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In Silico Analysis of Bioactive Compounds from *Imperata cylindrica* as Potential EGFR Inhibitors in Cervical Cancer

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Abstract

Cervical cancer remains a major cause of death in women globally. Conventional treatments often result in toxicity and resistance, prompting interest in natural alternatives. *Imperata cylindrica* has demonstrated potential anticancer activity, but its molecular interaction with EGFR in cervical cancer remains unexplored. Objective This study employed an in-silico approach to evaluate the potential of bioactive compounds from I. cylindrica as epidermal growth factor receptor (EGFR) inhibitors. **Methods**: An in-silico study was conducted using molecular docking using AutoDock v4.2.6 to assess the binding affinity of *I. cylindrica* bioactive compounds toward EGFR. Docking validation used redocking. ADMET predictions were performed using pkCSM and ProTox-II to evaluate pharmacokinetics, toxicity, and drug-likeness properties. **Results**: Jatrorrhizine, curcumin, and 5-hydroxyflavone showed strong binding to EGFR (ΔG: –8.00 to –7.67 kcal/mol) with key interactions at Asp855 and Lys745. These compounds also exhibited good oral absorption and low toxicity. Arundoin showed the highest affinity (–8.57 kcal/mol) but poor ADMET characteristics, reducing its therapeutic potential. **Conclusion**: Jatrorrhizine, curcumin, and 5-hydroxyflavone show potential as EGFR inhibitors, warranting further experimental validation and development.

Keywords: Cervical cancer; EGFR; In-silico; *Imperata cylindrica*.

INTRODUCTION

Cervical cancer remains a significant global health burden, ranking among the most prevalent malignancies affecting women, particularly in low-middle income countries (Lukac et al., 2018). According to the World Health Organization (WHO), an estimated 604,127 new cases and 341,831 deaths were reported in 2020 alone, accounting for approximately 12% of all female cancers worldwide (Singh et al., 2023). With a mortality rate of 7.2 per 100,000 women annually, this disease leads to the death of one woman every two minutes, underscoring its devastating impact on public health (Singh et al., 2023). Persistent infection with high-risk human papillomavirus (HPV), especially HPV types 16 and 18, has been identified in over 99.7% of cervical cancer cases, making it the most critical etiological factor (Kashyap et al., 2019). However, co-factors such as early sexual activity, multiple sexual partners, high parity, smoking, low socioeconomic status, unprotected intercourse, and polygamous relationships also contribute to the incidence and progression of the disease (Burmeister et al., 2022).

Early-stage cervical cancer is often asymptomatic, which delays diagnosis and treatment initiation. When symptoms appear, they may include post-coital bleeding, pelvic pain, abnormal vaginal discharge, or dyspareunia, though these signs are not exclusive to cervical malignancies (Setiawati & Hapsari, 2023). Diagnostic confirmation typically involves screening methods such as the Papanicolaou (Pap) smear, HPV DNA testing, colposcopy, and histopathological examination (Eun & Perkins, 2020) . Treatment modalities depend on the stage and patient condition, but for advanced-stage cases, chemotherapy remains the primary approach. Cisplatin, a platinum-based compound, induces cancer cell death by binding to DNA and inhibiting its replication, while paclitaxel disrupts mitosis by stabilizing microtubules, effectively halting cell division (Assi et al., 2021). Despite their efficacy, both drugs are associated with adverse effects such as anemia, myelosuppression, mucositis, neuropathy, and gastrointestinal toxicity (Federico et al., 2021).

Given the limitations of current treatments, there has been growing interest in identifying plant-based therapeutic agents with anticancer properties. *Imperata cylindrica* (cogongrass), a perennial herb widely distributed in Asia, has a long-standing history in traditional medicine systems. In Chinese medicine, it is utilized for treating fever, edema, hematuria, blood stasis, and urinary tract disorders (Jung & Shin, 2021). In

Indonesia, particularly on the island of Java, decoctions made from *I. cylindrica* roots are traditionally consumed to manage hypertension (Sulistyowati et al., 2017), and the plant is known to be a fast-growing, invasive species in tropical ecosystems (Syah & Hidayat, 2020). Pharmacological evaluations have confirmed its diverse bioactivities, including anti-inflammatory, antibacterial, diuretic, hemostatic, immunomodulatory, and notably, antitumor effects (Jung & Shin, 2021).

