represent electron-rich reactive regions within the molecule. These sites play a crucial role not only in intramolecular charge transfer processes but also in molecular recognition mechanisms by determining the hydrogen-bonding ability of quercetin. Therefore, the electron density distribution and the presence of oxygen-containing functional groups provide a structural basis for both the nonlinear optical response and the biological interaction capacity of the molecule. The calculated high first-order hyperpolarizability (β) value indicates that quercetin exhibits efficient intramolecular charge-transfer characteristics and may serve as a promising candidate for nonlinear optical (NLO) material design in optoelectronic and photonic applications. However, the electronic characteristics responsible for its optical response, including charge delocalization, polarizability, and electron-rich active regions, are also directly associated with its ability to interact with biological macromolecules. In this context, the high polarizability and hydrogen-bonding potential arising from oxygen-containing functional groups may facilitate favorable ligand–protein interactions by enhancing electrostatic and non-covalent interactions within biological targets. To further evaluate the biological relevance of these electronic and structural features, molecular docking analyses were performed against 6QGK and 2O21 enzyme targets associated with leukemia pathogenesis. The results revealed that quercetin can effectively interact with the active sites of both targets with high binding affinity. Particularly, the docking score of −8.50 kcal/mol obtained for the 2O21 enzyme was supported by strong interactions within the active pocket, including interactions involving THR-5 and VAL-96 Potential covalent bonds, hydrogen bonding with VAL-196, and additional hydrophobic interactions such as Pi-Sigma and Pi-Alkyl contacts. These findings suggest that the electron-rich regions and hydrogen-bonding capabilities identified through DFT calculations contribute significantly to the stabilization of ligand–protein complexes and provide a molecular basis for the observed binding affinity. Overall, when the electronic structure, high hyperpolarizability, and biological interaction profile of quercetin are considered together, this molecule emerges as a versatile molecular platform with potential applications in both NLO material development and targeted therapeutic strategies. The obtained theoretical findings demonstrate a meaningful relationship between the electronic properties governing optical behavior and the molecular interactions responsible for biological activity, supporting quercetin as a rational and promising scaffold for multifunctional applications.

References

Agbektas, T., Coskun, H., Genc, H. C., Cinar Kaya, G., Tas, A., Goren, K., Huseynzada, A., Guliyev, R., Hasanova, U., & Kaya, S. (2026). Evaluation of the Anticancer Effects of DODP on Gene Expression and Oxidative Stress in Gastric Cancer: An Integrated Docking, Bioinformatics, and Experimental Approach. *Life*, 16(4), 534. https://doi.org/10.3390/life16040534

Aghababaei, F., & Hadidi, M. (2023). Recent advances in potential health benefits of quercetin. *Pharmaceuticals*, 16(7), 1020. Doi: 10.3390/ph16071020

Bağlan, M., Gören, K., Kotan, G., Manap, S., & Yüksek, H. (2026). Synthesis, Desing, Characterizations, Antimicrobial and Antioxidant Activity of New 1-(Morpholin-4-ylmethyl)-3-R-4-(3-hydroxy-4-methoxybenzylideneamino)-4, 5-dihydro-1 H-1, 2, 4-triazol-5-ones. *Russian Journal of General Chemistry*, 96(7), 192. https://doi.org/10.1134/S1070363225606404

Bağlan, M., Gören, K., Tahiroğlu, V., Kotan, G., Manap, S., & Yüksek, H. (2026). Design, Synthesis, DFT-Based Characterization, Molecular Docking, and ADMET Evaluation of a Novel Mannich Base Derivative. *ChemistrySelect*, 11(9), e06617. https://doi.org/https://doi.org/10.1002/slct.202506617

Bağlan, M., Gören, K., & Yıldıko, Ü. (2023a). DFT Computations and Molecular Docking Studies of 3-(6-(3-aminophenyl) thiazolo [1, 2, 4] triazol-2-yl)-2H-chromen-2-one (ATTC) Molecule. *Hittite Journal of Science and Engineering*, 10(1), 11–19. https://doi.org/10.17350/HJSE19030000286

