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In Silico Modelling Studies to Identification of Lead Compounds from Swietenia Macrophylla Against Cancer

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ABSTRACT

Objective: Cancer, a malignant neoplasm, is a multifactorial disease characterized by the progressive accumulation of genetic and epigenetic alterations. The present study aimed to identify potential lead compounds from Swietenia macrophylla with anticancer activity using molecular docking and in silico pharmacokinetic and toxicity profiling.

Methods: Phytoconstituents of Swietenia macrophylla were identified and their structures retrieved from the PubChem database. Target proteins including Cyclin-Dependent Kinase-2 (PDB ID: 1DI8), Cyclin-Dependent Kinase-6 (PDB ID: 1XO2), Vascular Endothelial Growth Factor-2 (PDB ID: 2OH4), Anti-Apoptotic Protein (PDB ID: 2O2F), and Insulin Growth Factor (PDB ID: 2OJ9) were obtained from the Protein Data Bank. Molecular docking was performed using PyRx to evaluate binding affinity and interaction with active sites. Docking results were visualized using BIOVIA Discovery Studio Visualizer. Pharmacokinetic and toxicity parameters of the selected compounds were predicted using SWISS ADME and pkCSM tools.

Results: The compounds Catechin, 3β-Hydroxystigmast-5-en-7-one, 3-Hydroxystigmast-5-en-7-one, and Epicatechin demonstrated strong binding affinity and favorable interactions, including hydrogen bonding and hydrophobic interactions with target proteins. These compounds also exhibited good pharmacokinetic properties and safety profiles. In comparison, standard anticancer drugs such as Seliciclib, Palbociclib, Lucitanib, Venetoclax, and Ceritinib showed similar binding interactions but demonstrated suboptimal pharmacokinetic and safety profiles.

Conclusion: The study concludes that Catechin, 3β-Hydroxystigmast-5-en-7-one, 3-Hydroxystigmast-5-en-7-one, and Epicatechin are promising lead compounds from Swietenia macrophylla with potential application in cancer therapy.

Keywords: *Swietenia macrophylla*, *Molecular docking*, *Anti-Cancer*,

1. INTRODUCTION

Malignant neoplasm, the medical term for cancer, is a collection of disorders that are defined by unchecked cell development and the ability to spread to other parts of the body. The buildup of genetic mutations and epigenetic modifications that interfere with regular cellular functions including DNA repair, apoptosis, and cell cycle regulation causes this illness. Mutations in important regulatory genes, such as oncogenes, tumor suppressor genes, and cell cycle regulators, frequently cause the unchecked growth of cancer cells [1]. Drug resistance, toxicity, and limited treatment efficacy are still critical obstacles in the fight against cancer, despite tremendous advancements in treatment, including targeted treatments, chemotherapy, and radiotherapy [2].

Consequently, there is an increasing interest in discovering new therapeutic compounds from natural sources, especially plants, that can provide safer and more effective treatments with reduced side effects. Swietenia macrophylla, usually referred to as the mahogany tree, has demonstrated potential in traditional medicine for the treatment of several diseases,

including cancer. Recent studies have emphasized its bioactive components, including flavonoids and terpenoids, which exhibit anti-cancer effects by altering many cancer-related pathways [4].

Molecular docking studies have become a vital tool in the drug discovery process because they shed light on the atomic-level binding interactions between small compounds and target proteins [5]. These investigations can help rank prospects for additional research by forecasting the binding affinity, selectivity, and mode of action of possible molecules. Our goal in this work is to use molecular docking studies to investigate the potential of phytocompounds from Swietenia macrophylla as lead molecules for cancer therapy.

Cyclin-Dependent Kinase-2 (CDK-2), Cyclin-Dependent Kinase-6 (CDK-6), Vascular Endothelial Growth Factor-2 (VEGF-2), Anti-Apoptotic Protein (Bcl-2), and Insulin Growth Factor (IGF) are among the important proteins linked to cancer that we have chosen as targets. These proteins play a role in controlling critical processes that are frequently dysregulated in cancer, including angiogenesis, apoptosis, and cell cycle progression. Our goal is to evaluate the binding affinities, active site interactions, and potential for therapeutic use of a few chosen phytocompounds from Swietenia macrophylla by docking them to these proteins.

Tropical and subtropical regions of the world are home to the endangered and medicinally significant Swietenia macrophylla King (Meliaceae) plant. In traditional medicine, S. macrophylla has been used extensively to cure a variety of illnesses. According to phytochemical studies, the main components of S. macrophylla are limonoids and their derivatives [6,7,8]. Table 1 summarizes the large number of isolated pure compounds with a variety of pharmacological properties that have been found from various sections of S. macrophylla.