Recent studies have demonstrated the potential anticancer activity of methanolic root extracts of *I. cylindrica* on cervical cancer cell lines, such as HeLa (HPV-18) and CaSki (HPV-19). The extracts exhibited a dose and timedependent reduction in cell viability, induced apoptosis, and triggered G0/G1 phase cell cycle arrest. Furthermore, colony formation by CaSki cells was significantly inhibited. These effects have been attributed to the presence of secondary metabolites, including flavonoids, phenolic compounds, tannins, and saponins (Nayim, Sudhir, et al., 2021). One proposed mechanism involves interference with the epidermal growth factor receptor (EGFR) tyrosine kinase signaling pathway, which plays a critical role in promoting cell proliferation and survival in many cancers, including cervical carcinoma (Zhou et al., 2024).

With mounting evidence supporting the anticancer potential of *I. cylindrica*, further exploration of its active compounds using computational approaches is warranted. In silico studies, particularly molecular docking and virtual screening, provide a rapid and cost-effective platform to predict the binding affinity of phytochemicals to cancer-related molecular targets. Therefore, this study aims to identify candidate bioactive compounds from *Imperata cylindrica* with potential inhibitory effects on cervical cancer through an in-silico approach. This research not only contributes to the growing body of ethnopharmacological evidence but also supports the development of plant-based therapeutic alternatives to conventional chemotherapy.

MATERIALs AND METHODS

Materials

This study utilized several bioactive compounds found in *Imperata cylindrica*, including jaceidin (CID: 5464461), epicatechin (CID: 72276), curcumin (CID: 969516), myricetin (CID: 5281672), jatrorrhizine (CID: 72323), caffeic acid (CID: 689043), syringin (CID: 5316860), ferulic acid (CID: 445858), arundoin (CID: 12308619), tricin (CID: 5281702), and 5-hydroxyflavone (CID: 68112) (Jung & Shin, 2021). Carboplatin was selected as the reference drug due to its common application in cervical cancer therapy, particularly in combination regimens with agents such as paclitaxel. All compound structures, including both bioactive compounds and the control drug, were retrieved from the PubChem database (PubChem). The epidermal growth factor receptor (EGFR) was chosen as the molecular target in this research, with the protein structure accessed from the RCSB Protein Data Bank (RCSB PDB: Homepage) under the PDB ID: 3W2S (Yuliana et al., 2023). This target was selected based on previous studies indicating its involvement in similar pathological conditions, making it a suitable candidate for molecular docking studies.

Tools

The computational work was conducted using an MSI Modern 14 laptop equipped with an Intel Core i5-1235 processor, 16 GB of RAM, and a 512 GB SSD. A combination of software tools was employed in the research process, including Biovia Discovery Studio 2024, Avogadro, ChemOffice 2019, and AutoDock v4.2.6. Online databases and platforms such as the Protein Data Bank (RCSB PDB), PubChem, pKCSM, and ProTox-II were also utilized for compound sourcing, protein structure retrieval, pharmacokinetic prediction, and toxicity assessment.

Method

Protein and ligand preparation

All ligands, specifically the bioactive compounds derived from *Imperata cylindrica*, were first geometrically optimized using Avogadro. Energy minimization was then carried out using ChemOffice 2019 to ensure that the ligands achieved a stable and biologically relevant conformation. The target protein was subjected to a preprocessing step to prepare it for docking simulations. This included the removal of the native ligand, separation of protein chains, and exclusion of any cofactors or water molecules. These preparations were conducted using Biovia Discovery Studio 2024 and were essential to facilitate accurate molecular docking and redocking procedures.

