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In silico molecular docking analysis of quinaldic acid against cancer related targets

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ABSTRACT

The present study investigated the pharmacokinetic properties of quinaldic acid (QA) and the molecular interactions between QA and the breast cancer related protein targets by computational techniques. ADME prediction performed using the SwissADME revealed drug like features, including good absorption in gastrointestinal tract, blood-brain barrier penetration, medium lipophilicity, high bioavailability and absence of P-glycoprotein prediction. Moreover, the BOILED-Egg approach suggested good oral absorption and brain penetration. Molecular docking studies done using AutoDock Vina showed that QA has strong affinity towards several proteins associated with carcinogenesis. QA exhibited the strongest binding affinity toward BRCA2 (-8.4 kcal/mol), followed by iNOS (-7.3 kcal/mol), p53 (-7.2 kcal/mol), TNF-α (-7.2 kcal/mol), COX-2 (-7.2 kcal/mol), caspase-9 (-6.6 kcal/mol), caspase-3 (-6.3 kcal/mol), Bax (-6.3 kcal/mol), Bcl-2 (-6.0 kcal/mol), Nfkb (-5.8 kcal/mol), IL-6 (-5.5 kcal/mol) and BRCA1 (-5.2 kcal/mol). Based on the observed binding effects, there is an indication that QA can have interactions with proteins related to pathways of apoptosis, inflammation and DNA repair. The strong binding interactions of QA suggest that it can be considered for further *in vitro* and *in vivo* experimental studies of cancer prevention.

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INTRODUCTION

Cancer continues to be one of the serious public health problems around the world. One in six people dying from cancer around the world and is one of the three leading causes of death around the globe. Cancer also becomes health concern due to its impact on quality of life and economic burden (Bray *et al.*, 2022). Breast cancer is one of the most prevalent form of cancer among all other forms of cancers as well as one of the commonest causes of death in women. According to the data reported in 2022, around 2.3 million new breast cancer cases have been diagnosed throughout the world. Making up approximately a quarter of all cases of cancer among women. Breast cancer mortality is relatively higher in developing countries due to delayed diagnosis, lack of health care facilities and limited advanced treatment options (Łukasiewicz *et al.* 2021). In India, breast cancer affected 1,92,020 new cases and caused 98,337 deaths in 2022 (Bray *et al.* 2022; Freihat *et al.* 2025).

Breast cancer progression involves the accumulation of genetic and molecular changes in the cell that disturb the cellular balance. Genetic changes in the breast cancer tumor suppressor genes such as BRCA1 and BRCA2 contribute to about 5-10% of the hereditary breast cancer cases and enhance disease susceptibility significantly. The BRCA proteins maintain the genome stability through the regulation of homologous recombination DNA repair mechanisms and chromosome stability. Inactivation of BRCA1 and 2 leads to genome instability and carcinogenesis, causing an increased risk of developing early onset and aggressive breast cancer (Albert *et al.* 2020; Georgy *et al.* 2026).

In addition to genetic instability, oxidative stress, chronic inflammation and dysregulated apoptosis are key mechanisms that promote breast cancer initiation and progression (Gupta *et al.* 2009; Dandoti *et al.* 2024). Excessive production of reactive oxygen and nitrogen species induces oxidative damage to DNA, proteins and lipids, resulting in genomic instability and activation of oncogenic signaling pathways (Dong *et al.* 2025). Persistent oxidative stress also stimulates chronic inflammatory responses characterized by increased expression of cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS), nuclear factor-κB (NF-κB), tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), thereby favoring a tumor-promoting microenvironment (Nishida *et al.*, 2025).

Cancer cells evade programmed cell death through alterations in key apoptotic regulators.

The tumor suppressor p53, anti-apoptotic protein Bcl-2, pro-apoptotic protein Bax and the executioner caspases (caspase-3 and caspase-9) and cytochrome c together regulate the intrinsic apoptotic pathway. Dysregulation of these proteins promotes uncontrolled cell proliferation and therapeutic resistance, making them attractive molecular targets for anticancer drug discovery (Carneiro *et al.* 2020). Thus, proteins involved in DNA repair, inflammation and apoptosis serve as promising therapeutic targets for the development of novel cancer interventions.

Molecular docking has emerged as a valuable computational approach for identifying potential ligand-protein interactions, predicting binding affinities and characterizing the amino acid residues involved in molecular recognition before experimental validation (Ma *et al.* 2024). AutoDock Vina is one of the most widely used docking platforms for predicting ligand-binding conformations and estimating binding energies using an efficient search algorithm and scoring function (Trott and Olson 2010). In addition, early evaluation of pharmacokinetic characteristics is an important step in drug discovery. The SwissADME web server enables prediction of absorption, distribution, metabolism and excretion (ADME) properties of a compound. ADME predicts gastrointestinal absorption, oral bioavailability, blood-brain barrier permeability and drug-likeness as well (Daina *et al.* 2017), thereby facilitating the identification of promising lead compounds.

