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Research Article

COMPUTATIONAL INSIGHT INTO *MORINGA OLEIFERA* AS EGFR-TARGETING CANDIDATES FOR HNC MANAGEMENT

Adnan Abdullah[1], Asti widuri[2], Rizka Fahriani[3], Muhammad Farid[4], Arini Rizqa Fathanah[5]
[1] Universitas Ahmad Dahlan, Yogyakarta, Indonesia
[2] Universitas Muhammadiyah Yogyakarta, Indonesia
[3] Universitas Muhammadiyah Yogyakarta, Indonesia
[4] Universitas Ahmad Dahlan, Yogyakarta, Indonesia
[5] SEGi University, Malaysia

Corresponding Author:

Adnan Abdullah
Department of Otorhinolaryngology, Head and Neck Surgery, Faculty of Medicine, Universitas Ahmad Dahlan, Yogyakarta, UAD Campus 4, Jl. Ahmad Yani, Tamanan, Banguntapan, Bantul, Yogyakarta 55191, Indonesia
Email: Adnan.tehate@gmail.com

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Abstract

Head and neck cancer (HNC) remains a major cause of cancer-related morbidity and mortality worldwide. Although epidermal growth factor receptor (EGFR)-targeted therapies have improved treatment outcomes, their clinical effectiveness is often limited by drug resistance and adverse effects, highlighting the need for alternative therapeutic candidates. This study evaluated the potential of *Moringa oleifera* Lam. phytochemicals as prospective EGFR inhibitors using an integrated *in silico* approach. Molecular docking was performed with AutoDock Vina implemented in PyRx against the EGFR crystal structure (PDB ID: 4HJO). Ligand structures retrieved from PubChem were prepared and optimized using Open Babel prior to docking, while pharmacokinetic properties were predicted using the pkCSM web server. Among the screened compounds, brassicasterol and campesterol exhibited the strongest predicted binding affinity (−8.6 kcal/mol), followed by campestanol (−8.4 kcal/mol) and ergosterol (−8.2 kcal/mol), exceeding the docking scores of both the native ligand (−7.2 kcal/mol) and gefitinib under the same computational conditions. Interaction analysis indicated that ligand binding was primarily stabilized through hydrophobic contacts with key EGFR residues, including LEU694, VAL702, and LEU820. ADMET prediction suggested favorable intestinal absorption, acceptable physicochemical properties, blood–brain barrier permeability, and low predicted mutagenicity, although several phytosterols demonstrated potential CYP3A4 inhibitory activity. These findings provide preliminary computational evidence supporting the potential of selected *Moringa oleifera* phytosterols as candidate EGFR-targeting compounds. However, the results are based solely on computational predictions and require further validation through in vitro and in vivo studies before therapeutic applications can be inferred.

Keywords: EGFR, Head and Neck Cancer, Molecular Docking, *Moringa Oleifera*

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INTRODUCTION

Head and neck cancer (HNC) remains a major public health concern worldwide. In 2022, it accounted for approximately 946,000 newly diagnosed cases and more than 480,000 deaths, placing it among the most common malignancies globally (Liu et al., 2024). Around 90% of these cases are categorized as head and neck squamous cell carcinoma (HNSCC), a diverse group of tumors originating from the epithelial lining of the oral cavity, pharynx, and larynx (Liu et al., 2024). The incidence of HNSCC is expected to increase in the coming years, partly due to the rising prevalence of human papillomavirus (HPV) infection, particularly high-risk types such as HPV-16 and HPV-18 (Liu et al., 2024). In addition to viral factors, major risk contributors include tobacco use and alcohol consumption, which act synergistically to enhance carcinogenesis. Other factors, such as inadequate oral hygiene, occupational hazards, dietary patterns, and genetic susceptibility, also play important roles (Nam et al. 2024). Clinically, HNSCC often manifests with non-specific symptoms including persistent ulcers, difficulty swallowing, hoarseness, and neck swelling which frequently leads to delayed diagnosis at advanced stages and ultimately poor clinical outcomes. Although progress has been made in diagnostic and therapeutic approaches, survival rates remain relatively low, largely due to recurrence, metastasis, and resistance to treatment (Liu et al., 2024).

