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Multitarget Therapeutic Potential of Mimosa pudica (Linn.) in Luminal-Type Breast Cancer: A Bibliometric, Network Pharmacology, and Molecular Docking Analysis

Potensi Terapeutik Multitarget Mimosa pudica (Linn.) pada Kanker Payudara Tipe Luminal: Analisis Bibliometrik, Farmakologi Jaringan, dan Penambatan Molekuler

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ABSTRACT

The growing burden of breast cancer and the limitations of current treatment strategies underscore the need to identify alternative therapeutic approaches. This study investigated the multitarget therapeutic potential of *Mimosa pudica* (Linn.) against luminal-type breast cancer using an integrated computational framework that combined bibliometric analysis, drug-likeness and ADMET screening, network pharmacology, gene expression analysis, and molecular docking. Bioactive compounds reported from *M. pudica* were evaluated in silico to assess physicochemical characteristics, pharmacokinetic properties, and potential molecular targets. Predicted protein targets were further analyzed using protein–protein interaction network analysis and visualized in Cytoscape to identify key pathways associated with breast cancer progression. The analysis identified multiple candidate compounds with favorable pharmacological profiles and predicted interactions with proteins involved in critical biological processes, including cell cycle regulation, DNA metabolism, growth factor signaling, angiogenesis, migration, and invasion. Network analysis highlighted several hub proteins associated with luminal-type breast cancer, among which AURKA and CDK1 were prioritized for molecular docking based on network topology, pathway enrichment, biological relevance, and structural suitability. Molecular docking demonstrated favorable predicted interactions between selected flavonoids—apigenin, galangin, kaempferol, diosmetin, and chrysin—and both target proteins, with binding energies ranging from −7.6 to −8.9 kcal/mol. These findings provide mechanistic insight into the potential molecular actions of *M. pudica*-derived compounds and support their prioritization as candidate therapeutic molecules for further experimental investigation in luminal-type breast cancer.

Keywords: bibliometrics; luminal-type breast cancer; *Mimosa pudica*; molecular docking; multitarget therapy; network pharmacology

ABSTRAK

Peningkatan beban kasus kanker payudara serta keterbatasan strategi terapi yang tersedia saat ini menegaskan perlunya pengembangan pendekatan terapeutik alternatif. Penelitian ini bertujuan untuk mengevaluasi potensi terapeutik multitarget Mimosa pudica (Linn.) terhadap kanker payudara tipe luminal menggunakan kerangka kerja komputasional terintegrasi yang menggabungkan analisis bibliometrik, penyaringan drug-likeness dan ADMET, network pharmacology, analisis ekspresi gen, serta molecular docking. Senyawa bioaktif yang dilaporkan dari M. pudica dianalisis secara in silico untuk mengevaluasi karakteristik fisikokimia, sifat farmakokinetik, dan memprediksi target molekuler potensial. Target protein yang diprediksi kemudian dianalisis menggunakan jaringan interaksi protein–protein dan divisualisasikan dengan Cytoscape untuk mengidentifikasi jalur biologis utama yang terkait dengan progresi kanker payudara. Hasil analisis mengidentifikasi beberapa senyawa kandidat dengan profil farmakologis yang baik dan

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interaksi yang diprediksi terhadap protein-protein yang terlibat dalam proses biologis penting, termasuk regulasi siklus sel, metabolisme DNA, pensinyalan faktor pertumbuhan, angiogenesis, migrasi, dan invasi. Analisis jaringan menunjukkan beberapa protein hub yang berasosiasi dengan kanker payudara tipe luminal, di mana AURKA dan CDK1 diprioritaskan untuk analisis molecular docking berdasarkan topologi jaringan, hasil pathway enrichment, relevansi biologis, serta ketersediaan struktur tiga dimensi yang sesuai. Analisis molecular docking menunjukkan interaksi prediktif yang baik antara flavonoid terpilih—apigenin, galangin, kaempferol, diosmetin, dan chrysin—dengan kedua target protein tersebut, dengan energi ikatan berkisar antara −7,6 hingga −8,9 kkal/mol. Temuan ini memberikan wawasan mekanistik mengenai kemungkinan aksi molekuler senyawa turunan M. pudica serta mendukung prioritasnya sebagai kandidat molekul terapeutik yang memerlukan validasi eksperimental lebih lanjut pada kanker payudara tipe luminal.

Kata kunci: *Bibliometrik; farmakologi jaringan; kanker payudara tipe luminal; Mimosa pudica; penambatan molekuler; terapi multitarget*

INTRODUCTION

Breast cancer remains a major global health challenge, threatening women's health and life expectancy worldwide. In 2022, more than 2.3 million women were diagnosed with breast cancer globally, resulting in approximately 670,000 deaths (World Health Organization, 2024). In Indonesia, breast cancer incidence has also increased substantially, with 65,858 new cases reported in 2020, making it the most frequently diagnosed cancer among women (Kementerian Kesehatan, 2023). Although considerable progress has been made in breast cancer diagnosis and treatment, conventional therapies such as chemotherapy remain associated with significant adverse effects, including nausea, alopecia, fatigue, and immunosuppression (Ali *et al*., 2016; Li *et al.,* 2017; Lorizio *et al.,* 2012).

The molecular heterogeneity of breast cancer further complicates treatment strategies because each subtype exhibits distinct biological characteristics, prognosis, and therapeutic responses. Among these subtypes, Luminal A is the most prevalent, accounting for approximately 52.1% of breast cancer cases globally (Johnson *et al.,* 2021). Although Luminal-type breast cancer is generally associated with a more favorable prognosis than other molecular subtypes, it remains clinically important because disease progression, recurrence, and therapeutic resistance continue to contribute substantially to morbidity and mortality (Kulkarni *et al.,* 2019). In Indonesia, studies at Dr. Sardjito Hospital in Yogyakarta reported that Luminal A accounted for approximately 40% of breast cancer cases (Setyawati *et al.,* 2018; Widodo *et al.,* 2014). These challenges highlight the need to identify alternative or complementary therapeutic approaches that target multiple molecular pathways involved in tumor progression.