Quinaldic acid (quinoline-2-carboxylic acid) (Fig.1) is a biologically active quinoline derivative that has attracted increasing attention because of its diverse pharmacological activities. It is an endogenous metabolite of the kynurenine pathway of tryptophan metabolism. It is generated through the dehydroxylation of kynurenic acid by intestinal microbiota (Badawy *et al.* 2017). QA has also been isolated from natural sources such as *Ephedra pachyclada*. Previous studies have demonstrated the anti-inflammatory, antibacterial, antiviral, antidiabetic and anticancer activities of QA and quinoline derivatives (Langner *et al.* 2015; Okamoto *et al.* 1973; Tamilarasi *et al.* 2026). However, despite these promising biological activities, its molecular targets, binding interactions and mechanistic relevance in cancer remain poorly understood. Therefore, the present study has to investigated the molecular interactions of QA with key proteins involved in breast cancer pathogenesis (BRAC1 and 2) and other molecular markers including apoptosis-related proteins (p53, caspase-3, caspase-9, Bcl-2 and Bax) and inflammatory mediators (COX-2, iNOS, NF-κB, IL-6 and TNF-α), using molecular docking analysis. Furthermore, SwissADME was employed to evaluate the pharmacokinetic and drug-likeness properties of QA.

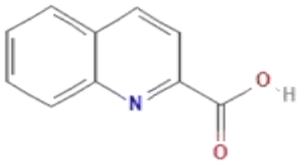

Fig. 1. Shows the molecular structure of QA

MATERIALS AND METHODS

In silico adme analysis

The pharmacokinetic properties of QA were predicted using the SwissADME web server (https://www.swissadme.ch/). The Simplified Molecular Input Line Entry System (SMILES) structure of QA was uploaded to the server and key ADME parameters, including gastrointestinal (GI) absorption, blood-brain barrier (BBB) permeability, P-glycoprotein (P-gp) substrate status, cytochrome P450 (CYP) enzyme inhibition and drug-likeness were evaluated. Gastrointestinal absorption and brain penetration were predicted using the BOILED-Egg model implemented in the SwissADME platform.

Molecular docking analysis

Ligand preparation

The three-dimensional (3D) structure of QA (PubChem CID: 5281647) was retrieved from the PubChem database. The ligand structure was visualized and prepared using PyMOL (Version 3.1) and the structure was converted into Protein Data Bank (PDB) format. Ligand preparation was subsequently performed using MGL Tools (Version 1.5.7), which included the addition of hydrogen atoms, assignment of Gasteiger charges and definition of rotatable bonds. The prepared ligand was then saved in PDBQT format for molecular docking analysis.

Protein preparation

The crystallographic structures of breast cancer-associated target proteins were retrieved from the RCSB Protein Data Bank (https://www.rcsb.org/). The selected inflammation-related targets included tumor necrosis factor-α (TNF-α; PDB ID: 1TNF), nuclear factor-κB (NF-κB; PDB ID: 1NFI), interleukin-6 (IL-6; PDB ID: 1ALU), cyclooxygenase-2 (COX-2; PDB ID: 5KIR) and inducible nitric oxide synthase (iNOS; PDB ID: 4NOS). The apoptosis-related proteins included B-cell lymphoma-2 (Bcl-2; PDB ID: 2WCL), caspase-3 (PDB ID: 5I9B), caspase-9 (PDB ID: 2AR9), Bcl-2-associated X protein (Bax; PDB ID: 4SO0) and tumor protein p53 (PDB ID: 2OCJ). In addition, the DNA repair proteins breast cancer susceptibility protein 1 (BRCA1; PDB ID: 1JNX) and breast cancer susceptibility protein 2 (BRCA2; PDB ID: 1NoW) were included in the study.

Protein preparation was performed using AutoDock Tools (Version 1.5.7) within the MGL Tools suite. Prior to docking, all water molecules, co-crystallized ligands and non-essential heteroatoms were removed from the protein structures. Polar hydrogen atoms were added and Kollman united atom charges were

assigned to each protein. The prepared protein structures were subsequently saved in PDBQT format for molecular docking analysis.

Binding site prediction

Potential ligand-binding sites of the target proteins were identified using the Computed Atlas of Surface Topography of Proteins (CASTp) server (Version 3.0). CASTp predicts solvent-accessible surface pockets and internal cavities based on the three-dimensional structure of proteins. For each target protein, the binding pocket with the largest surface area and volume corresponding to the reported functional region was selected for molecular docking. The docking grid box was defined to completely encompass the selected binding pocket and its surrounding amino acid residues. The grid box center coordinates were determined based on the geometric centroid of the selected binding pocket.

