In-silico studies of haematological effects of Corchorus olitorius Leaf Phytochemicals

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Research Article

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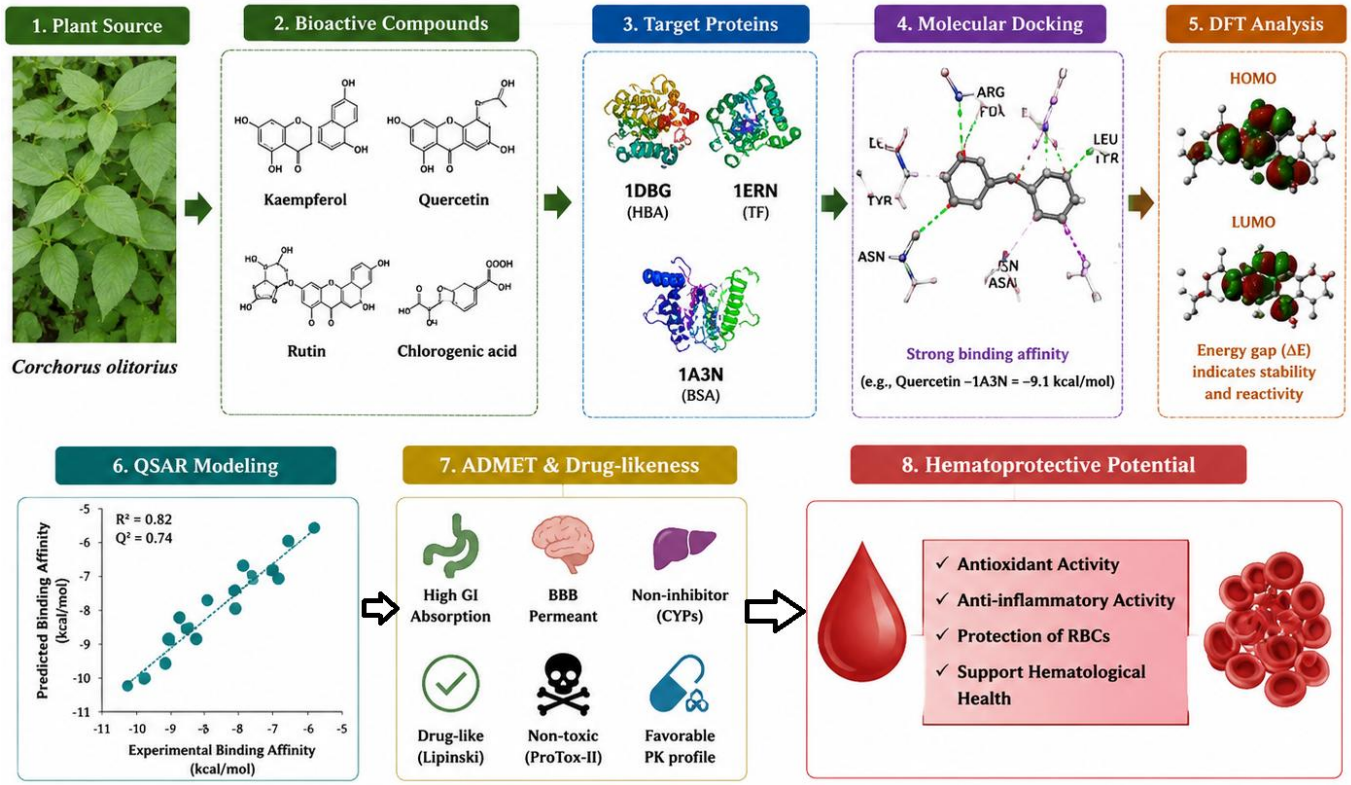
Abstract

This study investigated the theoretical effects of selected phytochemicals from *Corchorus olitorius* leaves on haematological-related targets using an integrated computational approach involving density functional theory (DFT), molecular docking, global reactivity descriptors, and ADMET prediction. Major bioactive compounds including caffeic acid, kaempferol, chlorogenic acid, and quercetin were evaluated against catalase (PDB ID: 1DBG), erythropoietin receptor (PDB ID: 1ERN), and hemoglobin (PDB ID: 1A3N), using erythropoietin as a reference compound. Geometry optimization confirmed stable molecular conformations suitable for quantum chemical analysis. Frontier molecular orbital analysis showed caffeic acid possessed the lowest HOMO–LUMO energy gap (2.868 eV), indicating high chemical reactivity, while quercetin exhibited the highest energy gap (8.176 eV), suggesting greater kinetic stability. Global reactivity descriptor analysis further revealed that caffeic and chlorogenic acids had the highest softness and electrophilicity, supporting favorable electron transfer potential and possible antioxidant activity. Molecular docking results demonstrated strong binding affinities of kaempferol and quercetin toward the studied protein targets, with kaempferol showing the highest affinity against catalase (−10.0 kcal/mol) and quercetin showing the strongest interaction with hemoglobin (−8.0 kcal/mol) and erythropoietin receptor (−6.9 kcal/mol). QSAR results demonstrated that descriptor contributions vary across protein targets, while correlation analysis confirmed strong relationships among electronic parameters and binding behavior. ADMET prediction indicated favorable drug-likeness, pharmacokinetic properties, and acceptable toxicity profiles for most compounds, particularly kaempferol and caffeic acid. Overall, the findings suggest that *Corchorus olitorius* phytochemicals possess promising hematoprotective potential and may serve as lead compounds for further experimental validation.

Keywords: *Corchorus olitorius*; phytochemicals; molecular docking; DFT; ADMET; hematoprotective activity.



1. Introduction

Medicinal plants continue to attract attention as important sources of bioactive compounds with therapeutic potential in managing various disorders, including haematological abnormalities [1]. Blood plays essential roles in oxygen transport, immune defense, nutrient distribution, and maintenance of homeostasis. As a result, haematological indices such as red blood cell count (RBC), white blood cell count (WBC), haemoglobin concentration (Hb), packed cell volume (PCV), and platelet count are widely used to assess health status [2]. Alterations in these parameters may result from oxidative stress, inflammation, anemia, or toxic exposure, highlighting the need for natural agents that can support blood-related functions [3]. One plant of growing interest is *Corchorus olitorius,* commonly known as jute mallow, which is widely consumed in Africa and Asia. It is rich in essential nutrients such as iron, calcium, folate, and vitamins A, C, and E, as well as bioactive compounds including flavonoids, phenolic acids, alkaloids, tannins, terpenoids, and glycosides [4]. These phytochemicals have been associated with antioxidant, anti-inflammatory, and immunomodulatory properties, suggesting potential benefits in haematological protection [5]. Key phytoconstituents such as quercetin, kaempferol, chlorogenic acid, and caffeic acid exhibit strong antioxidant activity, which may help reduce oxidative damage, stabilize erythrocyte membranes, and support hematopoiesis. Since oxidative stress is a major contributor to haematological dysfunction, antioxidant-rich plants like *C. olitorius* present promising therapeutic potential [1, 6]. Despite these benefits, the molecular mechanisms underlying the haematological effects of *C. olitorius* are not fully understood. Experimental studies often demonstrate biological

activity but provide limited insight into molecular interactions and chemical behavior. To address this gap, computational approaches have become increasingly important in natural product research [7]. In silico techniques such as molecular docking, density functional theory (DFT), and ADMET prediction, offer valuable tools for investigating phytochemical interactions with biological targets. Molecular docking predicts binding affinity between compounds and proteins involved in haematological regulation, while DFT provides insight into chemical reactivity [8]. ADMET analysis evaluates pharmacokinetic properties drug-likeness and toxicity. Therefore, this study applies an integrated computational approach to investigate selected phytochemicals from *Corchorus olitorius*. The findings are expected to provide molecular-level insights into its potential hematoprotective properties and support its relevance in drug discovery.

2.0 Computational Methods

This study employed an integrated in silico approach involving density functional theory (DFT), molecular docking, drug-likeness prediction, and toxicity prediction to investigate the interaction of selected phytochemicals from *Corchorus olitorius* with haematological targets.