Table 1: Binding affinity between phytoconstituents and target proteins

S. No	Name of the compounds	Binding affinity (-K/Cal)			
		Human CDK 2	Human CDK-6	VEGFR2	IGF-IR kinase
1	Hexadecanoic acid	-5.8	-5.3	-5	-5
2	Catechin	-9	-9.8	-7.6	-7.6
3	Epicatechin	-8.6	-9.7	-8.2	-8.2
4	3-Hydroxystigmast-5-en-7-one	-8	-8.7	-6.5	-6.5
5	Beta-sitosterol	-8.9	-6.8	-8.3	-8.3
6	Andirobin	-7.2	-7.2	-7.4	-7.4
7	Scopoletin	-7.1	-7.5	-6.7	-6.7
8	Stigmasterol	-9.7	-7.3	-8.8	-8.8
9	Germacrene D	-8.4	-7.5	-6.7	-6.7
10	Beta-sitostenone	-8.2	-9.9	-7.3	-7.3
11	Germacrene A	-7.9	-9	-6.7	-6.7
12	Cadina-1,4-diene	-8.8	-9.1	-7.7	-7.7
13	Swietenine J	-6.8	-7.3	-7	-7
14	Swietenolide monohydrate	-6.9	-6.9	-6.9	-7
15	Swietemahonin E	-6.4	-7.2	-7	-6.9
16	3beta,6-dihydroxydihydrocarapin	-6.9	-8.9	-7.5	-7.5
17	3-O-tigloyl-6-O-acetylswietenolide	-6.8	-6.8	-7.1	-7.1
18	Proceranolide	-6.6	-9.4	-7	-7
19	3,6-O,O-diacetylswietenolide	-6.7	-6.3	-6.9	-6.9
20	Khayanolide B	-7	-6.9	-7.1	-7.1
21	2-hydroxyswietenine	-6.4	-7.1	-7.1	-7.1

22	**1-O-deacetylkhayanolide E**	**-6.9**	**-7.1**	**-7**	**-7**
23	**1-O-acetylkhayanolide A**	**-6.9**	**-7.1**	**-6.6**	**-6.6**
24	**3-O-tigloylswietenolide**	**-6.5**	**-7.7**	**-6.9**	**-6.9**
25	**swietephragmin H**	**-6.4**	**-7.7**	**-6.8**	**-6.8**
26	**swietephragmin I**	**-6.3**	**-7.5**	**-6.8**	**-6.8**
27	**swietephragmin J**	**-6.5**	**-7.7**	**-6.5**	**-6.5**
28	**swietenitin Q**	**-7.2**	**-8.2**	**-6.6**	**-6.6**
29	**swietenitin W**	**-6.2**	**-7.6**	**-6.2**	**-6.2**
30	**Swietenitin X**	**-6.4**	**-7.4**	**-6.2**	**-6.2**
31	**Khayalactone**	**-8.3**	**-8.1**	**-7.8**	**-7.8**
32	**Swietemacrophyllanin**	**-9.8**	**-8.1**	**-8.8**	**-8.8**
33	**Ethylhexadecanoate**	**-5.4**	**-5.6**	**-4.9**	**-4.9**

The stem fraction of S. macrophylla exhibited antiviral activity [9], the seed extract demonstrated anti-inflammatory, anticancer, and antitumor activity [10], antimutagenic, and anti-infective activity [11], while the methanol extract of S. macrophylla exhibited antidiabetic activity [12], anti-nociceptive, anti-malarial, and hypolipidemic activity [13], as well as antioxidant [15]. The aqueous extract of S. macrophylla seeds demonstrated antimicrobial activity [16], while the petroleum ether extract of S. macrophylla seeds demonstrated antidiarrheal, antimalarial, antifeedant, and acaricidal properties [19]. The current study used in silico methods to assess the ADMET and anti-cancer activity of bioactive compounds from S. macrophylla.

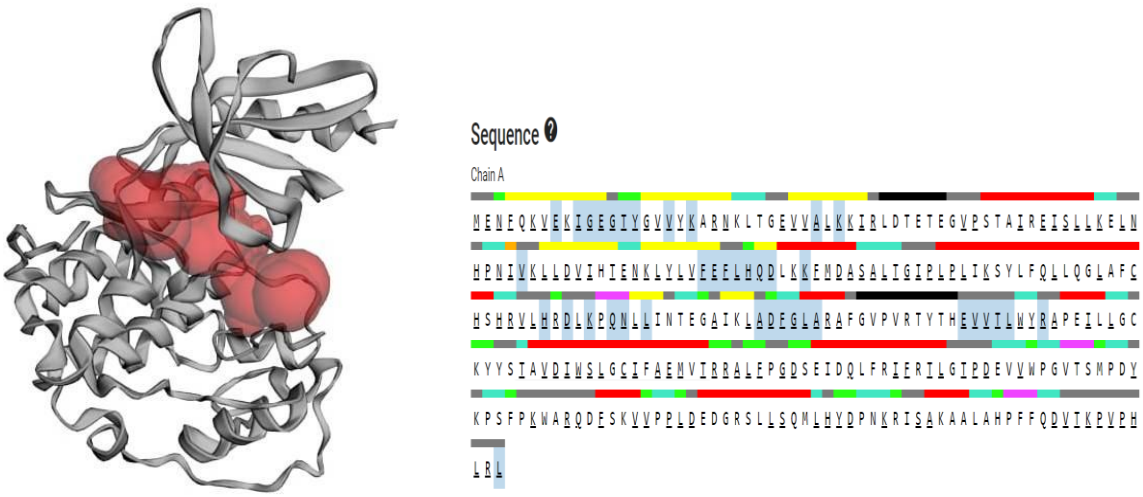
2. MATERIAL METHODS

2.1 3 D structure collection of Anticancer Phytobioactives and cancer targeted Protein preparation

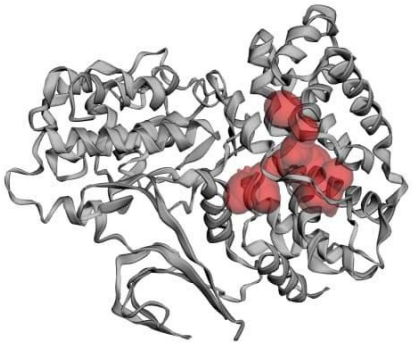
33 bioactive compounds of *Swietenia macrophylla*, were retrieved from literature [10] and bioactive compound's structure was retrieved from Pub Chem database (https://pubchem.ncbi.nlm.nih.gov/) as SDF format. Ligand optimization, energy minimization and conversion of retrieved ligands to 3D PDB format were done using Discovery Studio Visualizer [21]. Protein Data Bank (https://www.rcsb.org/) was used to retrieve the three-dimensional crystal structure of Cyclin-dependent kinase 2 (PDB ID:1DI8), Human cyclin-dependent kinase 6 (PDB ID:1XO2), vascular endothelial growth factor receptor 2 (VEGFR 2) (PDB ID:2OH4) and IGF-1R kinase (2OJ9). Protein actives site were predicted by using Computed Altas of Surface Topography of Proteins (CASTp) [22] (fig. 1) and BIOVIA Discovery studio 2017 R2 tool.

