

Anticancer potential of *Dendrocnide meyeniana*: phytochemical profiling, ADMET analysis, molecular docking, and in silico cytotoxicity evaluation

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Abstract

The study of phytochemicals offers opportunities for therapeutic development due to their source of bioactive metabolites with diverse pharmacological properties. This research focused on *Dendrocnide meyeniana*, a plant species analyzed to determine its phytochemical composition and anticancer properties using *in silico* approaches. Using GC-MS and UHPLC-QTOF-MS, a total of 78 compounds were identified, confirming the plant's chemical richness. To further assess the pharmaceutical applications, the absorption, distribution, excretion, and toxicity (ADMET) profiles of selected 31 compounds were examined. Among these, nine satisfied the drug-likeness criteria, with eight exhibiting favorable oral bioavailability. Molecular docking simulations were conducted to predict the inhibitory interactions against significant cancer-related targets: ERG, p53, MMP7, and CDK8/Cyclin C. Results revealed strong affinities with cryptotanshinone, emerging as a lead candidate, exhibiting docking scores ranging from -6.5 to -8.3 kcal/mol, surpassing fluorouracil, a standard chemotherapeutic drug. Supporting parameters such as ligand efficiency, inhibition constants, and the number of hydrogen bond interactions confirmed its anticancer potential. Furthermore, *in silico* cytotoxicity predictions identified Usnic acid, Cryptotanshinone, and related compounds as potential inhibitors of brain glioma and lymphoblastic leukemia cell lines. Overall, these findings highlight *D. meyeniana* as a valuable reservoir of bioactive metabolites with promising applications in plant-based anticancer drug development.

1. Introduction

Plants are widely recognized as rich sources of bioactive metabolites that exhibit diverse pharmacological properties¹. Globally, approximately 80–85% of the population relies on plant-based medicines for the management and treatment of various diseases^{2,3}. Numerous plant extracts, as well as isolated bioactive compounds and their derivatives, have shown considerable potential as candidates for both the prevention and treatment of cancer³.

The current interest in the properties of plant compounds represents a growing area of research aimed at discovering reliable and effective anticancer agents that can selectively target tumor cells while minimizing toxicity to normal cells^{4,5}. Many plant-derived compounds exert anticancer effects by modulating key cellular signaling pathways. These mechanisms include reducing oxidative stress, inducing cell cycle arrest at various checkpoints, downregulating anti-apoptotic proteins, suppressing the expression of P13K/Akt/MMP pathways, and upregulating tumor suppressor and apoptotic markers^{6,7}.

Dendrocnide meyeniana (Walpers) Chew, *Gard. Bull. Singapore* 21: 206 (1965) is a member of the Urticaceae family and is a deciduous shrub native to the Philippines and Taiwan. It typically grows to a height of 3 to 7 meters and is characterized by its large, broadly triangular leaves measuring 20 to 40 cm, densely clustered small flowers, and small fleshy fruits that range in color from white to pale violet⁸. Notably, the plant is covered with conspicuous stinging hairs, particularly on its twigs and leaf surfaces, which contain irritant compounds such as histamine, oxalic acid, and tartaric acid. These compounds can cause erythematous papules and a stinging sensation upon contact⁹. *D. meyeniana* holds cultural and medicinal importance. It has long been utilized by communities in traditional medicine, where it is valued for its purported therapeutic properties despite its toxic nature.

In silico techniques have become essential tools in modern drug discovery and development, offering cost-effective and rapid solutions to predict pharmacokinetic properties and optimize compounds^{10,11}. These computational approaches, including ADMET profiling and molecular docking, enable early assessment of drug candidates' safety and efficacy, reducing the likelihood of late-stage failures¹². While *in vitro* and *in vivo* methods remain crucial, *in silico* tools provide valuable initial insights, streamlining the drug development process and reducing reliance on expensive laboratory experiments¹³. The integration of *in silico*, *in vitro*, and *in vivo* techniques has shown promising results in enhancing predictive power and accelerating drug discovery^{13,14}. As computational methods continue to evolve, they are revolutionizing drug design by offering rapid, cost-effective solutions that bridge the gap between discovery and development.

In this study, we identified the phytochemical constituents of *D. meyeniana* utilizing GC-MS and UHPLC-QTOF-MS analysis. We also performed predictions of their ADMET properties and molecular docking analyses to assess their binding affinity with relevant anticancer targets. Finally, we evaluated the cytotoxic potential of the identified compounds against tumor and non-tumor cell lines using *in silico* analyses.

2. Materials and methods

2.1. Compliance with ethical standards

This study complied with institutional, national, and international guidelines and legislation on plant research. The study adhered to the IUCN Policy Statement on Research Involving Species at Risk of Extinction (Version 1.0, approved 1989)¹⁵ and the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES, 1973, with current appendices)¹⁶. *D. meyeniana* is currently assessed as Least Concern under the IUCN Red List Categories and Criteria (version 3.1, latest assessment 2022)¹⁷ and is not listed under any CITES Appendices. No endangered or protected species were involved in this research.

2.2 Plant collection and processing

Permission to collect *D. meyeniana* was obtained from the local officials of Sta. Fe, Nueva Vizcaya, Philippines and the Department of Environment and Natural Resources (DENR), Philippines. Voucher specimens were identified by Mr. Paul Henric Gojo Cruz, a taxonomist from the Department of Biological Sciences, Central Luzon State University, Nueva Ecija, Philippines, where the specimens are deposited in the department's public collection with Voucher ID No. EP0001.

The freshly harvested leaves were immediately placed in a sterile plastic bag and transported to the laboratory for further processing. The leaves were thoroughly washed with distilled water, followed by a final rinse with 70% (v/v) ethanol to remove surface contaminants¹⁸. The cleaned leaves were air-dried at room temperature for 15 days. Once completely dried, the leaves were ground into fine powder using a mechanical blender. The powdered plant materials were stored in a sterile, airtight 1000 ml container for further use.

2.3. Ethanol extraction

Fifty (50) grams of ground leaves of *D. meyeniana* were transferred to a separate container, and 500 mL of 95% ethanol was added. The solution was kept in the dark for 72 hours (3 days) at room temperature. After this period, the ethanol extracted solution was separated by filtration through filter paper. Subsequently, the resulting filtrates were concentrated under reduced pressure at 40°C using a rotary evaporator (IKA® RV 10/ HB 10/ 220 to 240/ 20 to 280 rpm, China). The crude extracts were sterilized by centrifugation at 10,000 x g for 30 min, followed by membrane filtration using an acrodisc 25mm Syringe Filter and stored at 4°C until further use.

2.4. Gas Chromatography-Mass Spectroscopy (GC-MS)

After concentrating the extracts using a rotary evaporator, 20 µL aliquots were transferred into individual vials. The extracts were dried using a vacuum centrifuge at 25 °C for 1.5 hours. Each vial was derivatized with 20 µL of methoxamine HCl in pyridine (30 mg/mL) at 37 °C for 2 hours with intermittent shaking, followed by the addition of 20 µL of N, O-Bis(trimethylsilyl)trifluoroacetamide (BSTFA) with 1% trimethylchlorosilane (TMCS) and further incubation at 37 °C for 1 hour. The sample solutions were then left to stand at room temperature for 1 hour before GC-MS analysis. A blank was prepared following the previous procedures.

Compound identification was performed using an Agilent 8890 GC system (Agilent Technologies, Santa Clara, CA, USA) equipped with a 5977B Mass Selective Detector (MSD) and an HP-5MS column (30m x 0.250 mm, 0.25-micron film thickness). The GC-MS operated in electron ionization mode (70eV) with a scan range of energy method 50 to 550 m/z and a scan time of 0.2 seconds. A 1 µL sample solution was injected using a 1:10 ratio at an injector temperature of 300°C. The oven was programmed to rise from 45 °C (0 min hold) to 300 °C at 10 °C/min, with a final hold for 9 minutes, totaling 34.5 minutes of routine. Peaks appearing at ~5.00 minutes corresponded to the derivatization agent. Compounds were identified by comparing retention times, peak data, and mass spectra with entries in the NIST library.

2.5. UHPLC-QTOF-MS Analysis

Metabolites were also identified using UHPLC-QTOF-MS (Agilent 1260 Infinity II HPLC with 6530 QTOF-MS/MS). Samples were analyzed in negative ionization mode over a 25- 1000m/z scan range at 5 sec/ spectrum and 200 ms/spectrum. A Poroshell 120 EC-C18 column (4.6 x 150mm, 4µm) was used with a mobile phase of ultrapure water (H₂O, with 0.1% MS-grade formic acid) and acetonitrile (CAN), both containing 0.1% MS-grade formic acid.

For sample preparation, 250µL of H₂O and 250µL MeOH were mixed, vortexed (1 min), sonicated (5 min), and centrifuged (12000 rpm, 5 min). A 50µL aliquot was reconstituted with the same solvent mix and processed similarly. The final 2 mL extract was transferred to vials for UHPLC-QTOF analysis. Gradient elution was carried out at a flow rate of 0.4 mL/min with a 10µL injection volume at 40 °C. Data were processed using the Agilent Mass Hunter Qualitative Analysis Navigator (B.08.00) and interpreted through Global Natural Products Social Molecular Networking (GNPS) software.

2.6. ADMET prediction

Nine (9) volatile and 22 non-volatile compounds were selected based on their higher percentage composition, cosine similarity, and relevant structures^{2,19}. The interaction of bioactive compounds with the human body involves their absorption, distribution, metabolism, excretion, and toxicity (ADMET). These properties are crucial for evaluating pharmacodynamic properties and therapeutic potential²⁰. The molecular structures and SMILES notation of identified compounds were retrieved from PubChem (<https://pubchem.ncbi.gov>, accessed May 2025), and computational approaches were done in a web-based system. Drug-likeness and pharmacokinetic properties were predicted using the SwissADME software (<http://www.swissadme.ch>). The toxicological profile, including oral, hepatotoxicity, cytotoxicity, mutagenicity, carcinogenicity, and immunotoxicity, was assessed via the ProTox-II tool (<https://tox.charite.de/protox3> accessed May 2025)^{19,21,22}.

2.7. Molecular Docking Analysis

Molecular docking was conducted to assess the interaction between selected bioactive ligands and cancer-related protein receptors. Four target proteins, such as EGFR (PD ID: 4lqm), p53 (PD ID: 3hf1), MMP7 (PD ID: 2y6d), and CDK8/ Cyclin C (PD ID: 6t41), were retrieved from the RCSB Protein Data Bank (PDB). These proteins play a critical role in cancer biology. The 3D structures of the proteins were prepared using the Biovia Discovery Studio- 2025 Client by removing water molecules and heteroatoms (HETATOMS) while adding polar hydrogen. The refined structures were then converted to PDB format for docking analysis.

Bioactive compounds from *D. meyeniana* were selected for molecular docking studies based on two criteria: binding energies below -6.0 kcal/mol and compliance with established drug-likeness rules, including the Lipinski rule and the filters proposed by Veber, Ghose, Egan, and Muegge². A total of nine compounds were selected from the 78 tentatively identified volatile and non-volatile metabolites obtained through GC-MS and UHPLC-QTOF-MS analyses (Tables 1 and 2). The corresponding chemical structures were retrieved from the PubChem database (<https://pubchem.ncbi.nlm.nih.gov>, accessed April 2025) in Structure data format (SDF) for docking studies. The selected ligand molecules, along with their PubChem Compound Identifiers (CIDs) such as (A) Usnic acid (CID: 5646); (B) Anisomycin (CID: 253602); (C) 5,6,2'-trimethoxyflavone (CID: 14484690); (D) Cinchonine (CID: 90454); (E) 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl(Z)-2-methylbut-2-enoate (CID: 51136479); (F) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one (CID:

102187241, 25763650); (G) 4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxo-13-azatricyclo [8.5.1.0^{13,16}] hexadec-10-ene-3,7-dione (CID: 9415) (H) Cryptotanshinone (CID 160254, 496348); ; (I) 6-(1,1-dimethylallyl)-2-(1-hydroxy-1-methylethyl)-2,3-dihydro-7H-furo[3,2-G]chromen-7-one (CID: 5287846).