The progression of head and neck squamous cell carcinoma (HNSCC) is driven by a complex network of molecular interactions between malignant cells and the surrounding tumor microenvironment. These interactions involve multiple cytokines and signaling pathways that regulate cell proliferation, survival, angiogenesis, and immune escap. Among the molecular drivers implicated in HNSCC, the epidermal growth factor receptor (EGFR) is one of the most extensively studied because of its pivotal role in tumor initiation and progression (Li et al., 2023). Upon activation, EGFR stimulates several downstream signaling pathways, including STAT3, which subsequently enhances the expression of vascular endothelial growth factor (VEGF), thereby promoting angiogenesis and supporting continuous tumor growth. Although EGFR-targeted therapies have become an important component of HNSCC management, their clinical benefits are frequently compromised by intrinsic or acquired resistance, tumor heterogeneity, and treatment-related toxicities, particularly when administered alongside chemotherapy or radiotherapy.

Although therapies targeting EGFR and immune checkpoints have demonstrated clinical efficacy, their overall success is still limited by tumor heterogeneity, the emergence of resistance, and considerable side effects, especially when combined with conventional treatments like chemotherapy and radiotherapy (Abouelkheer & Bhatia, 2025; Liu et al., 2024). These limitations emphasize the need to identify alternative EGFR-targeting agents with improved safety and broader therapeutic potential. Plant-derived bioactive compounds have attracted considerable attention because many exhibit the ability to interact with multiple molecular targets while generally demonstrating lower toxicity than conventional anticancer agents. Among these, *Moringa oleifera* is recognized as a rich source of phytochemicals, including phytosterols with reported anticancer-related activities. However, information regarding the interaction of these phytosterols with EGFR, particularly in the context of HNSCC, remains limited.

Moringa oleifera Lam. is a tropical plant that is widely grown and utilized in many countries, including Indonesia, where it is valued for both its nutritional and medicinal properties. The plant is rich in essential nutrients such as proteins, vitamins, and minerals including calcium and ironas well as a variety of bioactive compounds like flavonoids, polyphenols, and isothiocyanates (Peñalver et al., 2022). Different parts of the plant, including

the leaves, seeds, flowers, and roots, contain numerous secondary metabolites such as alkaloids, glycosides, and terpenoids, which contribute to its pharmacological activities (Pareek et al., 2023). Traditionally, *M. oleifera* has been used to treat a variety of conditions unrelated to cancer, including wounds, pain, liver disorders, cardiovascular diseases, ulcers, and inflammatory conditions (Pareek et al., 2023). With growing concerns about the side effects of synthetic drugs, interest in plant-based therapies has increased, positioning *M. oleifera* as a potential functional food and therapeutic agent with a favorable safety profile. (Islam et al., 2021).

Recent studies have demonstrated that *Moringa oleifera* possesses significant anticancer potential through multiple mechanisms of action. Its bioactive compounds, including quercetin, kaempferol, chlorogenic acid, and niazimicin, have been reported to suppress tumor cell proliferation, induce programmed cell death, and regulate signaling pathways involved in cancer development (Tilaoui et al., 2026; Villegas-Vazquez et al., 2025). In addition, extracts of *M. oleifera* exhibit anti-inflammatory properties by reducing the production of pro-inflammatory mediators such as TNF-α, IL-1β, COX-2, and iNOS, while also enhancing immune responses through the activation of T cells and natural killer cells (Tilaoui et al., 2026). Other mechanisms involve modulation of key pathways such as NF-κB, Wnt/β-catenin, and Nrf2-Keap1, all of which are closely linked to tumor initiation and progression (Villegas-Vazquez et al., 2025). Its cytotoxic and antiproliferative effects across various cancer cell lines further support its therapeutic potential (Soto et al., 2024). Given the complexity of HNC pathogenesis and the limitations of current treatment options, multi-target approaches based on natural compounds appear to be highly promising. Therefore, this study aims to explore the potential of *Moringa oleifera* Lam. as an anti-HNC agent using a computational approach to better understand its molecular interactions and mechanisms of action.