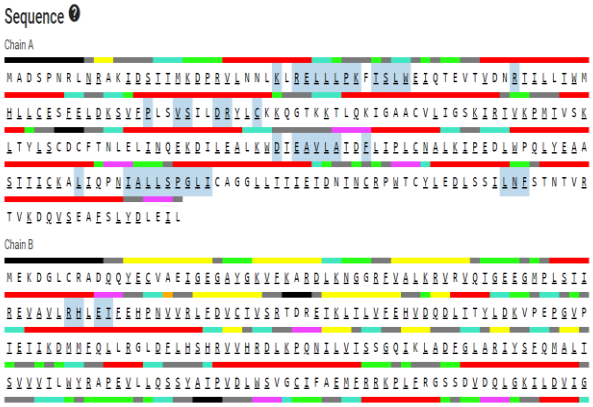
Fig. 1: Prediction of protein active sites

a) cyclin dependent kinase-2

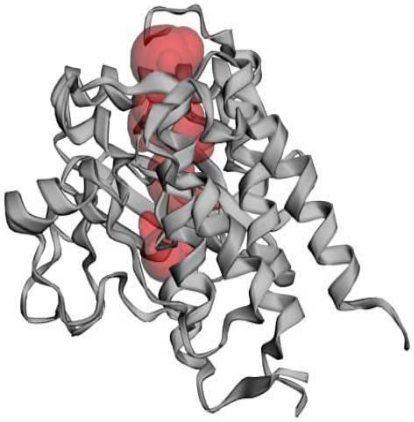


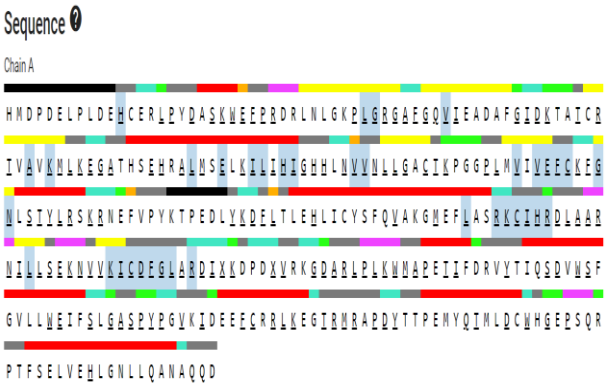
b) Human cyclin dependent kinase-6



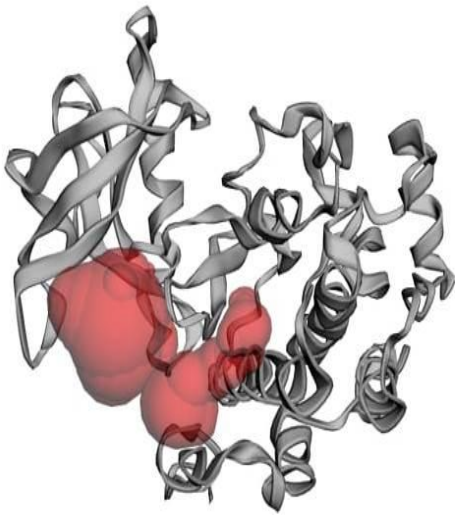


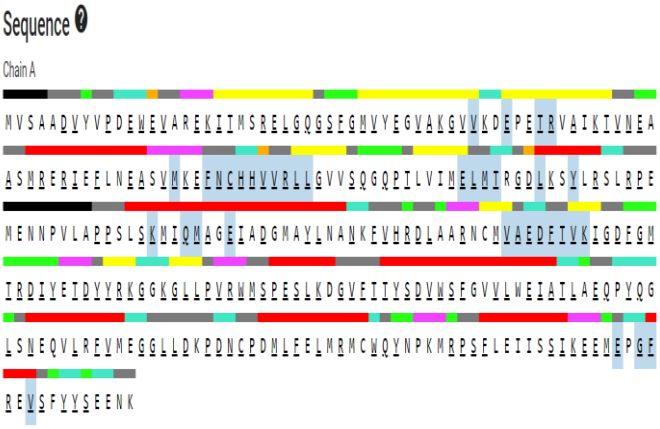
c) VEGFR-2





d) IGF-1R kinase





2.2 Virtual screening and molecular docking

A set of 33 compounds from *Swietenia macrophylla* was downloaded from the database. Virtual screening of the compounds with the 3D models was carried out using AutoDock Vina [23]. The virtual screening was performed by using PyRx virtual screening tool between bioactive compounds of *Swietenia macrophylla* and selected cancer targeted proteins and measure binding affinity and interaction visualization performed using Discovery studio 2017 R2 tool.

2.3 Pharmacokinetic parameters prediction by using SWISS ADME

ADMET (adsorption, distribution, metabolism, excretion and toxicity) of the bioactive compounds used SWISS-ADME is a website (https://www.swissadme.ch) [24] and pkCSM [25].