Method validation and molecular docking simulation

To validate the docking protocol, a redocking approach was employed in which the native ligand was re-docked into the active site of the EGFR protein. This step was performed using AutoDock v4.2.6, with the grid box centered on the coordinates of the native ligand's binding site. The grid box dimensions defined the docking space (X, Y, Z coordinates), which was later used for the docking of test compounds. The accuracy of the redocking process was evaluated based on the Root Mean Square Deviation (RMSD) value between the predicted pose and the original crystallographic pose. An RMSD of less than 2.0 Å was considered indicative of a valid docking protocol (Farid et al., 2025). Following validation, molecular docking simulations were performed using the selected *Imperata cylindrica* compounds, aligned to the same grid parameters.

Docking result analysis

The docking simulations provided key data such as binding affinity (ΔG) and inhibition constant (Ki). Lower values of both parameters indicated stronger and more stable ligand-protein interactions. Visualization and interaction analysis were carried out using Biovia Discovery Studio 2024, allowing detailed observation of ligand conformations and identification of interacting amino acid residues (Farid et al., 2025). These interactions were examined to assess the stability and specificity of binding within the active site.

Prediction of Bioavailability, Pharmacokinetics, and Toxicity

In silico predictions of bioavailability, pharmacokinetics, and toxicity were performed for each *Imperata cylindrica* compound to assess their drug-likeness and safety profile. Bioavailability was evaluated using Lipinski's Rule of Five, focusing on molecular weight, hydrogen bond donors and acceptors, and lipophilicity (LogP). Pharmacokinetic parameters were predicted using the pkCSM platform ***(pkCSM)***, included: human intestinal absorption (%), P-glycoprotein substrate status, blood-brain barrier (BBB) permeability, central nervous system (CNS) penetration, CYP2D6 and CYP3A4 substrate predictions, total clearance (log mL/min/kg), and renal OCT2 substrate status (Utami et al., 2025). Toxicity profiles were predicted via the ProTox-II platform ***(ProTox-3.0 - Prediction of TOXicity of chemicals)***, including assessments of toxicity class, hepatotoxicity, carcinogenicity, immunotoxicity, mutagenicity, cytotoxicity, and median lethal dose (LD50) (Banerjee et al., 2024).

RESULTS AND DISCUSSION

The docking protocol validation yielded a promising result, with a Root Mean Square Deviation (RMSD) value of 1.397 Å. This indicates a high degree of accuracy between the predicted ligand binding pose and the experimentally determined crystallographic structure (Farid et al., 2025). The grid configuration employed set to 40 points along the X, Y, and Z axes, with a central coordinate at (3.880, 1.496, 10.744) was effective in defining the active site region and capturing ligand-receptor interactions accurately. These findings are further supported by Figure 1, which shows minimal structural deviation between the pre-docking (gray) and post-docking (yellow) ligand conformations, confirming the reliability of the docking protocol. Overall, these results validate the docking setup and support its application in subsequent molecular docking analyses.

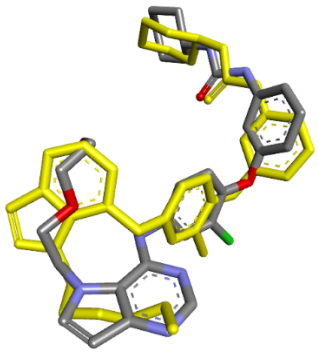

Figure 1. Native ligand pre and post redocking.

Among the tested compounds, several exhibited promising binding affinities toward the EGFR target protein. The native ligand demonstrated the strongest binding with a ΔG of –11.76 kcal/mol and an inhibition constant (Ki) of 2.38 µM, serving as the benchmark for comparison. Arundoin displayed the most favorable binding affinity among the *Imperata cylindrica* compounds –8.57 kcal/mol, although its inhibition constant was relatively high (518.96 µM), indicating weaker inhibitory potency. Jatrorrhizine and curcumin showed both strong binding energies –8.00 and –7.82 kcal/mol and low Ki values 1.38 and 1.85 µM, suggesting stable interactions and high inhibitory potential. Other compounds such as 5-hydroxyflavone –7.67 kcal/mol, Ki: 2.38 µM and tricin –7.15 kcal/mol, Ki: 5.71 µM also demonstrated relatively strong interactions.