The ligand structures were uploaded into PyRx Software, which integrates the Open Babel tool for molecular conversion and optimization. The energy minimization was performed using the Universal Force Field (UFF) by adding partial charges and optimizing the molecular geometry. Following minimization, the ligands were converted into AutoDock PDBQT format, the required input for molecular docking simulations. Docking simulations were carried out using the AutoDock Vina Wizard within PyRx to evaluate binding affinities and potential ligand-receptor interactions relevant to anticancer activity.

Protein and ligand files were selected using the Vina Wizard Control Panel, and docking was initiated by clicking the “Run Vina” command. Results were analyzed via “Analyze Vina” functions, and binding affinity scores were exported as CSV files for further interpretation.

The 2D and 3D visualization of docking poses and interaction profiles was performed using Biovia Discovery Studio 25 Client to illustrate ligand-receptor binding at the molecular level ^{19,23}.

2.8. *In silico* cytotoxicity prediction

The cytotoxic potential of the major compounds of *D. meyeniana* was subsequently evaluated using the *in silico* cell line cytotoxicity predictor (CLC-Pred) available at <http://www.way2drug.com/Cell-line/>. This web-based tool predicts the cytotoxic effects of chemical compounds on both human tumor and non-tumor cell lines by analyzing the structure-activity relationship. The results include two probability scores: Pa (probability of activity) and Pi (probability of inactivity). A compound is considered to have potential cytotoxic activity if Pa>Pi, indicating a higher likelihood of being active against the tested cell lines ²⁰.

3. Results

3.1 Phytochemical composition of *D. meyeniana* detected by GC-MS and UHPLC-QTOF-MS

The GC-MS analysis of the ethanolic extract of *D. meyeniana* revealed thirty-nine volatile compounds (Table 1 and Figure 1A). The major classes identified were sesquiterpenoids, fatty acids, and terpenoids. Among these, Stigmast-5-ene,3 β -(trimethylsiloxy)-,24semerged as the most abundant constituent, representing 26.99% of the total area. The second most prevalent compound was phytol (11.735), a diterpene alcohol. Several fatty acids were also prominent, including palmitic acid (10.28%), α -Linolenic acid (3.81%), and 9,12, 9,12-octadecadienoic (linoleic acid) (4.87 %). Furthermore, notable sesquiterpenoids such as Silphinene (3.75%) and Neophytadiene (2.96%) were detected.

Table 1. The GC-MS analysis results of *D. meyeniana*.

Peak No.	RT (min)	MW (g/mol)	Tentative compound	% Peak area	MF	Nature of Compound
1	7.021	90.08	Lactic acid*	0.29	C ₃ H ₆ O ₃	Alpha Hydroxy acid
2	8.206	60.056	Urea*	0.57	CH ₄ N ₂ O	Organic carbonic acid
3	9.671	106.12	Diethylene glycol*	0.53	C ₄ H ₁₀ O ₃	Organooxygen compound
4	10.157	92.09	Glycerol*	3.74	C ₃ H ₈ O ₃	Carbohydrate
5	10.884	204.35	Silphiperfol-5-ene	0.39	C ₁₅ H ₂₄	Sesquiterpenoid
6	11.176	204.35	Silphinene	3.75	C ₁₅ H ₂₄	Sesquiterpenoid
7	11.668	204.35	Modephene	0.62	C ₁₅ H ₂₄	Sesquiterpenoid
8	11.754	204.35	alpha-isocomene α-Isocomene	0.41	C ₁₅ H ₂₄	Sesquiterpenoid
9	12.04	204.35	(±)-β-Isocomene	0.40	C ₁₅ H ₂₄	Sesquiterpenoid
10	12.171	204.35	Caryophyllene	0.40	C ₁₅ H ₂₄	Sesquiterpenoid
11	13.298	122.12	Meso-erythritol	1.90	C ₄ H ₁₀ O ₄	Carbohydrate
			L-Threitol*		C ₄ H ₁₀ O ₄	Carbohydrate
12	13.625	206.32	2,4-Di-tert-butylphenoxytrimethylsilane	0.51	C ₁₄ H ₂₂ O	Phenylpropane
13	15.828	152.15	D- (+)-arabitol	1.83	C ₅ H ₁₂ O ₅	Carbohydrate
			L- (-)-arabitol		C ₅ H ₁₂ O ₅	Carbohydrate
		152.15	Xylitol*		C ₅ H ₁₂ O ₅	Carbohydrate
14	15.885	152.15	Adonitol*	0.48	C ₅ H ₁₂ O ₅	Carbohydrate
15	16.812	278.5	Neophytadiene	2.96	C ₂₀ H ₃₈	Sesquiterpenoid
16	16.915	228.37	Myristic acid*	1.13	C ₁₄ H ₂₈ O ₂	Fatty acid
17	17.064	280.5	2-hexadecen-1-ol, 3,7,11,15tetramethyl-, acetate, [R- [R*, R*- (E)]]-	1.21	C ₂₀ H ₄₀	Fatty acid
18	17.252	296.53	3,7,11,15-tetramethyl-2-hexadecen-1-ol	1.69	C ₂₀ H ₄₀ O	Isoprenoid
19	17.481	180.16	D-fructose, 1,3,4,5,6-pentakis-o(trimethylsilyl)-, o-methyl oxime	1.41	C ₁₆ H ₁₂ O ₆	Organooxygen compound
20	17.584	180.16	D- (-)-fructose, pentakis(trimethylsilyl) ether, methyloxime (syn)	0.34	C ₁₆ H ₁₂ O ₆	Organooxygen compound
21	17.745	180.16	D-glucose, 2,3,4,5,6-pentakis-O-(trimethylsilyl)-, o-methyloxime, (1Z)-	0.85	C ₁₆ H ₁₂ O ₆	Organooxygen compound
22	18.054	291.435	2,4,6 tri-tert-butylnitrobenzene	3.74	C ₁₈ H ₃₆ O ₂	Aromatic nitro compound
23	18.340	284.477	Hexadecenoic acid, ethyl ester	1.11	C ₁₈ H ₃₆ O ₂	Fatty acid
24	18.855	256.42	Palmitic acid	10.28	C ₁₆ H ₃₆ O ₂	Fatty acid
25	20.068	296.50	Phytol	11.73	C ₂₀ H ₄₀ O	Diterpene
26	20.382	280.45	9,12- octadecadienoic acid	4.87	C ₁₈ H ₃₂ O ₂	Fatty acid
27	20.455	278.40	α-linolenic acid	3.81	C ₁₈ H ₃₂ O ₂	Fatty acid
28	20.628	284.50	Stearic acid	2.14	C ₁₈ H ₃₂ O ₂	Fatty acid
29	22.271	312.50	Arachidic acid	0.64	C ₂₀ H ₄₀ O ₂	Fatty acid
30	24.250	342.30	Sucrose	0.37	C ₁₂ H ₂₂ O ₁₁	Carbohydrate

31	25.017	342.30	Lactose	0.47	C ₁₂ H ₂₂ O ₁₁	Carbohydrate
32	25.767	402.70	δ-tocopherol	1.94	C ₂₇ H ₄₆ O ₂	Quinone and hydroquinone
33	26.522	416.70	γ-tocopherol	0.36	C ₂₈ H ₄₈ O ₂	Quinone and hydroquinone
34	29.183	400.70	Campesterol	1.55	C ₂₈ H ₄₈ O	Ergosterol
35	30.350	484.87	Stigmast-5-ene,3β-(trimethylsiloxy)-,24s	26.99	C ₃₂ H ₅₆ O	Triterpenes
36	30.533	412.70	Isofucosterol	2.36	C ₂₉ H ₄₈ O	Sterol lipid
37	31.231	426.71	9,19-Cyclolanost-24-en-3-ol,(3β)-,	0.99	C ₃₀ H ₅₀ O	Triterpenoid
38	32.147	440.74	9,19-Cyclolanost-24-en-3-ol, 24-methylene-(3β)-,	0.41	C ₃₁ H ₅₂ O	
39	32.885	426.72	Citrostadienol*	0.42	C ₃₀ H ₅₀ O	Triterpenoid

*Tentatively identified compound was derivatize with methoxyamine HCl in pyridine and BSTFA with 1% TMCS

Table 2 and Figure 1B presents the phytochemical profile of *D. meyeniana* determined through UHPLC-QTOF-MS, which reveals thirty-nine (39) non-volatile compounds. The analysis showed that a chemical profiling of extracts revealed a diverse array of compounds, including alkaloids, fatty acids, flavonoids, terpenoids, and coumarins, which are known for their pharmacological significance. Among the alkaloids identified were Anisomycin, Cinchonine, and Indole-3-carboxaldehyde. Several structurally complex alkaloid derivatives were also detected, such as 3-methyl-8,10,20,22-tetraoxa-3-azapentacyclo[15.7.0.05,13.07,11.019,23]tetracos-1(17),5,7(11),12,18,23-hexaen-14-one, and monocrotaline. The fatty acid fraction included Docosanol, 6-hydroxypalmitic acid, and 13S-hydroxy-6Z,9Z,11E-octadecatrienoic acid (coriolic acid). Other notable fatty acids, such as 9,10-epoxy-12Z-octadecenoic acid [(+)-9(10)-], Decylbenzenesulfonic acid, 9-hydroxy-10,12-octadecadienoic acid, were also present, further contributing to the extract's therapeutic potential. The flavonoid content, characterized by polyphenolic aromatic compounds, included 5,6,2'-trimethoxyflavone and Methyl 2-[(3,4-diethoxyphenyl)methylene]-3-oxobenzo[b]furan-5-carboxylate. Terpenoids were well represented with complex structures such as Uracarinic acid and Cryptotanshinone, and highly oxygenated derivatives like 1R,2R,4aS,6aS,6bR,10S,12aR,14bS)-1,8,10-trihydroxy-1,2,6a,6b,9,9,12a-heptamethyl-2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydronicene-4a-carboxylic and others. Additionally, coumarins class was marked by bioactive molecules including 8-8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate and 6-(1,1-dimethyllyl)-21-hydroxy-1-methylethyl)-2,3-dihydro-7H-furo[3,2G]chromen-7-one.

Table 2. Phytochemical Profile of *D. meyeniana* using UHPLC-QTOF-MS.