Molecular docking and interaction analysis

Molecular docking of QA with the selected target proteins was performed using AutoDock Vina (Version 1.2.0). The ligand was treated as fully flexible by allowing rotation around all rotatable bonds, whereas the protein receptors were considered rigid throughout the docking simulations, which were performed using the default AutoDock Vina parameters. For each target protein, the docking pose with the lowest predicted binding free energy (kcal/mol) was selected as the optimal binding conformation. Protein-ligand interactions were subsequently analyzed using BIOVIA Discovery Studio Client 2025 (Version 25.1.0.0). Two-dimensional (2D) and three dimensional (3D) interaction maps were generated to identify and characterize key interactions between QA and amino acid residues within the binding pocket (hydrogen bonds, hydrophobic interactions, electrostatic interactions, π-interactions and other non-covalent contacts).

RESULTS

Pharmakinetic profile of QA

BOILED (Brain or intestinal estimated permeation)-Egg analysis

QA is located in the yellow yolk region of the BOILED-Egg model, suggesting a high likelihood of BBB penetration. This suggests that QA possesses physicochemical properties favorable for central nervous system (CNS) accessibility. Simultaneously, its placement also overlaps with the white region, implying good gastrointestinal absorption following oral administration. This suggests that QA is predicted to be both orally absorbable and capable of reaching the central nervous system after systemic exposure. QA was predicted to be a non-substrate of P-glycoprotein, indicating a lower probability of active efflux and supporting improved intracellular retention, as indicated by the red circular marker (Fig 2).

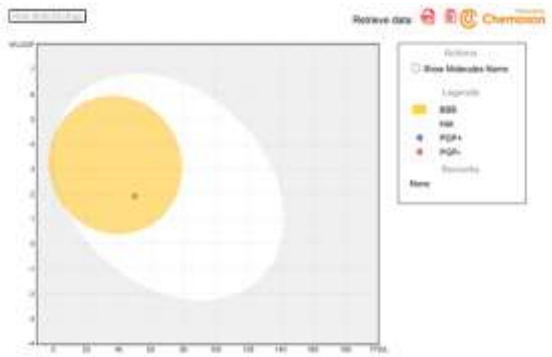

Fig. 2. Illustrates the BOILED-Egg model of QA's ADME prediction

ADME (absorption, distribution, metabolism and excretion) prediction of QA

QA possessed good predicted pharmacokinetics profile. It has a molecular formula $C_{10}H_7NO_2$ and a molecular weight of 173.17 g/mol, which indicates, it has all the necessary properties to be considered as a promising drug candidate. QA has 13 heavy atoms, 10 aromatic heavy atoms, 1 rotatable bond, 3 hydrogen bond acceptor and 1 hydrogen bond donor. Its topological polar surface area is 50.19 $Å^2$ which means that it has suitable polarity to be absorbed in the intestine.

Lipophilicity of QA was found moderate with the log P value of 1.57, which indicates that the compound has balanced hydrophilic-lipophilic character. The other models of lipophilicity also agreed with this result where iLOGP= 1.25, XLOGP3= 2.63, WLOGP= 1.93, MLOGP= 0.23 and SILICOS-IT=

1.82. Moderately lipophilic compounds are preferable as far as membrane permeability through passive diffusion and good water solubility are concerned.

This compound was predicted to have good water solubility with log S value ranging from -3.07 to -3.33. This compound was expected to show high absorption through the gastrointestinal tract and had the potential for oral bioavailability. The other property that was expected from this compound is its BBB permeation ability, which suggests that the drug can reach the central nervous system. The other expected property of the drug is that it is not a substrate of P-gp. The predicted skin permeation coefficient (Log Kp = -5.49 cm/s) indicates low dermal permeability, suggesting that QA is unlikely to be efficiently absorbed through the skin.

QA was expected to be an inhibitor of CYP1A2 enzyme but not an inhibitor of CYP2C19, CYP2C9, CYP2D6 and CYP3A4 enzymes. Thus, metabolic property indicates a reduced possibility of adverse cytochrome P450-mediated drug interactions with the major metabolic enzymes. Drug likeness prediction studies demonstrated that QA is a good candidate for an oral active small molecule. QA adhered to all Lipinski's Rules of Five, Ghose, Veber and Egan filters without any Lipinski rule violations. In addition, it obtained bioavailability score 0.85, which indicates good oral bioavailability. QA had however, one violation of Muegge filter, which considered QA is not a lead-like owing to the low value of its molecular weight (<200 g/mol). This does not however affect its medicinal properties. From the medicinal chemistry perspective, QA showed no PAINS or Brenk alerts, indicating the absence of structurally hindering or assay-interfering substructures that are commonly associated with false-positive biological activity. Moreover, the synthetic accessibility score of 1.21 suggests that the compound is relatively easy to synthesize, which is advantageous for future medicinal chemistry optimization and large-scale production. Pharmacokinetic data for QA are summarized in Table 1.