In contrast, compounds like syringin and caffeic acid displayed weaker binding affinities –5.02 and –5.33 kcal/mol and higher Ki values 210.64 and 124.83 µM, indicating lower docking performance. Notably, the positive control carboplatin exhibited the weakest binding affinity –4.04 kcal/mol but a low Ki 1.10 µM, which may reflect a different mode of action not solely reliant on binding strength. Overall, jatrorrhizine and arundoin emerged as the most promising bioactive candidates due to their favorable combination of strong binding affinity and potent inhibition.

The analysis of amino acid interactions derived from molecular docking results, the primary focus is identifying residues that play a dominant role in ligand receptor complex formation. The findings indicate that several amino acids consistently participate in interactions with various ligands, through both hydrogen and non-hydrogen bonding. Aspartate 855 (Asp 855) and Lysine 745 (Lys 745) appear most frequently, suggesting a crucial structural role in stabilizing ligand binding. These residues are involved in hydrogen bonds with more than half of the tested ligands, including the native ligand, curcumin, jaceidin, and epicatechin. This suggests that they are likely located within or near the protein's active or binding site. Asp 855's role as a hydrogen bond acceptor highlights its significant electronegative property in recognizing polar ligands. Conversely, Lys 745 functions effectively as a hydrogen bond donor due to its basic side chain.

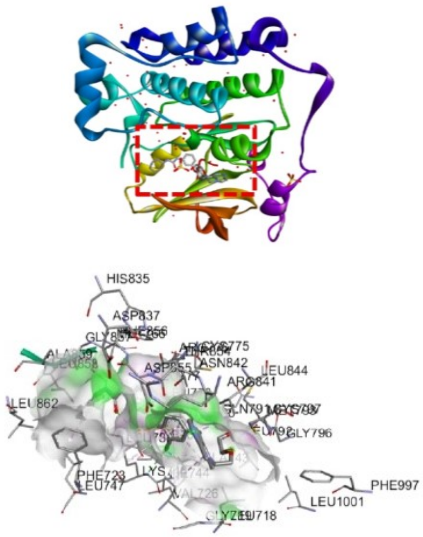

Figure 2. 3D structure of EGFR with native ligand bound at the active site.

Besides these two primary residues, Phenylalanine 856 (Phe 856) is also frequently involved in ligand interactions. Phe 856 participates in both hydrogen bonding and hydrophobic interactions, particularly with aromatic compounds such as curcumin, epicatechin, and syringin. Its aromatic side chain allows π-π stacking interactions, which strengthen ligand binding. Its involvement in ligands with relatively high affinity suggests a stabilizing function within the binding pocket. Additionally, the presence of Phe 856 in the native ligand complex further supports its potential location in a catalytic or binding hotspot. Though the interactions are largely non-covalent, their contribution to overall binding energy is considerable. Therefore, this residue is a promising target for structure-based drug design involving aromatic pharmacophores.