2.4 Biological activity Prediction

The potential biological properties of the selected compounds were investigated through the PASS web server [26]. It gives the prediction score for biological properties on the ratio of probability to be active (Pa) and probability to be inactive (Pi). A higher Pa means the biological property is having more probability for a compound.

3. RESULTS

3.1 Molecular docking studies

The binding affinity data indicates that several compounds from *Swietenia macrophylla* show promising interactions with the target cancer-related proteins. Notably, Catechin and Epicatechin exhibit strong binding affinity to Human CDK-2 and Human CDK-6, both having values as low as -9.0 Kcal/mol and -9.7 Kcal/mol, respectively. These results suggest that these compounds might inhibit the activity of these cyclin-dependent kinases, which are key regulators of the cell cycle, potentially halting the uncontrolled proliferation of cancer cells. Additionally, compounds like Stigmasterol and Beta-sitosterol also show significant affinity for VEGFR2 and IGF-IR kinase, with binding affinities of -9.7 Kcal/mol and -9.9 Kcal/mol, respectively. VEGFR2 is crucial for angiogenesis, while IGF-IR kinase is involved in cell growth and survival. The strong binding of these compounds to these targets could potentially disrupt cancer cell survival and the formation of new blood vessels, both of which are critical for tumor growth and metastasis. nterestingly, compounds like Swietemacrophyllanin and Catechin also exhibit high binding affinities for Human CDK-6 (-8.1 Kcal/mol) and VEGFR2 (-8.8 Kcal/mol), suggesting their potential to modulate multiple cancer-related pathways. These results, when compared to marketed drugs such as Seliciclib, Palbociclib, and Venetoclax, demonstrate that the compounds from *Swietenia macrophylla* could be viable candidates for further development in cancer therapy (table 1, fig. 2, fig. 3).

Fig. 2: 3D Visualisation interactions: a) Cyclin dependent kinase 2 (1DJ8) and Selicclib b) Human cyclin dependant kinase 6(1XO2) and Palbociclib c) VEGFR 2 (2OH4) and Lucitanib d) IGF-1R (2OJ9) and Ceritinib.

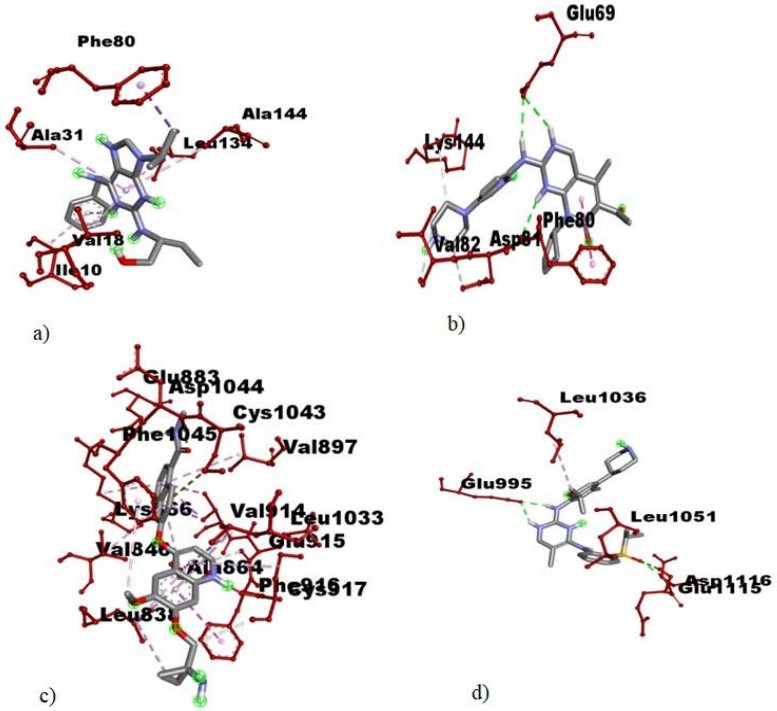
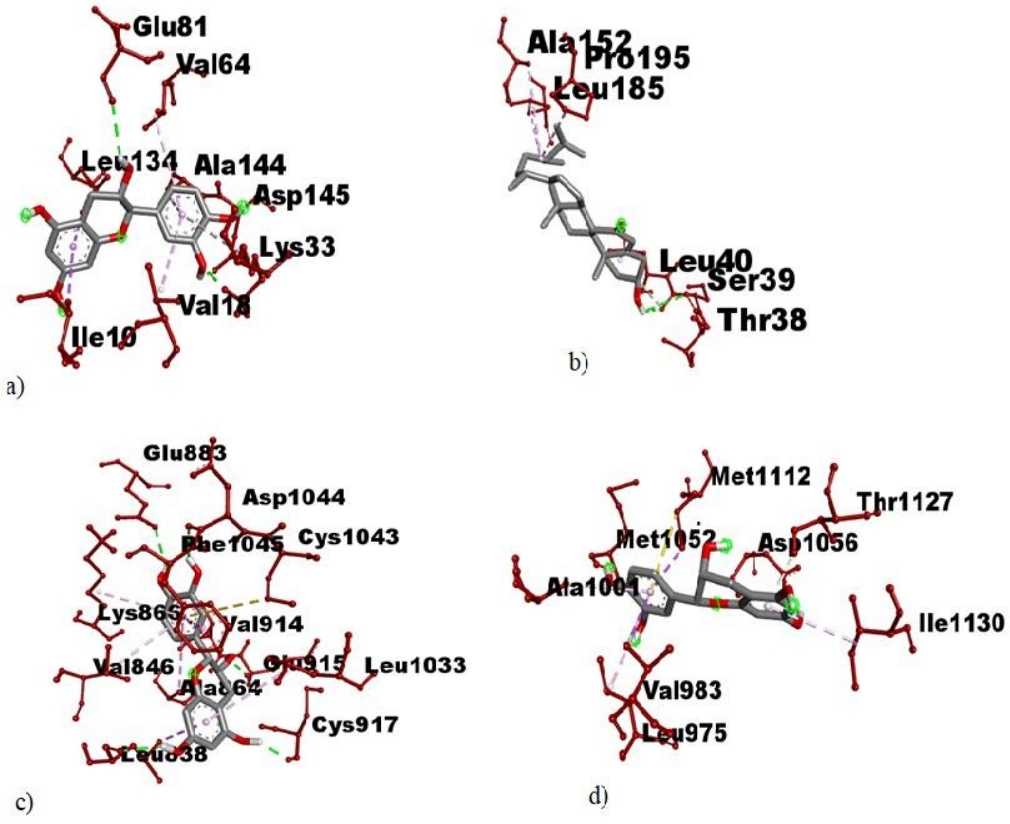


