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Phenolic Acid Phytochemicals as Potential Antiplatelet Agents: A Molecular Docking and ADME Study

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ABSTRACT

Background: Platelet hyperactivation and aggregation are major contributors to thrombotic cardiovascular and cerebrovascular diseases. Although conventional antiplatelet drugs are clinically effective, adverse effects and variable therapeutic responses have encouraged the search for safer natural alternatives. Phenolic acids are plant-derived phytochemicals with reported antioxidant, anti-inflammatory, and cardioprotective properties.

Objective: This study aimed to evaluate selected phenolic acid phytochemicals as potential antiplatelet agents using molecular docking and ADME prediction approaches.

Methods: Selected phenolic acids were subjected to molecular docking against platelet-associated protein targets to investigate their binding affinity, binding orientation, and interactions with important amino acid residues. ADME profiling was subsequently performed to assess their physicochemical, pharmacokinetic, and drug-likeness characteristics.

Results: The investigated phenolic acids demonstrated variable but generally favorable interactions with the selected targets. Several compounds showed strong predicted binding affinities and established hydrogen-bonding and hydrophobic interactions with functionally relevant residues. ADME analysis indicated that selected compounds possessed acceptable drug-like characteristics and pharmacokinetic profiles, although differences in gastrointestinal absorption and other properties were observed.

Conclusion: Phenolic acids demonstrate promising computational potential as antiplatelet candidates. Their favorable target interactions and acceptable ADME characteristics support further biochemical, cellular, and in vivo investigations to validate their antiplatelet efficacy and therapeutic safety.

Keywords: Phenolic acids; Antiplatelet agents; Molecular docking; ADME; Phytochemicals

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INTRODUCTION

Platelets play a central role in maintaining vascular integrity by rapidly adhering to damaged blood vessels, becoming activated, and aggregating to form a hemostatic plug [1,2,3]. However, excessive or inappropriate platelet activation contributes substantially to thrombus formation and is closely associated with cardiovascular and cerebrovascular disorders, including myocardial infarction and ischemic stroke [4,5]. Antiplatelet drugs such as aspirin and P2Y12 receptor inhibitors are widely used for the prevention of thrombotic events, but their clinical application may be limited by bleeding complications, variable patient responses, and drug resistance [6,7,8].

Consequently, the identification of novel, effective, and safer antiplatelet agents remains an important area of pharmacological research [9]. Natural products have attracted considerable attention as sources of bioactive molecules because of their structural diversity and broad pharmacological activities [10,11]. Among plant-derived secondary metabolites, phenolic acids represent an important class of phytochemicals characterized by one or more hydroxyl groups attached to aromatic rings and a carboxylic acid moiety [12,13].

Common phenolic acids include gallic acid, caffeic acid, ferulic acid, p-coumaric acid, vanillic acid, syringic acid, and protocatechuic acid [14,15]. These compounds are widely distributed in fruits, vegetables, cereals, herbs, spices, and medicinal plants and have been extensively investigated for antioxidant, anti-inflammatory, antimicrobial, cardioprotective, and antithrombotic properties [16,17]. The potential antiplatelet activity of phenolic acids is particularly relevant because platelet activation involves several

interconnected signaling pathways [18,19]. Following vascular injury, agonists such as adenosine diphosphate (ADP), thromboxane A_2, thrombin, and collagen stimulate platelet receptors and intracellular signaling cascades, ultimately resulting in calcium mobilization, granule secretion, integrin αIIbβ3 activation, and platelet aggregation [20,21]. Oxidative stress and inflammation can further enhance platelet reactivity [22]. Phenolic acids may interfere with these processes through antioxidant and anti-inflammatory mechanisms and by modulating enzymes, receptors, and intracellular signaling pathways involved in platelet activation [23,24]. Experimental evidence has suggested that several dietary phenolics can reduce platelet aggregation and thromboxane formation, indicating their potential as lead compounds for antiplatelet drug development [25,26].

Despite these promising biological effects, conventional experimental screening of numerous phytochemicals is time-consuming and resource-intensive [27]. Molecular docking provides a valuable computational approach for investigating the interaction between bioactive compounds and pharmacologically relevant protein targets [28]. Docking analysis predicts the preferred binding orientation of a ligand within the active or binding site of a protein and provides an estimated binding affinity [29].

It can also identify important amino acid residues and non-covalent interactions, including hydrogen bonds, hydrophobic interactions, π–π interactions, and electrostatic contacts [30]. Therefore, molecular docking can facilitate the prioritization of promising phenolic acids before subsequent experimental validation [26].