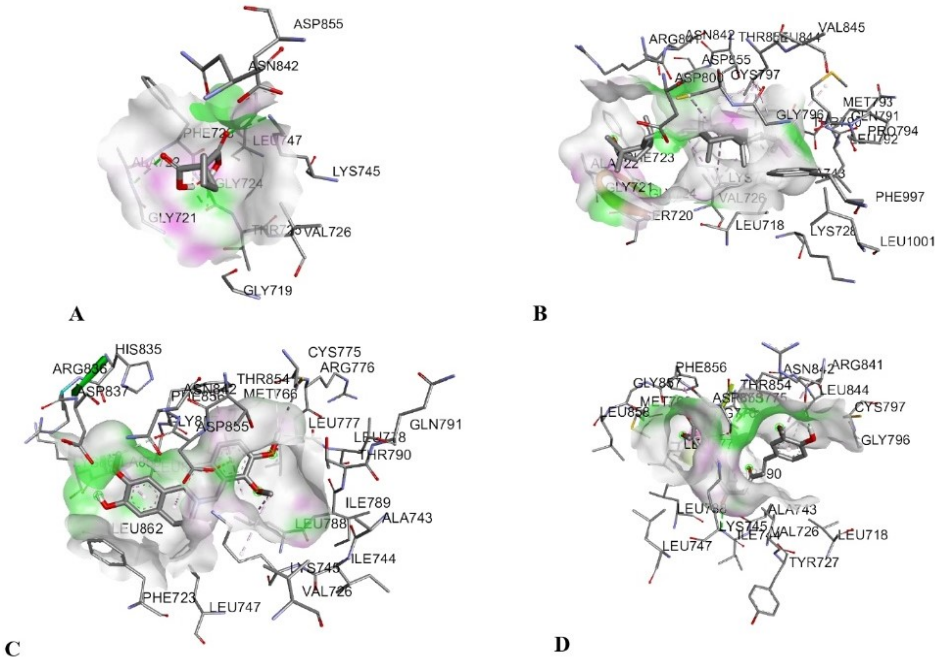

Figure 3. Binding pocket of (A) Carboplatin, (B) Arundoin, (C) Jatrorrhizine, and (D) Curcumin within the EGFR.

Other notable residues include Threonine 790 (Thr 790), Leucine 788 (Leu 788), and Methionine 766 (Met 766), which appear in several ligand complexes, albeit less frequently than Asp 855 or Lys 745. Thr 790 is relevant in hydrogen bonding with ligands like jatrorrhizine and caffeic acid, reflecting its polar side chain's versatility. Leu 788 and Met 766 are primarily involved in non-hydrogen interactions, supporting hydrophobic contacts with ligands containing non-polar side chains. These residues likely contribute to maintaining ligand orientation within the binding pocket. Their presence in several complexes with relatively favorable binding affinities suggests a structural rather than catalytic role. Hence, they function as auxiliary residues in ligand accommodation and stabilization during docking.

Table 1. Docking scores and key amino acid interactions of selected compounds with EGFR.

Compound	ΔG (kcal/mol)	Ki (μM)	Hydrogen Bond Interactions	Non-Hydrogen Bond Interactions
Native Ligand	-11.76	2.38	Phe856, Asp855, Lys745, Met793	Lys745, Phe723, Leu844, Val726, Thr790, Ala743, Leu788, Leu777
Jaceidin	-6.37	21.37	Gly724, Lys745, Asp855, Asp837, Asn842, Gly875	Lys745, Asp855, Asp837, Val726, Ala859
Epicatechin	-6.77	10.91	Asp837, Gly857, Phe856, Asp855	Phe856, Asp855, Leu788, Met766
Curcumin	-7.82	1.85	Arg841, Lys745, Phe856, Asp855	Arg841, Asp855, Phe856
Myricetin	-6.85	9.45	Thr854, Asp855, Leu788, Gln791, Met793	Lys745, Thr790, Ala743, Leu844, Val729, Leu718
Jatrorrhizine	-8.00	1.38	Thr790, Asp855, Cys775	Leu788, Leu777, Lys745, Phe856, Leu858, Ala859, Met766, Asp855
Caffeic Acid	-5.33	124.83	Thr790, Phe856, Gly857, Lys745, Cys755	Leu777, Met766
Syringin	-5.02	210.64	Thr854, Thr790, Leu788, Ala743, Phe856, Leu777, Lys745	Lys745, Val726, Cys775, Met793, Leu844, Asp855, Ala743
Ferulic Acid	-5.42	106.36	Thr790, Gly857, Lys745, Arg776	Leu777, Met766, Leu788
Arundoin	-8.57	518.96	–	Leu792, Met793, Val726, Ala743, Leu844, Cys797
Tricin	-7.15	5.71	Thr854, Leu777, Met766	Lys745, Leu747, Leu862, Leu858, Met766, Phe723, Leu777
5-Hydroxyflavone	-7.67	2.38	Thr854	Lys745, Met766, Leu858, Leu777
Carboplatin	-4.04	1.10	Phe723, Ala722, Lys745, Gly724	–