2.1 Selection and Preparation of Phytochemical Ligands

Major bioactive constituents of *Corchorus olitorius*, including quercetin, kaempferol, chlorogenic acid, and caffeic acid, were selected based on reported phytochemical composition and biological relevance [4, 5]. Three-dimensional structures of the phytochemicals and the standard reference drug (Erythropoietin), were retrieved from PubChem in SDF format, as shown in Figure 1. Ligands were imported into Avogadro for geometry optimization using the MMFF94 force field and saved in PDB format for further analysis [9].

2.2 Density Functional Theory (DFT) Calculations

Quantum chemical calculations were performed using ORCA at the B3LYP/6-31G* level of theory [10]. Geometry optimization was carried out for each phytochemical, followed by calculation of frontier molecular orbital energies including HOMO and LUMO and was use to evaluate the global reactivity descriptors were calculated using Koopmans' theorem [8]. The energy gap was determined using: where lower energy gaps indicate higher chemical reactivity and potential antioxidant activity [11].

2.3 Protein Selection and Preparation

Protein targets associated with haematological function were selected from the Protein Data Bank based on their relevance to erythropoiesis and oxidative stress regulation. Selected proteins included erythropoietin receptor (PDB ID: 1ERN), hemoglobin (PDB ID: 1A3N), and catalase (PDB ID: 1DGB). Protein structures were prepared using AutoDock Tools by removing water molecules and co-crystallized ligands, adding polar hydrogens, assigning Kollman charges, and converting structures to PDBQT format [12].

2.4 Molecular Docking Analysis

Molecular docking studies were carried out using AutoDock Vina to predict binding affinities and interaction profiles between phytochemicals and target proteins [13]. Grid box parameters were defined around active binding pockets based on co-crystallized ligand coordinates and literature reports. Docking scores were expressed as binding energies (kcal/mol), with lower binding energies indicating stronger predicted interactions. Docked complexes were visualized using PyMOL and Discovery Studio Visualizer to identify hydrogen bonding, hydrophobic interactions, and key amino acid residues involved in binding.

2.5 QSAR Modeling

Quantitative structure–activity relationship (QSAR) analysis was performed to correlate DFT-derived descriptors (ΔE, softness, and electrophilicity) with docking binding affinities. Multiple linear regression models were developed using Python (scikit-learn library), and separate models were generated for each protein target. The general QSAR model is expressed as:

$$Binding\ Affinity = a + b1(\Delta E) + b2(S) + b3(\omega) \qquad (1)$$

Model performance was evaluated using the coefficient of determination (R^2), and graphical plots of predicted versus actual values were generated.

2.6 Drug-Likeness and ADMET Prediction

The pharmacokinetic properties and drug-likeness of selected compounds were predicted using SwissADME [14]. Parameters evaluated included molecular weight, lipophilicity (LogP), hydrogen bond donors and acceptors, gastrointestinal absorption, and compliance with Lipinski's Rule of Five. Toxicity and pharmacological suitability were assessed theoretically to support selection of promising compounds for docking studies.

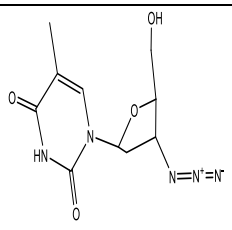
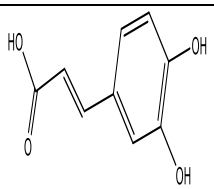
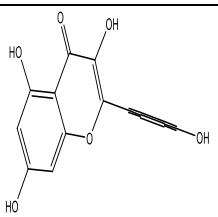
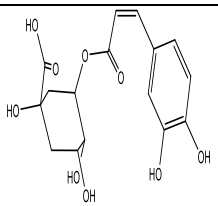
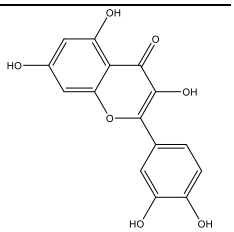
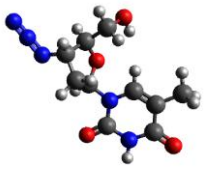
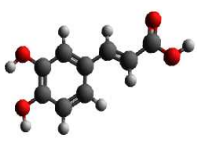
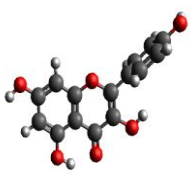
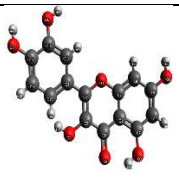
	Erythropoitein	**Caffeic acid**	**Kaempferol**	**Chlorogenic-acid**	**Quercetin**
2D					
3D					

Fig 1. 2D and 3D of the geometry structure of the ligands

3.0 Results and Discussion

3.1 Geometry Optimization of Ligands

The geometry-optimized structures of caffeic acid, kaempferol, chlorogenic acid, quercetin, and the reference ligand are presented in Figure 1. Geometry optimization produced stable minimum-energy conformations for all ligands, with no abnormal bond distortions, confirming suitability for subsequent DFT analysis [7, 8]. Structural differences among the ligands may influence their reactivity and biological interactions. Caffeic acid showed a relatively planar conjugated structure with hydroxyl and carboxyl groups favorable for electron donation and hydrogen bonding. Kaempferol and quercetin exhibited highly conjugated flavonoid skeletons with multiple hydroxyl substituents, suggesting enhanced π-electron delocalization and antioxidant potential [5]. Chlorogenic acid displayed a larger and more flexible structure due to its ester-linked quinic acid moiety, which may support multiple binding orientations. The high degree of planarity observed in quercetin and kaempferol is associated with improved electron delocalization and molecular stability, features often linked to favorable pharmacological activity [1]. Additionally, the abundance of oxygen-containing functional groups across the ligands suggests strong hydrogen bonding potential that may contribute to ligand–protein interactions observed in docking studies.

3.2 Frontier Molecular Orbitals (HOMO–LUMO Analysis)

Frontier molecular orbital (FMO) analysis provides insight into molecular stability, electron transfer potential, and chemical reactivity. The HOMO represents electron-donating ability, whereas the LUMO reflects electron-accepting capacity. Their spatial distributions are shown in Figure 2, while calculated orbital energies are presented in Table 1.

Table 1: HOMO–LUMO Energy Gap (ΔE) of Studied Compounds

Ligand	HOMO (eV)	LUMO (eV)	ΔE (eV)
Erythropoitein-refer	-5.894	-2.280	3.614
Caffeic	-5.217	-2.349	2.868
Kaempferol	-5.146	-2.086	3.060
Chlorogenic	-5.314	-2.337	2.977
Quercetin	−8.651	−0.475	8.176

Caffeic acid exhibited the lowest HOMO–LUMO gap (2.868 eV), indicating the highest predicted chemical reactivity and lowest kinetic stability among the studied compounds. Lower energy gaps generally facilitate charge transfer and are often associated with stronger antioxidant potential and easier interaction with biological targets [11, 15]. Chlorogenic acid and kaempferol also showed relatively low energy gaps, suggesting appreciable reactivity. In contrast, quercetin displayed the largest energy gap (8.176 eV), indicating greater electronic stability and lower

intrinsic reactivity. High HOMO–LUMO gaps are often associated with molecules possessing enhanced kinetic stability and reduced softness [8]. The HOMO surfaces of caffeic acid, kaempferol, and quercetin were predominantly localized around hydroxyl-substituted aromatic rings, suggesting these regions may act as electron-donating sites.