Bağlan, M., Gören, K., & Yıldıko, Ü. (2023b). HOMO–LUMO, NBO, NLO, MEP analysis and molecular docking using DFT calculations in DFPA molecule. *International Journal of Chemistry and Technology*, 7(1), 38–47. https://doi.org/10.32571/ijct.1135173

Bağlan, M., Yıldıko, Ü., & Gören, K. (2022). Computational investigation of 5.5", 7"-trihydroxy-3, 7-dimethoxy-4'-4"'-O-biflavone from flavonoids using DFT calculations and molecular docking. *Adıyaman University Journal of Science*, 12(2), 283–298. https://doi.org/10.37094/adyujsci.1121018

Bank, R. P. D. (2007). *Solution structure of the anti-apoptotic protein Bcl-2 in complex with an acyl-sulfonamide-based ligand*. RCSB Protein Data Bank. Retrieved 07 June from https://www.rcsb.org/structure/2O21

Bank, R. P. D. (2019). *Structure of human Bcl-2 in complex with THIQ-phenyl pyrazole compound*. RCSB Protein Data Bank. Retrieved 07 June from https://www.rcsb.org/structure/6QGK

Batiha, G. E.-S., Beshbishy, A. M., Ikram, M., Mulla, Z. S., El-Hack, M. E. A., Taha, A. E., Algammal, A. M., & Elewa, Y. H. A. (2020). The pharmacological activity, biochemical properties, and pharmacokinetics of the major natural polyphenolic flavonoid: quercetin. *Foods*, 9(3), 374. doi: 10.3390/foods9030374

BIOVIA, D. S. (2016). *Discovery Studio Visualizer*. In *Dassault Systèmes*

Boy, S., Ardahanlı, H., Gören, K., Manap, S., & Yüksek, H. (2026). Novel triazole derivative mannich bases as potential therapeutic agents: synthesis, in-vitro and in-silico studies. *Journal of Molecular Structure*, 146893. https://doi.org/https://doi.org/10.1016/j.molstruc.2026.146893

Dogan, S. C., & Goren, K. (2026). The Effects of Bisphosphonates Used in Osteoporosis Treatment on Breast Cancer: Analysis with Integrative Bioinformatics Methods, DFT, ADMET and Molecular Docking Analysis. *Biology*, 15(12), 952. https://doi.org/10.3390/biology15120952

Eberhardt, J., Santos-Martins, D., Tillack, A. F., & Forli, S. (2021). AutoDock Vina 1.2. 0: new docking methods, expanded force field, and python bindings. *Journal of chemical information and modeling*, 61(8), 3891–3898. https://doi.org/10.1021/acs.jcim.1c00203

G.W.T. M.J. Frisch, H. B. S., G.E. Scuseria, M.A. Robb, J.R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G.A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H.P. Hratchian, A.F. Izmaylov, J. Bloino, G. Zheng, J.L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J.A. Montgomery Jr., J.E. Peralta, F. Ogliaro, M. Bearpark, J.J. Heyd, E. Brothers, K.N. Kudin, V.N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J.C. Burant, S.S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J.M. Millam, M. Klene, J.E. Knox, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, R.L. Martin, K. Morokuma, V.G. Zakrzewski, G.A. Voth, P. Salvador, J.J. Dannenberg, S. Dapprich, A.D. Daniels, Ö. Farkas, J.B. Foresman, J.V. Ortiz, J. Cioslowski, D.J. Fox. (2009). *Gaussian 09*. In (Version Revision A.02)

Georgiou, N., Kakava, M. G., Routsi, E. A., Petsas, E., Stavridis, N., Freris, C., Zoupanou, N., Moschovou, K., Kiriakidi, S., & Mavromoustakos, T. (2023). Quercetin: a potential polydynamic drug. *Molecules*, 28(24), 8141. Doi: 10.3390/molecules28248141