Table 1. Pharmakinetic profiling of QA

Category	Parameter	Output
Physicochemical properties	Molecular Formula	C10H7NO2
	Molecular Weight	173.17 g/mol
	Heavy atoms	13
	Aromatic heavy atoms	10
	Fraction Csp^3	0.00
	Rotatable bonds	1
	H-bond acceptors	3
	H-bond donors	1
	Molar refractivity	48.70
	TPSA	50.19 $Å^2$
Lipophilicity	iLOGP	1.25
	XLOGP3	2.63
	WLOGP	1.93
	MLOGP	0.23
	SILICOS-IT	1.82
	Consensus Log $P_{o/w}$	1.57
Water Solubility	Log S (ESOL)	-3.07
	Solubility (ESOL)	1.46e-01 mg/mL ; 8.44e-04 mol/L
	Log S (Ali)	-3.33
	Solubility (Ali)	8.02e-02 mg/mL ; 4.63e-04 mol/L
	Log S (SILICOS-IT)	-3.07
	Solubility (SILICOS-IT)	1.47e-01 mg/mL ; 8.51e-04 mol/L
	Solubility class	Soluble
Pharmacokinetics	GI absorption	High
	BBB permeant	Yes
	P-gp substrate	No
	CYP1A2 inhibitor	Yes

	CYP2C19 inhibitor	No
	CYP2C9 inhibitor	No
	CYP2D6 inhibitor	No
	CYP3A4 inhibitor	No
	Log Kp (skin permeation)	-5.49 cm/s
Drug-Likeness	Lipinski rule	Yes (0 violations)
	Ghose filter	Yes
	Veber rule	Yes
	Egan rule	Yes
	Muegge rule	No (1 violation: MW < 200)
	Bioavailability score	0.85
Medicinal Chemistry	PAINS alerts	0
	Brenk alerts	0
	Lead-likeness	No (1 violation: MW < 250)
	Synthetic accessibility	1.21

RESULTS

Docking analysis with apoptosis-related proteins

The interaction between QA and its effect on modulation of the apoptotic proteins (p53, caspase-9 and 3, Bax and Bcl-2), was determined by molecular docking analysis (Fig 3 and Table 2).

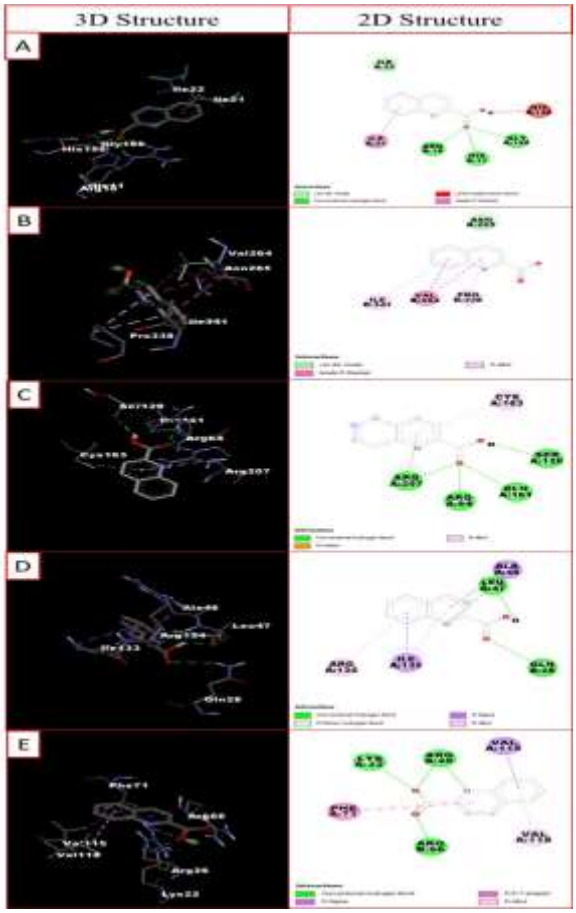

Fig. 3. 2D and 3D interactions of QA with apoptosis associated related proteins. A) P53 B) Caspase-9 C) Caspase-3 D) Bax E) Bcl-2 proteins interactions with QA

QA showed greater binding affinity towards the pro-apoptotic proteins compared to the anti-apoptotic protein Bcl-2. Among the all targets considered, QA showed the greatest predicted binding affinity towards p53 (-7.2 kcal/mol). This protein-ligand complex is stabilized by Hydrogen bonding, van der waals forces and amide-π stacking interactions with involving the amino acid residues Ile22, Ile21, Arg10, His11, Gly199 and His198. These amino acid residues are present in the functionally important site of the p53 protein.