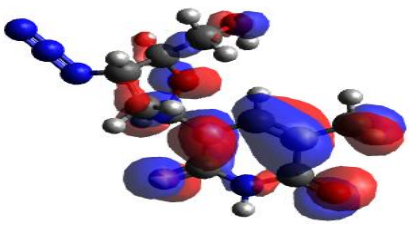
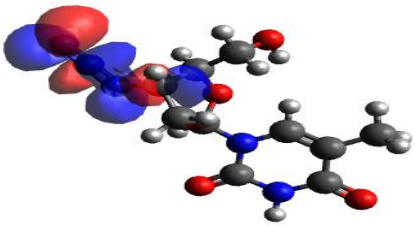
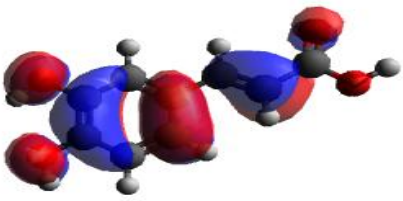
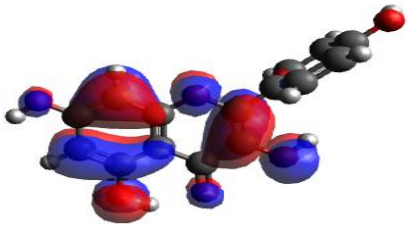
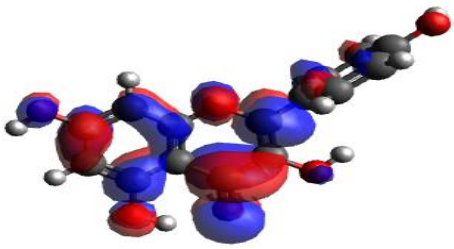
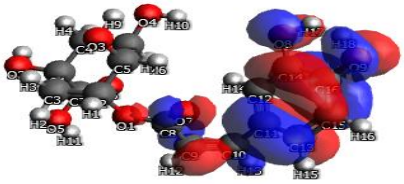
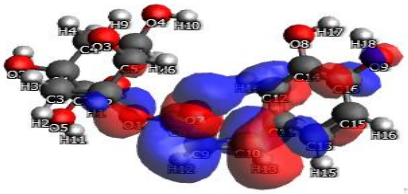
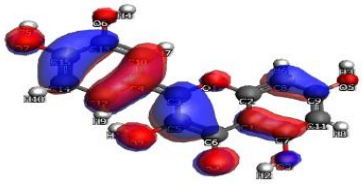
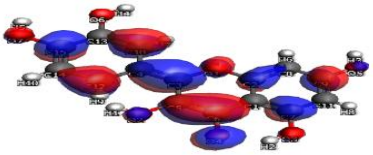
Ligand	HOMO	LUMO
Erythropoitein		
Caffeic		
Kaempferol		
Chlorogenic		
Quercetin		

Fig 2**.** Frontier molecular orbital (HOMO and LUMO) distributions of selected phytochemicals from *Corchorus olitorius*,

Conversely, the LUMO distributions were concentrated around carbonyl and oxygen-rich moieties, indicating preferred electron-accepting centers. Such donor–acceptor characteristics are important for radical scavenging and receptor interactions.

3.3 Global Reactivity Descriptors

The calculated global reactivity descriptors provided important insight into the chemical behavior and biological interaction potential of the studied ligands, as shown in Table 2. Caffeic acid and chlorogenic acid exhibited the lowest hardness values (1.434 and 1.489 eV) and highest softness values (0.349 and 0.336 eV^{-1}), indicating greater chemical reactivity and stronger electron transfer potential. Molecules with low hardness and high softness are generally associated with enhanced antioxidant activity and improved interaction with biological targets [15, 16]. In contrast, quercetin showed the highest hardness (4.088 eV) and lowest softness (0.122 eV^{-1}), suggesting greater kinetic stability but lower reactivity.

Table 2: Global Reactivity Descriptors of Studied Compounds

Ligand	ΔE (eV)	η (eV)	S (eV^{-1})	χ (eV)	μ (eV)	ω (eV)
Erythropoietin	3.614	1.807	0.277	4.087	-4.087	4.62
Caffeic acid	2.868	1.434	0.349	3.783	-3.783	4.99
Kaempferol	3.060	1.530	0.327	3.616	-3.616	4.27
Chlorogenic acid	2.977	1.489	0.336	3.826	-3.826	4.92
Quercetin	8.176	4.088	0.122	4.563	-4.563	2.55

The electronegativity values showed that quercetin had the highest electron-attracting tendency (4.563 eV), whereas caffeic acid, kaempferol, and chlorogenic acid displayed moderate values that favor balanced donor–acceptor interactions within protein binding sites. Similarly, the electrophilicity index revealed that caffeic acid (4.99 eV) and chlorogenic acid (4.92 eV) possessed the highest electrophilic character, indicating strong potential for interaction with nucleophilic residues in proteins and possible enhanced biological activity [8]. The global descriptor analysis suggests that caffeic acid and chlorogenic acid possess the most favorable reactivity characteristics, combining low hardness, high softness, and high electrophilicity, which may support antioxidant and hematoprotective activity. Kaempferol showed intermediate behavior, while quercetin appeared more chemically stable but less reactive. These findings support the frontier orbital results and agree with recent conceptual DFT studies linking softness and electrophilicity with bioactivity [17].

3.4 Molecular Docking

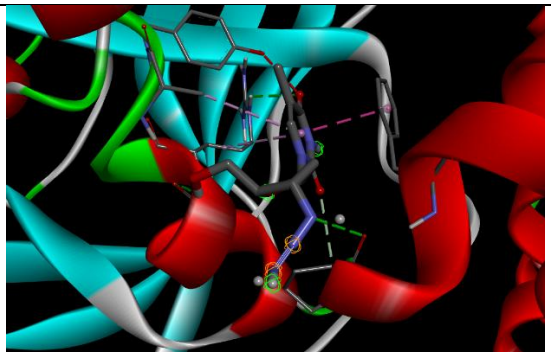
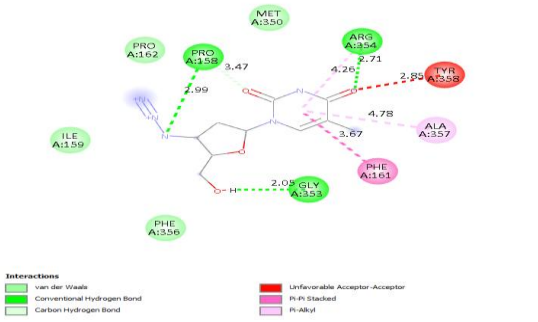
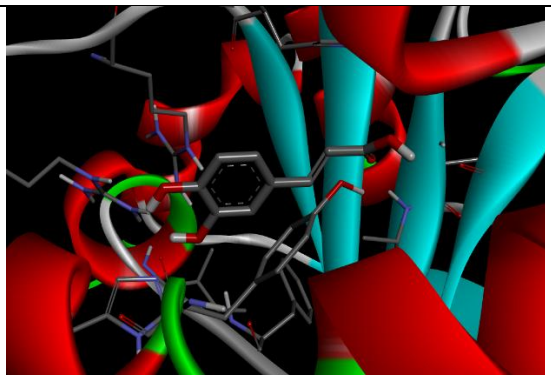
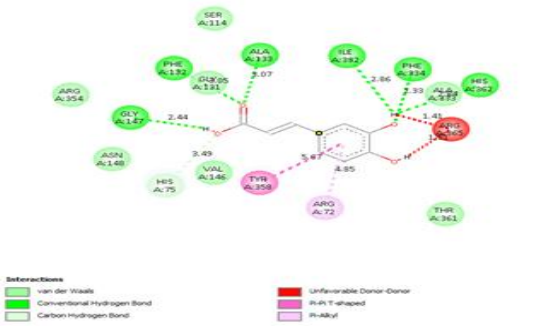
Molecular docking was performed to evaluate the binding affinities and interaction profiles of selected phytochemicals from *Corchorus olitorius* against three haematological-related protein targets: catalase (PDB ID: 1DBG), erythropoietin receptor (PDB ID: 1ERN), and hemoglobin (PDB ID: 1A3N). Binding affinity values obtained from docking simulations are presented in Table 3. In docking studies, more negative binding energy values indicate stronger ligand–protein interactions and greater binding stability [13].