Natural products have increasingly attracted attention as promising sources of bioactive compounds for anticancer drug discovery. Plant-derived metabolites, in particular, have been shown to modulate diverse molecular pathways involved in cancer initiation, proliferation, survival, angiogenesis, invasion, and metastasis (Manna *et al*., 2023; Rahmani *et al*., 2023; Rovik *et al.*, 2024). Among these, *Mimosa pudica* is a widely distributed medicinal plant traditionally used in folk medicine for various therapeutic purposes, including antimalarial, antifungal, antibacterial, and anticancer applications, as

well as for treating rheumatism, ulcers, and asthma (Desrini *et al.,* 2023; Jose *et al.,* 2016; Muhammad *et al.,* 2016). Previous phytochemical investigations have identified multiple classes of bioactive constituents in *M. pudica*, including flavonoids, terpenoids, sterols, tannins, fatty acids, and C-glycosides, several of which have been associated with anticancer biological activities (Hullatti *et al.*, 2013; Jose *et al.,* 2016; Parmar *et al.,* 2015). Despite growing interest in the pharmacological properties of *M. pudica*, evidence on its molecular mechanisms and target interactions in luminal-type breast cancer remains limited and fragmented. Existing studies have largely focused on general phytochemical characterization or broad anticancer activity, without systematically investigating the multitarget molecular interactions that underlie its therapeutic potential in specific breast cancer subtypes. In addition, not all reported constituents are necessarily suitable therapeutic candidates, underscoring the importance of prioritizing compounds based on pharmacological and safety considerations. Therefore, a comprehensive computational framework integrating bibliometric analysis, network pharmacology, drug-likeness and ADMET evaluation, and molecular docking may provide a systematic strategy for identifying candidate compounds and elucidating their underlying molecular mechanisms. Accordingly, the present study aimed to investigate the multitarget therapeutic potential of *Mimosa pudica* in luminal-type breast cancer using an integrated approach that combined bibliometric analysis, network pharmacology, compound prioritization, and molecular docking. This study aimed to identify candidate bioactive compounds and characterize their interactions with key molecular targets associated with breast cancer progression.

METHOD

Bibliometric Analysis: A literature search was conducted using the keywords "*Mimosa pudica*" AND "cancer" across three electronic databases: Scopus, Web of Science, and PubMed. The retrieved records were exported in RIS/Zotero-compatible format and screened for relevance. The bibliographic data were then imported into VOSviewer (version 1.6.20) for bibliometric mapping and keyword co-occurrence analysis. Network visualization was configured to identify major research themes, publication trends, and keyword relationships related to *M. pudica* and cancer research.

Drug-Likeness and ADMET Prediction: Drug-likeness and ADMET screening were conducted using SwissADME (https://swissadme.ch/) and pkCSM (http://biosig.unimelb.edu.au/pkcsm/), two web-based platforms that predict the physicochemical properties, pharmacokinetic behavior, and toxicity of small molecules. The bioactive compounds of Mimosa pudica were compiled from the phytochemical data reported by Desrini *et al.* (2023). Each compound was evaluated with SwissADME to predict physicochemical properties, including molecular weight, lipophilicity (LogP), water solubility, pharmacokinetic characteristics, and drug-likeness according to Lipinski's rule of five. To complement these analyses, pkCSM was used to estimate ADMET parameters, including human intestinal absorption, blood–brain barrier permeability, cytochrome P450 interactions, total clearance, hepatotoxicity, and AMES toxicity.

Compounds with favorable drug-likeness and ADMET profiles were prioritized for subsequent analyses.

Target Prediction Using SwissTargetPrediction: Potential molecular targets of the prioritized bioactive compounds were predicted using SwissTargetPrediction (http://www.swisstargetprediction.ch/). Canonical SMILES structures of the selected compounds were used as input, and predictions were restricted to *Homo sapiens*. Predicted target proteins were compiled and further analyzed to investigate the potential molecular mechanisms underlying the biological activity of *M. pudica.*

Gene Expression Analysis Using UALCAN: Gene expression analysis was conducted using UALCAN (https://ualcan.path.uab.edu/analysis.html) to evaluate expression profiles of genes encoding the predicted target proteins in luminal-type breast cancer. Expression levels in tumor and normal tissues were compared to identify potential biomarkers and therapeutically relevant targets.

Protein-Protein Interaction (PPI) Network Analysis: Protein interaction analysis was conducted using the STRING database (https://string-db.org/) to explore interactions among predicted target proteins. The resulting interaction network was imported into Cytoscape (version 3.10.1) for visualization and topological analysis. Network clustering was performed with clusterMaker2 (version 2.1.0) to identify functionally connected protein groups. Hub proteins were prioritized based on network topology and biological relevance to luminal-type breast cancer pathways.

Molecular docking: Molecular docking simulations were conducted to evaluate the binding affinity of selected bioactive compounds—apigenin (CID: 5280443), galangin (CID: 5281616), kaempferol (CID: 5280863), diosmetin (CID: 5281612), and chrysin (CID: 5281607)—to hub proteins involved in cell cycle regulation, namely AURKA (UniProt ID: O14965; PDB ID: 1MQ4) and CDK1 (UniProt ID: P06493; PDB ID: 5HQ0). Target selection for molecular docking was based on predefined criteria, including: (1) identification as hub proteins in the Cytoscape network, (2) involvement in significantly enriched biological pathways associated with cell cycle regulation, (3) biological relevance to luminal-type breast cancer progression, and (4) availability of experimentally determined three-dimensional structures suitable for docking analysis. Three-dimensional ligand structures were retrieved from the PubChem database and prepared using AutoDockTools-1.5.7. Protein receptors were prepared by removing water molecules and co-crystallized ligands, adding polar hydrogens, and assigning Kollman charges. Ligands were prepared by assigning Gasteiger charges and defining rotatable bonds. Prepared receptor and ligand files were saved in pdbqt format. Docking simulations were performed using the Lamarckian Genetic Algorithm (LGA) implemented in AutoDockTools-1.5.7. Docking protocol validation was performed by redocking the native ligand into the corresponding receptor binding site. Validation accuracy was assessed by calculating the Root Mean Square Deviation (RMSD) between the redocked pose and the original crystallographic ligand conformation. Docking procedures were considered acceptable when RMSD ≤ 2.0 Å. Post-docking analysis included evaluation of binding affinity scores, characterization of intermolecular interactions, and three-dimensional visualization of docked complexes using BIOVIA Discovery Studio 2016 Client.

RESULTS AND DISCUSSION

The sensitive plant (*Mimosa pudica*) is a widely distributed medicinal plant that has attracted growing interest for its diverse phytochemical composition and reported pharmacological activities (Desrini *et al.,* 2023; Muhammad *et al.,* 2016). In the present study, bioactive compounds were compiled from previously published phytochemical profiling data generated by high-resolution mass spectrometry in positive ionization mode of the ethyl acetate fraction of *M. pudica* aerial parts (Desrini *et al.,* 2023). The analysis identified multiple compound classes, including flavonoids, amino acids, and other secondary metabolites (Supplementary Table S1). To prioritize compounds with potential therapeutic relevance, the identified constituents underwent drug-likeness and ADMET screening before subsequent computational analyses. This step enabled the selection of compounds with more favorable pharmacological and predicted safety profiles for downstream target prediction and molecular docking analyses.

Predicted target proteins for prioritized *M. pudica* compounds were identified via computational target prediction and subsequently evaluated in the context of luminal-type breast cancer. Gene expression analysis showed that several predicted targets were elevated in breast cancer tissues compared with normal tissues (Table 1).