ID	RT (min)	m/z	Tentative compound	MW (g/mol)	MF	Cosine Similarity	Nature of Compound
1	23.29	325.30	Docosanol	326.6	C ₂₂ H ₄₆ O	0.96	Fatty acid
2	19.61	343.08	Usnic acid	344.3	C ₁₈ H ₁₆ O ₇	0.96	Polyketides
3	21.65	297.14	Decylbenzenesulfonic acid	298.4	C ₁₆ H ₂₆ O ₃ S	0.96	Polyketides
4	16.61	264.10	Anisomycin	265.3	C ₁₄ H ₁₉ NO ₄	0.96	Alkaloid
5	19.95	311.10	5,6,2'-trimethoxyflavone	312.3	C ₁₈ H ₁₆ O ₅	0.95	Flavonoid
6	20.24	293.16	Cinchonine	294.4	C ₁₉ H ₂₂ N ₂ O	0.94	Alkaloid
7	23.95	271.23	16-hydroxypalmitic acid	272.42	C ₁₆ H ₃₂ O ₃	0.94	Fatty acid
8	20.25	293.20	13S-hydroxy-6Z,9Z,11E-octadecatrienoic acid13(S)	294.4	C ₁₈ H ₃₀ O ₃	0.93	Fatty acid
9	27.35	341.10	8,8-dimethyl-2,10-dioxo-9h-pyrano [2,3-f] chromen-9-yl) (Z)-2-methylbut-2-enoate	342.3	C ₁₉ H ₁₈ O ₆	0.93	Coumarin
10	23.05	483.30	1-hexadecanoyl-2-(9z-octadecenoyl)-sn-glycero-3-phospho- (1'-rac-glycerol)	749	C ₄₀ H ₇₇ O ₁₀ P	0.92	glycerophospholipid
11	21.13	311.20	Benzenesulfonic acid, 4-undecyl-	312.5	C ₁₇ H ₂₈ O ₃ S	0.92	Benzenesulfonic
12	10.14	144.00	Indole-3- carboxaldehyde	145.2	C ₉ H ₇ NO	0.89	Alkaloid
13	14.88	487.343	(1R,2R,4aS,6aS,6bR,10S,12aR,14bS)-1,8,10-trihydroxy- 1,2,6a,6b,9,9,12a-heptamethyl- 2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydronicene- 4a-carboxylic acid	488.7	C ₃₀ H ₄₈ O ₅	0.85	Triterpenoid
14	21.65	295.20	9,10-eode 9,10-epoxy-12z-octadecenoic acid (+)-9(10)-	296.4	C ₁₈ H ₃₂ O ₃	0.83	Fatty acid
15	14.80	487.30	(1R,2R,4aS,6aS,6bR,9R,10R,11R,12aR)-1,10,11-trihydroxy-9- (hydroxymethyl)-1,2,6a,6b,9,12a-hexamethyl- 2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydronicene- 4a-carboxylic acid. (Uncaric acid)	504.7	C ₃₀ H ₄₈ O ₆	0.83	Triterpenoid
16	21.65	297.14	Decylbenzenesulfonic acid	298.4	C ₁₆ H ₂₆ O ₃ S	0.81	Fatty acid
17	21.88	295.20	9-hydroxy-10,12-octadecadienoic acid	296.4	C ₁₈ H ₃₂ O ₃	0.81	Fatty acid
18	8.29	352.1	3-methyl-8,10,20,22-tetraoxa-3-azapentacyclo [15.7.0.05,13.07,11.019,23] tetracos- 1(17),5,7(11),12,18,23-hexaen-14-one	No available data	C ₂₀ H ₁₉ NO ₅	0.81	Alkaloids
19	17.57	535.20	(1R,2R,4S,7S,8R,9R,10S,11R,12S,13S,14R,17R,18R,19R)-8- Acetoxy-10,19-dihydroxy-1,9,18-trimethyl-15-oxo-16,20- dioxahexacyclo [15.3.2.0~2,13~.0~4,12~.0~7,11~.0~14,19~] docos-5-ene- 5-carboxylic acid	490.5	C ₂₆ H ₃₄ O ₉	0.80	Terpenoid
20	20.67	751.30	Glc-glc-octadecatrienoyl-sn-glycerol	No available data			
21	20.6	559.3	Glc-octadecatrienoyl-sn-glycerol	No available data			
22	18.2	311.1	5,6,2'-trimethoxyflavone	312.3	C ₁₈ H ₁₆ O ₅	0.79	Flavonoid
23	21.65	368.10	methyl 2-[(3,4-diethoxyphenyl) methylene]-3- oxobenzo[b]furan-5-carboxylate	368.4	C ₂₁ H ₂₀ O ₆	0.78	Flavonoid
24	19.61	138.01	4-nitrophenol	139.11	C ₆ H ₅ NO ₃	0.76	Phenolic
25	30.68	324.10	4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxa-13-azatricyclo [8.5.1.013,16] hexadec-10-ene-3,7-dione	314.4	C ₁₉ H ₂₂ O ₄	0.77	Ornithine alkaloid
26	29.03	134.90	Cyclohomonervilasterol			0.78	Terpenoid
27	7.42	297.14	Cryptotanshinone	296.4	C ₁₉ H ₂₀ O ₃	0.75	Diterpenoid
28	21.38	313.50	6-(1,1- dimethylallyl)-21-hydroxy-1-methylethyl)-2,3-dihydro-	314.4	C ₁₉ H ₂₂ O ₄	0.75	Coumarin

7H-furo[3,2-G] chromen-7-one							
29	11.57	372.94	6-O-methylarthothelin	375.6	C ₁₅ H ₉ C ₁₃ O ₅	0.74	Xanthone
30	16.14	329.23	(10E,12E,14E)-16-hydroxy-9-oxooctadeca-10,12,14-trienoic acid	330.5	C ₁₈ H ₃₄ O ₅	0.74	Octadecanoid
31	9.90	539.10	Cynarin	516.4	C ₂₅ H ₂₄ O ₁₂	0.73	Phenylpropanoid
32	21.88	482.2	2-[hydroxy-[(2R)-2-hydroxy-3-pentadecanoyloxypropoxy] phosphoryl] oxyethyl-trimethylazaniu	482.6	C ₂₃ H ₄₉ NO ₇ P ⁺	0.72	Phospholipid
33	17.16	710.4	[3-[2-[3-[[10,13-dimethyl-17-(6-methylheptan-2-yl)2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl] oxycarbonylamino] propoxy] ethoxy]-2-hydroxypropoxy]-propan-2-ylphosphinate	710.9	C ₃₉ H ₆₉ NO ₈ P ⁻	0.72	Steroid
34	15.61	539.1	4',4'',5,5'',7,7''-hexahydroxy-3,8''-biflavone	538.5	C ₃₀ H ₁₈ O ₁₀	0.72	Flavonoid
35	16.89	307.1	(10E,12E,14E)-16-hydroxy-9-oxooctadeca-10,12,14-trienoic acid	308.4	C ₁₈ H ₂₈ O ₄	0.72	Fatty acid
36	15.6	309.	(E)-4-[(1R,2S,3S,4R,8aS)-2,3,4-trihydroxy-2,5,5,8a-tetramethyl-3,4,4a,6,7,8-hexahydro-1H-naphthalen-1-yl]but-3-en-2-one	310.4	C ₁₈ H ₃₀ O ₄	0.71	Terpenoid
37	18.7	313.2	12,13-Dihome	314.5	C ₁₈ H ₃₄ O ₄	0.71	Fatty acid
38	9.00	356.3	(2S)-2-amino-3-methylbutanoic acid; hexadecenoic acid	373.6	C ₂₁ H ₄₃ NO ₄	0.70	Octadecanoid
39	10.5	343.2	(. +/-.)-4-Hydroxy-5E,7Z,10Z,13Z,16Z,19Z-docosaheptaenoic acid	344.5	C ₂₂ H ₃₂ O ₃	0.70	Fatty acid

3.2. ADMET properties

Nine compounds satisfied all five drug-likeness filters of Lipinski, Ghose, Veber, Egan, and Muegge without any violations (Tables 3a and 3b). These compounds include includes (A) Usnic acid; (B) Anisomycin; (C) 5,6,2'-trimethoxyflavone (D) Cinchonine (E) 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate (F) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one (G) 4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxa-13-azatricyclo [8.5.1.013,16] hexadec-10-ene-3,7-dione (8) Cryptotanshinone (9) 6-(1,1-dimethallyl)-2-(1-hydroxyl-1-methylethyl)-2,3-dihydro-7H-furo[3,2-G]chromen-7-one.

The Abbot Bioavailability Score (ABS) indicated a moderate probability of oral bioavailability (55 – 56%) for all compounds, except Cryptotanshinone, which exhibited a comparatively high score. Although these compounds satisfied major drug-likeness criteria, each presented at least one lead-likeness violation, indicating the need for structural optimization during lead development. Furthermore, compounds (E) 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate (F) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one (I) 6-(1,1-dimethallyl)-2-(1-hydroxyl-1-methylethyl)-2,3-dihydro-7H-furo[3,2-G]chromen-7-one triggered two BRENK alerts suggesting the presence of potentially problematic substructures that may compromise safety or synthetic feasibility.

The basic physicochemical properties of the selected compounds are summarized in Tables 4a and 4b. Molecular weights ranged from 265.3 to 344.32 g/mol, all below the 500 g/mol threshold, which supports compliance with Lipinski's rule. The computed consensus Log P value (lipophilicity) varied between 0.9 and 3.87, indicating moderate lipophilicity favorable for oral absorption (Table 5a and 5b). ADME analysis revealed favorable pharmacokinetic characteristics for all compounds (Table 6a and 6b). All nine compounds demonstrated high gastrointestinal (GI) absorption, suggesting good oral bioavailability. Blood-brain barrier (BBB) permeability was predicted for several compounds, including (C) 5,6,2'-trimethoxyflavone; (D) Cinchonine; (F) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy] chromen-2-one; (G). 4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxa-13-azatricyclo [8.5.1.013,16] hexadec-10-ene-3,7-dione (H) Cryptotanshinone; (I) 6-(1,1-dimethallyl)-2-(1-hydroxyl-1-methylethyl)-2,3-dihydro-7H-furo[3,2-G] chromen-7-one, indicating potential central nervous system activity. Among these, (C) Cinchonine and (H) Cryptotanshinone were also predicted to be P-gp substrates.

Regarding cytochrome P450 (CYP) inhibition, Usnic acid and Anisomycin exhibited no inhibitory activity against any of the CYP isoforms (Table 6a and 6b). Conversely, (C) 5,6,2'-trimethoxyflavone inhibited five CYP isoforms, while (H) Cryptotanshinone, and (I) 6-(1,1-dimethallyl)-2-(1-hydroxyl-1-methylethyl)-2,3-dihydro-7H-furo[3,2-G]chromen-7-one inhibited four isoforms. Compounds (E) 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate, (F) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one, and (G) 4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxa-13-azatricyclo [8.5.1.013,16] hexadec-10-ene-3,7-dione [4[8.5.1.013,16] hexadec-10-ene-3,7-dione inhibited three isoforms each, whereas (D) Cinchonine inhibited one isoform.

Table 7 presents the predicted toxicity profile of bioactive compounds present in *D. meyeniana* extract. Compounds (C) 5,6,2'-trimethoxyflavone; (F) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one, (G) 4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxa-13-azatricyclo [8.5.1.013,16] hexadec-10-ene-3,7-dione, and (H) Cryptotanshinone exhibited LD₅₀ values exceeding 2000 mg kg⁻¹, indicating low acute oral toxicity. Several compounds, including (B) Anisomycin, (C) 5,6,2'-trimethoxyflavone, (D) Cinchonine, (F) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one, and (G) 4,5-dihydroxy-4,5,6-

trimethyl-2,8-dioxa-13-azatricyclo [8.5.1.013,16] hexadec-10-ene-3,7-dione, were predicted to be non-hepatotoxic, non-carcinogenic, non-cytotoxic, and non-mutagenic, suggesting a favorable safety profile. In contrast, (A) Usnic acid and (H) Cryptotanshinone were carcinogenic. Additionally, (E) 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate and (I) 6-(1,1-dimethylallyl)-2-(1-hydroxyl-1-methylethyl)-2,3-dihydro-7H-furo[3,2-G] chromen-7-one were predicted to exhibit immunotoxicity and mutagenicity, respectively, indicating potential structural concerns. For comparison, the reference anticancer drug displayed more pronounced toxicity, while fluorouracil showed carcinogenic potential, with other toxicological parameters remaining inactive.