Table 3. The Docking Score of the studies ligands

Ligand name	Binding Affinity (Kcal/mol)		
	1DBG	1ERN	1A3N
Erythropoitein-refer	-6.9	-5.8	-6.4
Caffeic	-7.7	-5.2	-6.5
Kaempferol	-10.0	-6.5	-7.7
Chlorogenic	-7.2	-5.8	-7.0
Quercetin	-9.3	-6.9	-8.0

3.4.1 Interaction with Catalase (PDB ID: 1DBG)

Among all ligands, kaempferol exhibited the strongest binding affinity toward catalase with a docking score of −10.0 kcal/mol, followed by quercetin (−9.3 kcal/mol) and caffeic acid (−7.7 kcal/mol), all showing stronger binding than the reference ligand (−6.9 kcal/mol). This suggests superior interaction of these phytochemicals with the oxidative stress-related target. Kaempferol formed hydrogen bond interactions with ARG112 and GLY147, while π-interactions were observed with TYR358, HIS75, ARG72, and ALA146. Additional hydrophobic interactions involving HIS362, SER114, PHE132, and ARG354 further stabilized the complex, as shown in Figure 3.

Binding Affinity (PDB ID: 1DBG)		
Ligand	**3D**	**2D**
Erythro poitein-refer		
Caffeic		

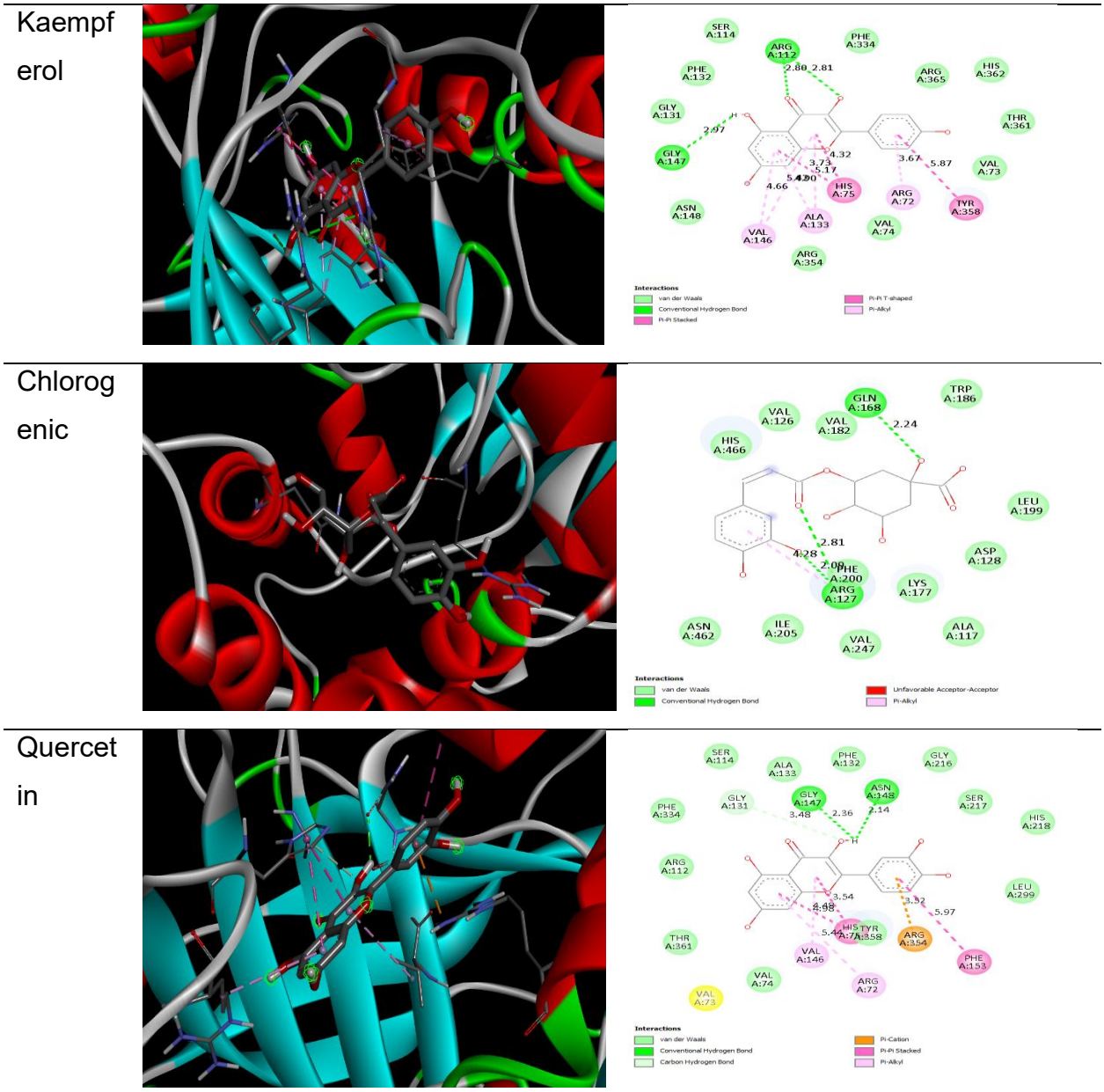
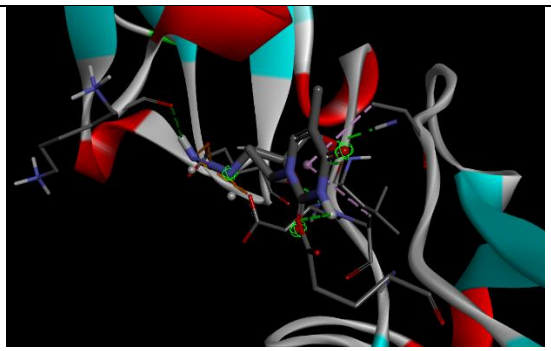
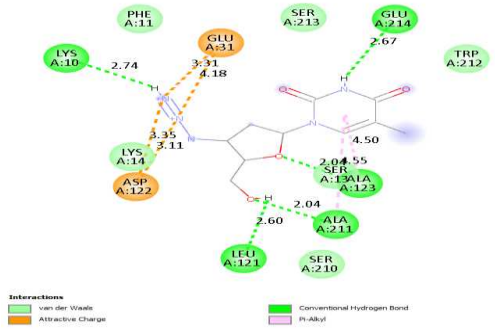
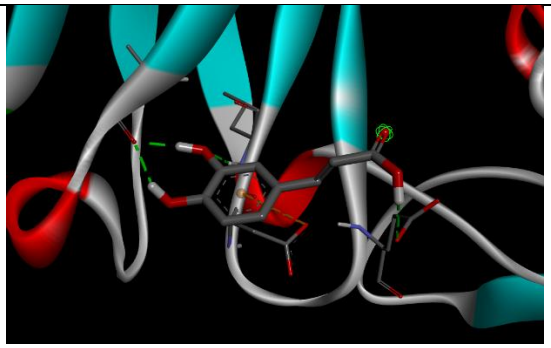
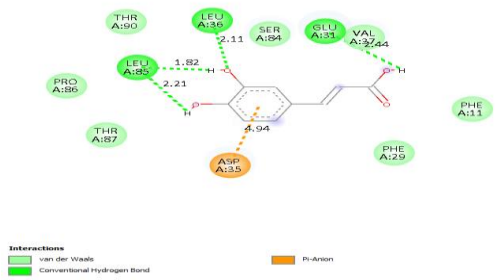
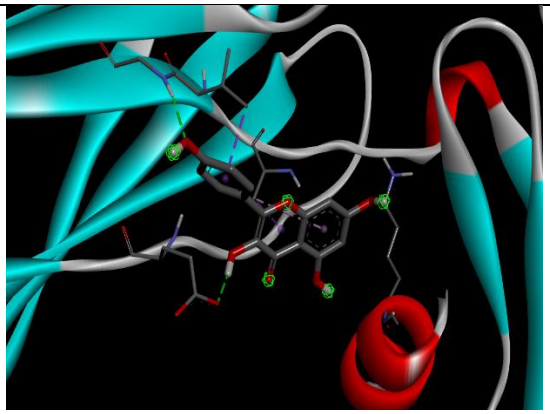
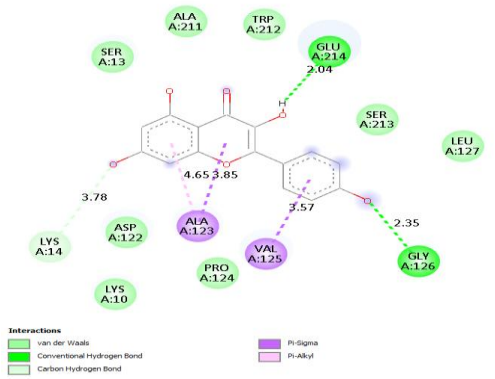


Fig 3. 3D and 2D binding interaction of the ligands with the amino-acid residues of (PDB ID: 1DBG) receptors.