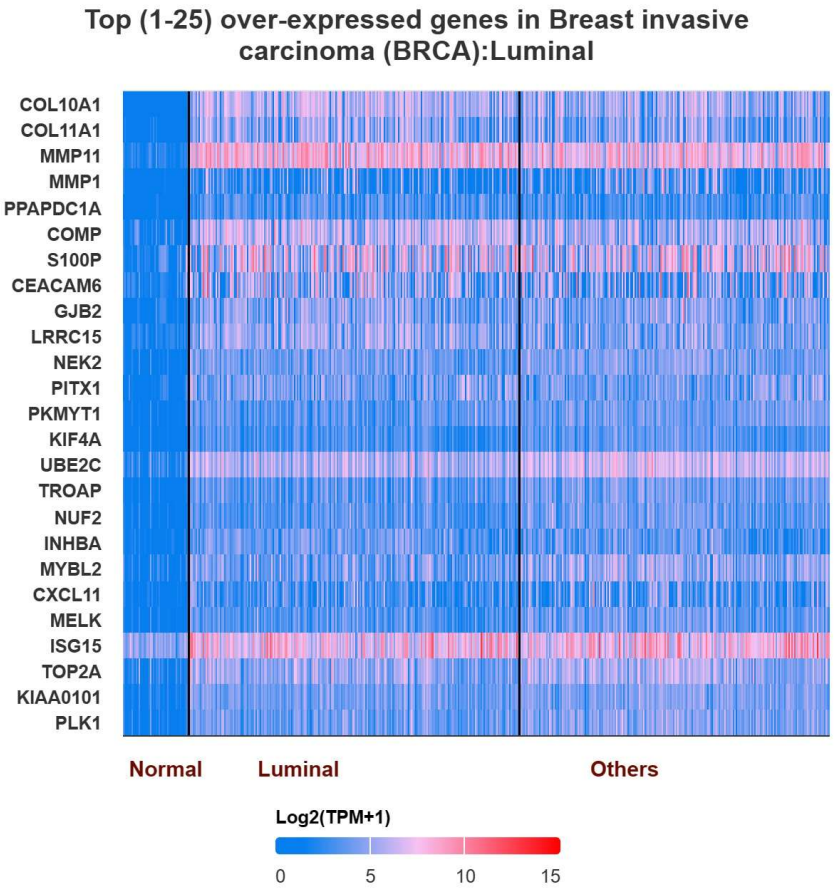


Figure 1. UALCAN analysis of gene expression levels in luminal-type breast cancer

Supplementary Table S1. Drug-Likeness and ADMET Screening of *Mimosa pudica*-Derived Compounds

No	Compound	CID	Molecular Weight (g/mol)	Log P <5	#Rotatable Bonds	#Acceptors	#Donors	Surface Area	Solubility (log mol/L)	Caco2 (log Papp in 10-6 cm/s)	Human intestinal absorption (%)	P-gp substrate	VDss (log L/kg)	Fraction unbound	CYP3A4 Inhibitor	Total Clearance (log mL/min/kg)	AMES Toxicity	Mx tolerated dose (log mg/kg /day)	LD50 (mol/ kg)	Hepatotoxicity
1	(-)-Caryophyllene oxide	1742210	220.356	3.936	0	1	0	99.255	-4.433	1.509	95.421	No	0.586	0.324	No	0.905	No	0.12	1.532	No
2	(1S)-1,5-Anhydro-2-O-(6-deoxy-α-L-mannopyranosyl)-1-[5,7]-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-6-yl]-D-glucitol	no data																		
3	(1ξ)-1,5-Anhydro-1-[2-(3,4-dihydroxy phenyl)-5,7-dihydroxy-4-oxo-4H-chromen-8-yl]-D-galactitol	no data																		
4	1,5-Anhydro-1-[5,7-dihydroxy-3-(4-hydroxyphenyl)-4-oxo-4H-chromen-8-yl]hexit	no data																		
5	3-Hydroxypyridine	7971	95.101	0.787	0	2	1	41.445	-0.628	1.721	98.882	No	-0,046	0.747	No	0.575	No	0.481	2.067	No
6	3-Methoxy-5,7,3',4'-tetrahydroxy-flavone	no data																		
7	4-Coumaric acid	637542	164.16	1.49	2	2	2	69.587	-2.378	1.21	93.494	No	-1.151	0.428	No	0.662	No	1.111	2.155	No
8	5-Methoxysalicylic acid	75787	168.148	1.099	2	3	2	69.025	-2.139	0.359	77.879	No	-1.617	0.563	No	0.651	No	1.025	2.331	No
9	5-O-Methylgenistein	5748551	284.267	2.8798	2	5	2	119.203	-3.307	1.14	95.62	No	0	0.038	Yes	0.301	No	0.199	2.248	No
10	5,7-Dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl β-L-xylofuranoside	no data																		
11	9S,13R-12-Oxophytodienoic acid	14037063	292.419	4.5293	11	2	1	127.676	-4.542	1.506	95.212	No	-0.704	0.124	No	1.65	No	-0.691	1.621	No
12	Adenine																			
13	Aflatoxin G1	14421	328.276	1.8605	1	7	0	134.908	-3.357	1.353	99.276	No	-0.384	0.103	No	0.585	Yes	-0.001	4.494	No
14	Aflatoxin G2	2724362	330.292	1.736	1	7	0	135.597	-3.329	1.357	99.593	No	-0.386	0.104	No	0.58	Yes	-0.005	3.069	No
15	Apigenin	5280443	270.24	2.5768	1	5	3	112.519	-3.329	1.007	93.25	No	0.822	0.147	No	0.566	No	0.328	2.45	No
16	Avicularin	5490064	434.353	0.1002	4	11	7	172.742	-2.976	0.233	57.226	Yes	1.745	0.226	No	0.402	No	0.576	2.543	No
17	Choline	305	104.173	-0.3151	2	1	1	44.963	0.765	1.473	100	Yes	0.224	0.865	No	0.932	No	0.952	1.939	No
18	Chrysin	5281607	254.241	2.8712	1	4	2	107.725	-3.538	0.945	93.761	Yes	0.403	0.136	No	0.405	No	0.016	2.289	No
19	Cynaroside	5280637	448.38	-0.2445	4	11	7	179.107	-2.716	0.248	37.556	Yes	0.884	0.224	No	0.478	No	0.584	2.547	No
20	D-(+)-Proline																			
21	Diosmetin	5281612	300.266	2.585	2	6	3	123.998	-3.238	0.326	79.898	Yes	0.709	0.068	No	0.598	No	0.42	2.338	No
22	Esculetin	5281416	178.143	1.204	0	4	2	72.668	-2.497	0.301	86.291	Yes	0.528	0.484	No	0.671	No	-0.262	2.337	No
23	Galangin	5281616	270.24	2.576	1	5	3	112.519	-3.335	0.999	93.985	Yes	0.816	0.142	No	0.256	No	0.333	2.45	No
24	Hexadecanamide	69421	255.446	4.953	14	1	1	113.715	-6.511	1.525	90.399	No	0.319	0.117	No	1.837	No	-0.074	1.802	No
25	Isokaempferide	5280862	300.266	2.5854	2	6	3	123.998	-0.383	-0.319	84.294	Yes	-0.102	0.043	No	0.525	No	0.34	2.395	No