Table 3a. Predicted drug-likeness results of the volatile and non-volatile bioactive compounds of *D. meyeniana*

Volatile bioactive compound	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
ADME Properties																
Lipinski # violations	No; 1	No; 1	No; 1	No; 1	No; 1	No; 1	Yes; 0	No;1	No; 1	No;1	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0
Ghose # violations	No; 3	No; 1	Yes; 0	No; 1	No; 1	Yes; 0	No;2	No; 1	No; 3	No; 1	Yes; 0	No; 1	Yes; 0	Yes; 0	Yes; 0	No; 3
Veber # violations	Yes;0	No; 1	No; 1	No; 1	No; 1	Yes;0	Yes; 0	No; 1	Yes; 0	No; 1	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0
Egan # violations	No; 1	No; 1	Yes; 1	No; 1	No; 1	Yes; 0	Yes; 0	No; 1	No; 1	No; 1	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0
Muegge # violations	No; 2	No; 2	No; 1	No; 1	No; 1	No; 2	No; 2	No; 2	No; 2	No; 3	Yes; 0	No; 1	Yes; 0	Yes; 0	Yes; 0	Yes; 0
Bioavailability score	0.55	0.55	0.85	0.85	0.85	0.55	0.55	0.55	0.55	0.55	0.56	0.85	0.55	0.55	0.55	0.56
Pan assay interference compounds (PAINS) # alerts	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Brenk # alerts	1	1	0	1	1	1	0	1	1	0	1	1	0	0	1	1
Lead likeness # violations	2	2	2	2	2	2	1	2	2	2	0	2	0	0	0	2
Synthetic accessibility	6.29	4.3	2.31	3.1	3.1	5.04	4.08	4.08	6.15	2.99	4.19	3.08	3.14	3.46	4.18	6.61

Table 3b. Predicted drug-likeness results of the volatile and non-volatile bioactive compounds of *D. meyeniana*.

Volatile bioactive compound	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
ADME Properties																
Lipinski # violations	Yes; 0	Yes; 0	No; 2	No; 1	Yes; 0	Yes; 0	Yes; 0	No; 1	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0
Ghose # violations	Yes; 0	Yes; 0	No; 4	No; 1	No; 2	No; 3	Yes; 0	No; 3	Yes; 0	No; 1	Yes; 0	No; 3	Yes; 0	Yes; 0	Yes; 0	No; 3
Veber # violations	No; 1	Yes; 0	No; 2	No; 1	Yes; 0	Yes; 0	No; 1	Yes; 0	No; 1	Yes; 0	Yes; 0	Yes; 0	Yes;0	Yes; 0	Yes; 0	Yes; 0
Egan # violations	Yes; 0	Yes; 0	No; 2	No; 1	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0	No; 1	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0
Muegge # violations	No; 1	Yes;0	No; 4	No; 1	No; 1	Yes; 0	No; 1	Yes; 0	No; 1	Yes; 0	Yes; 0	No; 1	Yes; 0	Yes; 0	Yes; 0	No; 2
Bioavailability score	0.85	0.55	0.11	0.85	0.55	0.56	0.85	0.56	0.85	0.56	0.55	0.55	0.55	0.85	0.55	0.55
Pan assay interference compounds (PAINS) # alerts	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0
Brenk # alerts	0	2	3	1	1	1	2	1	1	1	2	2	2	1	2	0
Lead likeness # violations	2	0	3	2	1	2	2	2	2	1	1	1	1	1	1	1
Synthetic accessibility	2.35	4.09	8.08	2.77	1	6.61	4.18	6.73	4.18	6.73	3.57	1.41	3.57	4.11	4	1.52

(1) Stigmast-5-ene,3 β -(trimethylsiloxy)-,24s (2) Phytol (3) Palmitic acid (4) 9,12-Octadecadienoic acid (5) α -Linolenic acid (6) Silphinene (7) 2,4,6 Tri-tert-butylNitrobenzene (8) Neophytadiene (9) Isofucosterol (10) Docosanol (11) Usnic acid (12) Decylbenzenesulfonic acid (13) Anisomycin (14) 5,6,2'-

Trimethoxyflavo (15) Cinchonine (16) 16-hydroxypalmitic acid (17) 13S-hydroxy-6Z,9Z,11E-octadecatrienoic acid|13(S) (18) 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate (19) 1-Hexadecanoyl-2-(9Z-octadecenoyl)-sn-glycero-3-phospho-(1'-rac-glycerol) (20) Benzenesulfonic acid, 4-undecyl- (21) Indole-3-carboxyaldehyde (22) (1R,2R,4aS,6aS,6bR,10S,12aR,14bS)-1,8,10-trihydroxy-1,2,6a,6b,9,9,12a-heptamethyl-2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydronicene-4a-carboxylic acid (23) 9,10-epoxy-12Z-octadecenoic acid|(+)-9(10)-epome (24) (1R,2R,4aS,6aS,6bR,9R,10R,11R,12aR)-1,10,11-trihydroxy-9-(hydroxymethyl)-1,2,6a,6b,9,12a-hexamethyl-2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydronicene-4a-carboxylic acid (25) 9-hydroxy-10,12-octadecadienoic acid (26)1R,2R,4S,7S,8R,9R,10S,11R,12S,13S,14R,17R,18R,19R)-8-acetoxy-10,19-dihydroxy-1,9,18-trimethyl-15-oxo-16,20 dioxahexacyclo[15.3.2.0~2,13~.0~4,12~.0~7,11~.0~14,19~]docos-5-ene-5-carboxylic acid (27) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one (28) 4-nitrophenol - (29) 4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxa-13-azatricyclo[8.5.1.013,16]hexadec-10-ene-3,7-dione (30) Cryptotanshinone (31)6-(1,1-dimethylallyl)-2-(1-hydroxy-1-methylethyl)-2,3-Dihydro-7H-furo[3,2-G]chromen-7-one (32) Fluorouracil

Table 4a. Physiochemical properties and computational descriptors of the volatile and non-volatile bioactive compounds of *D. meyeniana*.

Volatile bioactive compound	1	2	3	4	5	6	7	8	9	10	11	12	13	14
ADME Properties														
Size (MW) g/mol	398.71	296.53	256.42	280.45	278.43	204.35	180.16	278.52	412.69	326.6	344.32	272.42	265.3	312.32
Lipophilicity XLOGP3)	10.87	8.19	7.17	6.98	6.98	5.25	-3.24	9.62	8.85	10.36	2.88	5.73	0.9	3.09
Solubility Log S (ESOL)														
Solubility Log S (ESOL)	-8.76	-5.98	-5.02	-5.05	-5.05		1.15	-6.77	-7.64	-7.07	-3.83	-4.86	-1.96	-3.97
Saturation Fraction Csp3	0.93	0.9	0.94	0.72	0.61	0.87	1	0.8	0.86	1	0.33	0.62	0.5	0.17
Flexibility (Num, rotatable bonds)	6	13	14	14	13	0	1	13	5	20	2	10	5	4
Num. H-bond acceptors	0	1	2	2	2	0	6	0	1	1	7	3	5	5
Num. H-bond donors	0	1	1	1	1	0	5	0	1	1	2	1	2	0
Molar refractivity	132.07	98.94	80.8	89.46	88.99	66.62	35.74	97.31	132.75	109.3	86.54	73.79	87.4	87.4

Table 4b. Physiochemical properties and computational descriptors of the volatile and non-volatile bioactive compounds of *D. meyeniana*.

Volatile bioactive compound	17	18	19	20	21	22	23	24	25	26	27	28	29	30
ADME Properties														
Size (MW) g/mol	294.43	342.34	749.01	312.47	145.16	488.7	296.44	504.7	296.44	490.54	314.38	139.1	314.38	296.36
Lipophilicity XLOGP3	5.6	3.2	12.33	6.28	1.93	4.59	5.57	4.29	5.35	1.43	3.52	1.91	3.52	3.8
Solubility Log S (ESOL)														
Solubility Log S (ESOL)	-4.08	-9.55	-9.55	-5.22	-2.5	-5.7	-4.26	-5.54	-4.12	-3.58	-3.93	-2.28	-3.93	-4.27
Saturation Fraction Csp3	0.61	0.32	0.9	0.65	0	0.9	0.83	0.9	0.72	0.81	0.32	0	0.32	0.47
Flexibility (Num, rotatable bonds)	13	3	41	11	1	1	14	2	14	3	6	1	6	0
Num. H-bond acceptors	3	6	10	3	1	5	3	6	3	9	4	3	4	3
Num. H-bond donors	2	0	3	1	1	4	1	5	2	3	1	1	1	0
Molar refractivity	90.15	91.55	210.81	89.34	43.69	139.28	88.91	140.44	121.76	121.76	92.49	37.29	92.49	85.13

(1) Stigmast-5-ene,3 β -(trimethylsiloxy)-,24s (2) Phytol (3) Palmitic acid (4) 9,12-Octadecadienoic acid (5) α -Linolenic acid (6) Silphinene (7) 2,4,6 Tri-tert-butylNitrobenzene(8) Neophytadiene (9) Isofucosterol (10) Docosanol (11) Usnic acid (12) Decylbenzenesulfonic acid (13) Anisomycin (14) 5,6,2'-Trimethoxyflavo (15) Cinchonine (16) 16-hydroxypalmitic acid (17) 13S-hydroxy-6Z,9Z,11E-octadecatrienoic acid|13(S) (18) 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate (19) 1-Hexadecanoyl-2-(9Z-octadecenoyl)-sn-glycero-3-phospho-(1'-rac-glycerol) (20) Benzenesulfonic acid, 4-undecyl- (21) Indole-3-carboxyaldehyde (22) (1R,2R,4aS,6aS,6bR,10S,12aR,14bS)-1,8,10-trihydroxy-1,2,6a,6b,9,9,12a-heptamethyl-2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydronicene-4a-carboxylic acid (23) 9,10-epoxy-12Z-octadecenoic acid|(+-)9(10)-epome (24) (1R,2R,4aS,6aS,6bR,9R,10R,11R,12aR)-1,10,11-trihydroxy-9-(hydroxymethyl)-1,2,6a,6b,9,12a-hexamethyl-2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydronicene-4a-carboxylic acid (25) 9-hydroxy-10,12-octadecadienoic acid (26) 1R,2R,4S,7S,8R,9R,10S,11R,12S,13S,14R,17R,18R,19R)-8-acetoxy-10,19-dihydroxy-1,9,18-trimethyl-15-oxo-16,20 dioxahexacyclo[15.3.2.0~2,13~.0~4,12~.0~7,11~.0~14,19~]docos-5-ene-5-carboxylic acid (27) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one (28) 4-nitrophenol - (29) 4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxo-13-azatricyclo[8.5.1.0^{13,16}]hexadec-10-ene-3,7-dione (30) Cryptotanshinone (31) 6-(1,1-dimethylallyl)-2-(1-hydroxy-1-methylethyl)-2,3-Dihydro-7H-furo[3,2-G]chromen-7-one (32) Fluorouracil

Table 5a. Lipophilicity results of the volatile and non-volatile bioactive compounds of *D. meyeniana*.