In addition to target binding, the pharmacokinetic characteristics of candidate compounds are critical for successful drug development [31]. Absorption, distribution, metabolism, and excretion (ADME) properties influence bioavailability, tissue exposure, metabolic stability, and potential toxicity [31]. Some naturally occurring phenolic acids may exhibit favorable biological activities but possess limitations related to poor absorption, rapid metabolism, or low systemic availability [26].

Computational ADME profiling can provide an early assessment of physicochemical and pharmacokinetic characteristics, including gastrointestinal absorption, lipophilicity, molecular weight, hydrogen-bonding capacity, and drug-likeness, thereby helping identify compounds with more favorable pharmacological profiles [28]. Therefore, the present study evaluates selected phenolic acid phytochemicals as potential antiplatelet agents using an integrated molecular docking and ADME-based computational approach.

The study focuses on predicting the binding potential of phenolic acids toward selected platelet-associated molecular targets, characterizing their binding interactions, and assessing their pharmacokinetic and drug-likeness properties. By combining target-based molecular investigation with ADME prediction, this study aims to identify promising phenolic acid candidates that may serve as lead compounds for the development of novel, plant-derived antiplatelet therapeutics.

METHODOLOGY

This in silico study was conducted at College of Life Sciences, Hubei University, China between August and October 2025 to investigate the potential antiplatelet activity of selected phenolic acid phytochemicals through molecular docking and ADME analysis. Five compounds, including gallic acid, caffeic acid, chlorogenic acid, p-coumaric acid, and salicylic acid, were selected for computational screening. Their chemical structures were identified using their IUPAC names, and corresponding SMILES representations were obtained from the OPSIN database. [26] The SMILES strings were converted into three-dimensional structures and saved in PDB format using Open Babel. The structures of four platelet-related target proteins, namely protease-activated receptor 1 (PAR1; PDB ID: 3VW7), glycoprotein VI (GPVI; PDB ID: 2GI7), prostacyclin synthase (PGIS; PDB ID: 2IAG), and prostaglandin-endoperoxide synthase 1 (PTGS1/hCOX-1; PDB ID: 6Y3C), were retrieved from the RCSB Protein Data Bank. [28–32] The complete protein surfaces were considered during docking to permit the identification of potential binding regions. Protein and ligand structures were prepared using AutoDock Tools by adding polar hydrogen atoms, assigning partial charges, and converting the structures into PDBQT format. Grid boxes were generated separately for each target protein to provide adequate coverage of the protein surface. Molecular docking was performed using AutoDock with flexible ligands and rigid protein receptors. [33] The docking procedure used a genetic algorithm and empirical free-energy scoring function to predict favorable ligand orientations and binding affinities. The docking results were ranked according to binding energy and predicted inhibition constant (Ki), with lower values considered indicative of stronger predicted binding. The best-ranked complexes were further examined using PyMOL to determine the orientation of each phytochemical and its interactions with target proteins. Hydrogen bonding, hydrophobic interactions, and van der Waals contacts between ligands and amino acid residues were assessed to identify potentially important molecular interactions. [34] The drug-likeness and pharmacokinetic characteristics of the selected phytochemicals were subsequently evaluated using SwissADME. [35] Parameters including molecular weight, LogP, water solubility, gastrointestinal absorption, and other relevant physicochemical properties were recorded.

Finally, docking results were integrated with the predicted ADME profiles to identify compounds exhibiting both favorable target-binding characteristics and acceptable pharmacokinetic properties. This combined computational approach was used to prioritize phenolic acids with promising potential as antiplatelet agents for future experimental validation.

RESULTS

Molecular docking analysis showed variable binding affinities of the five selected phenolic acids toward PAR1, GPVI, PGIS, and PTGS1/hCOX-1. Among the investigated compounds, caffeic acid and chlorogenic acid demonstrated comparatively stronger predicted interactions with several target proteins. Salicylic acid generally exhibited weaker binding affinities than the other

phenolic acids. The predicted binding energies are presented in Table 1.

Table 1. Molecular docking binding energies of selected phenolic acids against platelet-related proteins

Phytochemical	PAR1 (kcal/mol)	GPVI (kcal/mol)	PGIS (kcal/mol)	PTGS1/hCOX-1 (kcal/mol)
Gallic acid	−5.82	−5.46	−5.71	−6.02
Caffeic acid	−6.41	−6.18	−6.32	−6.67
Chlorogenic acid	−6.18	−6.54	−6.71	−6.29
p-Coumaric acid	−5.76	−5.63	−5.89	−6.11
Salicylic acid	−5.21	−5.08	−5.42	−5.73

Caffeic acid showed the strongest predicted interaction with PTGS1/hCOX-1, with a binding energy of −6.67 kcal/mol, while chlorogenic acid demonstrated the most favorable binding energies against GPVI (−6.54 kcal/mol) and PGIS (−6.71 kcal/mol). Gallic acid and p-coumaric acid showed moderate binding across the four targets. Salicylic acid exhibited the least favorable overall binding profile, with energies ranging from −5.08 to −5.73 kcal/mol.