26	Jasmonic acid	5281166	210.273	2.4127	5	2	1	90.175	-2.452	1.278	94.103	No	-0.649	0.425	No	0.455	No	0.538	1.669	No
27	Kaempferol	5280863	286.239	2.2824	1	6	4	117.313	-3.04	0.032	74.29	Yes	1.274	0.178	No	0.477	No	0.531	2.449	No
28	L-Isoleucine																			
29	N-(2,4-Dimethylphenyl) formamide	no data																		
30	N, N-Dimethylaniline	no data																		
31	Nicotinamide	936	122.127	0.1805	1	2	1	52.517	-0.719	1.159	92.547	No	-0.224	0.703	No	0.608	No	1.15	2.116	No
32	Nicotinic acid	938	123.111	0.7798	1	2	1	51.972	-2.124	1.17	94.099	No	-1.015	0.776	No	0.652	No	0.907	2.24	No
33	NP-000358	no data																		
34	NP-000465	no data																		
35	NP-003294	no data																		
36	NP-015559	no data																		
37	NP-018720	no data																		
38	NP-019811	no data																		
39	NP-021018	no data																		
40	Oleamide	5283387	281.484	5.509	15	1	1	125.755	-7.074	1.55	90.218	No	0.281	0.067	No	1.959	No	-0.265	1.805	No
41	Poliprolol	no data																		
42	Pyridoxine	1054	169.18	0.08022	2	4	3	70.129	-2.108	0.561	94.139	No	0.589	0.819	No	0.688	No	-0.18	1.852	No
43	Pyrrole-2-carboxylic acid	12473	111.1	0.7129	1	1	2	45.961	-2.059	1.127	88.643	No	-1.027	0.74	No	0.662	No	0.778	2.206	No
44	Quercetin-3β-D-glucoside	5280343	302.238	1.988	1	7	5	122.108	-2.925	-0.299	77.207	No	1.559	0.206	No	0.407	No	0.499	2.471	No
45	Rutin	5280805	610.521	-1.6871	6	16	10	240.901	-2.892	-0.949	23.446	Yes	1.663	0.187	No	-0.369	No	0.452	2.491	No
46	Scopoletin	5280460	192.17	1.5072	1	4	1	79.352	-2.504	1.184	95.277	No	0.034	0.363	No	0.73	No	0.614	1.95	No
47	Stearamide	31292	283.5	5.7332	16	1	1	126.445	-7.17	1.561	89.712	No	0.306	0.066	No	1.906	No	-0.202	1.822	No
48	Tropine	449293	141.214	0.6039	0	2	1	61.836	-0.514	1.444	93.575	Yes	0.54	0.796	No	1.063	No	0.896	1.91	Yes
49	Vitexin	5280441	432.381	0.0917	3	10	7	173.994	-2.845	-0.956	46.695	Yes	1.071	0.242	No	0.444	No	0.577	2.595	No
50	α-Pyrrolidinopropiophenone	209045	203.285	2.3536	3	2	0	90.902	-2.071	1.161	92.082	No	0.76	0.71	No	0.994	No	-0.306	3.052	Yes

Note: No data means no validated CID/SMILES available; excluded from ADMET prioritization

The top 25 overexpressed genes were identified in luminal-type breast cancer (Figure 1). The observed expression patterns suggest that these targets participate in molecular processes associated with tumor progression and may represent candidate therapeutic intervention points. Notably, several overexpressed genes correspond to proteins involved in regulating proliferation, cell cycle progression, and oncogenic signaling.

Table 1. Protein target analysis using Swiss Target Prediction

Compounds	Protein Target	Potential Target
(-)-Caryophyllene oxide	100	CA12 ERBB2
3-Hydroxypyridine	43	MMP1 MMP9 CA12 ESR1 KMO ERBB2 MIF
4-Coumaric acid	100	MMP1 NEK2 AURKB MMP9 SQLE CA12 KMO MIF
5-Methoxysalicylic acid	100	KIF11 PTK6 CA12 ESR1 MIF
5-O-Methylgenistein	100	ESR1
9S,13R-12-Oxophytodienoic acid	100	NEK2 PLK1 CDK1 AURKB MMP9 CA12 ESR1
Apigenin	100	TOP2A PLK1 CDK1 ARKB MMP9 CA12 ESR1
Chrysin	100	NEK2

Compounds	Protein Target	Potential Target
		PLK1 CDK1 AURKB MMP9 CA12 ESR1
Diosmetin	100	NEK2 PLK1 AURKB AURKA MMP9 SQLE CA12 ESR1 TYMS ERBB2 MIF
Esculetin	100	NEK2 TOP2A PLK1 CDK1 AURKB MMP9 CA12 ESR1
Galangin	100	TOP2A KMO MIF
Isokaempferide	100	NEK2 PLK1 CDK1 AURKB MMP9 CA12 ESR1
Jasmonic acid	100	CA12 TYMP
Kaempferol	100	NEK2 PLK1 CDK1 AURKB MMP9 CA12 ESR1
Nicotinamide	100	TOP2A KIF11 CA12 MIF
Nicotinic acid	76	TOP2A

Compounds	Protein Target	Potential Target
		KIF11 CA12 MIF
Pyrrole-2-carboxylic acid	71	MMP9 CA12
Quercetin-3β-D-glucoside	100	NEK2 TOP2A PLK1 CDK1 AURKB MMP9 CA12
Scopoletin	100	PLK1 AURKB AURKA SQLE CA12 ESR1 ERBB2
Tropine	100	FAP
α-Pyrrolidinopropiophenone	100	-

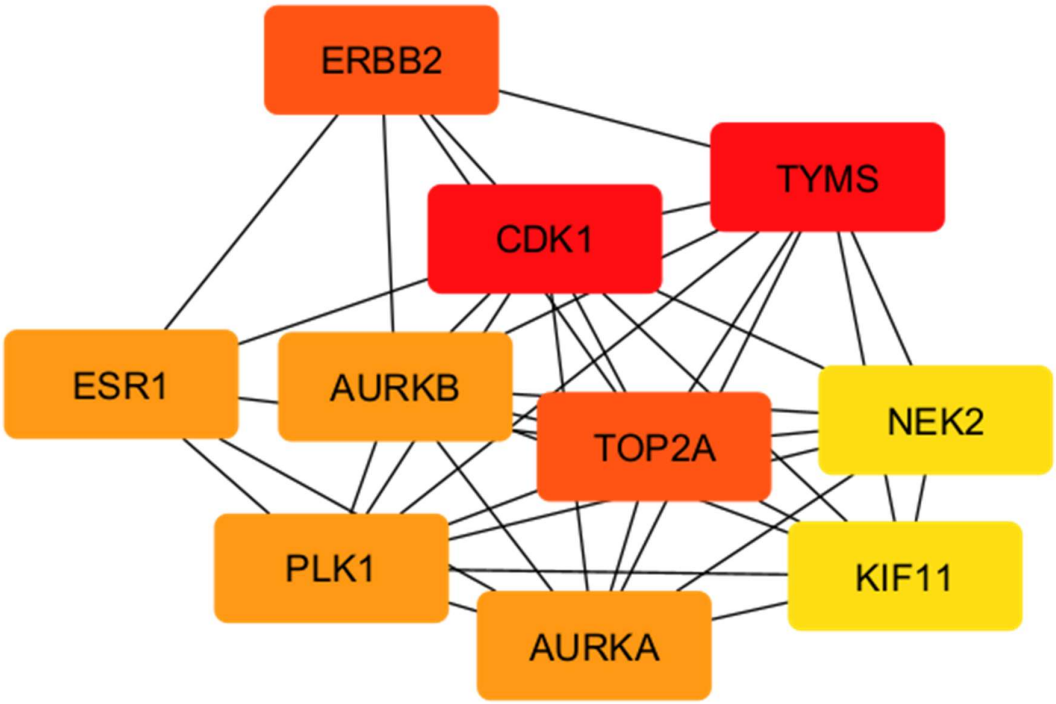


Figure 2. Protein-to-protein networking analysis using STRING and Cytoscape

Protein–protein interaction analysis indicated that *M. pudica* compounds may interact with multiple molecular targets linked to breast cancer progression. The interaction network identified several hub proteins, including AURKA, AURKB, CA12, CDK1, ERBB2, ESR1, KIF11, KMO, MIF, MMP1, MMP9, NEK2, PLK1, PTK6, SQLE, TOP2A, TYMP, and TYMS (Figure 2).