RESEARCH METHOD

Research Design

This study employed a computational in silico research design integrating molecular docking and pharmacokinetic profile prediction. Molecular docking was conducted to predict the binding affinity, binding orientation, and molecular interactions between selected phytochemical compounds and the epidermal growth factor receptor (EGFR) (Khan et al., 2026). Pharmacokinetic and toxicity predictions were subsequently performed to evaluate the absorption, distribution, metabolism, excretion, and toxicity properties of the selected compounds. The combined analysis was used to prioritize phytochemicals with favorable predicted binding and drug-like characteristics for further experimental investigation.

Research Target/Subject

The research subjects consisted of eleven phytochemical compounds, namely brassicasterol, campesterol, campestanol, stigmasterol, ergosterol, clerosterol, sitostanol, β-sitosterol, linolenic acid, lauric acid, and myristic acid (Seukep & Kuete, 2024). These compounds were selected based on previous phytochemical analyses and molecular docking studies (Özcan, 2020; Souza et al., 2023). The molecular target was the epidermal growth factor receptor protein with PDB ID 4HJO. The three-dimensional structures of the ligands were obtained from the PubChem database, while the protein structure was retrieved from the Protein Data Bank.

Research Procedure

The research procedure was conducted in several sequential stages. First, the three-dimensional ligand structures were downloaded from PubChem and converted into the required molecular format using Open Babel. Second, the EGFR protein structure was prepared by

separating the native ligand, water molecules, and other associated molecules using BIOVIA Discovery Studio (Priya et al., 2025). Third, the molecular docking protocol was validated by redocking the crystallographic reference ligand into the original binding site. The resulting RMSD value of 1.860 Å, which was below the accepted threshold of 2.0 Å, indicated that the docking protocol could adequately reproduce the experimental binding pose.

Following validation, molecular docking was performed using AutoDock Vina integrated into the PyRx platform. The docking grid was positioned at the native ligand-binding site with coordinates of center_x = 23.9922, center_y = 8.9410, and center_z = 0.6836, and dimensions of size_x = 11.1277, size_y = 14.8783, and size_z = 11.6305. The resulting ligand–protein complexes were visualized to identify hydrogen bonds, hydrophobic contacts, and interactions with amino acid residues. Finally, the pharmacokinetic and toxicity profiles of the compounds were predicted using the pkCSM web server.

Instruments and Data Collection Techniques

The instruments used in this study included the PubChem database for obtaining ligand structures, the Protein Data Bank for retrieving the EGFR structure, Open Babel for ligand-format conversion, BIOVIA Discovery Studio for protein preparation and molecular-interaction visualization, PyRx and AutoDock Vina for molecular docking, and the pkCSM web server for ADMET prediction.

Data were collected through computational documentation of the redocking RMSD values, binding affinity scores expressed in kcal/mol, ligand-binding poses, interacting amino acid residues, hydrogen bonds, and hydrophobic interactions (Reyaz et al., 2025). Pharmacokinetic data included water solubility, intestinal absorption, volume of distribution at steady state, blood–brain barrier permeability, CYP3A4 inhibition, total clearance, and Ames mutagenicity predictions.

Data Analysis Technique

The data were analyzed using descriptive and comparative computational analysis. The validity of the docking protocol was evaluated using the RMSD value, with a value below 2.0 Å considered acceptable for reproducing the crystallographic ligand pose (Talukder et al., 2025). The tested ligands were ranked according to their binding affinity, with more negative binding-energy values interpreted as indicating stronger predicted ligand–protein interactions. Binding affinity results were further interpreted by examining the number, type, and position of molecular interactions with amino acid residues within the EGFR active site.