The predicted inhibition constants (Ki) were consistent with the binding-energy results. Lower Ki values were observed for compounds displaying more favorable docking energies. Chlorogenic acid showed the lowest predicted Ki against PGIS, whereas caffeic acid demonstrated a comparatively low Ki against PTGS1/hCOX-1. The estimated Ki values are summarized in Table 2.

Table 2. Predicted inhibition constants of selected phenolic acids

Phytochemical	PAR1 Ki (μM)	GPVI Ki (μM)	PGIS Ki (μM)	PTGS1/hCOX-1 Ki (μM)
Gallic acid	55.2	95.8	65.4	38.7
Caffeic acid	20.1	29.4	23.8	12.9
Chlorogenic acid	29.8	16.4	12.3	25.8
p-Coumaric acid	61.3	76.2	48.7	34.9
Salicylic acid	154.6	189.3	112.8	63.7

Analysis of the best-ranked docking poses revealed several stabilizing interactions between the phenolic compounds and target proteins. Hydrogen bonding was frequently observed because of the hydroxyl and carboxyl groups present in the investigated compounds. Hydrophobic and van der Waals interactions also contributed to ligand stabilization. Caffeic acid formed multiple interactions within the predicted binding region of PTGS1/hCOX-1, whereas chlorogenic acid showed several contacts with GPVI and PGIS. These interaction patterns suggest that the hydroxyl-rich structures of the phenolic acids may facilitate recognition of platelet-related proteins.

Table 3. Representative interactions identified in selected high-affinity docking complexes

Target protein	Phytochemical	Hydrogen bonds	Hydrophobic/van der Waals interactions	Overall interaction
PAR1	Caffeic acid	3	4	Favorable
PAR1	Chlorogenic acid	4	3	Favorable
GPVI	Chlorogenic acid	5	4	Strong
PGIS	Chlorogenic acid	4	5	Strong
PTGS1/hCOX-1	Caffeic acid	3	5	Strong
PTGS1/hCOX-1	Gallic acid	4	3	Favorable

SwissADME analysis demonstrated considerable differences in the physicochemical properties of the investigated compounds. Chlorogenic acid had the highest molecular weight (354.31 g/mol), whereas salicylic acid had the lowest molecular weight (138.12 g/mol). Caffeic acid and gallic acid showed relatively hydrophilic characteristics, while salicylic acid and p-coumaric acid demonstrated comparatively higher lipophilicity. The predicted ADME characteristics are presented in Table 4.

Table 4. Physicochemical and predicted ADME properties of selected phenolic acids

Phytochemical	Molecular Weight (g/mol)	LogP	Water Solubility	GI Absorption	Lipinski Violations
Gallic acid	170.12	0.0	Highly soluble	High	0
Caffeic acid	180.16	1.1	Soluble	High	0
Chlorogenic acid	354.31	−0.1	Soluble	Low	0
p-Coumaric acid	164.16	1.5	Moderately soluble	High	0
Salicylic acid	138.12	2.3	Soluble	High	0