A favorable binding affinity was also observed with caspase-9 (-6.6 kcal/mol) with amino acid residues such as ASN265, VAL264, ILE341 and PRO338 these interaction stailized by stabilized by van der Waals, amide-π stacking and π-alkyl, indicating efficient interaction within the catalytic domain. The pro-apoptotic protein caspase-3 (-6.3 kcal/mol) and Bax (-6.3 kcal/mol) also showed favourable binding interactions. These interactions stabilized by H-bond, π-cation, π-alkyl, π-sigma, π -donor H-bond with amino acid residues Ser120, Arg64, Gln161, Arg207, Cys163 in caspase-3 and H-bond, π-sigma, π-alkyl, π -donor H-bond in Bax., indicating potential involvement in mitochondrial outer membrane permeabilization. In contrast, QA showed comparatively lower binding affinity toward the anti-apoptotic protein Bcl-2 (-6.0 kcal/mol). The interaction was mainly mediated by H-bond, π-sigma, π–π T-shaped and π-alkyl with amino acid residues such as Lys22, Arg26, Arg66, Val115, Val118, Phe71, indicating weaker stabilization relative to pro-apoptotic targets.

Table 2. Molecular docking interactions profile of QA with cancer associated apoptosis-related proteins

Target protein	Binding energy (kcal/mol)	Key interacting residues	Interactions
p53	-7.2	Ile22, Ile21, Arg10, His11, Gly199, His198	Hydrogen bonding, van der waals forces and amide-π stacking interactions
Caspase-9	-6.6.	Asn265, Val264, Pro338, Ile341	van der Waals, amide-π stacking, π-alkyl
Caspase-3	-6.3	Ser120, Arg64, Gln161, Arg207, Cys163	H-bond, π-cation, π-alkyl
Bax	-6.3	Ala46, Leu47, Ile133, Arg134, Gln28	H-bond, π-sigma, π-alkyl, π -donor H-bond
Bcl-2	-6.0	Lys22, Arg26, Arg66, Val115, Val118, Phe71	H-bond, π-sigma, π–π T-shaped, π-alkyl

Table 3. Molecular docking interactions profile of QA with cancer associated inflammatory signaling proteins

Target protein	Binding energy (kcal/mol)	Key interacting residues	Major Interaction Types
iNOS	-7.3	ARG381, TRP461, TRP463, SER118, TRP90, MET120, PHE476	H-bond, π-π stacking, π-sulfur, π-cation, C-H bond
TNF-α	-7.2	TYR119 (2), GLN61, PRO117 (2)	H-bond, π-alkyl, π-donor H
COX-2	-7.2	VAL349, ALA523, VAL527, GLY526	C-H bond, π-σ, amide-π stacking, π-alkyl
NF-κB	-5.8	ARG73, ASN139	H-bond
IL-6	-5.5	THR43, ASP160, THR163, ARG104	H-bond, π-alkyl

Docking analysis with inflammatory signaling proteins

The binding interaction between QA and inflammatory associated proteins such as TNF-α, iNOS, COX-2), NF-κB and IL-6 showed in Table 3 and Fig. 4.

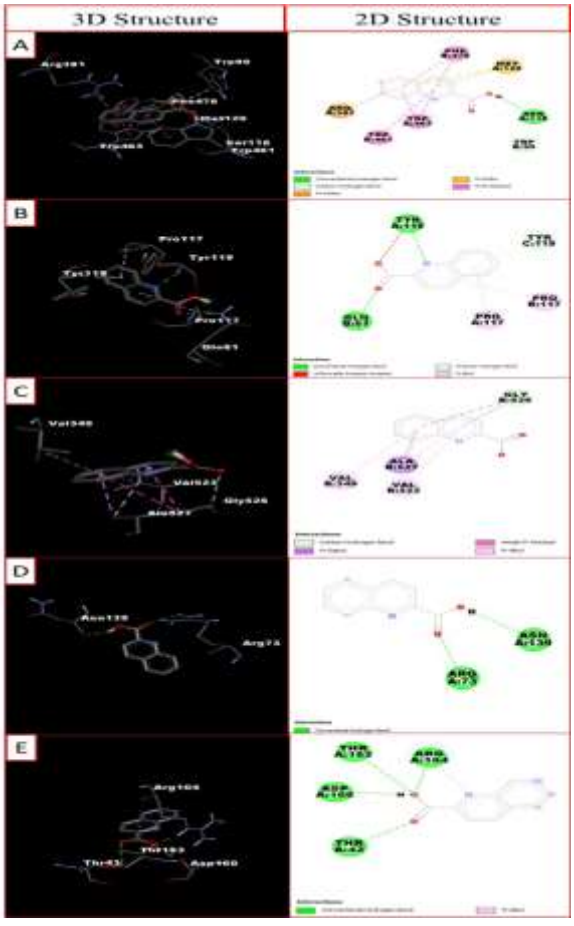

Fig. 4. 2D and 3D interactions of QA with cancer-associated inflammation-related proteins. A) iNOS B) TNF-α C) COX-2 D) NF-κB E) IL-6 proteins interactions with QA