Imperata cylindrica has emerged as a promising plant-based candidate for anticancer therapy, including against cervical cancer. Nayim, Mbaveng, et al in 2021 reported that the methanolic root extract of *I. cylindrica* (IC-MeOH) significantly inhibited the proliferation of HeLa and CaSki cervical cancer cells. The extract induced apoptosis and cell cycle arrest at the G0/G1 phase in a concentration- and time-dependent manner (Nayim, Sudhir, et al., 2021). Metabolite profiling using UHPLC-HRMS identified ten active compounds with documented anticancer properties, such as epicatechin, curcumin, myricetin, jatrorrhizine, syringin, and caffeic acid many of which are known to modulate key pathways in apoptosis and cell cycle regulation. These findings are reinforced by the work of Keshava et al (2020), which demonstrated the selective cytotoxicity of methanolic *I. cylindrica* leaf extract against SCC-9 oral carcinoma cells, with no significant effect on normal cells, highlighting its safety profile. Moreover, the active hexane fraction induced apoptosis via caspase-3 and -8 gene expression, indicating a potential mechanistic overlap with pathways involved in cervical cancer cell death. This evidence suggests that *I. cylindrica* not only exerts cytotoxicity but also interferes with cancer cell survival mechanisms relevant to cervical carcinoma.

Further support for the anticancer potential of *I. cylindrica* comes from additional studies on different cancer models that share mechanistic similarities with cervical cancer. Roeslan and Tasha (2021) showed that ethanol extract of *I. cylindrica* leaves significantly inhibited proliferation and migration of HSC-3 oral squamous carcinoma cells by modulating MMP-2 and MMP-9 expression and arresting the cell cycle in G1/S and G2/M phases mechanisms also implicated in cervical cancer progression. Indriyanti et al (2024) further explored the synergistic potential of *I. cylindrica* root ethanol extract in combination with erlotinib on A549 lung cancer cells, demonstrating that most extract-drug combinations exhibited synergistic effects in reducing cell viability. Although conducted in lung and oral cancer models, the shared cellular processes such as apoptosis induction, cell cycle arrest, and metastasis inhibition enhance the translational relevance of these findings to cervical cancer. Taken together, these studies collectively affirm that *I. cylindrica*, through both single-agent activity and combinatorial potential, holds significant promise as a natural anticancer agent, including for the treatment of cervical carcinoma.

Prediction of Bioavailability, Pharmacokinetics, and Toxicity

A comprehensive in silico pharmacokinetic and toxicity profiling was conducted on twelve bioactive compounds derived from Imperata cylindrica, namely curcumin, kaempferol, jatrorrhizine, tricin, syringin, arundoin, myricetin, catechin, epigallocatechin, hesperidin, 5-hydroxyflavone, and apigenin, Using pkCSM predictions, most compounds demonstrated favorable intestinal absorption, particularly jatrorrhizine (94.47%), 5-hydroxyflavone (94.77%), and curcumin (89.29%), indicating their potential for good oral bioavailability (Bultum et al., 2022). Nonetheless, all compounds were identified as substrates of P-glycoprotein, raising concerns over possible intracellular efflux and reduced pharmacological activity due to drug efflux mechanisms.

Distribution analysis revealed that most compounds exhibit negative log BB and log PS values, suggesting limited ability to cross the blood–brain barrier (BBB), which is favorable for non-neuroactive agents. However, 5-hydroxyflavone was predicted to penetrate the BBB (log BB = 0.462), warranting further assessment of its CNS-specific effects (Bultum et al., 2022). Regarding metabolic interaction potential, nearly all compounds were predicted not to be substrates of CYP2D6 or CYP3A4 isoenzymes, with the exception of arundoin. This suggests a generally low risk of metabolic drug–drug interactions for most compounds, although arundoin may require closer investigation due to its potential involvement in CYP3A4-mediated metabolism (Utami et al., 2025). In terms of excretion, variability was observed among compounds. Jatrorrhizine showed a high total clearance rate (1.222 log mL/min/kg), indicating efficient elimination, whereas curcumin displayed a markedly low clearance value (–0.002), implying a possible risk of systemic accumulation upon prolonged administration. Furthermore, arundoin and tricin were identified as substrates of renal OCT2 transporters, suggesting the potential for transporter-mediated drug interactions, particularly in co-administration scenarios involving OCT2 inhibitors (Utami et al., 2025).