Gören, K., Bağlan, M., & Çakmak, İ. (2022). Theoretical investigation of ^{1}H and ^{13}C NMR Spectra of diethanol Amine dithiocarbamate RAFT agent. *Journal of the Institute of Science and Technology*, 12(3), 1677–1689. https://doi.org/10.21597/jist.1103750

Gören, K., Bağlan, M., Tahiroğlu, V., & Yıldıko, Ü. (2024). Theoretical calculations and molecular docking analysis of 4-(2-(4-bromophenyl) hydrazineylidene)-3, 5-diphenyl-4H-pyrazole molecule. *Journal of Advanced Research in Natural and Applied Sciences*, 10(4), 786–802. https://doi.org/10.28979/jarnas.1516154

Gören, K., Bağlan, M., Tahiroğlu, V., & Yıldıko, Ü. (2025). The Relationship Between AChE and BChE Enzymes and Alzheimer's Disease: ADME, Molecular Docking, and DFT Studies of Schiff Base-Substituted Phenylpyrimidine. *Celal Bayar University Journal of Science*, 21(4), 1–15. https://doi.org/10.18466/cbayarfbe.1538029

Gören, K., Bağlan, M., & Yıldıko, Ü. (2024a). Antimicrobial, and Antitubercular Evaluation with ADME and Molecular Docking Studies and DFT Calculatıons of (Z)-3-((1-(5-amino-1, 3, 4-thiadiazol-2-yl)-2-Phenylethyl) imino)-5-nitroindolin-2-one Schiff Base. *Karadeniz Fen Bilimleri Dergisi*, 14(4), 1694–1708. https://doi.org/10.31466/kfbd.1423367

Gören, K., Bağlan, M., & Yıldıko, Ü. (2024b). Melanoma Cancer Evaluation with ADME and Molecular Docking Analysis, DFT Calculations of (E)-methyl 3-(1-(4-methoxybenzyl)-2, 3-dioxoindolin-5-yl)-acrylate Molecule. *Journal of the Institute of Science and Technology*, 14(3), 1186–1199. https://doi.org/10.21597/jist.1467666

GÖREN, K., BAĞLAN, M., YILDIKO, Ü., & TAHİROĞLU, V. (2024). Anti-Kanser ve Anti-Üreaz Aktivitesi için Tiazolidinon-Bis Schiff Bazının Moleküler Yerleştirme ve DFT Analizi. *Journal of the Institute of Science & Technology/Iğdır Üniversitesi Fen Bilimleri Enstitüsü Dergisi*, 14(2). Doi: 10.21597/jist.1416223

Gören, K., Bağlan, M., Yıldıko, Ü., & Tahiroğlu, V. (2024). Molecular Docking and DFT analysis of Thiazolidinone-Bis schiff base for anti-Cancer and anti-Urease activity. *Journal of the Institute of Science and Technology*, 14(2), 822–834. https://doi.org/10.21597/jist.1416223.

Gören, K., Kotan, G., Manap, S., & Yüksek, H. (2024). Synthesis, Antimicrobial and Antioxidant Activities of 3-Alkyl (aryl)-4-(3-methoxy-4-hydroxybenzylideneamino)-4, 5-dihydro-1 H-1, 2, 4-triazol-5-one Derivatives. *Chemistry Africa*, 7(10), 5273–5289. https://doi.org/10.1007/s42250-024-01139-2

Gören, K., & Yıldıko, Ü. (2024). Aldose reductase evaluation against diabetic complications using ADME and molecular docking studies and DFT calculations of spiroindoline derivative molecule. *Süleyman Demirel Üniversitesi Fen Bilimleri Enstitüsü Dergisi*, 28(2), 281–292. https://doi.org/10.19113/sdufenbed.1474689

Janjua, M. R. S. A., Mahmood, A., Nazar, M. F., Yang, Z., & Pan, S. (2014). Electronic absorption spectra and nonlinear optical properties of ruthenium acetylide complexes: a DFT study toward the designing of new high NLO response compounds. *Acta Chimica Slovenica*, 61(2).