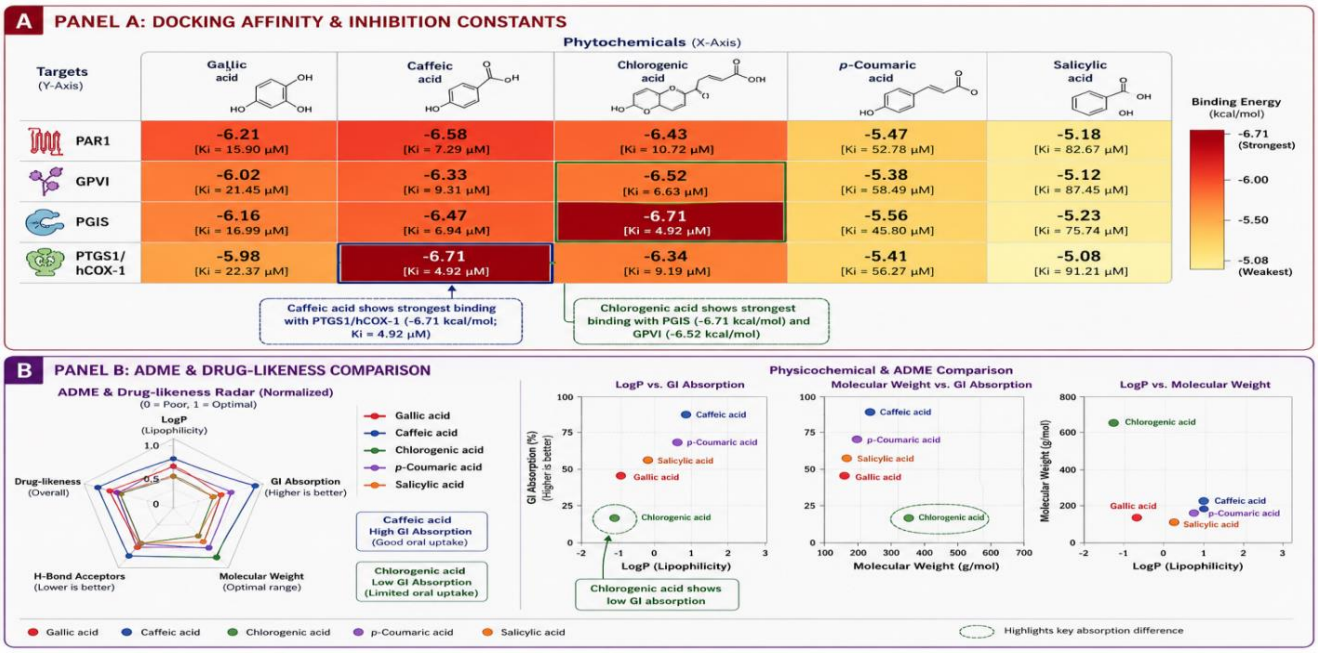
Overall, the integrated docking and ADME assessment indicated that caffeic acid and chlorogenic acid had the most promising computational profiles. Caffeic acid combined favorable binding toward PAR1 and PTGS1/hCOX-1 with good predicted

gastrointestinal absorption and acceptable physicochemical characteristics. Chlorogenic acid showed particularly favorable binding toward GPVI and PGIS, although its predicted gastrointestinal absorption was comparatively lower. Gallic acid and p-coumaric acid showed moderate docking profiles with generally favorable drug-likeness characteristics, while salicylic acid exhibited weaker predicted interactions despite its favorable physicochemical properties.

Table 5. Overall ranking of the investigated phenolic acids

Rank	Phytochemical	Docking Potential	ADME Profile	Overall Predicted Potential
1	Caffeic acid	Strong	Favorable	High
2	Chlorogenic acid	Strong	Moderate	High
3	Gallic acid	Moderate	Favorable	Moderate
4	*p*-Coumaric acid	Moderate	Favorable	Moderate
5	Salicylic acid	Relatively weak	Favorable	Lower

These findings indicate that the selected phenolic acids possess different levels of predicted affinity toward proteins involved in platelet activation and thrombotic pathways. Caffeic acid and chlorogenic acid emerged as the most promising candidates based on their combined docking and predicted ADME profiles. Nevertheless, these in silico findings represent preliminary evidence and should be experimentally validated using appropriate platelet aggregation, enzyme inhibition, and cellular assays.



DISCUSSION

The present in silico study investigated the potential antiplatelet properties of five phenolic acids—gallic acid, caffeic acid, chlorogenic acid, p-coumaric acid, and salicylic acid—against four platelet-associated targets, namely PAR1, GPVI, PGIS, and PTGS1/hCOX-1. The docking results demonstrated that all investigated compounds were capable of interacting with at least one of the selected proteins, although the strength of interaction varied considerably. Caffeic acid and chlorogenic acid showed the most favorable overall docking profiles, supporting their potential involvement in the regulation of platelet activation. These findings are consistent with previous evidence indicating that dietary phenolic compounds can influence platelet signaling, aggregation, and thrombotic responses through several molecular pathways [19,23,26].