Physicochemical property assessments confirmed that all compounds conform to Lipinski's Rule of Five, with molecular weights under 500 g/mol. Nonetheless, arundoin exhibited an excessively high lipophilicity (log P = 8.67), raising concerns regarding its bioaccumulation potential and overall toxicity. Syringin, with its high number of hydrogen bond donors and acceptors, presents increased polarity, which may impact its solubility and permeability profiles (Bultum et al., 2022).

Toxicological predictions based on the ProTox III platform provided valuable insights into the safety margins of these compounds. Acute toxicity classification placed epicatechin in Class 6 (LD_{50} > 5000 mg/kg), consistent with its reported safety at doses up to 200 mg/day (Barnett et al., 2015). Myricetin and jatrorrhizine were classified under Class 3, denoting moderate toxicity, potentially triggered by flagged structural alerts (Zhong et al., 2022). Other compounds, including curcumin, ferulic acid, tricin, syringin, and 5-hydroxyflavone, were distributed between Class 4 and 5, indicating low to intermediate toxicity.

Hepatotoxicity, all compounds were categorized as non-hepatotoxic. However, arundoin (0.82), syringin (0.83), and jaceidin (0.70) presented probability scores approaching the hepatotoxic threshold. These findings contrast with the lower-risk profiles of epicatechin (0.72), tricin (0.71), and curcumin (0.61), which have been supported by experimental evidence of hepatoprotective effects (Barnett et al., 2015; He et al., 2015). Interestingly, myricetin and jatrorrhizine displayed borderline values (0.69 and 0.81, respectively), which align with reports of ROS-induced hepatotoxicity (Hobbs et al., 2015).

In other toxicity domains, myricetin and 5-hydroxyflavone exhibited potential carcinogenicity and mutagenicity, both having been associated with DNA damage and oxidative stress mechanisms (Hobbs et al., 2015; Bronikowska et al., 2017). Meanwhile, curcumin, syringin, and epicatechin showed low carcinogenic probability, supporting their use in long-term therapeutic settings. Immunotoxicity scores were elevated for curcumin (0.92), syringin (0.92), and arundoin (0.98), suggesting potential immunomodulatory effects that are context-dependent (He et al., 2015). 5-hydroxyflavone alone demonstrated notable cytotoxicity (0.52), which may be linked to its apoptotic activity in cancer cells (Bronikowska et al., 2017), while curcumin, tricin, epicatechin, and caffeic acid showed no significant cytotoxicity, supporting their safety in systemic use.

Table 2. Predicted ADME properties of tested compounds using pkCSM.

Compound	Intestinal Absorption (%)	p-glycoprotein substrate	BBB Permeability	CNS Permeability	CYP2D6 Substrate	CYP3A4 Substrate	Total Clearance	Renal OCT2 Substrate	Hydrogen Donor	Hydrogen acceptor	Molecular weight (g/mol)	Log P
Jaceidin	77.265	Yes	-1.463	-3.277	No	No	0.561	No	3	8	360.318	2.6026
Epicatechin	68.829	Yes	-1.054	-3.298	No	No	0.183	No	5	6	290.271	1.5461
Curcumin	82.19	Yes	-0.562	-2.99	No	Yes	-0.002	No	2	6	368.385	3.3699
Myricetin	65.93	Yes	-1.493	-3.709	No	No	0.422	No	6	8	318.237	1.6936
Jatrorrhizine	94.465	Yes	-0.15	-2.142	No	No	1.222	No	1	4	338.383	3.0818
Caffeic acid	69.407	No	-0.647	-2.608	No	No	0.508	No	3	3	180.159	1.1956
Syringin	44.025	Yes	-1.25	-3.909	No	No	0.215	No	5	9	372.37	-1.112
Ferulic acid	93.685	No	-0.239	-2.612	No	No	0.623	No	2	3	194.186	1.4986
Arundoin	96.924	No	0.823	-1.547	No	Yes	0.158	No	0	1	440.756	8.6789
Tricin	89.713	Yes	-1.115	-3.411	No	No	0.62	No	3	7	2.594	2.594
5-Hydroxyflavone	94.776	Yes	0.462	-1.733	No	Yes	0.325	No	1	3	238.242	3.1656

Table 3. Toxicity predictions of compounds based on ProTox III analysis.