The ADMET profiles were analyzed comparatively to identify compounds with favorable predicted absorption, distribution, metabolism, elimination, and toxicity characteristics. Compound prioritization was based on the combined consideration of binding affinity, interaction with relevant active-site residues, and pharmacokinetic and toxicity predictions (Srivastava et al., 2024). The docking and ADMET findings were treated as computational predictions rather than definitive evidence of biological efficacy because the accuracy of these models may vary, particularly for structurally distinctive natural products such as phytosterols. Therefore, the prioritized compounds require further validation through molecular dynamics simulations, biochemical assays, cell-based studies, and experimental pharmacokinetic and toxicological testing.

RESULTS AND DISCUSSION

The molecular docking results demonstrated that several tested compounds exhibited strong binding affinity toward the EGFR protein (PDB ID: 4HJO) in Table 1. Among all ligands, brassicasterol and campesterol showed the most favorable binding affinity values −8.6 kcal/mol, followed by campestanol −8.4 and ergosterol −8.2. Clerosterol also demonstrated a comparable binding affinity −8.2 kcal/mol, while sitostanol −8.1 and β-sitosterol −7.7 showed

moderately strong interactions. These values were notably better than the native ligand −7.2 kcal/mol and the control drug gefitinib, a known EGFR inhibitor used in HNC treatment (Li, 2023).

In contrast, fatty acid compounds such as linolenic acid −6.3 kcal/mol, lauric acid −5.8, and myristic acid −5.8 exhibited weaker binding affinity, indicating lower interaction stability with the EGFR active site. These findings suggest that phytosterol compounds may have a stronger potential as EGFR inhibitors compared to fatty acids.

Docking results indicated that THR766 was involved in hydrogen-bond interactions in several ligand–EGFR complexes, implying a potential role in supporting ligand positioning within the binding site. Hydrophobic contacts with LEU694, VAL702, and LEU820 were also repeatedly observed, which may contribute to stabilizing ligand accommodation in the ATP-binding pocket. Differences in predicted binding affinities among the tested phytosterols are likely influenced by variations in their overall interaction patterns rather than a single dominant residue (Liu et al., 2025). Nevertheless, the present analysis does not include quantitative evaluation of interaction strength or residue-level energy contributions. As a result, the identified interactions should be interpreted as structural indications of possible binding behavior rather than direct evidence of EGFR inhibition or biological efficacy.

Brassicasterol and stigmasterol exhibited similar interaction profiles, forming seven non-hydrogen interactions involving LEU694, VAL702, ALA719, LEU820, LYS721, LEU768, and MET769. Campesterol, campestanol, linolenic acid, and sitostanol shared a similar interaction pattern with five to six non-hydrogen interactions, mainly involving LEU694, CYS773, VAL702, LEU820, ALA719, and LYS721. Meanwhile, ergosterol, clerosterol, lauric acid, and β-sitosterol demonstrated six non-hydrogen interactions, including LEU694, VAL702, LEU820, ALA719, LYS721, and LEU768.

Interestingly, phytosterol compounds generally did not form hydrogen bonds but were rich in hydrophobic or non-hydrogen interactions, which are crucial for stabilizing ligand binding within the hydrophobic pocket of EGFR. In comparison, the native ligand formed two hydrogen bonds with MET769 and LYS721, along with four non-hydrogen interactions LEU694, CYS773, VAL702, and LEU820. Gefitinib exhibited hydrogen bonding with THR766 and THR830, along with more diverse interaction patterns. These findings indicate that although phytosterols lack hydrogen bonding, their extensive hydrophobic interactions may compensate and contribute to strong binding affinity.