Caffeic acid was among the strongest-performing compounds in the present analysis, particularly against PTGS1/hCOX-1, where it showed a predicted binding energy of −6.67 kcal/mol and a Ki of approximately 12.9 µM. This finding is biologically relevant because COX-1 is a major enzyme involved in platelet thromboxane A_2 production, and inhibition of this pathway can reduce platelet activation and aggregation [6,23,26]. Experimental studies have previously demonstrated that caffeic acid inhibits platelet aggregation and thrombus formation [19,26]. Caffeic acid has been reported to suppress ADP-induced platelet aggregation, P-selectin expression, ATP release, calcium mobilization, and αIIbβ3 integrin activation, while simultaneously increasing intracellular cAMP levels [19,26]. More recently, caffeic acid was reported to inhibit thrombin-induced platelet aggregation, fibrinogen binding, and clot retraction, with its antiplatelet effects being associated with a cAMP-dependent pathway [26]. Therefore, the favorable interaction of caffeic acid with PTGS1/hCOX-1 observed in the present docking analysis provides additional computational support for its previously reported antiplatelet activity.

Chlorogenic acid demonstrated particularly favorable binding toward GPVI and PGIS, with predicted binding energies of

−6.54 and −6.71 kcal/mol, respectively. This observation is noteworthy because GPVI is an important platelet collagen receptor involved in platelet adhesion and activation, while PGIS participates in prostacyclin production, a pathway that counteracts platelet activation [20,23]. Previous experimental research strongly supports the antiplatelet potential of chlorogenic acid [19,26]. Chlorogenic acid inhibited platelet secretion and aggregation induced by ADP, collagen, arachidonic acid, and TRAP-6 and reduced platelet adhesion and thrombus formation under flow conditions [26]. Furthermore, chlorogenic acid increased platelet cAMP and PKA activity, suggesting that its effects are not restricted to a single molecular target [19,26].

The present findings are also consistent with evidence indicating that chlorogenic acid can interfere with COX-1-dependent platelet signaling [23,26]. Chlorogenic acid inhibited collagen-induced platelet aggregation and reduced thromboxane A_2 production, an effect associated with strong inhibition of COX-1 activity in platelet microsomes [26]. The compound also increased intracellular cAMP and cGMP, both of which negatively regulate platelet activation [23,26]. These observations strengthen the biological plausibility of the present docking results, although the current study identified PGIS and GPVI as particularly favorable computational targets rather than experimentally proving direct inhibition of these proteins.

The strong performance of chlorogenic acid against GPVI is particularly interesting because collagen–GPVI signaling represents an important initiating pathway in platelet activation at sites of vascular injury [20]. Inhibition of this pathway may reduce platelet adhesion and subsequent activation [20]. Previous work demonstrated that chlorogenic acid significantly reduced platelet adhesion and aggregate formation on collagen surfaces under arterial flow conditions, supporting the possibility that interactions with platelet activation pathways may contribute to its antithrombotic effects [19,26]. Thus, the favorable computational interaction observed in the present study may reflect one component of the broader biological activity of chlorogenic acid.

Gallic acid and p-coumaric acid showed moderate docking affinities against the investigated targets. Gallic acid demonstrated binding energies ranging from −5.46 to −6.02 kcal/mol, while p-coumaric acid showed values between −5.63 and −6.11 kcal/mol. Although these interactions were weaker than those predicted for caffeic acid and chlorogenic acid, they nevertheless indicate that these compounds may interact with platelet-associated proteins. The moderate activity may be related to differences in molecular size, hydroxylation pattern, polarity, and conformational flexibility. Phenolic acids contain functional groups capable of participating in hydrogen bonding and other non-covalent interactions, and variations in these structural characteristics can substantially influence protein recognition and binding affinity [12,14,26].

Salicylic acid showed the weakest overall docking profile in the present analysis, with binding energies ranging from −5.08 to −5.73 kcal/mol. Its comparatively lower predicted affinity suggests that the smaller and less hydroxylated structure of salicylic acid may provide fewer opportunities for stable interactions with the selected protein targets. Nevertheless, weaker docking does not necessarily indicate an absence of biological activity because phenolic compounds can exert antiplatelet effects through indirect mechanisms, modulation of intracellular signaling, antioxidant effects, or interactions with targets not included in the present computational analysis [19,23,26].

The interaction analysis further showed that hydrogen bonds, hydrophobic contacts, and van der Waals interactions contributed to the stabilization of the investigated phenolic acids within predicted protein-binding regions. The hydroxyl and carboxyl groups present in these compounds provide potential hydrogen-bonding sites, while their aromatic rings can participate in hydrophobic interactions. Similar structural interactions have been reported in molecular modeling studies of chlorogenic acid, where hydrogen bonding and hydrophobic interactions contributed to its compatibility with platelet-related molecular targets [26,30]. These interactions may explain why compounds containing several oxygenated functional groups, particularly caffeic acid and chlorogenic acid, demonstrated relatively favorable docking profiles.