The abundance of aromatic residues involved in π-interactions suggests favorable stacking interactions between the flavonoid aromatic system and active-site residues [8]. Quercetin similarly showed strong binding, supported by hydrogen bonding with GLY147 and ASN148, and π-interactions involving PHE152, HIS75, and ARG354. These interactions may be associated with antioxidant-related inhibitory mechanisms, consistent with reports that polyphenolic flavonoids exhibit strong affinity toward oxidative enzymes [5, 18]. The stronger binding of kaempferol and quercetin correlates with their polyhydroxylated flavonoid structures and conjugated aromatic frameworks, which favor hydrogen bonding and hydrophobic interactions.

3.4.2 Interaction with Erythropoietin Receptor (PDB ID: 1ERN)

For the erythropoietin receptor, quercetin showed the highest binding affinity (−6.9 kcal/mol), followed by kaempferol (−6.5 kcal/mol), both outperforming the reference ligand (−5.8 kcal/mol). This suggests possible modulatory interactions relevant to erythropoietic signaling. Quercetin established multiple hydrogen bond interactions with SER13, ASP122, PRO124, GLY126, and TRP212, while hydrophobic interactions involved GLU214, ALA211, VAL125, and ALA123. The presence of several hydrogen bonds indicates strong ligand accommodation within the receptor binding pocket, as shown in Figure 4.

Ligand	Binding interaction (PDB ID: 1ERN)	
	3D	2D
Erythropoitein-refer		
Caffeic		
Kaempferol		

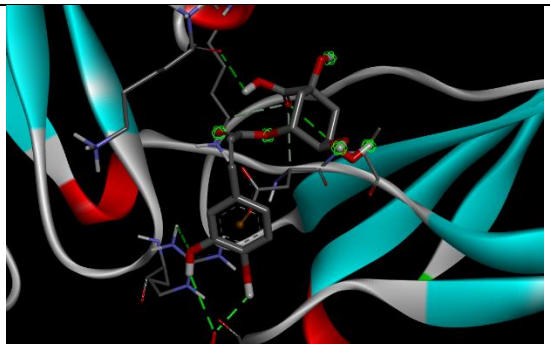
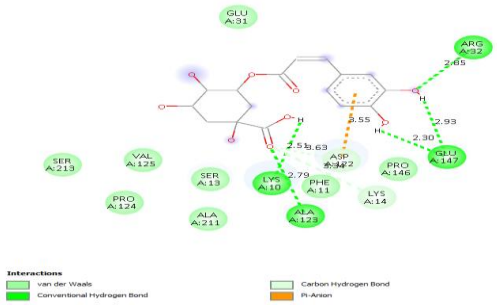
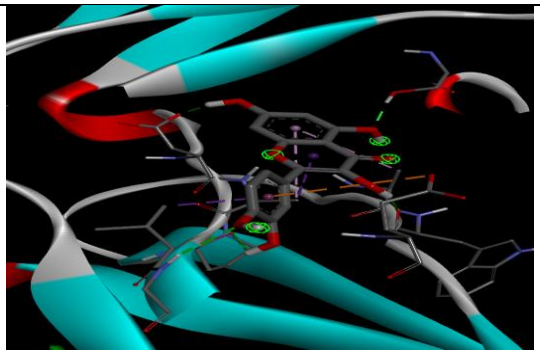
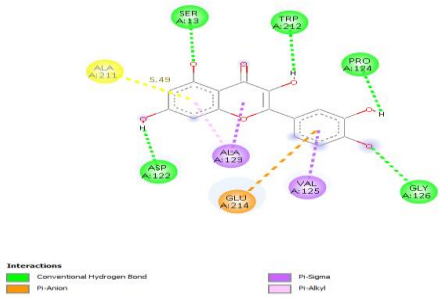
Chlorogenic		
Quercetin		

Fig 4. 3D and 2D binding interaction of the ligands with the amino-acid residues of (PDB ID: 1ERN) receptors

Kaempferol also formed important hydrogen bonds with GLU214 and GLY126, supported by π-interactions with ALA123 and VAL125. These residues have been implicated in ligand recognition and receptor stabilization. Caffeic acid exhibited the weakest interaction (−5.2 kcal/mol), suggesting comparatively lower affinity for the receptor.

3.4.3 Interaction with Hemoglobin (PDB ID: 1A3N)

For hemoglobin, quercetin again showed the strongest binding affinity (−8.0 kcal/mol), followed by kaempferol (−7.7 kcal/mol) and chlorogenic acid (−7.0 kcal/mol), all stronger than the reference compound. Quercetin displayed π-interactions with VAL93, LEU91, and PHE43, alongside additional stabilizing contacts with HIS45, LYS90, and MET32. Although no hydrogen bonds were recorded, the extensive hydrophobic and π-stacking interactions appear sufficient to stabilize the complex, as shown in Figure 5.