Fig. 3: a) Catechin and cyclin dependent kinase 2 b) 3-betaHydroxystigmast-5-en-7-one and human cyclin dependent kinase 6 c) Catechin and VEGFR 2 d) Epicatechin and IGF-1R kinase



3.2 Toxicity prediction using pkCSM database

AMES Toxicity: AMES toxicity is an important measure of a compound's mutagenic potential. Based on the results, all compounds tested, except for Germacrene D, Germacrene A, Cadina-1,4-diene, Swietenine J, Swietenolide monohydrate, Swietemahonin E, 3beta,6-dihydroxydihydrocarapin, 3-O-tigloyl-6-O-acetylswietenolide, Proceranolide, Swietenitin W, Swietenitin X, and Khayalactone, were not identified as mutagenic (negative Ames toxicity). This is a positive indicator that most of the compounds from *Swietenia macrophylla* do not pose a high risk of mutagenesis, which is important for their potential use in therapeutics (table 2, table 3).

Table 2: Toxicity prediction using pkCSM database

S.no	Name of the compound	AMES toxicity	Hepatotoxicity	Skin sensitization
1	Hexadecanoic acid	No	No	Yes
2	Catechin	No	No	No
3	Epicatechin	No	No	No
4	3β-hydroxystigmast-5-en-7-one	No	No	No
5	Beta-sitosterol	No	No	No
6	Andirobin	No	Yes	No
7	Scopoletin	No	No	No
8	Stigmasterol	No	No	No
9	Germacrene D	No	No	Yes
10	Beta-sitostenone	No	No	No
11	Germacrene A	No	No	Yes

12	Cadina-1,4-diene	No	No	Yes
13	Swietenine J	No	Yes	No
14	Swietenolide monohydrate	No	Yes	No
15	Swietemahonin E	No	Yes	No
16	3beta,6-dihydroxydihydrocarapin	No	Yes	No
17	3-O-tigloyl-6-O-acetylswietenolide	No	Yes	No
18	Proceranolide	No	Yes	No
19	3,6-O,O-diacetylswietenolide	No	No	No
20	Khayanolide B	No	No	No
21	2-hydroxyswietenine	No	No	No
22	1-O-deacetylkhayanolide E	No	No	No
23	1-O-acetylkhayanolide A	No	No	No
24	3-O-tigloylswietenolide	No	No	No
25	swietephragmin H	No	No	No
26	swietephragmin I	No	No	No
27	swietephragmin J	No	No	No
28	swietenitin Q	No	No	No
29	swietenitin W	No	Yes	No
30	Swietenitin X	No	Yes	No
31	Khayalactone	No	Yes	No
32	Swietemacrophyllanin	No	No	No
33	Ethylhexadecanoate	No	No	Yes

Table 3: ADME Prediction of phytoconstituents

S.no	**Name of The Compound**	**GI absorption**	**Blood brain barrier**	**P-gp substrate**	**CYP1A2 inhibitor**	**CYP2C19 inhibitor**	**CYP2C9 inhibitor**	**CYP2D6 inhibitor**	**CYP3A4 inhibitor**
1	Hexadecanoic Acid	High	Yes	No	Yes	No	Yes	No	No
2	Catechin	High	No	Yes	No	No	No	No	No
3	Epicatechin	High	No	Yes	No	No	No	No	No
4	3β-Hydroxystigmast-5-En-7-One	Low	No	No	No	No	No	No	No
5	Beta-Sitosterol	Low	No	No	No	No	No	No	No
6	Andirobin	High	No	Yes	No	No	No	No	No
7	Scopoletin	High	Yes	No	Yes	No	No	No	No

8	Stigmasterol	Low	No	Yes	No	No	No	No	Yes
9	Germacrene D	Low	No	No	No	No	Yes	No	No
10	Beta-Sitostenone	Low	No	No	No	No	Yes	No	No
11	Germacrene A	Low	No	No	No	Yes	Yes	No	No
12	Cadina-1,4-Diene	High	Yes	No	Yes	No	Yes	No	No
13	Swietenine J	Low	No	Yes	No	No	No	No	Yes
14	Swietenolide Monohydrate	Low	No	Yes	No	No	No	No	Yes
15	Swietemahonin E	Low	No	Yes	No	No	No	No	No
16	3beta,6-Dihydroxydihydrocarapin	High	No	Yes	No	No	No	Yes	Yes
17	3-O-Tigloyl-6-O-Acetylswietenolide	Low	No	Yes	No	No	No	No	No
18	Proceranolide	High	No	Yes	No	No	No	No	Yes
19	3,6-O,O-Diacetylswietenolide	Low	No	Yes	No	No	No	No	No
20	Khayanolide B	Low	No	Yes	No	No	No	No	No
21	2-Hydroxyswietenine	Low	No	Yes	No	No	No	No	No
22	1-O-Deacetylkhayanolide E	Low	No	Yes	No	Yes	No	Yes	No
23	1-O-Acetylkhayanolide A	High	No	Yes	No	No	No	Yes	No
24	3-O-Tigloylswietenolide	Low	No	Yes	No	No	No	No	No
25	Swietephragmin H	Low	No	Yes	No	No	No	No	No
26	Swietephragmin I	Low	No	Yes	No	No	No	No	Yes
27	Swietephragmin J	Low	No	No	No	No	No	No	No
28	Swietenitin Q	Low	No	Yes	No	No	No	No	Yes