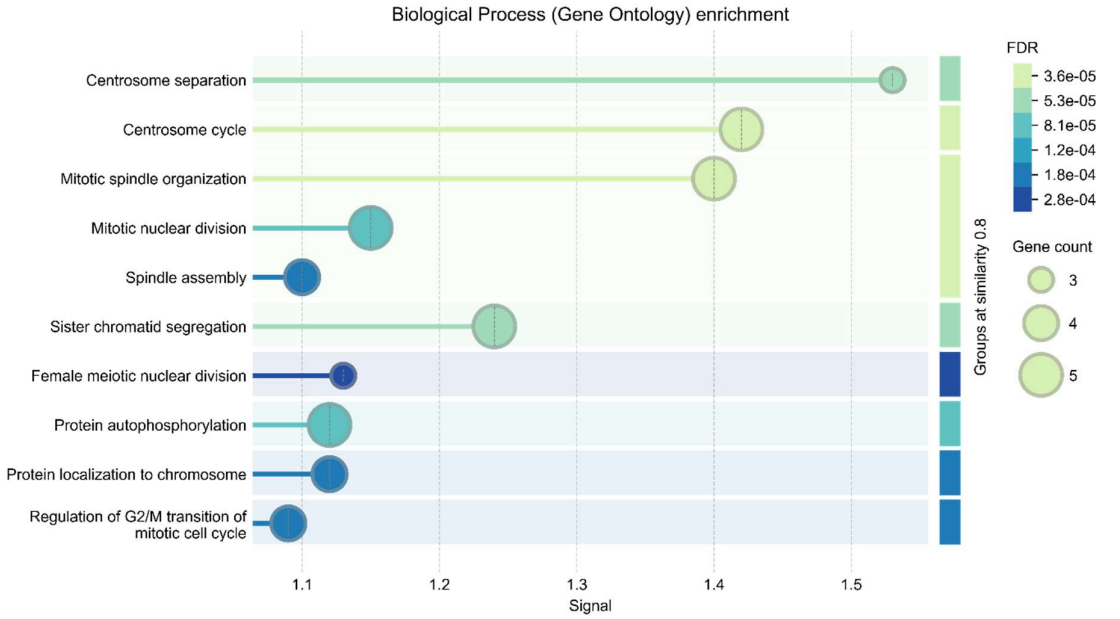
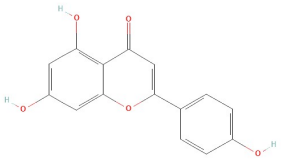
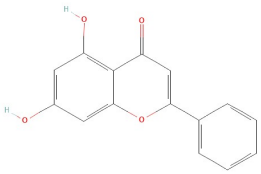
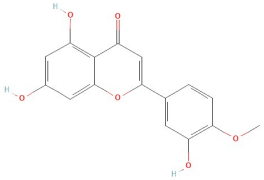
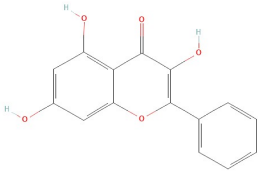
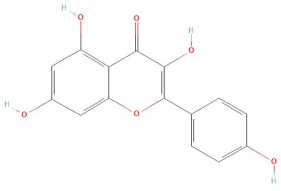


Figure 3. Enrichment analysis of protein targets

Functional enrichment analysis indicated that these proteins are primarily involved in biological processes related to cell cycle regulation, cytokine-mediated signaling, cell migration, and DNA replication (Figure 3). Among these pathways, cell cycle regulation was the most significantly enriched, supporting its potential role as a central mechanism underlying the predicted therapeutic activity of *M. pudica* compounds. Based on network topology, biological relevance to luminal-type breast cancer, enrichment results, and structural suitability for docking analysis, CDK1 and AURKA were selected as representative targets for molecular docking validation.

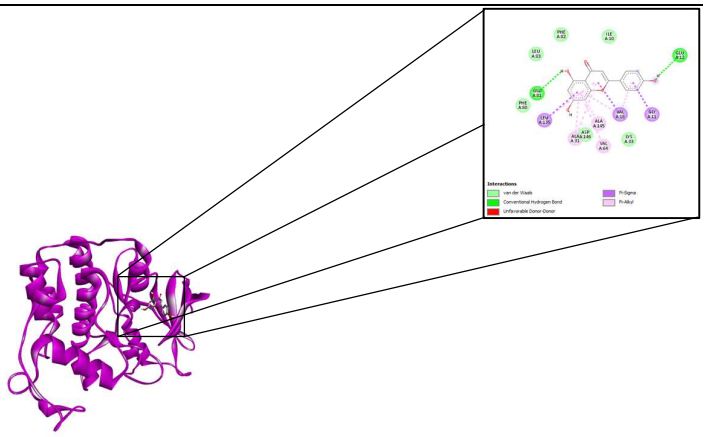
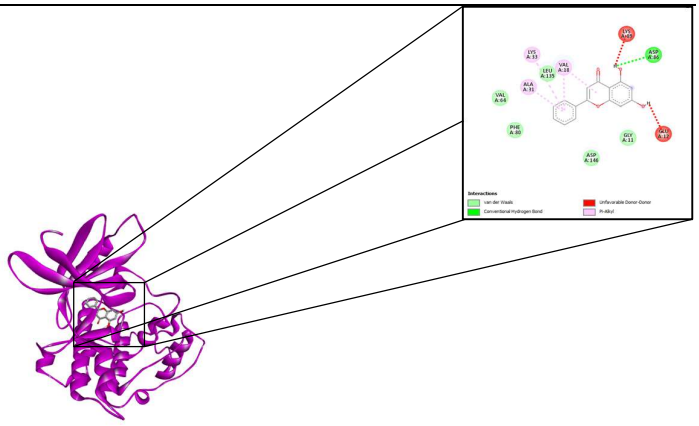
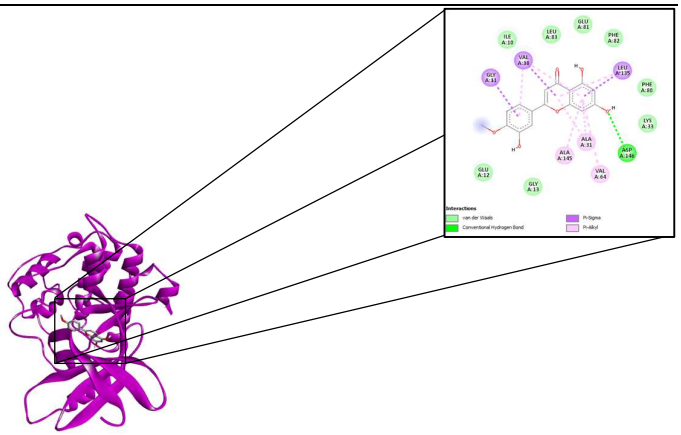
Table 2. Chemical structure of the chosen *Mimosa pudica*-derived compounds