Volatile bioactive compound	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
ADME Properties																
Polarity TPSA	0	20.23	37.3	37.3	37.3	0	110.38	0	20.23	20.23	117.97	62.75	67.79	57.9	36.36	57.53
XLOGP3	10.87	8.19	7.17	6.98	6.98	5.25	-3.24	9.62	8.85	10.36	2.88	5.73	0.9	3.09	2.68	5.6
ILOGP	5.17	4.85	3.85	4.14	4.14	3.17	0.35	5.05	5.08	5.73	0.85	1.2	2.34	3.1	3.07	3.39
WLOGP	9.05	6.36	5.55	5.88	5.66	4.42	-3.22	7.17	7.94	7.8	1.5	5.7	0.12	3.49	2.46	4.52
MLOGP	8.72	5.25	4.19	4.47	4.47	5.65	-2.75	6.21	6.62	5.84	-0.52	4.01	0.71	1.25	2.59	3.31
SILICOS-IT	7.93	6.57	5.25	5.77	5.77	3.91	-2.3	7.3	6.88	8.3	2.8	4.03	1.4	4.08	3.08	4.69
Lipophilicity average	8.35	6.25	5.2	5.45	5.45	4.48	-2.23	7.07	7.08	7.61	1.5	4.13	1.1	3	2.78	4.3

Table 5b. Lipophilicity results of the volatile and non-volatile bioactive compounds of *D. meyeniana*.

Volatile bioactive compound	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
ADME Properties															
Polarity TPSA	57.53	82.81	158.63	62.75	32.86	97.99	49.83	118.22	139.59	139.59	59.67	66.05	59.67	43.37	59.67
XLOGP3	5.6	3.2	12.33	6.28	1.93	4.59	5.57	4.29	5.35	1.43	3.52	1.91	3.52	3.8	3.87
ILOGP	3.39	2.71	8.39	2.81	1.12	3.37	3.83	2.93	3.83	0	3.6	0.77	3.6	2.81	3.53
WLOGP	4.63	3.02	10.45	6.09	1.98	5.18	5.1	4.15	4.86	1.5	3.84	1.3	3.84	3.44	3.33
MLOGP	3.31	1.76	4.64	4.26	0.88	4.14	3.29	3.33	3.59	2.02	2.66	0.26	2.66	2.66	2.74
SILICOS-IT	4.69	3.76	11.93	4.44	2.69	4.07	5.44	3.46	5.04	0.52	4.37	-0.79	4.37	4.37	4.48
Lipophilicity average	4.3	2.89	9.55	4.77	1.72	4.27	4.65	3.63	4.53	1.09	3.6	0.69	3.6	3.6	3.59

(1) Stigmast-5-ene,3 β -(trimethylsiloxy)-,24s (2) Phytol (3) Palmitic acid (4) 9,12-Octadecadienoic acid (5) α -Linolenic acid (6) Silphinene (7) 2,4,6 Tri-tert-butylnitrobenzene (8) Neophytadiene (9) Isofucosterol (10) Docosanol (11) Usnic acid (12) Decylbenzenesulfonic acid (13) Anisomycin (14) 5,6,2'-Trimethoxyflavo (15) Cinchonine (16) 16-hydroxypalmitic acid (17) 13S-hydroxy-6Z,9Z,11E-octadecatrienoic acid|13(S) (18) 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate (19) 1-Hexadecanoyl-2-(9Z-octadecenoyl)-sn-glycero-3-phospho-(1'-rac-glycerol) (20) Benzenesulfonic acid, 4-undecyl- (21) Indole-3-carboxyaldehyde (22) (1R,2R,4aS,6aS,6bR,10S,12aR,14bS)-1,8,10-trihydroxy-1,2,6a,6b,9,9,12a-heptamethyl-2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydronicene-4a-carboxylic acid (23) 9,10-epoxy-12Z-octadecenoic acid|(+-)9(10)-epome (24) (1R,2R,4aS,6aS,6bR,9R,10R,11R,12aR)-1,10,11-trihydroxy-9-(hydroxymethyl)-1,2,6a,6b,9,12a-hexamethyl-2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydronicene-4a-carboxylic acid (25) 9-hydroxy-10,12-octadecadienoic acid (26) 1R,2R,4S,7S,8R,9R,10S,11R,12S,13S,14R,17R,18R,19R)-8-acetoxy-10,19-dihydroxy-1,9,18-trimethyl-15-oxo-16,20 dioxahexacyclo[15.3.2.0~2,13~.0~4,12~.0~7,11~.0~14,19~]docos-5-ene-5-carboxylic acid (27) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one (28) 4-nitrophenol - (29) 4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxa-13-azatricyclo[8.5.1.013,16]hexadec-10-ene-3,7-dione (30) Cryptotanshinone (31) 6-(1,1-dimethylallyl)-2-(1-hydroxy-1-methylethyl)-2,3-Dihydro-7H-furo[3,2-G]chromen-7-one (32) Fluorouracil

Table 6a. Predicted pharmacokinetics results of the volatile and non-volatile bioactive compounds of *D. meyeniana*.

Volatile bioactive compound	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
ADME Properties																
Gastrointestinal (GI) absorption	Low	Low	High	High	High	Low	Low	Low	Low	Low	High	High	High	High	High	High
Blood-brain barrier (BBB) permeability	No	No	Yes	Yes	Yes	No	No	No	No	No	No	No	No	Yes	Yes	Yes
P-gp substrate	No	Yes	No	No	No	No	Yes	Yes	No	No	No	No	No	No	Yes	No
CYP1A2 inhibitor	No	No	Yes	Yes	Yes	No	No	No	No	Yes	No	No	No	Yes	No	No
CYP2C19 inhibitor	No	No	No	No	No	Yes	No	No	No	No	No	Yes	No	Yes	No	No
CYP2C9 inhibitor	No	Yes	Yes	Yes	No	Yes	No	Yes	No	No	No	Yes	No	Yes	No	No
CYP2D6 inhibitor	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	Yes	Yes
CYP3A4 inhibitor	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No
Log Kp (skin permeation) cm/s	-1.01	-2.29	-2.77	-3.05	-2.19	-3.82	-9.7	-1.17	-2.53	-0.94	-6.36	-4.05	-7.28	-6.01	-6.19	-3.99

Table 6b. Predicted pharmacokinetics results of the volatile and non-volatile bioactive compounds of *D. meyeniana*.

Volatile bioactive compound	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
ADME Properties																
Gastrointestinal (GI) absorption	High	High	Low	High	High	High	High	High	High	High	High	High	High	High	High	High
Blood-brain barrier (BBB) permeability	Yes	No	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
P-gp substrate	No	No	Yes	No	No	Yes	No	No	No	No	No	No	No	Yes	No	No
CYP1A2 inhibitor	No	No	No	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	Yes	Yes	No
CYP2C19 inhibitor	No	Yes	No	Yes	No	No	No	No	No	No	Yes	No	Yes	Yes	Yes	No
CYP2C9 inhibitor	No	Yes	No	Yes	No	No	Yes	No	Yes	No	Yes	No	Yes	Yes	Yes	No
CYP2D6 inhibitor	Yes	No	No	No	No	No	No	No	Yes	No	No	No	No	No	Yes	No
CYP3A4 inhibitor	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No
Log Kp (skin permeation) cm/s	-3.99	-6.12	-2.11	-3.75	-5.82	-6.02	-4.15	-6.33	-4.31	-8.28	-5.72	-5.79	-5.72	-5.41	-5.47	-7.73

(1) Stigmast-5-ene,3 β -(trimethylsiloxy)-,24s (2) Phytol (3) Palmitic acid (4) 9,12-Octadecadienoic acid (5) α -Linolenic acid (6) Silphinene (7) 2,4,6 Tri-tert-butylnitrobenzene (8) Neophytadiene (9) Isofucosterol (10) Docosanol (11) Usnic acid (12) Decylbenzenesulfonic acid (13) Anisomycin (14) 5,6,2'-Trimethoxyflavo (15) Cinchonine (16) 16-hydroxypalmitic acid (17) 13S-hydroxy-6Z,9Z,11E-octadecatrienoic acid|13(S) (18) 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate (19) 1-Hexadecanoyl-2-(9Z-octadecenoyl)-sn-glycero-3-phospho-(1'-rac-glycerol) (20) Benzenesulfonic acid, 4-undecyl- (21) Indole-3-carboxyaldehyde (22) (1R,2R,4aS,6aS,6bR,10S,12aR,14bS)-1,8,10-trihydroxy-1,2,6a,6b,9,9,12a-heptamethyl-2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydropicene-4a-carboxylic acid (23) 9,10-epoxy-12Z-octadecenoic acid|(+)9(10)-epome (24) (1R,2R,4aS,6aS,6bR,9R,10R,11R,12aR)-1,10,11-trihydroxy-9-(hydroxymethyl)-1,2,6a,6b,9,12a-hexamethyl-2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydropicene-4a-carboxylic acid (25) 9-hydroxy-10,12-octadecadienoic acid (26) 1R,2R,4S,7S,8R,9R,10S,11R,12S,13S,14R,17R,18R,19R)-8-acetoxy-10,19-dihydroxy-1,9,18-trimethyl-15-oxo-16,20 dioxahexacyclo[15.3.2.0~2,13~.0~4,12~.0~7,11~.0~14,19~]docos-5-ene-5-carboxylic acid (27) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one (28) 4-nitrophenol - (29) 4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxa-13-azatricyclo[8.5.1.013,16]hexadec-10-ene-3,7-dione (30) Cryptotanshinone (31) 6-(1,1-dimethylallyl)-2-(1-hydroxy-1-methylethyl)-2,3-Dihydro-7H-furo[3,2-G]chromen-7-one (32) Fluorouracil

Table 7. Toxicological properties of selected bioactive compounds of *D. meyeniana*.

Code	Bioactive compound	Hepatotoxicity		Carcinogenicity		Cytotoxicity		Immunotoxicity		Mutagenicity		Predicted LD50 (mg kg ⁻¹)	Toxicity class
		Pr	Pb	Pr	Pb	Pr	Pb	Pr	Pb	Pr	Pb		
A	Usnic acid	Inactive	0.61	Active	0.57	Inactive	0.72	Inactive	0.51	Inactive	0.89	995	4
B	Anisomycin	Inactive	0.89	Inactive	0.73	Inactive	0.63	Inactive	0.66	Inactive	0.78	72	3
C	5,6,2'-trimethoxyflavone	Inactive	0.69	Inactive	0.53	Inactive	0.82	Inactive	0.81	Inactive	0.69	4000	5
D	Cinchonine	Inactive	0.93	Inactive	0.67	Inactive	0.8	Inactive	0.6	Inactive	0.68	720	4
E	8,8-dimethyl-2,10-dioxo-9H-pyrano [2,3-f] chromen-9-yl) (Z)-2-methylbut-2-enoate	Inactive	0.63	Inactive	0.54	Inactive	0.67	Active	0.9	Inactive	0.54	832	4
F	7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy] chromen-2-one	Inactive	0.78	Inactive	0.56	Inactive	0.78	Inactive	0.89	Inactive	0.54	3200	5
G	4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxo-13-azatricyclo [8.5.1.013,16] hexadec-10-ene-3,7-dione	Inactive	0.78	Inactive	0.56	Inactive	0.78	Inactive	0.89	Inactive	0.54	3200	5
H	Cryptotanshinone	Inactive	0.74	Active	0.51	Inactive	0.78	Active	0.96	Inactive	0.79	8000	6
I	6-(1,1-dimethylallyl)-2-(1-hydroxy-1-methylethyl)-2,3-dihydro-7H-furo[3,2-G] chromen-7-one	Inactive	0.69	Inactive	0.58	Inactive	0.7	Inactive	0.98	Active	0.82	1500	4
J	Fluorouracil	Inactive	0.78	Active	0.85	Inactive	0.93	Inactive	0.99	Inactive	0.88	1923	4