29	Swietenitin W	Low	No	Yes	No	No	No	No	No
30	Swietenitin X	Low	No	Yes	No	No	No	No	No
31	Khayalactone	Low	No	Yes	No	No	No	Yes	Yes
32	Swietemacrophyllanin	Low	No	No	No	No	Yes	No	No
33	Ethylhexadecanoate	Low	No	Yes	No	No	No	No	No

Hepatotoxicity: Hepatotoxicity refers to the potential of a compound to cause liver damage. Most of the compounds, including Catechin, Epicatechin, 3β-hydroxystigmast-5-en-7-one, Beta-sitosterol, Scopoletin, Stigmasterol, and others, showed no hepatotoxicity, which is a favorable result for their safety profile. However, several compounds such as Andirobin, Swietenine J, Swietenolide monohydrate, Swietemahonin E, 3beta,6-dihydroxydihydrocarapin, 3-O-tigloyl-6-O-acetylswietenolide, Proceranolide, Swietenitin W, Swietenitin X, and Khayalactone did show hepatotoxic potential. This indicates that some compounds may have the potential to cause liver damage and should be further evaluated for their pharmacokinetics and liver safety before they can be considered for therapeutic use.

Skin Sensitization: Skin sensitization is an allergic response that occurs upon skin contact with a compound. Most compounds, including Catechin, Epicatechin, 3β-hydroxystigmast-5-en-7-one, Beta-sitosterol, Andirobin, Scopoletin, Stigmasterol, Beta-sitostenone, and others, did not show skin sensitization. However, compounds such as Hexadecanoic acid, Germacrene D, Germacrene A, Cadina-1,4-diene, and Ethylhexadecanoate exhibited skin sensitization, suggesting that they might trigger allergic reactions upon skin contact, which is a critical consideration for any potential topical formulations.

3.3 ADME prediction

Pharmacokinetic properties suggest that compounds from *Swietenia macrophylla* exhibit diverse behaviors. Catechin, Epicatechin, and Andirobin show good GI absorption and may have peripheral effects, though their interactions with P-gp could affect their distribution and bioavailability. Compounds like Hexadecanoic Acid and Scopoletin are notable for their BBB penetration, indicating possible neuroactive properties. The potential for drug-drug interactions via CYP450 inhibition should be considered, especially for compounds like Hexadecanoic Acid and Andirobin, which may interfere with the metabolism of other drugs (table 3).

3.4 Biological activity prediction

Many compounds like Andirobin and Swietenine J show strong anticancer (antineoplastic) potential, with additional effects like anti-inflammatory and antioxidant properties. Compounds such as Swietemahonin E and Swietenolide Monohydrate exhibit anti-inflammatory activity, which is crucial for conditions involving chronic inflammation, including cancer. -Sitosterol and Stigmasterol show antihypercholesterolemic effects, which could aid in treating hyperlipidemia and cardiovascular diseases. Catechin and Epicatechin help maintain membrane integrity, indicating potential use in neurodegenerative diseases and mucosal protection. Several compounds, like Swietenine J and Proceranolide, act as phosphatase inhibitors, which could modulate cellular signaling in cancer and immune disorders. Swietemacrophyllanin shows free radical scavenging activity, suggesting potential use in combating oxidative stress-related diseases. AR expression inhibitors, such as those found in Andirobin, point to potential use in treating androgen-dependent cancers like prostate cancer. Cytochrome P450 Interaction: Some compounds, such as Hexadecanoic Acid, are substrates for cytochrome P450 enzymes, relevant for drug metabolism (table 4).

Table 4: Biological activity prediction using PASS online database

S.no	Name of the Compound	Biological activity				
1	Hexadecanoic Acid	Acylcarnitine hydrolase	Alkylacetylglycerophosphatase inhibitor (0,966)	Alkenylglycerophosphocholine	CYP2J substrat	CYP2J2 substrate (0,961)