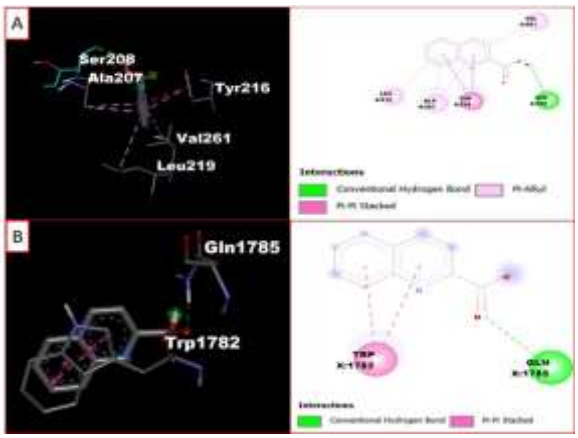

Fig. 5. Shows the 2D and 3D interactions of QA with breast cancer- susceptibility proteins. A) BRAC2 and B) BRAC1

The highest binding energy was noticed to be for iNOS (-7.3 kcal/mol). The interaction between the ligand and protein was formed via H-bond, π-π stacking, π-sulfur, π-cation, C-H bond and interactions with ARG381, TRP461, TRP463, SER118, TRP90, MET120, PHE476 amino acids residues.

Followed by the strong binding was observed in TNF-α (-7.2 kcal/mol) and COX-2 (-7.2 kcal/mol) with amino acid residues such as TYR119 (2), GLN61 and PRO117 (2) and VAL349, ALA523, VAL527 and GLY526,

respectively. These interactions were stabilized by H-bond, π-alkyl, π-donor H, C-H bond, π-σ and amide-π stacking. Comparatively, the lowest binding affinity was observed in NF-κB (-5.8 kcal/mol) followed by IL-6 (-5.5 kcal/mol). These predicted binding affinities were stabilized by amino acid residues such as ARG73, ASN139 and THR43, ASP160, THR163, ARG104, respectively, through H and π-alkyl bonds.

Table 4. Molecular docking interaction profile of QA with breast cancer susceptibility proteins

Target protein	Binding energy (kcal/mol)	Key interacting residues	Major interaction types
BRCA2	-8.4	VAL261, SER208, TYR216, ALA207, LEU219	H-bond, π-alkyl, π-π stacking
BRCA1	-5.2	TRP1782, GLN1785	H-bond, π-π stacking

Docking Analysis with Breast Cancer Susceptibility Proteins (BRCA1 and BRCA2)

The strongest binding affinity was observed with BRCA2 (-8.4) with amino acid residues such as VAL261, SER208, TYR216, ALA207 and LEU219 and stabilized by H-bond, π-alkyl and π-π stacking, suggesting the formation of a highly stable ligand-protein complex and effective accommodation of QA's within the binding pocket. In contrast, QA demonstrated a moderate binding affinity toward BRCA1 (-5.2 kcal/mol). Thee ligand-protein complex was stabilized by H-bond, and π-π stacking with interactions TRP1782, GLN1785 amino acid residues (Table 4 and Fig. 5).

DISCUSSION

Breast cancer remains a major global health challenge and current therapeutic strategies are often limited by drug resistance, systemic toxicity and suboptimal pharmacokinetic properties (Tufail *et al.* 2022; Cemali *et al.* 2025). Therefore, growing interest in identifying small bioactive molecules capable of multitarget modulation with improved safety and favorable drug-like characteristics are in progress. QA, a quinoline-derived compound has been attracted considerable attention due to its antioxidant, anti-inflammatory, antidiabetic and anticancer activities (Tamilarasi *et al.* 2026). However, its molecular mechanisms underlying anticancer activity remain poorly understood. Therefore, the present study employed integrated molecular docking and in silico pharmacokinetic analyses to investigate the potential interactions of QA with cancer-associated molecular targets, including breast cancer associated genes.

ADME prediction and the BOILED-Egg approach have become essential components in early-stage drug discovery for the assessment of pharmacokinetic properties of prospective molecules. The molecules demonstrating high absorption rate in the gastrointestinal tract, moderate lipophilicity and good oral bioavailability are usually considered as good drug candidates (Daina *et al.* 2016). In the current research, QA demonstrated all these favourable ADME properties. In addition, QA does not belong to the substrates of P-glycoprotein and thus is less likely to demonstrate active efflux. Furthermore, QA did not inhibit the activity of major CYP enzymes. These characteristics making it less susceptible to cause the drug-drug interactions (Deodhar *et al.* 2020).

The BOILED-Egg model offers an easy visual prediction of gastrointestinal absorption and BBB penetration (Daina *et al.* 2016). According to the BOILED-Egg plot, compounds with high probability of human intestinal absorption to be present in the white area (egg white), while compounds with a high probability of blood-brain barrier permeability to be located in the yellow area (egg yolk). Compounds found in areas other than these two are generally considered poor absorbtion with low BBB permeability (Islam *et al.* 2025). The QA molecule was placed in the yellow egg yolk area close to the white region, implying its high gastrointestinal absorption and the ability to pass through the blood-brain barrier.