*Pr: prediction; Pb: probability

The bioavailability radar plot (Figure 2) illustrates the drug-likeness profiles of the bioactive compounds, evaluating six key physicochemical properties: lipophilicity, size, polarity, solubility, flexibility, and saturation. Eight bioactive compounds namely (A) Usnic acid; (B) Anisomycin; (D) Cinchonine; (E) 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate; (F) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one; (G) 4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxo-13-azatricyclo [8.5.1.013,16] hexadec-10-ene-3,7-dione (H) Cryptotanshinone and (I) 6-(1,1-dimethylallyl)-2-(1-hydroxyl-1-methylethyl)-2,3-dihydro-7H-furo[3,2-G]chromen-7-one fully occupy the pink area of the radar, indicating compliance with optimal ranges for oral bioavailability. In contrast, (C) 5,6,2'-trimethoxyflavone did not meet the saturation criterion (sp³ carbon fraction, greater than 0.25)

3.4. Molecular docking analysis

Table 8 summarizes the binding interactions of *D. meyeniana* compounds that satisfied all drug-likeness criteria. These selected compounds include: (A) Usnic acid; (B) Anisomycin; (C) 5,6,2'-trimethoxyflavone (D) Cinchonine; (E) 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate; (F) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one; (G) 4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxo-13-azatricyclo [8.5.1.013,16] hexadec-10-ene-3,7-dione (H) Cryptotanshinone; (I) 6-(1,1-dimethylallyl)-2-(1-hydroxyl-1-methylethyl)-2,3-dihydro-7H-furo[3,2-G]chromen-7-one. Molecular docking performed against four key cancer-related targets: epidermal growth factor receptor (EGFR; PD ID: 4lqm), tumor suppressor protein p53 (PD ID: 3hf1), matrix metalloproteinase-7 (MMP7; PD ID: 2y6d), and cyclin-dependent kinase 8/ Cyclin C (CDK8/Cyclin C; PD ID: 6t41). Fluorouracil (5-FU), an FDA-approved chemotherapeutic agent for various carcinomas, served as a reference drug for comparison ^{24,25}.

Four bioactive compounds showed strong binding affinity to EGFR, with cryptotanshinone exhibiting the lowest binding energy (-8.3 kcal/mol), followed by (E) 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate (-7.3 kcal/mol); (F) 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one (-7.2 kcal/mol) and (I) 6-(1,1-dimethylallyl)-2-(1-hydroxyl-1-methylethyl)-2,3-dihydro-7H-furo[3,2-G]chromen-7-one (-7.2 kcal/mol). These binding energies were significantly lower (strong binding) compared to 5U-fluorouracil (-4.3 kcal/mol). The matrix metalloproteinase-7 (MMP-7), binding affinities from -5.3 to -7.2 kcal/mol, indicating moderate interaction. Cryptotanshinone again demonstrated the best binding energy (-7.2 kcal/mol). In the case of cyclin-dependent kinase 8 (CDK8/Cyclin C), all the compounds showed strong binding, with energies between -6.8 and -8.3 kcal/mol. Cryptotanshinone was the top-performing compound (-8.3 kcal/m), surpassing the binding energy of the reference chemotherapeutic drug, fluorouracil (-5.4 kcal/mol).

Ligand efficiency (LE) values for the bioactive compounds ranged from 0.29 to 0.38. Usnic acid showed a high LE of 0.33 against CDK8/ Cyclin C. Compounds (C) 5,6,2'-trimethoxyflavone, (D) Cinchonine, and (H) Cryptotanshinone had high LE values across all targets. Fluorouracil exhibited slightly higher LE (0.47 to 0.53). The predicted inhibition constant (K_i) values for the bioactive compounds ranged from 0.42 to 8.43 μM, significantly better than those of the reference drug Fluorouracil (7.63 to 25.32 μM).

The ligand-protein interactions of the top-ranked bioactive compounds and with each target are illustrated in Figures 3, highlighting key interactions that contribute to binding stability. For Cryptotanshinone interacting with the epidermal growth factor receptor (Figure 3A), the complex was stabilized primarily through a hydrogen bond with Arg 65; van der Waals interactions involving Val 147, Trp 146, Arg 150, and Asn 181; and an alkyl with Leu 148. In its interaction with tumor suppressor protein p53 (Figure 3B), Cryptotanshinone formed van der Waals interactions with Asn 106, Leu 107, and Asn 132; a pi-cation bond interaction with Asp 100 and Glu 105; a pi-sigma interaction with Glu 105; and alkyl (pi-alkyl) with Ile 128 and Val 108. For matrix metalloproteinase-7 (MMP7; PD ID: 2y6d) (Figure 3C), Cryptotanshinone established van der Waals interaction with aPro 187, Gly 188, Phe 185, Ala 184, TQJ 1271, Pro 184, and ASN 105, a pi-sigma bond with Ala 186, a pi-pi-T-shaped interaction with Phe103; and several alkyl (pi-alkyl) interactions involving Pro 107 and Pro 103. Lastly, the Cryptotanshinone interaction with cyclin-dependent kinase 8/ Cyclin C (CDK8/Cyclin C; PD ID: 6t41) (Figure 3D) showed van der Waals interactions were observed with Asn 181, Tyr 146, Leu 148, Arg 65.

3.5. *In silico* cytotoxicity prediction

Table 9 shows the *in-silico* cytotoxicity prediction and analysis. Compounds are evaluated based on the probability of being active (PA) and inactive (PI) across various cancer cell lines, tumor types, and tissues. Usnic acid exhibited a high probability of cytotoxic activity with 0.767 PA and a low inactivity probability of 0.005 against the U-251 Oligodendroglioma cell line located in brain glioma. Anisomycin showed moderate cytotoxic activities with 0.472 PA and 0.068 PI against NCI-H838 small cell lung carcinoma.

Table 8. Binding energy of bioactive compounds with target cancer-related protein receptors.

Code	Ligand	EGFR (PD ID: 4lqm)				p53 (PD ID: 3hf1)				MMP7 (PD ID: 2y6d)		
		Binding Energy	Ligand Efficiency	Inhibitory Constant (µM)	No of H Bonds	Binding Energy	Ligand Efficiency	Inhibitory Constant (µM)	No of H Bonds	Binding Energy	Ligand Efficiency	Inhibitor Constan (µM)
A	Usnic acid (CID: 5646)	-6.9	-0.28	1.70	2	-7.2	-0.29	1.26	4	-6.6	-0.26	2.30
B	Anisomycin (CID 253602)	-6.3	-0.33	3.10	0	-7.1	-0.37	1.39	3	-5.3	-0.28	8.43
C	5,6,2'-trimethoxyflavone (CID: 14484690)	-6.9	-0.30	1.70	0	-7.1	-0.31	1.39	1	-6.1	-0.27	3.79
D	Cinchonine (CID: 90454)	-6.8	-0.31	1.88	1	-7.7	-0.35	0.76	1	-6.5	-0.30	2.54
E	8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate (CID: 51136479)	-7.3	-0.29	1.14	1	-7.7	-0.31	0.76	2	-6.5	-0.26	2.54
F	7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one (CID: 25763650)	-7.2	-0.31	1.26	0	-7.1	-0.31	1.39	1	-6.3	-0.27	3.10
G	4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxo-13-azatricyclo [8.5.1.0 ^{13,16}] hexadec-10-ene-3,7-dione	-6.4	-0.28	2.81	0	-6.6	-0.29	2.30	0	-5.8	-0.25	5.11
H	Cryptotanshinone (CID: 160254)	-8.3	-0.38	0.42	1	-8.3	-0.38	0.42	0	-7.2	-0.33	1.26
I	6-(1,1-dimethyallyl)-2-(1-hydroxyl-1-methylethyl)-2,3-dihydro-7H-furo[3,2-G]chromen-7-one (CID: 151467)	-7.2	-0.31	1.26	1	-6.9	-0.30	1.70	0	-6.5	-0.28	2.54
J	Fluorouracil CID: 3385) (reference drug)	-4.3	-0.48	22.9	3	-4.8	-0.53	13.9	3	-4.2	-0.47	25.32

Table 9. *In silico* cytotoxicity prediction and analysis of bioactive compounds from *D. meyeniana*.

Code	Bioactive compound	PA	PI	CELL LINE	CANCER TYPE/CELL TYPE	TISSUE	TUMOR TYPE
A	Usnic acid (CID: 5646)	0.767	0.005	U-251	Oligodendroglioma	Brain	Glioma
B	Anisomycin (CID 253602)	0.472	0.068	NCI-H838	Small-cell lung carcinoma	Lung	Carcinoma
C	5,6,2'-trimethoxyflavone (CID: 14484690)	0.45	0.029	HepG2	Hepatoblastoma	Liver	hepatoblastoma
D	Cinchonine (CID: 90454)	0.436	0.003	5637	Urothelial bladder carcinoma	Urinary Tract	carcinoma
E	8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate (CID: 51136479)	0.556	0.021	HL-60	Promyeloblast leukemia	Lymphoid	Leukemia
F	7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy] chromen-2-one (CID: 25763650)	0.37	0.91	NALM-6	Lymphoblastic leukemia	Hematopoietic and lymphoid tissue	Leukemia
G	4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxo-13-azatricyclo [8.5.1.0 ^{13,16}] hexadec-10-ene-3,7-dione	0.37	0.91	NALM-6	Lymphoblastic leukemia	Hematopoietic and lymphoid tissue	Leukemia
H	Cryptotanshinone (CID: 160254)	0.536	0.023	HL-60	Promyeloblast leukemia	Hematopoietic and lymphoid tissue	Leukemia
I	6-(1,1-dimethylallyl)-2-(1-hydroxyl-1-methylethyl)-2,3-dihydro-7H-furo[3,2-G]chromen-7-one (CID: 151467)	0.553	0.021	HL-60	Promyeloblast leukemia	Hematopoietic and lymphoid tissue	Leukemia

*PA: probability of being active; PI: probability of being inactive

4. Discussion

D. meyeniana possesses a wide range of pharmacological properties due to its diverse chemical secondary metabolites, as revealed through GC–MS and UHPLC-QTOF-MS analyses. The identified compounds include sesquiterpenoids, terpenoids, fatty acids, and Silphinene, and each associated with significant biological activities. Sesquiterpenoids are well-documented for their biological activities, exhibiting antitumor, antibacterial, anti-inflammatory, anti-viral ²⁶, and anticancer properties ²⁷. Fatty acids, characterized by a long hydrocarbon chain and a terminal carboxyl group, have demonstrated inhibitory effects on carcinogenesis in various tumor cell lines ²⁸.

Similarly, terpenoids are recognized for their ability to interfere with multiple stages of cancer progression, contributing to their anticancer properties. Among the volatile constituents, Stigmast-5-ene,3 β -(trimethylsiloxy)-,24s is the most abundant compound. This molecule has been reported to exert strong anticancer activity by inducing apoptosis, causing cell arrest, inhibiting angiogenesis, and suppressing metastasis. Its mechanism involves targeting specific proteins such as Na⁺/K⁺ ATPase, leading to disruption of cancer survival pathways ²⁹. The second most prominent compound was phytol, a diterpenoid, which is known for its pro-apoptotic and necrotic effects on sarcoma 180 and human leukemia carcinoma cells ³⁰.