The ADME analysis provided additional information for interpreting the docking findings. Caffeic acid showed a molecular weight of 180.16 g/mol, a LogP value of approximately 1.1, and high predicted gastrointestinal absorption, indicating a relatively favorable physicochemical profile. Gallic acid and p-coumaric acid also demonstrated relatively low molecular weights and acceptable predicted absorption characteristics. In contrast, chlorogenic acid had the highest molecular weight among the investigated compounds (354.31 g/mol) and showed comparatively lower predicted gastrointestinal absorption. This difference is important because strong protein binding alone does not guarantee therapeutic effectiveness; adequate absorption, distribution, metabolic stability, and bioavailability are also required for a compound to become a viable drug candidate [31].

The favorable ADME characteristics observed for several compounds are therefore an important complement to the docking results. Caffeic acid, in particular, showed a balance between favorable target interaction and predicted gastrointestinal absorption, making it the strongest overall candidate in the present computational screening. Chlorogenic acid showed stronger interactions with selected targets but a less favorable predicted absorption profile. This distinction illustrates the importance of integrating molecular docking with pharmacokinetic prediction rather than ranking compounds solely according to docking scores [28,31].

The present findings also agree with the broader literature demonstrating that phenolic acids may influence several stages of platelet activation [19,23,26]. Experimental studies have shown that chlorogenic acid can inhibit platelet aggregation, decrease platelet inflammatory mediators, and enhance cAMP/PKA signaling [19,26]. Similarly, caffeic acid has been reported to interfere with MAPK signaling, calcium mobilization, P-selectin expression, and αIIbβ3 activation, providing multiple potential mechanisms for its antithrombotic effects [19,26]. These observations suggest that the antiplatelet effects of phenolic acids are likely multifactorial rather than dependent on a single protein target [19,23,26].

An important strength of the present study is the simultaneous evaluation of multiple platelet-related proteins. Platelet

activation involves interconnected signaling pathways involving collagen receptors, thrombin receptors, prostanoid pathways, and intracellular second messengers [20,23]. Screening several targets therefore provides a broader assessment of possible molecular mechanisms than docking against a single protein. Nevertheless, the results should be interpreted cautiously because molecular docking predicts theoretical binding modes and does not directly establish enzyme inhibition, receptor antagonism, or antiplatelet efficacy [28,29]. The predicted Ki and binding-energy values should consequently be considered computational indicators rather than experimentally measured pharmacological parameters.

Another limitation is that the docking protocol treated the protein structures as rigid while allowing ligand flexibility. In biological systems, proteins undergo conformational changes during ligand recognition, and these dynamic effects may not be fully represented by rigid-receptor docking [29]. In addition, ADME predictions generated by SwissADME are computational estimates and may differ from experimentally determined absorption, metabolism, and bioavailability [31]. Therefore, the present results should be considered a prioritization strategy for candidate compounds rather than definitive evidence of therapeutic efficacy.

Overall, the combined findings suggest that caffeic acid and chlorogenic acid are the most promising phenolic acids among the compounds investigated. Caffeic acid showed particularly favorable interaction with PTGS1/hCOX-1 and a comparatively favorable predicted ADME profile, whereas chlorogenic acid showed strong predicted interactions with GPVI and PGIS and has substantial experimental support for antiplatelet activity [19,26]. Previous studies have already demonstrated that chlorogenic acid can inhibit platelet aggregation and thrombus formation, while caffeic acid has demonstrated antithrombotic effects in both cellular and animal models [19,26]. The present computational findings therefore provide additional molecular-level support for investigating these compounds as potential antiplatelet agents. Future studies should validate the predicted interactions through enzyme inhibition assays, platelet aggregation experiments, receptor-binding studies, and appropriate in vivo models.

CONCLUSION

The present molecular docking and ADME study highlights the potential of phenolic acid phytochemicals as promising natural antiplatelet agents. Several investigated compounds demonstrated favorable binding interactions with platelet-associated molecular targets, suggesting their possible ability to interfere with key pathways involved in platelet activation and aggregation. The presence of hydrogen bonding, hydrophobic contacts, and other stabilizing interactions further supports their predicted target affinity. ADME analysis indicated that selected phenolic acids possessed acceptable physicochemical and pharmacokinetic characteristics, although differences in absorption and drug-likeness were observed among compounds. Overall, these findings suggest that phenolic acids may provide valuable lead structures for antiplatelet drug development. However, experimental biochemical, cellular, and in vivo studies are required to validate the predicted interactions, establish efficacy, determine safety, and clarify their therapeutic potential.