Ligand	**Binding Interaction (PDB ID: 1A3N)**	
	3D	**2D**

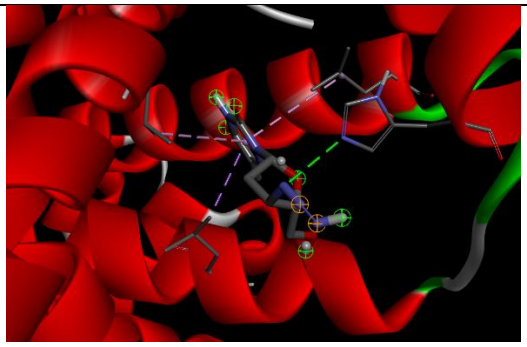
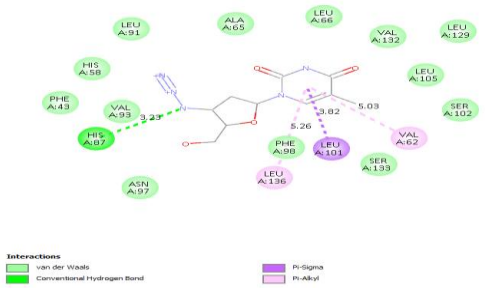
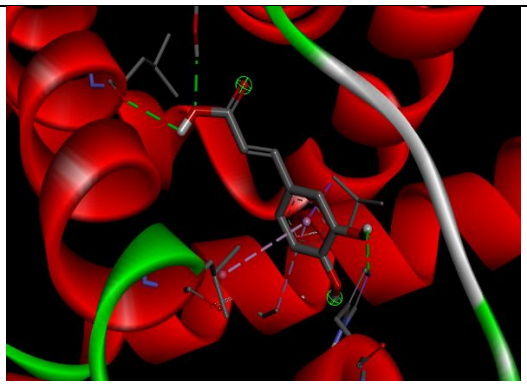
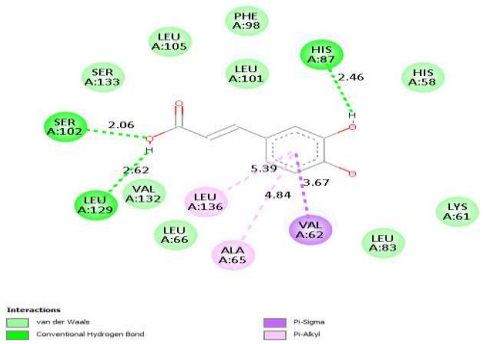
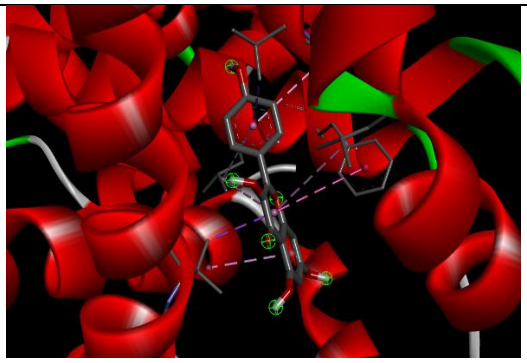
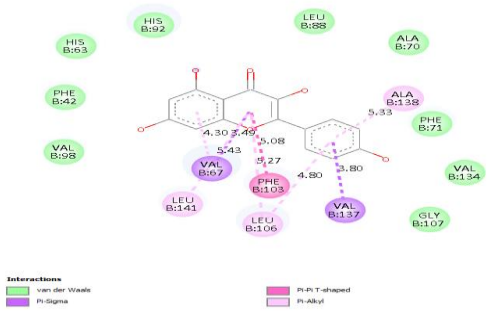
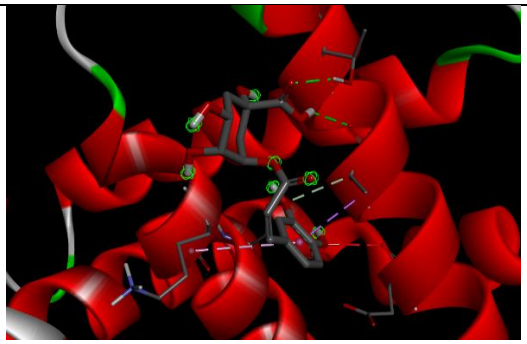
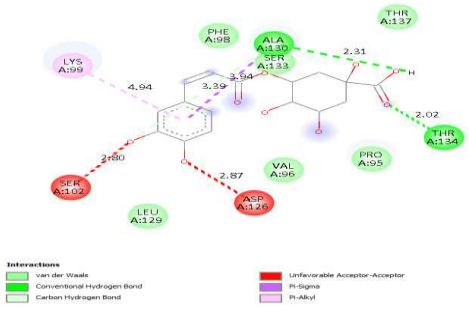
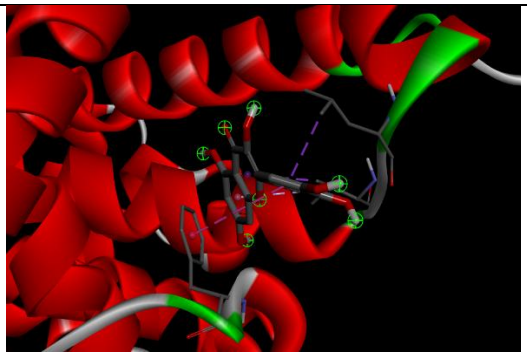
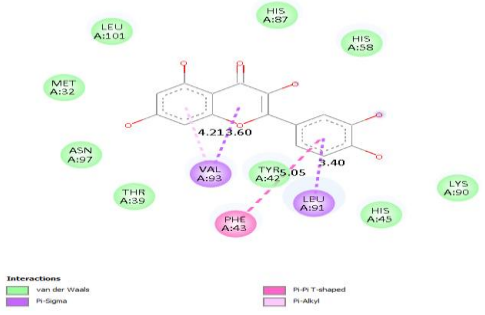
Erythropoitein		
Caffeic		
Kaempferol		
Chlorogenic		
Quercetin		

Fig 5. 3D and 2D binding interaction of the ligands with the amino-acid residues of (PDB ID: 1A3N) receptors

Kaempferol similarly formed multiple hydrophobic contacts involving VAL67, PHE103, LEU106, and ALA138, suggesting a well-packed ligand–protein complex. The superior binding of quercetin and kaempferol to hemoglobin may indicate potential membrane or protein stabilizing roles, supporting possible hematoprotective relevance.

Interestingly, these docking results complement the earlier frontier orbital analysis. Although caffeic acid showed highest electronic reactivity from global descriptor analysis, kaempferol and quercetin demonstrated superior receptor binding. This suggests that electronic reactivity alone does not solely govern docking performance; structural complementarity and interaction geometry also play major roles [13, 15]. The docking results therefore suggest that kaempferol and quercetin may represent the most promising phytochemical candidates for potential hematoprotective activity among the studied ligands.

3.5 Quantitative Structure–Activity Relationship (QSAR) Analysis

QSAR analysis was performed to correlate DFT-derived descriptors—energy gap (ΔE), softness (S), and electrophilicity (ω)—with docking-derived binding affinities. The resulting regression models for each protein are:

- **1DBG:**

$$Binding = -3.728 - 1.169(\Delta E) - 76.346(S) + 5.216(\omega)$$

- **1ERN:**

$$Binding = -38.876 + 2.759(\Delta E) + 66.557(S)$$

- **1A3N:**

$$Binding = -35.430 + 2.345(\Delta E) + 54.795(S) + 0.618(\omega)$$

The QSAR results indicate that descriptor influence varies across targets. For 1DBG, ΔE and electrophilicity contribute significantly, suggesting that balanced reactivity and electron-accepting ability enhance binding. In contrast, for 1ERN and 1A3N, positive contributions from ΔE and softness indicate that molecular stability and flexibility are the dominant factors governing ligand–protein interactions.