The detected fatty acids, such as palmitic acid, α -linolenic acid, and linoleic acid, are linked to apoptosis induction, inhibition of cell migration, invasion, and angiogenesis ^{31–33}. Linoleic acid further supports cellular metabolism and holds therapeutic potential. Other fatty acids, including Docosanol, 6-hydroxypalmitic acid, and Coriolic acid, also exhibit anticancer properties. Docosanol inhibits CHO-K1 and melanoma cell lines ³⁴, 6-hydroxypalmitic acid is a candidate for anticancer drug development ³⁵, and Coriolic acid targets breast cancer stem cells by downregulating c-Myc ²⁹.

Additional compounds like Epoxy-octadecenoic acid, Decylbenzenesulfonic acid, and Hydroxy-octadecadienoic acid may also contribute to anticancer effects. Flavonoids, known for their antiproliferative, pro-apoptotic, and antiangiogenic properties ³⁶, include 5,6,2'-trimethoxyflavone, which shows activity against Aspc-1 pancreatic cancer cells ³⁷. Another compound, methyl 2-[(3,4-diethoxyphenyl)methylene]-3-oxobenzo[b]furan-5-carboxylate, adds to the anticancer potential. Terpenoids, bioactive molecules with mechanisms such as mitochondrial apoptosis induction and PI3K/AKT and NF- κ B pathway inhibition ³⁸, include Uracaric acid and Cryptotanshinone. Cryptotanshinone notably inhibits lung cancer invasion, tumorigenesis, and proliferation ³⁹. Coumarins also exhibit strong anticancer activity by regulating the cell cycle, angiogenesis, apoptosis, and autophagy ⁴⁰. Key coumarins identified include derivatives such as 8-8-dimethyl-2,10-dioxochromen and 6-(1,1-dimethylallyl)-2,3-dihydrochromen. The diverse phytochemicals in *D. meyeniana* highlight its potential as a promising source for anticancer drug development.

Silphinene has demonstrated strong binding affinity to cancer-related proteins, including ERG, HER2, ABL1, and P13K- α , suggesting its potential as a molecular inhibitor in cancer therapy ⁴¹. Neophytadiene, another bioactive compound, exhibited a broad pharmacological spectrum, including anti-inflammatory, antioxidant ⁴², antimicrobial, and anticancer ⁴³. Collectively, these findings highlight that *D. meyeniana* is a rich source of bioactive compounds with significant anticancer potential.

Non-volatile compounds profiling showed alkaloids, fatty acids, flavonoids, terpenoids, and coumarins, each associated with significant anticancer properties. Alkaloids such as Anisomycin, Cinchonine, Indole-3- caboxaldehyde, 3-methyl-8,10,20,22-tetraoxa-3-azapentacyclo[15.7.0.05,13.07,11.019.23]tetracos-1(17),5,7(11),12,18,23-hexaen-14-one and monocrotaline were identified in the extract. Alkaloids are widely recognized for their antiproliferative and cytotoxic effects, with several already established as chemotherapeutic agents, including vinblastine,

vinorelbine, vincristine, and vindesine ⁴⁴. Specifically, Anisomycin, inhibits the growth, survival, and migration of non-small cell lung cancer ⁴⁵ while Cinchonine disrupts autophagy by blocking autophagosome degradation via the inhibition of lysosomal hydrolases maturation ⁴⁶. Indole-3-carboxaldehyde has also demonstrated both antimycobacterial and anticancer agents ⁴⁷.

In the early stages of drug development, assessing physicochemical properties, pharmacokinetics, drug-likeness, and medicinal chemistry characteristics is essential for identifying promising therapeutic candidates. This evaluation optimizes a compound's potential toxicity and helps prevent time-consuming and costly failures in later clinical trials. For a bioactive compound to qualify as a potential drug candidate, it must not only demonstrate the desired biological activity but also possess favorable pharmacokinetic properties ³⁹. In this study, we utilized *in silico* approaches to evaluate the pharmacokinetics, drug-likeness, and key medicinal chemistry properties of bioactive compounds derived from *D. meyeniana*.

Lipophilicity, which indicates a compound's ability to dissolve in lipids and nonpolar solvents, is crucial for determining its ADMET profile. It impacts distribution, metabolism, elimination, and membrane interactions. An optimal lipophilicity range of 0 to 5 is recommended for drug development ^{48,49}. In this analysis, all nine compounds exhibited favorable lipophilicity, suggesting efficient membrane permeability and systemic bioavailability.

Solubility also plays a significant role in drug absorption and distribution ⁴⁹. Effective drug absorption requires sufficient solubility in aqueous solutions at the site of uptake ³⁹. Eight compounds showed moderate solubility, indicating good oral bioavailability potential, while anisomycin demonstrated high solubility, which may necessitate formulation strategies for optimal systemic circulation.

ADME properties are essential for understanding a compound's pharmacokinetic behavior and influence on pharmacological activity. Efficient gastrointestinal absorption is critical for orally administered drugs. This study revealed that all nine compounds had good absorption potential via the gastrointestinal tract, with most predicted to cross the blood-brain barrier (BBB). However, Usnic acid and 8-8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl (Z)-2-methylbut-2-enoate were less likely to penetrate the BBB, potentially reducing neurotoxic risks.

P-glycoprotein (P-gp) functions as an efflux transporter, reducing plasma and tissue concentrations of xenobiotics and drugs by actively pumping them back into the intestinal lumen. In this study, seven compounds were predicted to be non-substrates of P-gp, except for cinchonine and cryptotanshinone, which may decrease their intercellular concentrations and therapeutic efficacy. Additionally, interactions with cytochrome P450 (CYP) isoenzymes critically influence pharmacokinetic behavior, as CYP enzymes are central to drug metabolism and clearance ⁴⁹. Inhibition of CYP isoforms can hinder drug clearance, potentially leading to toxicity. This analysis found that usnic acid, anisomycin, and the reference drug fluorouracil exhibited low inhibitory potential against major CYP isoforms, suggesting effective hepatic metabolism and clearance, thereby minimizing toxicity risks and pharmacokinetic interactions.

Drug-likeness evaluates a compound's potential for clinical development by assessing the alignment of its physicochemical and structural features with those of approved drugs. This serves as a valuable tool for reducing research costs by eliminating compounds with poor pharmacokinetic profiles ⁵⁰. In this study, five well-known computational filters - Lipinski, Ghose, Veber, Egan, and Muegge - were used to assess drug-likeness, revealing that all nine compounds met the criteria, indicating promising characteristics for further development.

The compounds were also screened for pan-assay interference compounds (PAINS) and BRENK alerts. Except for cryptotanshinone, none triggered PAINS alerts, suggesting the absence of structural motifs that could cause false positives during *in silico* screening ³⁹. However, several compounds displayed BRENK alerts, indicating potentially toxic structural fragments, particularly usnic acid and anisomycin. While such alerts require attention, they do not disqualify compounds and can often be addressed through structural optimization in lead development.

Pro-Tox-II was used to assess the cytotoxicity of selected compounds from *D. meyeniana*, examining acute toxicity (LD50 values), organ toxicity, genotoxicity, and carcinogenicity. The compounds 5,6,2'-trimethoxyflavone, 7-(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxychromen-2-one, 5-dihydroxy-4,5,6-trimethyl-2,8-dioxo-13-azatricyclo [8.5.1.0^{13,16}] hexadec-10-ene-3,7-dione, and Cryptotanshinone all exhibited LD50 values higher than 2000 mg/kg and were not active in organ toxicity, except for cryptotanshinone, which showed carcinogenic activity.

The bioavailability radar plot visually represents drug-like characteristics by evaluating six key pharmacokinetic properties: lipophilicity, size, polarity, solubility, flexibility, and saturation ². The pink area indicates optimal drug-likeness, defining acceptable ranges for key parameters. Eight bioactive compounds from this study - Usnic acid, Anisomycin, Cinchonine, 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl(Z)-2-methylbut-2-enoate, 7-(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxychromen-2-one, 4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxo-13-azatricyclo [8.5.1.0^{13,16}] hexadec-10-ene-3,7-dione, Cryptotanshinone, and 6-(1,1-dimethylethyl)-2-(1-hydroxy-1-methylethyl)-2,3-dihydro-7H-furo[3,2-g]chromen-7-one - fell entirely within this optimal zone, indicating strong potential for oral bioavailability. In contrast, 5,6,2'-trimethoxyflavone was outside the acceptable range for saturation, suggesting potential limitations in oral bioavailability. Comparatively, compounds from *D. meyeniana* exhibited superior bioavailability profiles than standard anticancer agents like fluorouracil, which partially falls outside the optimal zone ⁵¹. This suggests that these phytochemicals are likely capable of achieving efficient systemic absorption and distribution, supporting their potential as promising drug candidates ⁵².

Among the evaluated compounds, Cryptotanshinone demonstrated the most favorable ADMET characteristics and drug-likeness profile, justifying further investigation of its anticancer potential through molecular docking. This established *in silico* modeling technique assesses the interaction between small-molecule ligands and proteins ⁵³, with binding energy serving as a measure of affinity, in which lower energies indicate stronger interactions. Docking analysis focused on four key cancer-related proteins: epidermal growth factor receptor (EGFR), tumor suppressor protein p53, matrix metalloproteinase-7 (MMP7), and cyclin-dependent kinase 8/Cyclin C (CDK8/Cyclin C). EGFR, a transmembrane receptor tyrosine kinase, mediates signals in cell proliferation, differentiation, and migration ⁵⁴. The p53 protein prevents phenotypic and genomic changes linked to cancer progression ⁵⁵. MMP7 facilitates cancer cell invasion and angiogenesis via extracellular matrix degradation ⁵⁶, while CDK8 regulates transcription and cell cycle progression, influencing tumor

development⁵⁷. These targets were chosen due to their significant roles in oncogenesis and cancer progression. The strong binding affinity of Cryptotanshinone for these proteins emphasizes its potential as a multi-target anticancer agent.

Cryptotanshinone demonstrated strong binding potential to all four targets, forming multiple interactions within or near their active sites. For EGFR, cryptotanshinone established a hydrogen bond with the active site Arg 65, contributing significantly to binding stability. In interaction with the tumor suppressor protein p53 and matrix metalloproteinase-7 with alkyl chains and pi-cation interaction further reinforced ligand binding. Although cryptotanshinone did not directly interact with catalytic residues of cyclin-dependent kinase 8/ Cyclin C (CDK8/Cyclin C), it formed van der Waals interactions with residues adjacent to the active site cleft, which may alter protein conformation and disrupt enzymatic activity³⁹. The docking results indicated that van der Waals forces played a central role in binding stabilization, supported by hydrophobic interactions, π -alkyl, and π - π stacking⁵⁸. These interactions collectively enhance binding affinity and selectivity, suggesting that cryptotanshinone may effectively inhibit these cancer-related proteins.

Cryptotanshinone consistently emerged as the most promising compound, exhibiting robust binding interactions across all targets. These findings highlight the therapeutic potential of *D. meyeniana*-derived phytochemicals as novel anticancer agents, possibly with reduced adverse effects compared to the conventional chemotherapy drug, fluorouracil. However, further experimental validation and structural optimization are essential to confirm efficacy and optimize pharmacological profiles for future drug development^{59,60}.

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CLC-Pred, based on the Prediction of Activity Spectra for Substances (PASS) algorithm, was employed to estimate the biological activity profile of cryptotanshinone. The PASS tool utilizes a leave-one-out cross-validation approach, with a reported predictive accuracy of approximately 96% compared to experimental *in vivo* data. The analysis predicted a notable cytotoxic potential of cryptotanshinone against promyeloblast leukemia cells, further supporting its relevance as a candidate for anticancer drug development. Overall, cryptotanshinone consistently emerged as the most promising compound, exhibiting robust binding interactions across all evaluated cancer-related targets.