		inhibitor (0,973)		hydrolase inhibitor (0,963)	e (0,962)	
2	Catechin	Membrane integrity agonist (0,983)	Mucomembranous protector (0,962)	TP53 expression enhancer (0,959)	HMOX 1 expression enhancer (0,939)	Sulfotransferase substrate (0,927)
3	Epicatechin	Membrane integrity agonist (0,983)	Mucomembranous protector (0,962)	TP53 expression enhancer (0,959)	HMOX 1 expression enhancer (0,939)	Sulfotransferase substrate (0,927)
4	3β-Hydroxystigmast-5-En-7-One	Prostaglandin-E2 9-reductase inhibitor (0,970)	Testosterone 17beta-dehydrogenase (NADP+) inhibitor (0,955)	Antihypercholesterolemic (0,950)	CYP4B substrate (0,937)	Cholesterol antagonist (0,932)
5	Beta-Sitosterol	Prostaglandin-E2 9-reductase inhibitor (0,962)	Antihypercholesterolemic (0,953)	Cholesterol antagonist (0,937)	Testosterone 17beta-dehydrogenase (NADP+) inhibitor (0,932)	Alkenylglycerophosphocholine hydrolase inhibitor (0,929)
6	Andirobin	Antineoplastic (0.863)	Antieczematic (0.824)	HMOX1 expression enhancer (0.788)	AR expression inhibitor (0.739)	Antimetastatic (0.713)
7	Scopoletin	CYP2C12 substrate (0.958)	Chloredecone reductase inhibitor (0.938)	Aspulvinonedimethylallytransferase inhibitor (0.931)	CYP2A11 substrate (0.926)	4-Nitrophenol2-monooxygenase inhibitir (0.921)
8	Stigmasterol	DELTA14-sterol reductase inhibitor (0,965)	Antihypercholesterolemic (0,960)	Prostaglandin-E2 9-reductase inhibitor (0,959)	Cholesterol antagonist (0,957)	Alkenylglycerophosphocholine hydrolase inhibitor (0,952)
9	Germacrene D	Antieczematic (0,915)	Carminative (0,885)	Antineoplastic (0,817)	Testosterone agonist (0,732)	Phosphatase inhibitor (0,712)
10	Beta-Sitostenone	Antihypercholesterolemic (0.970)	Cholesterol antagonist (0.965)	Testosterone 17beta-dehydrogenase inhibitor (0.915)	Oxidoreductase inhibitor (0.933)	Prostaglandin-E2 9-reductase inhibitor (0.913)

11	Germacrene A	CYP2B1 substrate (0,965)	Carminative (0,956)	Retinol dehydrogenase inhibitor (0,928)	CYP2B Substrate (0,925)	Antieczematic (0,886)
12	Cadina-1,4-Diene	Carminative (0,846)	Glutamate-5-semialdehyde dehydrogenase inhibitor (0,829)	Antieczematic (0,810)	Ubiquinol-cytochrome-c reductase inhibitor (0,782)	Alkylacetylglycerophosphatase inhibitor (0,732)
13	Swietenine J	Antineoplastic (0,860)	Antiinflammatory (0,772)	Hepatoprotectant (0,737)	Phosphatase inhibitor (0,651)	Antifungal (0,625)
14	Swietenolide Monohydrate	Phosphatase inhibitor (0,667)	HMOX1 expression enhancer (0,649)	Antineoplastic (0,637)	Beta glucuronidase inhibitor (0,582)	AR expression inhibitor (0,577)
15	Swietemahonin E	Antineoplastic (0.873)	Antiinflammatory (0.721)	Antifungal (0.661)	HMOX1 expression enhancer (0.649)	Phosphatase inhibitor (0.650)
16	3beta,6-Dihydroxydihydrocarapin	AR expression inhibitor (0.693)	HMOX1 expression enhancer (0.696)	Phosphatase inhibitors (0.667)	Antineoplastic (0.673)	CYP2A11 substrate (0.621)
17	3-O-Tigloyl-6-O-Acetylswietenolide	Antineoplastic (0.889)	Antiinflammatory (0.822)	Hepatoprotectant (0.699)	Beta glucuronidase inhibitor (0.643)	Antifungal (0.634)
18	Proceranolide	Antineoplastic (0.786)	Antieczematic (0.682)	Phosphatase inhibitors (0.647)	Beta glucuronidase inhibitor (0.573)	HMOX1 expression enhancer (0.571)
19	3,6-O, O-Diacetylswietenolide	Antiinflammatory (0.834)	Antineoplastic (0.797)	Beta glucuronidase inhibitor (0.665)	Phosphatase inhibitor (0.636)	Paraoxonase substrate (0.574)
20	Khayanolide B	HMOX1 expression enhancer (0,741)	Antineoplastic (0,689)	AR expression inhibitor (0,657)	Phosphatase inhibitor (0,667)	Antifungal (0,623)
21	2-Hydroxyswietenine	Vanilloid agonist (0.899)	antineoplastic (0.656)	AR expression inhibitor (0.622)	Phosphatase inhibiotr (0.636)	CY2H substrate (0.621)

22	1-O-Deacetylkhayanolide E	HMOX1 expression enhancer (0,750)	Antineoplastic (0,740)	AR expression inhibitor (0,664)	Phosphatase inhibitor (0,661)	Beta glucuronidase inhibitor (0,575)
23	1-O-Acetylkhayanolide A	HMOX1 expression enhancer (0,723)	Antineoplastic (0,723)	AR expression inhibitor (0,670)	Antifungal (0,638)	Beta glucuronidase inhibitor (0,627)
24	3-O-Tigloylswietenolide	Vanilloid agonist (0.897)	Antifungal (0.725)	Antineoplastic (0.731)	Phosphatase inhibitors (0.647)	AR expression inhibitor (0.576)
25	Swietephragmin H	Antineoplastic (0,901)	Vanilloid 1 agonist (0,581)	Beta glucuronidase inhibitor (0,567)	Nitric oxide antagonist (0,517)	Phosphatase inhibitor (0,567)
26	Swietephragmin I	Antineoplastic (0,871)	Vanilloid 1 agonist (0,574)	Beta glucuronidase inhibitor (0,560)	Phosphatase inhibitor (0,559)	Antieczematic (0,514)
27	Swietephragmin J	Antineoplastic (0,905)	Vanilloid 1 agonist (0,588)	Beta glucuronidase inhibitor (0,573)	Nitric oxide antagonist (0,536)	Phosphatase inhibitor (0,574)
28	Swietenitin Q	Antineoplastic (0,893)	Nitric oxide antagonist (0,617)	Vanilloid 1 agonist (0,578)	Beta glucuronidase inhibitor (0,576)	Phosphatase inhibitor (0,565)
29	Swietenitin W	Antineoplastic (0,916)	Nitric oxide antagonist (0,696)	Antieczematic (0,615)	Phosphatase inhibitor (0,596)	Beta glucuronidase inhibitor (0,587)
30	Swietenitin X	Antineoplastic (0,887)	Nitric oxide antagonis (0,678)	Antieczematic (0,630)	Beta glucuronidase inhibitor (0,579)	Phosphatase inhibitor (0,588)
31	Khayalactone	Antineoplastic (0,741)	Antieczematic (0,745)	Phosphatase inhibitor (0,657)	Ryanodine receptor antagonist (0,600)	Ryanodine receptor 1 antagonist (0,600)
32	Swietemacrophyllanin	Membrane integrity agonist (0,948)	TP53 expression enhancer (0,852)	HMOX1 expression enhancer (0,822)	Free radical scavenger (0,819)	Fibrinolytic (0,792)