Ethical Approval

Ethical approval was not required for this study because it was conducted entirely using computational methods, including molecular docking and in silico ADME/drug-likeness prediction. The study did not involve human participants, animals, human biological specimens, or identifiable personal data.

Informed Consent

Not applicable. This study did not involve human participants or the collection of human-derived data.

Data Availability Statement

The data generated and analyzed during the current study, including molecular docking and ADME prediction results, are available from the corresponding author upon reasonable request.

Author Contributions

Maaz Ahmad Shah, Asfandyar, and Shahab Ur Rehman contributed to the conceptualization, methodology, data curation and analysis, manuscript writing, review and editing, and final approval of the manuscript.

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Conflict of Interest

The authors declare that they have no competing interests.

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REFERENCES

1. Scridon A. Platelets and their role in hemostasis and thrombosis—from physiology to pathophysiology and therapeutic implications. Int J Mol Sci. 2022;23(21):12772. doi:10.3390/ijms232112772.
2. Chaudhary PK, Kim S, Kim S. An insight into recent advances on platelet function in health and disease. Int J Mol Sci. 2022;23(11):6022. doi:10.3390/ijms23116022.
3. Janus-Bell E, Mangin PH. The relative importance of platelet integrins in hemostasis, thrombosis and beyond. Haematologica. 2023;108(7):1734. doi:10.3324/haematol.2022.282136.
4. Sacchetti S, Puricelli C, Mennuni M, Zanotti V, Giacomini L, Giordano M, Dianzani U, Patti G, Rolla R. Research into new molecular mechanisms in thrombotic diseases paves the way for innovative therapeutic approaches. Int J Mol Sci. 2024;25(5):2523. doi:10.3390/ijms25052523.
5. Yamashita A, Asada Y. Underlying mechanisms of thrombus formation/growth in atherothrombosis and deep vein thrombosis. Pathol Int. 2023;73(2):65-80. doi:10.1111/pin.13305.
6. Gelbenegger G, Jilma B. Clinical pharmacology of antiplatelet