These findings highlight the therapeutic potential of *D. meyeniana*-derived phytochemicals as novel anticancer agents, potentially with reduced adverse effects compared to conventional chemotherapy drugs, such as fluorouracil. However, further experimental validation and structural optimization are essential to confirm efficacy and enhance pharmacological profiles for future drug development^{59,60}.

Advancements in computational techniques and structure-based drug design have become essential for predicting the pharmacokinetic properties and drug-like profiles of natural products⁶¹. This study highlights the phytochemical diversity of *D. meyeniana*, which is crucial for identifying bioactive compounds that modulate key signaling pathways and exhibit diverse biological activities. Through comprehensive *in silico* analyses, including phytochemical profiling, ADMET prediction, drug-likeness evaluation, molecular docking, and cytotoxicity prediction, numerous phytochemicals from *D. meyeniana* were identified, exhibiting strong affinities with various cancer-related molecular targets.

These compounds exhibit promising pharmacological profiles and support their potential as multi-target therapeutics. Their natural origins may reduce the risk of adverse effects typically associated with traditional chemotherapeutic agents, which often involve significant toxicity and cost. The predicted cytotoxic activities of select bioactive compounds highlight *D. meyeniana* as a valuable source for anticancer agents, warranting further validation through *in vitro* and *in vivo* studies. Overall, this research highlights the efficacy of phytochemicals as cost-effective alternatives in cancer therapy and provides crucial data on their cytotoxic potential, ADMET profiles, and binding affinities, potentially clarifying their mechanisms of action in improving existing chemotherapy regimens.

5. Conclusion

D. meyeniana exhibits remarkable phytochemical diversity, which shows its potential as a valuable source of bioactive compounds. The *in silico* analyses highlighted the strong affinities of these compounds for various cancer-related molecular targets, demonstrating their capacity to influence key signaling pathways associated with cancer progression. These findings suggest that the phytochemicals from *D. meyeniana* could serve as promising lead candidates for the development of novel anticancer therapeutics, potentially offering more effective and safer treatment options compared to conventional therapies.

Declarations

Data availability

The data presented in this study are available in this article. Further inquiries can be directed to the corresponding authors.

Author contributions

E.E.P.: Sample collection, Methodology, Data curation, Formal analysis, Resources, Software, Visualization, Writing – original draft; K.G.J.C.: Conceptualization, Supervision, Validation, Data curation, Formal analysis, Investigation, Methodology, Writing & Reviewing; E.A.A.: Supervision, Validation, Reviewing; A.K.C.L.: Methodology, Formal analysis; A.B.M.M.K.I.: Methodology, Formal analysis; K.W.: Funding acquisition, Project administration, Resources, Supervision, Validation, Writing – review & editing.

Competing interests

The authors declare no competing interests.

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Figures

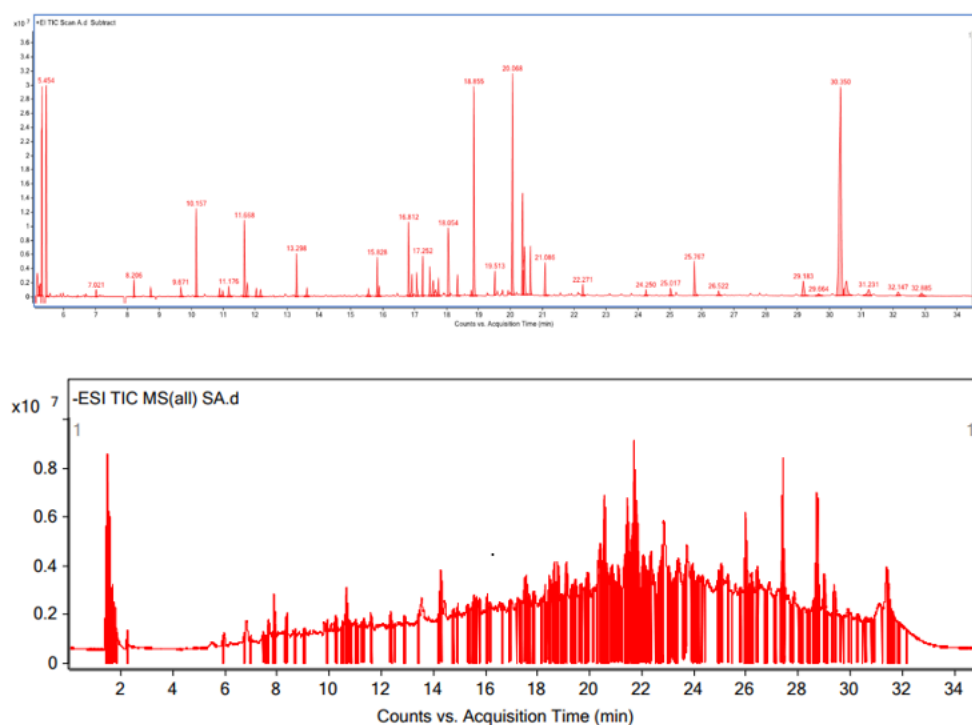


Figure 1

Chromatogram results of *D. meyeniana*. (A) GC-MS, and (B) UHPLC-QTOF-MS

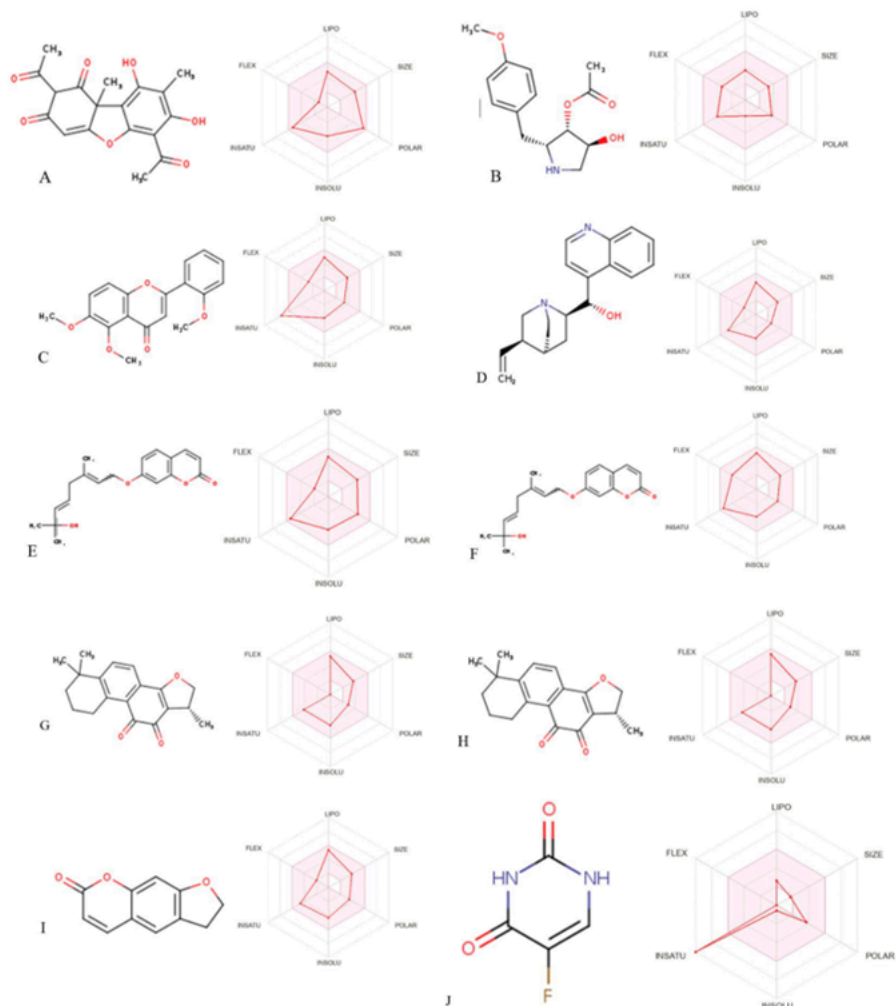


Figure 2

Bioavailability radar of the bioactive compounds of *D. meyeniana* **(A)** Usnic acid; **(B)** Anisomycin; **(C)** 5,6,2'-trimethoxyflavone **(D)** Cinchonine **(E)** 8,8-dimethyl-2,10-dioxo-9H-pyrano[2,3-f]chromen-9-yl) (Z)-2-methylbut-2-enoate **(F)** 7-[(2E,5E)-7-hydroxy-3,7-dimethylocta-2,5-dienoxy]chromen-2-one **(G)** 4,5-dihydroxy-4,5,6-trimethyl-2,8-dioxo-13-azatricyclo [8.5.1.0] hexadec-10-ene-3,7-dione **(H)** Cryptotanshinone **(I)** 6-(1,1-dimethallyl)-2-(1-hydroxyl-1-methylethyl)-2,3-dihydro-7H-furo[3,2-G]chromen-7-one and reference drug **(J)** Fluorouracil.

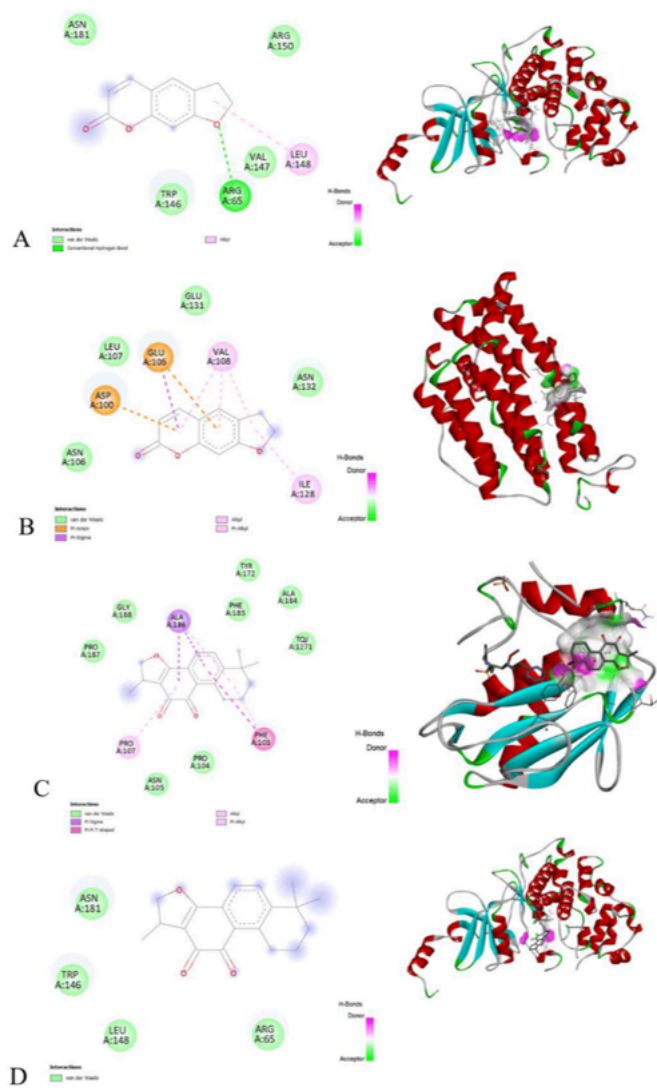


Figure 3

2D and 3D docking interaction of Cryptotanshinone with cancer-related protein receptors (A) EGFR: PD ID 4lqm, (B) p53: PD ID 3hfl, (C) MMP7: PD ID: 2y6d, (D) CDK8/Cyclin C: PD ID:6t41.