Apoptosis is a strictly controlled type of programmed cell death, crucial for the maintenance of tissue homeostasis by removal of the dysfunctional and

malignant cells (Mustafa *et al.* 2024). The current study showed favorable binding ability of QA to apoptosis-regulating proteins. The strong binding ability of QA with p53 suggested that such interactions might affect p53-regulated cell cycle arrest and apoptosis (Marvalim *et al.* 2023). On the other hand, due to its high binding affinities towards caspase-9, caspase-3 and Bax suggested that, QA interacted with proteins associated with the intrinsic mitochondrial pathway of apoptosis. In addition, the relatively low binding affinity towards the anti-apoptotic protein Bcl-2, indicated less interaction between QA and survival-related proteins. Overall, these binding profiles suggest that QA may preferentially interact with proteins involved in apoptosis, although further experimental studies are necessary to determine the functional significance of these interactions.

Chronic inflammation has been found to play an essential role in the initiation and progression of carcinogenesis (Danforth *et al.* 2021). In this study, QA was found to have strong binding affinity for key inflammatory mediators like iNOS, TNF-α and COX-2, which are reported as the major causative agents in inflammation-induced carcinogenesis (Myśliwiec *et al.* 2025; Valenzuela-Cardenas and Nowicki 2026). The high binding affinity for iNOS suggested that QA has the ability to modulate the production of nitric oxide and oxidative stress. Similarly, interaction with TNF-α can affect the inflammatory signaling pathways. The favourable binding affinities of QA with NF-κB and IL-6, suggested that QA could modulate inflammatory transcriptional and cytokine signaling pathways. Overall, docking analysis showed that QA has the ability to interact with various inflammatory proteins associated with carcinogenesis.

Tumor suppressor proteins associated with breast cancer BRCA1 and BRCA2, are essential regulators of genomic stability and mediate the repair of DNA double-strand breaks through the homologous recombination pathway (Liu *et al.* 2001; Georgy *et al.* 2026). In the present study, QA exhibited a stronger binding affinity toward BRCA2 than BRCA1, suggesting that BRCA2 may represent a more favourable molecular target. Since BRCA2 plays a central role in regulating RAD51-mediated homologous recombination and maintaining genomic stability (Holloman *et al.* 2011), its strong interaction with QA may be relevant to the compound's molecular activity. Interaction to BRCA2 suggests a potential influence on DNA double-strand break repair mechanisms, which are critical for preserving genome integrity and preventing tumor progression. Although the interaction with BRCA1 was comparatively moderate, the observed binding also suggests a possible association with DNA damage response pathways. These findings indicated that QA could interact with proteins involved in DNA repair mechanisms.

In summary, the *in silico* ADME screening showed that QA has multiple desirable pharmacokinetic and drug-likeness properties such as high oral absorption, moderately high lipophilicity, considerable water solubility, BBB permeability, low efflux potential by P-glycoprotein and satisfaction of multiple drug-likeness filters. Furthermore, the PAINS and Brenk alerts observations explored it as a very promising lead compound for further small molecule-based drug design.

CONCLUSION

The integrated ADME, BOILED-Egg and molecular docking analyses indicated that QA possesses favourable pharmacokinetic characteristics and exhibits promising interactions with proteins involved in apoptosis, inflammation and DNA repair pathways associated with carcinogenesis. The observed findings revealed QA as attractive lead compound for further research. Further extensive in vitro and in vivo studies are needed to confirm its biological activity and mechanisms against carcinogenesis.

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REFERENCES

Albert C, Haase M, Albert A, Kropf S, Bellomo R, Westphal S, Westerman M, Braun-Dullaeus RC, Haase-Fielitz A, Lee A, Moon BI. 2020. BRCA1/BRCA2 pathogenic variant breast cancer: treatment and prevention strategies. Annals of Laboratory Medicine **40(2)**, 114-121.

Badawy AA. 2017. Kynurenine pathway of tryptophan metabolism: Regulatory and functional aspects. International Journal of Tryptophan Research **10**, 1178646917691938.

Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. 2024. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians **74(3)**, 229-263.

Carneiro BA, El-Deiry WS. 2020. Targeting apoptosis in cancer therapy. Nature Reviews Clinical Oncology **17(7)**, 395-417.

Cemali SH, Poyraz S, Belveren S, Taş S, Tamer MA, Döndaş NY, Döndaş HA, Sansano JM. 2025. Recent insights in multi-target drugs in pharmacology and medicinal chemistry. ChemMedChem **20(18)**, e202500447.

Daina A, Michielin O, Zoete V. 2017. SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Scientific Reports **7(1)**, 42717.