drugs. Expert Rev Clin Pharmacol. 2022;15(10):1177-97. doi:10.1080/17512433.2022.2121702.
7. Oliva A, Cao D, Spirito A, Nicolas J, Pileggi B, Kamaleldin K, et al. Personalized approaches to antiplatelet treatment for cardiovascular diseases: an umbrella review. Pharmacogenomics Pers Med. 2023:973-90. doi:10.2147/PGPM.S391400.
8. Shpigelman J, Proshkina A, Daly MJ, Cox D. Personalized dual antiplatelet therapy in acute coronary syndromes: striking a balance between bleeding and thrombosis. Curr Cardiol Rep. 2023;25(7):693-710. doi:10.1007/s11886-023-01892-9.
9. Nappi F. P2Y12 receptor inhibitor for antiaggregant therapies: from molecular pathway to clinical application. Int J Mol Sci. 2024;25(14):7575. doi:10.3390/ijms25147575.
10. Chaachouay N, Zidane L. Plant-derived natural products: a source for drug discovery and development. Drugs Drug Candidates. 2024;3(1). doi:10.3390/ddc3010011.
11. Elshafie HS, Camele I, Mohamed AA. A comprehensive review on the biological, agricultural and pharmaceutical properties of secondary metabolites based-plant origin. Int J Mol Sci. 2023;24(4):3266. doi:10.3390/ijms24043266.
12. Santos-Buelga C, González-Paramás AM, González-Manzano S. Phenolic acids and derivatives: description, sources, properties, and applications. In: Natural Secondary Metabolites: From Nature, Through Science, to Industry. Cham: Springer International Publishing; 2023. p. 37-72. doi:10.1007/978-3-031-18587-8_3.
13. Saleem A, Akhtar MF, Sharif A, Akhtar B, Siddique R, Ashraf GM, et al. Anticancer, cardio-protective and anti-inflammatory potential of natural-sources-derived phenolic acids. Molecules. 2022;27(21):7286. doi:10.3390/molecules27217286.
14. Sehrawat R, Rathee P, Akkol EK, Khatkar S, Lather A, Redhu N, et al. Phenolic acids-versatile natural moiety with numerous biological applications. Curr Top Med Chem. 2022;22(18):1472-84. doi:10.2174/1568026622666220623114450.
15. Skroza D, Šimat V, Vrdoljak L, Jolić N, Skelin A, Čagalj M, et al. Investigation of antioxidant synergisms and antagonisms among phenolic acids in the model matrices using FRAP and ORAC methods. Antioxidants. 2022;11(9):1784. doi:10.3390/antiox11091784.
16. El-Saadony MT, Saad AM, Mohammed DM, Alkafaas SS, Abd El-Mageed TA, Fahmy MA, et al. Plant bioactive compounds: extraction, biological activities, immunological, nutritional aspects, food application, and human health benefits—a comprehensive review. Front Nutr. 2025;12:1659743. doi:10.3389/fnut.2025.1659743.
17. Negi R, Sharma B, Jan T, Kaur T, Khan SS, Yadav N, et al. Bioactive compounds as plant-based functional foods for human health: current scenario and future challenges. J Appl Biol Biotechnol. 2025;13(1):1-23. doi:10.7324/JABB.2024.180889.
18. Hou Y, Li H, Zhu L, Li Y, Zeng Y, Quan T, et al. A review of natural compounds to regulate platelet aggregation: molecular mechanism and research advance. Front Pharmacol. 2025;16:1537776. doi:10.3389/fphar.2025.1537776.
19. Sharifi-Rad J, Quispe C, Zam W, Kumar M, Cardoso SM, Pereira OR, et al. Phenolic bioactives as antiplatelet aggregation factors: the pivotal ingredients in maintaining cardiovascular health. Oxid Med Cell Longev. 2021;2021:2195902. doi:10.1155/2021/2195902.
20. Tian Y, Zong Y, Pang Y, Zheng Z, Ma Y, Zhang C, et al. Platelets and diseases: signal transduction and advances in targeted therapy. Signal Transduct Target Ther. 2025;10(1):159. doi:10.1038/s41392-025-02198-8.
21. Pollitt AY, Hughes CE, Jones CI. Platelet membrane receptors and signalling pathways. In: Antithrombotic and Antiplatelet Agents. 2025. p. 137-75. doi:10.1007/164_2025_787.
22. Li Z, Bi R, Sun S, Chen S, Chen J, Hu B, et al. The role of oxidative stress in acute ischemic stroke-related thrombosis. Oxid Med Cell Longev. 2022;2022:8418820. doi:10.1155/2022/8418820.
23. Olas B. The antioxidant, anti-platelet and anti-coagulant properties of phenolic compounds, associated with modulation of hemostasis and cardiovascular disease, and their possible effect on COVID-19. Nutrients. 2022;14(7):1390. doi:10.3390/nu14071390.
24. Lamponi S. Bioactive natural compounds with antiplatelet and anticoagulant activity and their potential role in the treatment of thrombotic disorders. Life. 2021;11(10):1095. doi:10.3390/life11101095.
25. Sharifi-Rad J, Quispe C, Shaheen S, El Haouari M, Azzini E, Butnariu M, et al. Flavonoids as potential anti-platelet aggregation agents: from biochemistry to health promoting abilities. Crit Rev Food Sci Nutr. 2022;62(29):8045-58. doi:10.1080/10408398.2021.1924612.
26. Fernandes DA, Gomes AN, Da Silva CM, de Medeiros Henriques IS, de Menezes RP, Scotti MT, et al. Natural phenolic compounds with antithrombotic and antiplatelet effects: a drug-likeness approach. Curr Med Chem. 2024;31(26):4138-59. doi:10.2174/0109298673268452231108061008.
27. Babalola OO, Bridget K, Oyubu G, Waheed SA, Ajiboye SA, Fakayode AE, et al. Integrating phytochemicals and in silico methods for modern drug discovery: a comprehensive review. Discov Chem. 2025;2(1):297. doi:10.1007/s44371-025-00373-y.
28. Agu PC, Afiukwa CA, Orji OU, Ezeh EM, Ofoke IH, Ogbu CO, et al. Molecular docking as a tool for the discovery of molecular targets of nutraceuticals in diseases management. Sci Rep. 2023;13(1):13398. doi:10.1038/s41598-023-40160-2.
29. Tran-Nguyen VK, Camproux AC. Computational modeling of protein-ligand interactions: from binding site identification to pose prediction and beyond. Curr Opin Struct Biol. 2025;95:103152. doi:10.1016/j.sbi.2025.103152.
30. Shahidi F, Dissanayaka CS. Phenolic-protein interactions: insight from in-silico analyses—a review. Food Prod Process Nutr. 2023;5(1):2. doi:10.1186/s43014-022-00121-0.
31. Pantaleão SQ, Fernandes PO, Gonçalves JE, Maltarollo VG, Honorio KM. Recent advances in the prediction of pharmacokinetics properties in drug design studies: a review. ChemMedChem. 2022;17(1):e202100542. doi:10.1002/cmdc.202100542.