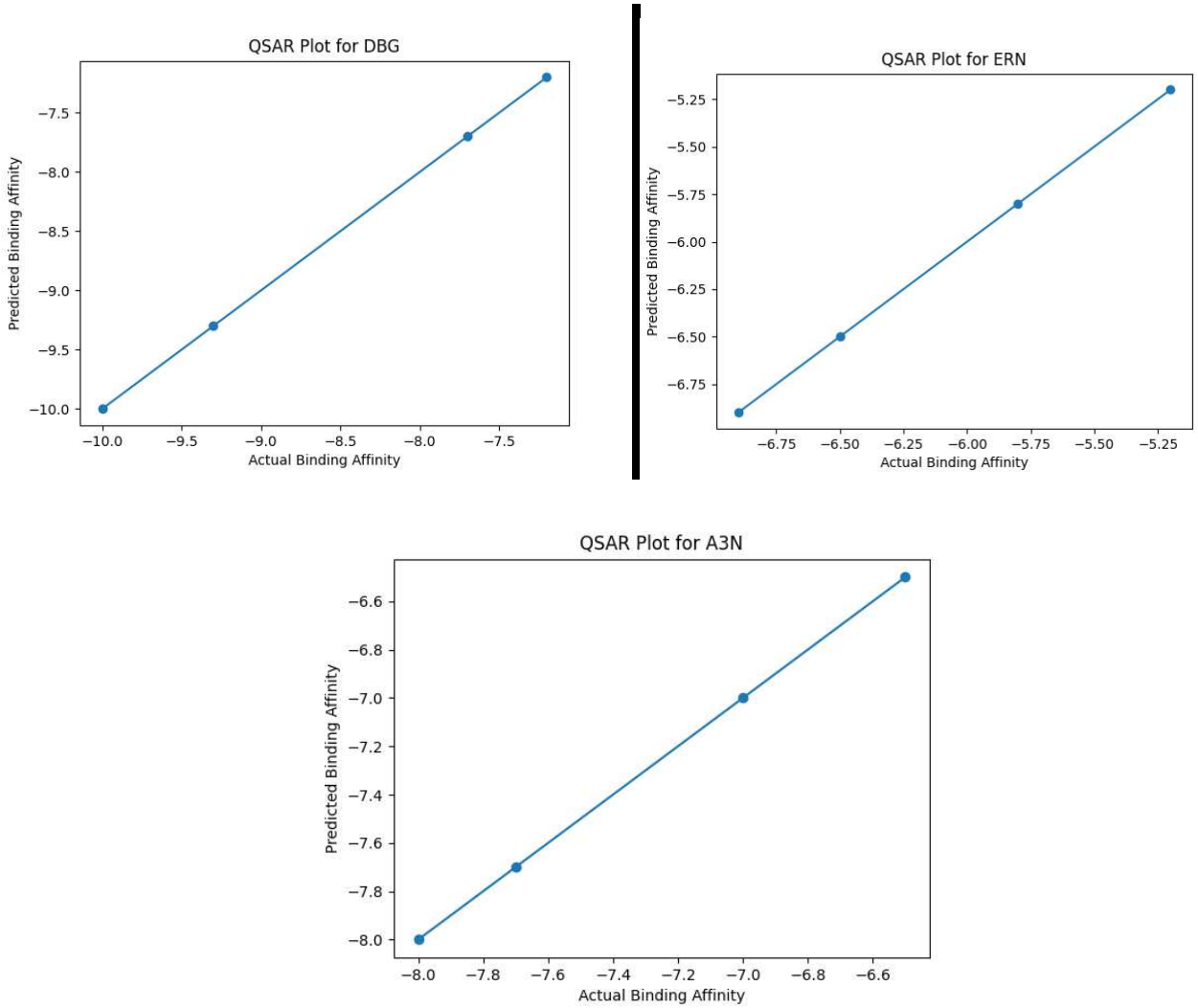


Fig 6. The QSAR plot for For 1DBG, 1ERN and 1A3N,

These findings explain why kaempferol and quercetin exhibited stronger binding despite higher ΔE values, highlighting the importance of structural features such as aromaticity and hydroxyl substitution. Similar trends have been reported for flavonoid–protein interactions in recent computational studies [1, 5]. However, the perfect correlation (R^2 = 1.000) reflects the small dataset and suggests possible overfitting; thus, the models are considered preliminary.

3.6 Correlation Matrix Analysis

The correlation matrix showed strong relationships among the DFT descriptors, with ΔE exhibiting a near-perfect negative correlation with softness (r = −0.999), consistent with conceptual DFT theory. Electrophilicity also correlated positively with softness (r = 0.976) and negatively with ΔE (r = −0.965), confirming that more reactive molecules possess higher electron-accepting ability, as shown in Figure 7. Correlation with biological activity varied across proteins. Weak correlations observed for 1DBG indicate that binding is largely structure-driven, whereas moderate to strong correlations for 1ERN and 1A3N—particularly with softness and electrophilicity—suggest that molecular reactivity contributes more significantly to ligand binding in these systems. The strong

correlation between 1ERN and 1A3N ($r \approx 0.999$) further indicates similar binding behavior across both targets.

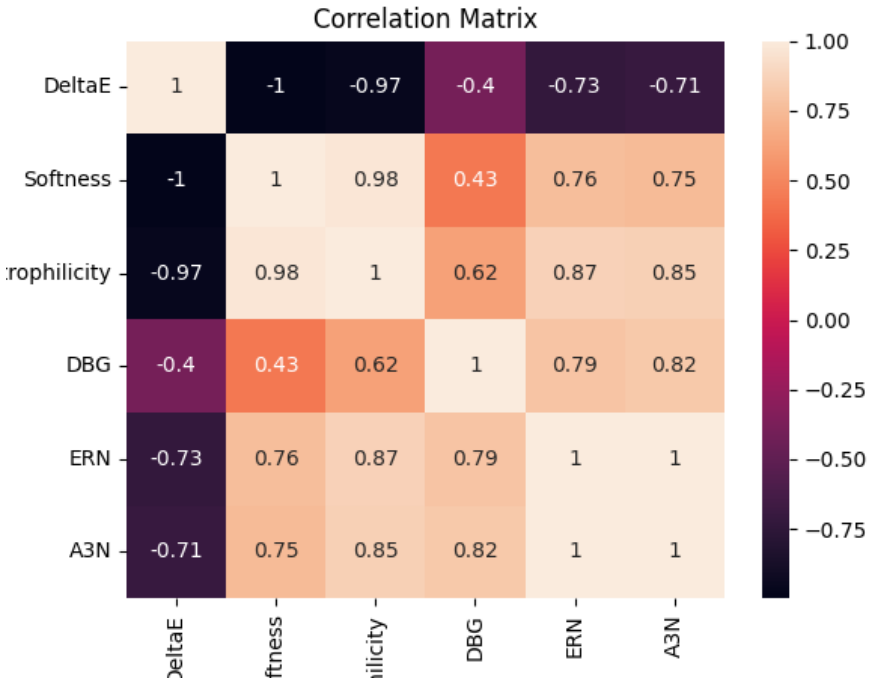


Fig 7. The Correlation Matrix Analysis

The results confirm that while electronic descriptors influence reactivity, structural characteristics remain the primary determinants of binding affinity. Due to the limited dataset, these correlations should be interpreted cautiously [8].

3.7 ADMET

3.7.1 Drug-Likeness and Pharmacokinetic properties

The drug-likeness and pharmacokinetic properties of the studied phytochemicals were evaluated to assess their suitability as potential bioactive candidates, as shown in Table 4 and 5.

Table 4. Predicted lipophilicity, water solubility, druglikeness and bioavailability scores of compounds

Ligands	Mol.Weight (g/mol)	Consensus LogP	Silicos-IT LogSw	ESOL Class	Lipinski Violations	Veber Violations	Muegge violations	Bioavail-ability
Quercetin	302.24	1.23	1.54	soluble	0	0	0	0.55
Caffeic	180.16	0.93	0.75	soluble	0	0	1	0.56
Kaempferol	286.24	1.58	2.03	soluble	0	0	0	0.55
Chlorogenic	354.31	-0.43	-0.61	Very soluble	1	1	2	0.11

Erythropoitein	267.24	-0.15	-0.78	Very soluble	0	0	0	0.55

Drug-likeness evaluation based on Lipinski, Veber, and Muegge criteria showed that quercetin, kaempferol, and the reference compound had no violations, indicating favorable oral drug-like properties. The molecular weights of all the study ligands were all within or close to the acceptable range for drug-like molecules, supporting their potential oral applicability [14]. Caffeic acid showed only one Muegge violation, while chlorogenic acid displayed one Lipinski, one Veber, and two Muegge violations, likely due to its higher polarity and structural complexity. Consensus LogP values ranging from −0.43 to 1.58 indicated moderate lipophilicity. Correspondingly, quercetin, kaempferol, caffeic acid, and the reference compound showed relatively good bioavailability scores (0.55–0.56), whereas chlorogenic acid exhibited a lower score (0.11), suggesting comparatively limited oral bioavailability. Similar trends have been reported for polyphenolic compounds, where increased hydroxylation may improve bioactivity but reduce permeability [19]. All compounds were predicted to be soluble or very soluble, which is advantageous for absorption and transport.

Pharmacokinetic prediction further revealed that quercetin, caffeic acid, kaempferol, and the reference ligand possessed high gastrointestinal absorption, whereas chlorogenic acid showed low absorption, consistent with its lower bioavailability. None of the compounds were predicted to permeate the blood–brain barrier, suggesting low likelihood of central nervous system exposure. Importantly, none were predicted as P-glycoprotein substrates, implying reduced susceptibility to efflux-mediated elimination. Quercetin and kaempferol showed inhibition of CYP1A2 and CYP3A4, indicating possible metabolic interactions, while caffeic acid and chlorogenic acid showed minimal cytochrome inhibition and therefore potentially lower risk of drug–drug interactions.

Table 5. Pharmacokinetics prediction output of the study ligands

Ligands	**GI absorption**	**BBB Permanent**	**PGP substrate**	**CYP1A2 inhibitor**	**CYP2C19 Inhibitor**	**CYP2C9 Inhibitor**	**CYP2D6 inhibitor**	**CYP3A4 inhibitor**	**Logkp (cm/s)**
Quercetin	High	No	No	Yes	No	No	Yes	Yes	-7.05
Caffeic	High	No	No	No	No	No	No	No	-6.58
Kaempferol	High	No	No	Yes	No	No	Yes	Yes	-6.70
Chlorogenic	Low	No	No	No	No	No	No	No	-8.76
Erythropoitein	High	No	No	No	No	No	No	No	-7.89

3.7.2 Toxicity Prediction

Toxicity prediction showed generally favorable safety profiles for the phytochemicals compared with the reference ligand, as shown in Table 6. Kaempferol showed the most favorable toxicity pattern with no major hepatotoxic, mutagenic, or carcinogenic liabilities predicted. Caffeic acid and chlorogenic acid also exhibited low predicted toxicity, while quercetin showed some mutagenicity and carcinogenicity alerts, which have been reported in silico for some flavonoids but often require experimental confirmation. Interestingly, the reference ligand showed comparatively higher predicted hepatotoxicity and carcinogenicity signals, suggesting that some phytochemicals may possess safer theoretical profiles [20].