33	Ethylhexadecanoate	Acrocylindropepsin inhibitor (0,957)	Chymosin inhibitor (0,957)	Saccharopepsin inhibitor (0,957)	Polyporopepsin inhibitor (0,932)	Pro-opiomelanocortin converting enzyme inhibitor (0,917)

4. DISCUSSION

The current work used molecular docking studies to find possible lead compounds from Swietenia macrophylla for cancer treatment. The study concentrated on how identified phytocompounds interacted with important proteins linked to cancer, such as Vascular Endothelial Growth Factor-2 (VEGF-2), Cyclin-Dependent Kinase-2 (CDK-2), Cyclin-Dependent Kinase-6 (CDK-6), Anti-Apoptotic Protein (Bcl-2), and Insulin Growth Factor (IGF). These proteins were chosen because they play important roles in the angiogenesis, survival, and proliferation of cancer cells.

According to the molecular docking results, the compounds that were chosen—Catechin, 3-Hydroxystigmast-5-en-7-one, Epicatechin, and 3 Beta-Hydroxystigmast-5-en-7-one—showed positive interactions with the target proteins, especially through hydrophobic and hydrogen bonding interactions. These interactions may account for the chemicals' possible therapeutic benefits and are essential for preventing the function of proteins linked to cancer. The chosen compounds' binding affinities, which indicate how strongly they interact with the target proteins, were revealed by the docking experiments. With docking scores comparable to those of commercially available medications such as Seliciclib, Palbociclib, Lucitanib, Venetoclax, and Ceritinib, the compounds demonstrated substantial binding affinities. These medications are well-known for their ability to treat cancer, especially by increasing apoptosis in cancer cells and blocking cyclin-dependent kinases (CDK).

Hydrogen bonds and hydrophobic interactions, which are essential for maintaining the stability of the binding complex, were notably present in the interactions between the drugs and cancer proteins. This implies that the chemicals found may successfully block the targeted proteins, perhaps causing apoptosis or cancer cell cycle halt. Research on catechin has shown that it can disrupt a number of cancer pathways, especially by modifying CDKs [27]. Similar to this, epicatechin has been shown to exhibit strong anti-cancer effects, particularly in models of breast cancer [28]. Similar potential is shown by the chemicals from Swietenia macrophylla, suggesting that they might make good candidates for cancer treatment medication development.

The chosen drugs showed advantageous pharmacokinetic characteristics, including good oral bioavailability, lipophilicity, and adequate solubility, according to the pharmacokinetic analysis conducted using SWISS ADME and pKCSM. These characteristics are necessary for the chemicals to reach the intended locations in the body and to be absorbed efficiently when taken orally. These chemicals are also good candidates for additional preclinical testing because the toxicity prediction indicated that they are safe and do not pose any serious toxicity risks. Seliciclib and Palbociclib, two commercially available medications utilized for comparison, on the other hand, had respectable pharmacokinetic profiles but varied in their levels of toxicity and off-target effects. For instance, in certain clinical contexts, seliciclib has been linked to liver damage [29].

Drug development must take into account the toxicity and adverse effects of marketed medications, highlighting the benefits of natural substances such as those obtained from Swietenia macrophylla.which might provide safer substitutes. The chemicals from Swietenia macrophylla showed similar or even superior binding interactions when compared to commercially available cancer medications like Seliciclib, Palbociclib, Lucitanib, Venetoclax, and Ceritinib, especially when it came to hydrogen bonding and hydrophobic interactions. The durability of drug-protein complexes depends on these interactions, which raises the drugs' possible effectiveness. The molecules also demonstrated minimal toxicity, which is a crucial benefit over manufactured medications, which can have serious adverse consequences [30].

The study's findings are consistent with earlier investigations on plant-derived chemicals as potential cancer treatments. Bioactive substances with anti-cancer properties have long been found in natural goods [31]. Particularly when used as adjuvant medicines to overcome resistance to traditional chemotherapy, the chemicals under investigation may provide novel therapeutic paths.

5. CONCLUSION

The present study demonstrates the potential of Catechin, 3 Beta-Hydroxystigmast-5-en-7-one, Catechin, 3-Hydroxystigmast-5-en-7-one, and Epicatechin as promising lead compounds from *Swietenia macrophylla* for cancer therapy. The molecular docking results suggest that these compounds could effectively interact with key cancer-related proteins and have favorable pharmacokinetic and toxicity profiles. These compounds hold promise as potential candidates for further drug development and cancer treatment.

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