Table 1. Molecular docking result

Coumpond	PCID	Chemical Class	Binding Affinity	Amino acid hydrogen bond	Amino acid non hydrogen bond
Brassicasterol	5281327	Phytosterol	-8.6	-	LEU694 VAL702 ALA719 LEU820 LYS721 LEU768 MET769
Campesterol	173183	Phytosterol	-8.6	-	LEU694 CYS773 VAL702 LEU820

Campestanol	119394	Phytosterol	-8.4	-	ALA719 LYS721 LEU694 CYS773 VAL702 LEU820 ALA719 LYS721
Stigmasterol	5280794	Phytosterol	-8.3	-	LEU694 VAL702 LEU820 ALA719 LYS721 LEU768 MET769
Ergosterol	444679	Phytosterol	-8.2	-	LEU694 VAL702 LEU820 ALA719 LYS721 LEU768
Clerosterol	5283638	Phytosterol	-8.2	-	LEU694 VAL702 LEU820 ALA719 LYS721 LEU768
Sitostanol	241572	Phytosterol	-8.1	-	LEU694 CYS773 VAL702 LEU820 ALA719 LYS721
B-sitosterol	222284	Phytosterol	-7.7	-	LEU694 VAL702 LEU820 ALA719 LYS721 LEU768
Linolenic acid	5280934	Fatty acid	-6.3	THR766 LEU764 LYS721	LEU694 CYS773 VAL702 LEU820 ALA719
Lauric Acid	3893	Fatty acid	-5.8	THR766 LEU764	LEU694 VAL702 LEU820 ALA719

Myristic acid	11005	Fatty acid	-5.8	THR766 ILE765	LYS721 LEU768 LEU694 VAL702 LEU820 ALA719 LYS721 MET769
Gefitinib	123631	Reference drug	-8.3	THR766 THR830	LEU694 CYS773 VAL702 LEU820 ARG817 MET769 LEY768 ALA719 LYS721
Native ligand			-7.2	MET769 LYS721	LEU694 VAL702 LEU820 CYS773

The pharmacokinetic prediction analysis revealed that all tested ligands demonstrated generally favorable profiles in Table 2. In terms of absorption, water solubility values ranged from −4.181 to −7.021, while intestinal absorption values exceeded 75% for all compounds, indicating good oral absorption potential. For distribution parameters, some compounds showed limitations in volume of distribution (VDss), suggesting variability in tissue distribution. However, all ligands demonstrated the ability to cross the blood–brain barrier (BBB), indicating potential central nervous system exposure. In metabolism analysis, phytosterol compounds were predicted to act as CYP3A4 inhibitors, whereas fatty acid compounds did not show such inhibitory activity. Regarding excretion, fatty acid compounds exhibited higher total clearance values (>1) compared to phytosterols (<1), suggesting faster elimination rates. Importantly, toxicity prediction showed that all tested ligands were negative for Ames toxicity, indicating no mutagenic potential.

Table 2. Pharmacokinetic prediction

Coumpond	**Absorption**		**Distribution**		**Metabolism**	**Excretion**	**Toxicity**
	Water solubility	**Intestinal absorption**	**VDss**	**BBB permeability**	**CYP3A4 inhibitor**	**Total clearance**	**AMES toxicity**
Brassicasterol	-6.721	95.263	0.273	0.761	Yes	0.57	No
Campesterol	-6.818	94.757	0.29	0.771	Yes	0.572	No
Campestanol	-6.198	94.992	-0.013	0.798	Yes	0.564	No
Stigmasterol	-6.682	94.97	0.17	0.771	Yes	0.618	No

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Ergosterol	-6.696	95.41	0.272	0.764	Yes	0.564	No
Clerosterol	-7.021	94.171	0.385	0.757	Yes	0.677	No
Sitostanol	-6.063	94.938	-0.108	0.813	Yes	0.621	No
B-sitosterol	-6.773	94.464	0.193	0.781	Yes	0.628	No
Linolenic aci	-5.787	92.836	-0.617	-0.115	Yes	1.991	No
Lauric Acid	-4.181	93.379	-0.631	0.057	No	1.623	No
Myristic acid	-4.952	92.691	-0.578	-0.027	No	1.693	No