Daina A, Zoete V. 2016. A boiled-egg to predict gastrointestinal absorption and brain penetration of small molecules. ChemMedChem **11(11)**, 1117-1121.

Dandoti S. 2021. Mechanisms adopted by cancer cells to escape apoptosis- A review. Biocell **45(4)**, 863-884.

Danforth DN. 2021. The role of chronic inflammation in the development of breast cancer. Cancers **13(15)**, 3918.

Deodhar M, Al Rihani SB, Arwood MJ, Darakjian L, Dow P, Turgeon J, Michaud V. 2020. Mechanisms of CYP450 inhibition: Understanding drug-drug interactions due to mechanism-based inhibition in clinical practice. Pharmaceutics **12(9)**, 846.

Dong R, Wang J, Guan R, Sun J, Jin P, Shen J. 2025. Role of oxidative stress in the occurrence, development andtreatment of breast cancer. Antioxidants **14(1)**, 104.

Freihat O, Sipos D, Kovacs A. 2025. Global burden and projections of breast cancer incidence and mortality to 2050: A comprehensive analysis of GLOBOCAN data. Frontiers in Public Health **13**, 1622954.

Georgy DM, Sedeek HN, Abaza NE, Eldeeb SE, Khamis SM, Elgamil MR, Magar RW. 2026. From mutation to treatment: The dual role of BRCA1 and BRCA2 in gynecological malignancy development and management a systematic review. Biochemistry and Biophysics Reports **46**, 102564.

Gupta S, Kass GE, Szegezdi E, Joseph B. 2009. The mitochondrial death pathway: A promising therapeutic target in diseases. Journal of Cellular and Molecular Medicine **13(6)**, 1004-1033.

Holloman WK. 2011. Unraveling the mechanism of BRCA2 in homologous recombination. Nature Structural and Molecular Biology **18(7)**, 748-754.

Islam MD, Saha JK, Marufa SS, Kundu TK, Hossain I, Nishino H, Alam MS, Haque MA, Rahman MM. 2025. Synthesis, antibacterial activity, in silico ADMET prediction, docking andmolecular dynamics studies of substituted phenyl and furan ring containing thiazole Schiff base derivatives. PLOS ONE **20(3)**, e0318999.

Langner E, Walczak K, Jeleniewicz W, Turski WA, Rajtar G. 2015. QA inhibits proliferation of colon cancer HT-29 cells in vitro: effects on signaling pathways. European Journal of Pharmacology **757**, 21-27.

Liu Y, West SC. 2001. Distinct functions of BRCA1 and BRCA2 in double-strand break repair. Breast Cancer Research **4(1)**, 9.

Łukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. 2021. Breast cancer-epidemiology, risk factors, classification, prognostic markers andcurrent treatment strategies-an updated review. Cancers **13(17)**, 4287.

Ma Z, Ajibade A, Zou X. 2024. Docking strategies for predicting protein-ligand interactions and their application to structure-based drug design. Communications in Information and Systems **24(3)**, 199.

Marvalim C, Datta A, Lee SC. 2023. Role of p53 in breast cancer progression: An insight into p53 targeted therapy. Theranostics **13(4)**, 1421.

Mustafa M, Ahmad R, Tantry IQ, Ahmad W, Siddiqui S, Alam M, Abbas K, Moinuddin, Hassan MI, Habib S, Islam S. 2024. Apoptosis: A comprehensive overview of signaling pathways, morphological changes andphysiological significance and therapeutic implications. Cells **13(22)**, 1838.

Myśliwiec A, Bartusik-Aebisher D, Aebisher D. 2025. The role of nitric oxide in cancer treatment: ally or foe? Molecules **30(13)**, 2802.

Nishida A andoh A. 2025. The role of inflammation in cancer: mechanisms of tumor initiation, progression andmetastasis. Cells **14(7)**, 488.

Okamoto H, Miyamoto S, Mabuchi H, Yoneyama Y, Takeda R. 1973. Insulin-releasing effect of QA and its relatives on isolated Langerhans islets. Biochemical and Biophysical Research Communications **53(4)**, 1297-1303.

Tamilarasi S, Kamali T, Sivasankaran SM, Deepa B. 2026. Pharmacological properties of QA: A concise review. European Journal of Biomedical **13(6)**, 066-070.

Trott O, Olson AJ. 2009. Software news and update AutoDock Vina: Improving the speed and accuracy of docking with a new scoring function, efficient optimization andmultithreading. Effic. Optim. Multithreading **31**, 455-461.

Tufail M, Cui J, Wu C. 2022. Breast cancer: molecular mechanisms of underlying resistance and therapeutic approaches. American Journal of Cancer Research **12(7)**, 2920.

Valenzuela-Cardenas M, Nowicki TS. 2026. TNF-alpha: Roles in pathogenesis and therapeutics in cancer. Journal of Biological Chemistry **111251**.