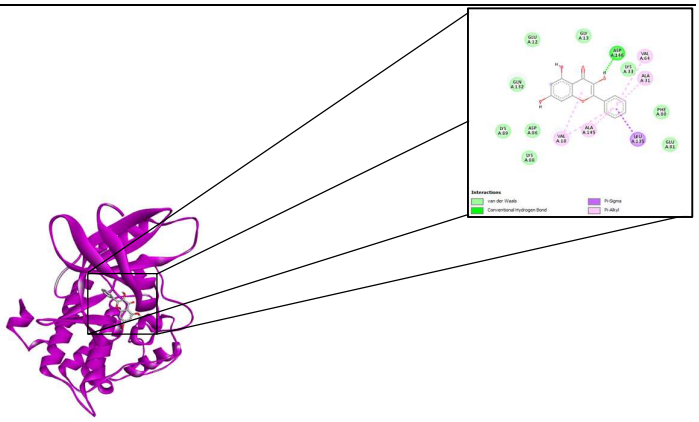
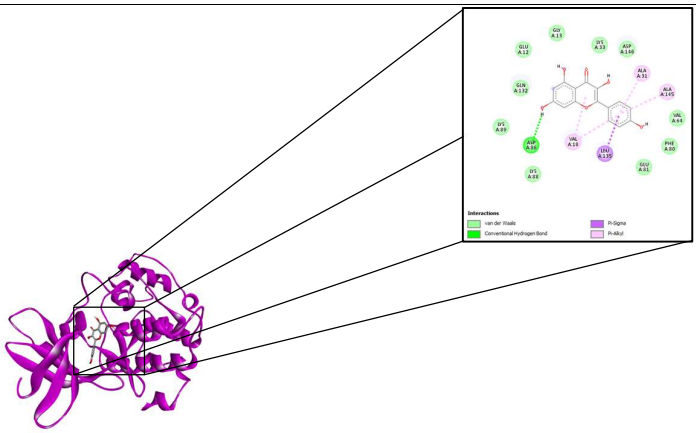
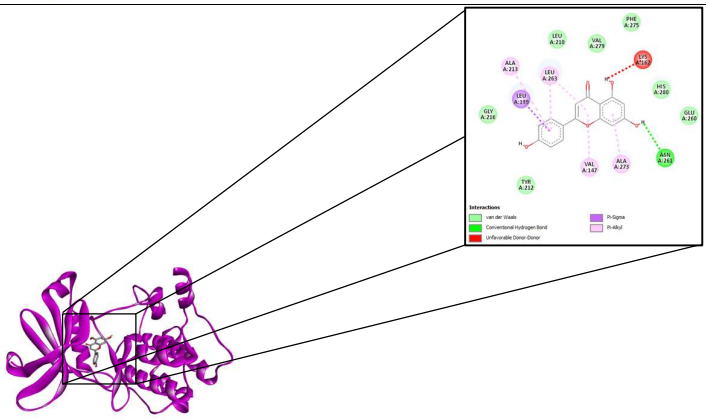
Compound	Chemical Structure	PubChem ID
Apigenin		5280443
Chrysin		5281607
Diosmetin		5281612
Galangin		5281616
Kaempferol		5280863

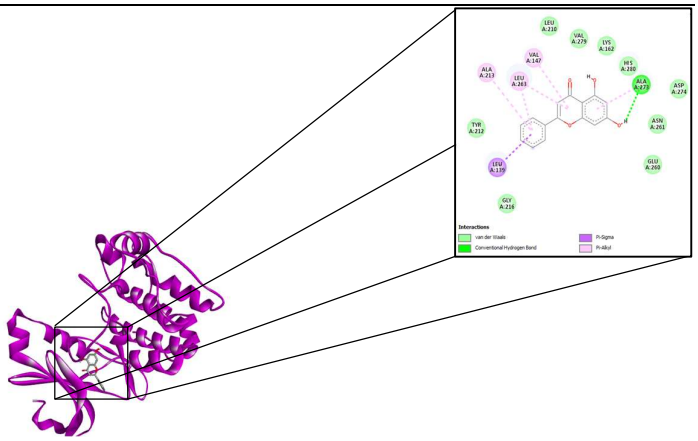
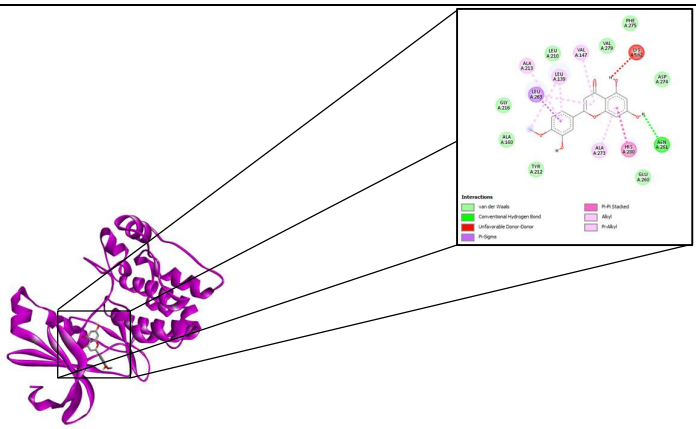
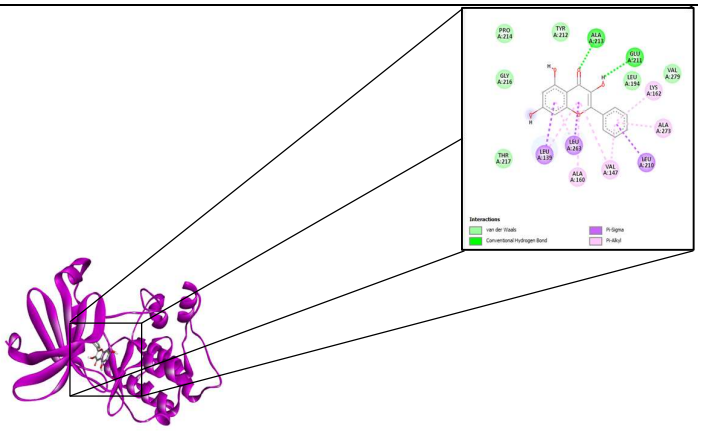
Molecular docking was conducted to assess interactions between selected M. pudica compounds and two prioritized cell-cycle regulators, CDK1 and AURKA (Table 3). Five compounds—apigenin, chrysin, diosmetin, galangin, and kaempferol—were selected