Kartal, B., Bağlan, M., & Gören, K. (2026). DFT, Molecular Docking and In-Silico ADME Studies of 2-(2-(4-Chlorophenyl) Benzo [D]-Oxazol-5-Yl) Propanoic Acid Compound. *Erciyes Üniversitesi Fen Bilimleri Enstitüsü Fen Bilimleri Dergisi*, 42(1). https://doi.org/10.65520/erciyesfen.1791980

Kelly, G. S. (2011). Quercetin. *Alternative medicine review*, 16(2).

Khan, J., Deb, P. K., Priya, S., Medina, K. D., Devi, R., Walode, S. G., & Rudrapal, M. (2021). Dietary flavonoids: Cardioprotective potential with antioxidant effects and their pharmacokinetic, toxicological and therapeutic concerns. *Molecules*, 26(13), 4021. https://doi.org/10.3390/molecules26134021

Kotan, G., Gören, K., Manap, S., Bağlan, M., & Yüksek, H. (2025). Novel Mannich Bases Based on Schiff Bases: Synthesis, Biological Activities, Computational Approach, and Anticancer Analysis with Molecular Docking. *Acta Chimica Slovenica*, 72(4). Doi: 10.17344/acsi.2025.9285

Li, Y., Yao, J., Han, C., Yang, J., Chaudhry, M. T., Wang, S., Liu, H., & Yin, Y. (2016). Quercetin, inflammation and immunity. *Nutrients*, 8(3), 167. https://doi.org/10.3390/nu8030167

Noureddine, O., Issaoui, N., & Al-Dossary, O. (2021). DFT and molecular docking study of chloroquine derivatives as antiviral to coronavirus COVID-19. *Journal of King Saud University-Science*, 33(1), 101248. Doi: 10.1016/j.jksus.2020.101248

Ramalingam, A., Sambandam, S., Medimagh, M., Al-Dossary, O., Issaoui, N., & Wojcik, M. J. (2021). Study of a new piperidone as an anti-Alzheimer agent: Molecular docking, electronic and intermolecular interaction investigations by DFT method. *Journal of King Saud University-Science*, 33(8), 101632. Doi:10.1016/j.jksus.2021.101632

Sharma, A., Kashyap, D., Sak, K., Tuli, H. S., & Sharma, A. K. (2018). Therapeutic charm of quercetin and its derivatives: a review of research and patents. *Pharmaceutical patent analyst*, 7(1), 15–32. https://doi.org/10.4155/ppa-2017-0030

Tahiroğlu, V., Gören, K., & Bağlan, M. (2025). In Silico drug evaluation by molecular docking, ADME studies and DFT calculations of 2-(6-chloro-2-(4-chlorophenyl) imidazo [1, 2-a] pyridin-3-yl)-N, N-dipropylacetamide. *BMC Pharmacology and Toxicology*, 26(1), 116. https://doi.org/10.1186/s40360-025-00958-4

Tahiroğlu, V., Gören, K., Kotan, G., & Yüksek, H. (2025a). Correction: In silico drug evaluation by molecular docking, ADME studies and synthesis, characterization, biological activities, DFT, SAR analysis of the novel Mannich bases. *BMC chemistry*, 19(1), 265. doi: 10.1186/s13065-025-01644-6

Tahiroğlu, V., Gören, K., Kotan, G., & Yüksek, H. (2025b). In silico drug evaluation by molecular docking, ADME studies and synthesis, characterization, biological activities, DFT, SAR analysis of the novel Mannich bases. *BMC chemistry*, 19(1), 249. https://doi.org/10.1186/s13065-025-01615-x

Tahiroğlu, V., Gören, K., Yıldıko, Ü., & Bağlan, M. (2024). IInvestigation, structural characterization and evaluation of the biological potency by molecular docking of amoxicillin analogue of a schiff base molecule. *International Journal of Chemistry and Technology*, 8(2), 190–199. https://doi.org/10.32571/ijct.1410570