Table 6. Toxicity profile of compounds

Ligands	Hepatotoxicity	Mutagenicity	carcinogenicity	Immunotoxicity	Cytotoxicity
Quercetin	-	+	+	-	-
Caffeic	-	--	++	-	--
Kaempferol	-	-	--	--	--
Chlorogenic	--	--	-	++	--
Erythropoitein	+	++	++	--	--
Non-Toxic (−) Toxic (+)					

The ADMET results suggest that quercetin, kaempferol, and caffeic acid possess favorable drug-likeness, pharmacokinetic behavior, and acceptable toxicity profiles, supporting their potential as promising bioactive candidates. Although chlorogenic acid showed lower predicted bioavailability, its strong solubility and low toxicity still indicate possible pharmacological relevance.

Conclusion

This study demonstrated, through computational and theoretical approaches, that selected phytochemicals from *Corchorus olitorius* possess promising properties relevant to haematological modulation. DFT analysis revealed favorable electronic characteristics, with caffeic acid and chlorogenic acid showing high chemical reactivity, while quercetin exhibited greater electronic stability. Global reactivity descriptors supported these findings by identifying caffeic acid and chlorogenic acid as soft and electrophilic molecules with potential antioxidant and biointeractive advantages. Molecular docking results showed strong ligand–protein interactions across the studied targets, with kaempferol and quercetin exhibiting superior binding affinities compared with the reference compound in several cases, suggesting possible hematoprotective relevance. QSAR results demonstrated that descriptor contributions vary across protein targets, while correlation analysis confirmed strong relationships among electronic parameters and binding behavior. In addition, ADMET prediction indicated that most of the phytochemicals possess

favorable drug-likeness, good pharmacokinetic behavior, and acceptable theoretical safety profiles. The combined results suggest that kaempferol, quercetin, caffeic acid, and chlorogenic acid may contribute to the potential haematological benefits associated with *Corchorus olitorius*. Among them, kaempferol and quercetin emerged as promising lead compounds based on docking performance, while caffeic acid and chlorogenic acid showed strong electronic reactivity advantages. These findings provide a molecular basis for the medicinal relevance of *Corchorus olitorius* and support further in vitro and in vivo validation of its hematoprotective potential.

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Author contributions Seun Ayorinde: Writing-Review & Editing, Visualization, insilico analysis, methodology, investigation.

Clinical trial number: not applicable.

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Declarations

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical Approval

This study is based entirely on computational simulations and analysis of publicly available structural data. No experiments involving humans, animals, or biological samples were conducted. Therefore, ethical approval was not required for this research.

Consent to Participate

Not applicable. This study did not involve human participants or animals.

Consent to Publish

Not applicable. This study does not contain any individual person's data in any form.

References

1. Kudumela RG, Ramadwa TE, Mametja NM, Masebe TM. Corchorus species: Botany, phytochemistry, nutritional content and pharmacological properties. *Plants* 2024, 13(8), 1096. https://doi.org/10.3390/plants13081096
2. Guyton AC, Hall JE. *Textbook of Medical Physiology*. 14th ed.; Elsevier: 2021.
3. Ukpai OM, Ijioma SN, Kanu K, Okafor CE, Nwankwo CP, Odo CC. Phytochemical composition, toxicological profiling and effect on pup birth weight of *Corchorus olitorius* leaf

extract in rats. *J Ethnopharmacol* 2024, 319, 117170. https://doi.org/10.1016/j.jep.2023.117170

4. Abdel-Razek MA, Abdelwahab MF, Abdelmohsen UR, Hamed ANE. Pharmacological and phytochemical biodiversity of *Corchorus olitorius* L. *RSC Adv* 2022, 12(54), 35103–35114. https://doi.org/10.1039/D2RA07406K
5. Biswas A, Dey S, Huang S, Deng Y, Birhanie ZM, Zhang J, Li D. A comprehensive review of *Corchorus capsularis* and *Corchorus olitorius*: Sources of nutrition, essential phytoconstituents and pharmacological activities. *Antioxidants* 2022, 11(7), 1358. https://doi.org/10.3390/antiox11071358
6. Mokgalaboni K, Phoswa WN. *Corchorus olitorius* extract exhibits anti-hyperglycemic and anti-inflammatory properties in rodent models. *Front Nutr* 2023, 10, 1099880. https://doi.org/10.3389/fnut.2023.1099880
7. Richard KA, Idayat S, Sunday WB, Wahab AO, Sikiru AA, Olusola OJ. Computational studies of suitability of triarylmethane-coumarins as sensitizer for dye. *Turk Comp Theor Chem* 2024, 8(3), 66–73. https://doi.org/10.33435/tcandtc.1349520
8. Adeleke RK, Garuba MH, Aremu AA, Ogunleye OD, Bello SA. Computational assessment of CNT–NH_2 and enzyme-functionalized nanomaterials for polycyclic aromatic hydrocarbon remediation. *Discov Chem* 2026, 3, 203. https://doi.org/10.1007/s44371-026-00665-x
9. Hanwell MD, Curtis DE, Lonie DC, Vandermeersch T, Zurek E, Hutchison GR. Avogadro: An advanced semantic chemical editor, visualization, and analysis platform. *J Cheminform* 2012, 4, 17. https://doi.org/10.1186/1758-2946-4-17
10. Neese F. Software update: The ORCA program system, version 4.0. *WIREs Comput Mol Sci* 2018, 8(1), e1327. https://doi.org/10.1002/wcms.1327
11. Sharma P, Ranjan P, Chakraborty T. Applications of conceptual density functional theory in reference to quantitative structure–activity/property relationship. *Mol Phys* 2024, 122(4), e2331620. https://doi.org/10.1080/00268976.2024.2331620
12. Morris GM, Huey R, Lindstrom W, Sanner MF, Belew RK, Goodsell DS, Olson AJ. AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. *J Comput Chem* 2009, 30(16), 2785–2791. https://doi.org/10.1002/jcc.21256
13. Trott O, Olson AJ. AutoDock Vina: Improving the speed and accuracy of docking with a new scoring function. *J Comput Chem* 2010, 31(2), 455–461. https://doi.org/10.1002/jcc.21334
14. Daina A, Michielin O, Zoete V. SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness. *Sci Rep* 2017, 7, 42717. https://doi.org/10.1038/srep42717

15. Domingo LR, Ríos-Gutiérrez M, Pérez P. Applications of conceptual density functional theory indices to organic chemistry reactivity. *Molecules* 2016, 21(6), 748. https://doi.org/10.3390/molecules21060748
16. Geerlings P, De Proft F, Langenaeker W. Conceptual density functional theory. *Chem Rev* 2003, 103(5), 1793–1874. https://doi.org/10.1021/cr990029p
17. Melin J, Aparicio F, Subramanian V, Galván M, Chattaraj PK. Is the Fukui function a right descriptor of hard-hard interactions? *J Phys Chem A* 2004, 108(13), 2487–2491. https://doi.org/10.1021/jp037841f
18. Ge Y, Zhang L, Wang X. Flavonoid–protein interactions and molecular docking approaches in antioxidant drug discovery. *J Mol Struct* 2023, 1285, 135515. https://doi.org/10.1016/j.molstruc.2023.135515
19. Pires DEV, Blundell TL, Ascher DB. pkCSM: Predicting small-molecule pharmacokinetic and toxicity properties using graph-based signatures. *J Med Chem* 2015, 58(9), 4066–4072. https://doi.org/10.1021/acs.jmedchem.5b00104
20. Banerjee P, Eckert AO, Schrey AK, Preissner R. ProTox-II: A webserver for toxicity prediction. *Nucleic Acids Res* 2018, 46(W1), W257–W263. https://doi.org/10.1093/nar/gky318