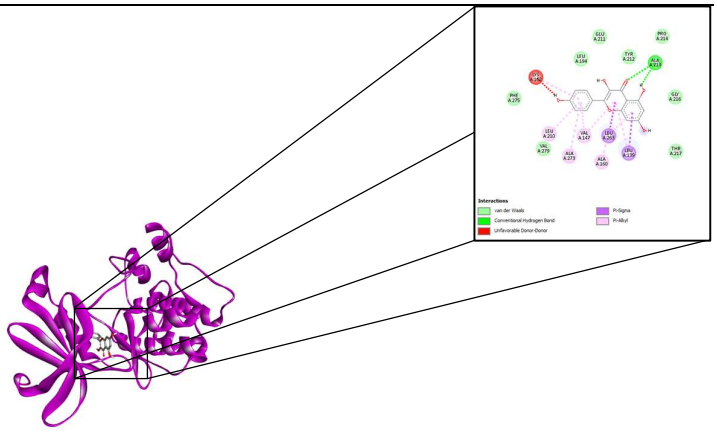
based on an integrated assessment of drug-likeness, ADMET characteristics, network pharmacology relevance, and biological plausibility.

Table 3. Molecular docking result

Protein	Ligand	Binding Affinity (kcal/mol)	Hydrogen bond	3D and 2D Visualization
CDK-1	Apigenin	-7.7	GLU81 GLU12	
CDK-1	Chrysin	-7.6	ASP86	
CDK-1	Diosmetin	-7.6	ASP146	

Protein	Ligand	Binding Affinity (kcal/mol)	Hydrogen bond	3D and 2D Visualization
CDK-1	Galangin	-7.7	ASP146	
CDK-1	Kaempferol	-7.6	ASP86	
AURKA	Apigenin	-8.8	ASN261	

Protein	Ligand	Binding Affinity (kcal/mol)	Hydrogen bond	3D and 2D Visualization
AURKA	Chrysin	-8.9	ALA273	
AURKA	Diosmetin	-8.7	ASN261	
AURKA	Galangin	-8.3	GLU211 ALA213	

Protein	Ligand	Binding Affinity (kcal/mol)	Hydrogen bond	3D and 2D Visualization
AURKA	Kaempferol	-8.4	ALA213	

Docking analysis showed that all selected compounds exhibited favorable binding interactions with CDK1 (Table 3). Apigenin and galangin showed the strongest predicted binding affinity for CDK1 (−7.7 kcal/mol), followed closely by chrysin, diosmetin, and kaempferol (−7.6 kcal/mol), suggesting potential modulation of proteins involved in cell cycle progression. Similarly, all evaluated compounds showed strong predicted interactions with AURKA. Chrysin and apigenin exhibited the highest binding affinities for AURKA, with binding energies of −8.9 kcal/mol and −8.8 kcal/mol, respectively. These findings suggest that flavonoid-rich compounds from *M. pudica* may exert multitarget therapeutic effects by interacting with key regulators of cell proliferation and mitotic control. However, these findings should be interpreted as computational predictions and require further experimental validation to confirm biological activity and therapeutic relevance.

Discussion

Current breast cancer management relies on multimodal therapeutic approaches, including surgery, chemotherapy, radiotherapy, endocrine therapy, and targeted treatment. Although luminal-type breast cancer generally responds well to endocrine therapy, long-term disease control remains limited by treatment resistance, disease recurrence, and adverse effects associated with prolonged pharmacological intervention. Consequently, there is growing interest in identifying alternative therapeutic strategies that can simultaneously modulate multiple molecular pathways.

In this study, an integrated framework combining network pharmacology, gene expression analysis, drug-likeness and ADMET screening, and molecular docking was used to explore the therapeutic potential of *Mimosa pudica* in luminal-type breast cancer. The findings suggest that selected bioactive compounds from *M. pudica* may interact with multiple molecular targets implicated in tumor progression, particularly pathways

involved in cell cycle regulation, DNA metabolism, growth factor signaling, migration, and invasion (Table 4).

Table 4. Gene targets clustering analysis

Molecular Function	Gene/Protein
Cell cycle regulation	KIF11, NEK2, PLK1, AURKB, AURKA, TOP2A, CDK1
DNA metabolism	TYMS, TOP2A
Growth factor signaling	ERBB2, ESR1, PTK6
Angiogenesis, metastasis, and invasion	TYMP, MMP1, MMP9
Inflammation and immunity	MIF

The network analysis identified several highly connected proteins associated with luminal breast cancer, including ESR1, ERBB2, TOP2A, AURKA, AURKB, CDK1, and matrix metalloproteinases. These proteins participate in interconnected signaling networks that regulate proliferation and disease progression (Ali *et al.*, 2016; Li *et al.*, 2017). ESR1 is a central regulator of estrogen-dependent transcriptional programs and remains a dominant therapeutic target in luminal breast cancer. In contrast, altered ERBB2 signaling contributes to increased proliferative capacity and more aggressive clinical behavior in selected luminal subgroups (Aman *et al.*, 2019; Iqbal & Iqbal, 2014). Likewise, dysregulation of DNA replication and genomic maintenance pathways, including TOP2A overexpression, has been linked to accelerated cell division and unfavorable prognosis (Bobustuc *et al.*, 2018; Kaya *et al.*, 2024).

Among the identified targets, cell cycle regulation was one of the most enriched biological processes. Consequently, molecular docking analysis focused on AURKA and CDK1 as representative hub proteins, based on their network centrality, functional enrichment results, relevance to luminal breast cancer progression, and the availability of experimentally determined structures suitable for docking. AURKA is a critical regulator of mitotic spindle formation and chromosome segregation and has been associated with increased tumor aggressiveness, enhanced migration, and extracellular matrix remodeling (Du *et al.*, 2021; Noh *et al.*, 2015; Tang *et al.*, 2017; Wang *et al.*, 2012). Similarly, CDK1 plays a central role in the G2/M transition and sustained proliferative signaling and has emerged as a potential therapeutic target across multiple breast cancer subtypes (Kim *et al.*, 2014; Talatam *et al.*, 2023; Teotia *et al.*, 2024).

The enrichment of pathways associated with migration and invasion also underscores the role of matrix remodeling mechanisms in luminal breast cancer progression. Matrix metalloproteinases, particularly MMP1 and MMP9, facilitate extracellular matrix degradation and contribute to tumor dissemination and metastatic behavior (Augoff *et al.*, 2022; Kwon, 2023; Wang *et al.*, 2017). Their association with poor prognosis further supports the value of multitarget approaches capable of simultaneously modulating multiple hallmarks of cancer.

Phytochemical prioritization identified several flavonoid-derived compounds from *M. pudica*, including apigenin, galangin, kaempferol, diosmetin, and chrysin, as the most promising candidates for further investigation (Table 2). These compounds were selected based on an integrated assessment of drug-likeness, ADMET predictions, network

pharmacology relevance, and mechanistic plausibility, rather than on a single screening parameter. Flavonoids are increasingly recognized for their ability to interact with multiple signaling pathways involved in proliferation, apoptosis, oxidative stress, and cell cycle regulation.