Compound	Toxicity Class	Hepatotoxicity	Carcinogenicity	Immunotoxicity	Mutagenic	Cytotoxic
Jaceidin	5	Inactive (0.70)	Inactive (0.69)	Active (0.94)	Inactive (0.82)	Inactive (0.75)
Epicatechin	6	Inactive (0.72)	Inactive (0.51)	Inactive (0.96)	Inactive (0.55)	Inactive (0.84)
Curcumin	4	Inactive (0.61)	Inactive (0.84)	Active (0.92)	Inactive (0.88)	Inactive (0.88)
Myricetin	3	Inactive (0.69)	Active (0.68)	Inactive (0.86)	Active (0.51)	Inactive (0.99)
Jatrorrhizine	3	Inactive (0.81)	Inactive (0.54)	Active (0.98)	Active (0.52)	Inactive (0.51)
Caffeic acid	5	Inactive (0.57)	Active (0.78)	Inactive (0.50)	Inactive (0.98)	Inactive (0.86)
Syringin	5	Inactive (0.83)	Inactive (0.85)	Active (0.92)	Inactive (0.80)	Inactive (0.76)
Ferulic acid	4	Inactive (0.51)	Inactive (0.61)	Active (0.91)	Inactive (0.96)	Inactive (0.88)
Arundoin	4	Inactive (0.82)	Inactive (0.54)	Active (0.98)	Inactive (0.92)	Inactive (0.88)
Tricin	5	Inactive (0.71)	Inactive (0.69)	Inactive (0.57)	Inactive (0.91)	Inactive (0.90)
5-Hydroxyflavone	5	Inactive (0.63)	Active (0.56)	Inactive (0.98)	Inactive (0.62)	Active (0.52)

The cross-analysis between molecular docking results and ADMET predictions reveals a critical balance between binding affinity and pharmacokinetic suitability. Notably, arundoin, jatrorrhizine and curcumin, which exhibited strong binding energies and low inhibition constants, also demonstrated favorable ADMET profiles, including high intestinal absorption and minimal metabolic interaction risks, suggesting their potential as orally bioavailable EGFR inhibitors. In contrast, arundoin, despite showing the highest binding affinity among the *Imperata cylindrica* compounds, exhibited poor ADMET characteristics such as extremely high lipophilicity (log P = 8.67), being a CYP3A4 substrate, and high immunotoxicity risk raising concerns over its systemic safety and drug-likeness. Meanwhile, 5-hydroxyflavone balanced strong docking results with acceptable ADMET properties, though its potential mutagenicity and cytotoxicity warrant further scrutiny. These findings underscore the necessity of integrating docking data with ADMET evaluation to prioritize candidates with both strong target engagement and favorable pharmacological profiles.

This *in silico* study offers a foundational understanding of the interaction between *Imperata cylindrica* compounds and the EGFR target; however, it is limited by the static nature of molecular docking and the predictive nature of ADMET modeling. Docking simulations do not capture the dynamic flexibility of protein-ligand interactions or solvent effects, which are crucial for assessing binding stability under physiological conditions. Therefore, future research should incorporate molecular dynamics simulations to evaluate the conformational behavior and binding persistence of top compounds. Additionally, the pharmacokinetic and toxicity predictions require experimental validation through in vitro assays and in vivo studies to confirm therapeutic efficacy, safety, and bioavailability. These integrative approaches are essential to substantiate the therapeutic potential of candidates like jatrorrhizine, curcumin, and 5-hydroxyflavone for further development in cervical cancer treatment.

CONCLUSIONS

This in silico study identified arundoin, jatrorrhizine, curcumin, and 5-hydroxyflavone as promising EGFR inhibitors from *Imperata cylindrica*, showing strong binding affinities and favorable ADMET profiles. Key interactions with residues like Asp855 and Lys745 support their potential efficacy. While arundoin had the highest docking score, its poor pharmacokinetics limit its suitability. These findings warrant further validation through molecular dynamics, in vitro, and in vivo studies to confirm therapeutic potential against cervical cancer.

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