Consistent with this rationale, molecular docking analysis predicted favorable interactions between all selected compounds and the prioritized protein targets. Apigenin and galangin showed the strongest predicted binding affinity for CDK1 (−7.7 kcal/mol), whereas chrysin and apigenin showed the strongest predicted interactions with AURKA (−8.9 and −8.8 kcal/mol, respectively). These findings suggest that selected *M. pudica* flavonoids may modulate kinase-mediated pathways associated with cell cycle progression (Table 4). However, binding affinity alone does not establish biological inhibition or therapeutic efficacy, and these computational findings should therefore be interpreted as hypothesis-generating evidence requiring experimental validation.

Importantly, although multiple compounds were initially identified from previously published phytochemical datasets, not all detected constituents were considered suitable therapeutic candidates. Compound prioritization incorporated drug-likeness and toxicity screening to prioritize compounds with more favorable predicted pharmacological profiles. Therefore, the present findings should not be interpreted as supporting the direct administration of crude *M. pudica* extracts but rather as identifying candidate bioactive molecules for future isolation, purification, and experimental investigation.

Future directions

Bibliometric mapping identified two dominant research clusters: one centered on *Mimosa pudica* and its biological activities, and another focused on cancer-related research (Figure 4). The connecting cluster, characterized by terms such as human cell, in vitro study, and cytotoxicity, suggests growing interest in evaluating the anticancer properties of *M. pudica*-derived compounds. In addition, keywords such as antioxidant activity and flavonoids indicate growing attention to phytochemical constituents that may contribute to cancer-related biological effects.

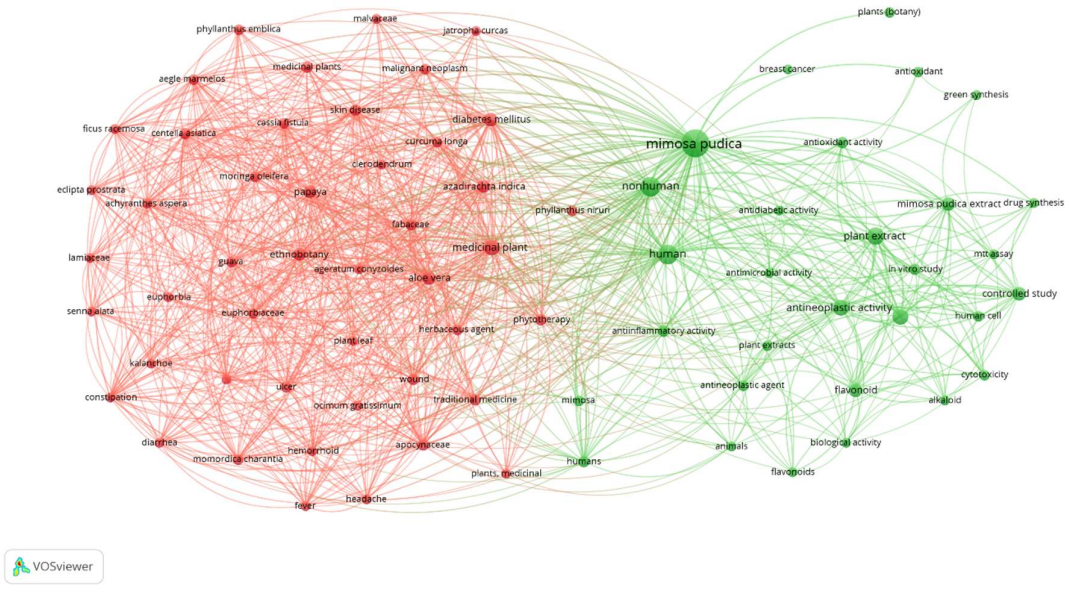


Figure 4. Network analysis visualization on '*Mimosa pudica*' and 'cancer' related topics

Despite this growing interest, current evidence remains limited and largely restricted to phytochemical characterization and in vitro investigations. Although multiple compounds reported in prior phytochemical studies were initially cataloged in the present analysis, not all constituents were deemed suitable therapeutic candidates. Drug-likeness, pharmacokinetic prediction, and toxicity screening were used to prioritize compounds with more favorable pharmacological profiles. Compounds with known toxicological concerns, including aflatoxin derivatives, were excluded from downstream network pharmacology and molecular docking analyses. Therefore, the present findings should not be interpreted as supporting the direct therapeutic use of crude *M. pudica* extracts but rather as a computational prioritization strategy to identify candidate compounds for further development.

The integrated network pharmacology analysis suggests that selected *M. pudica* compounds may influence multiple biological pathways linked to luminal breast cancer progression. The identified targets were associated not only with cell cycle regulation and DNA metabolism but also with pathways involved in growth factor signaling, migration, angiogenesis, and invasion. Such multitarget characteristics may be advantageous for addressing the complexity and molecular heterogeneity of breast cancer, in which compensatory signaling pathways frequently contribute to therapeutic resistance.

However, these findings remain predictive and should be interpreted as hypothesis-generating rather than as confirmatory evidence of therapeutic activity. Future studies should prioritize experimental validation of the selected compounds, particularly flavonoid-derived candidates such as apigenin, chrysin, diosmetin, galangin, and kaempferol. Initial validation may include in vitro assays in luminal-type breast cancer cell models (e.g., MCF-7) to assess cell viability, proliferation, apoptosis, migration, and cell cycle progression.

Subsequent studies may assess pharmacological efficacy, bioavailability, and toxicity in vivo using breast cancer models. In parallel, medicinal chemistry approaches may be pursued to optimize compound potency, selectivity, and pharmacokinetic performance. Additional computational methods, including molecular dynamics simulations, binding free-energy calculations, and transcriptomic or multi-omics integration, may further elucidate the molecular mechanisms underlying the therapeutic potential of *M. pudica*-derived compounds.

CONCLUSION

This study demonstrated the potential of *Mimosa pudica* as a source of bioactive compounds with multitarget therapeutic relevance for luminal-type breast cancer. Several candidate compounds and molecular targets linked to breast cancer progression were identified. Network analysis revealed that the predicted target proteins—including AURKA, AURKB, CA12, CDK1, ERBB2, ESR1, KIF11, KMO, MIF, MMP1, MMP9, NEK2, PLK1, PTK6, SQLE, TOP2A, TYMP, and TYMS—are involved in key biological processes such as

cell cycle regulation, DNA metabolism, growth factor signaling, angiogenesis, migration, and invasion. Among these, AURKA and CDK1 were prioritized for molecular docking based on network topology, pathway enrichment, biological relevance to luminal-type breast cancer, and structural suitability. Selected flavonoid-derived compounds from M. *pudica* (apigenin, chrysin, diosmetin, galangin, and kaempferol) showed favorable predicted interactions with AURKA and CDK1, with binding energies ranging from −7.6 to −8.9 kcal/mol. These findings suggest that *M. pudica*-derived compounds may modulate pathways associated with cell cycle progression and tumor development.

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