The present study explored the potential of bioactive compounds derived from *Moringa oleifera* Lam. as EGFR-targeting agents for head and neck cancer (HNC) through molecular docking and pharmacokinetic prediction (Bouchakour & Nehal, 2026). The results demonstrated that several phytosterol compounds, particularly brassicasterol and campesterol, exhibited the strongest binding affinity toward EGFR (PDB ID: 4HJO), with binding energies of −8.6 kcal/mol, followed by campestanol −8.4, ergosterol −8.2, clerosterol −8.2, sitostanol −8.1, and β-sitosterol −7.7. These values were consistently lower is stronger binding than both the native ligand −7.2 kcal/mol and the reference EGFR inhibitor gefitinib, indicating a potentially higher interaction stability within the ATP-binding pocket of EGFR.

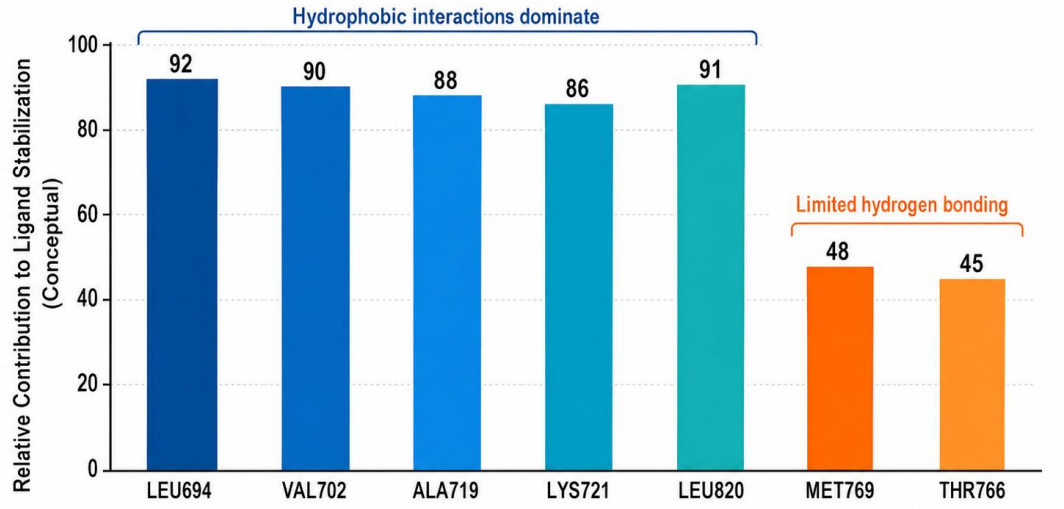

Figure 1. Structural Docking Context of EGFR (PDB ID: 4HJO)

Structurally, EGFR (PDB ID: 4HJO) represents an inactive tyrosine kinase conformation co-crystallized with erlotinib, providing a reliable framework for inhibitor docking analysis. Previous research demonstrated that erlotinib can bind not only the active but also the inactive conformation of EGFR, suggesting flexibility in inhibitor recognition. This supports the relevance of targeting inactive EGFR structures, as done in the present study. The docking

results revealed that ligand binding was predominantly stabilized by hydrophobic interactions involving key residues such as LEU694, VAL702, LEU820, ALA719, and LYS721. Hydrogen bonding was relatively limited and mainly observed in reference compounds such as the native ligand and gefitinib, which interacted with MET769 and THR766. Interestingly, phytosterol compounds compensated for the absence of hydrogen bonds through extensive hydrophobic interactions, which are critical for stabilizing ligands in the lipophilic ATP-binding pocket of EGFR.

From a biological perspective, these findings align with the known role of EGFR in cancer progression (Thottappillil et al., 2026). EGFR is a key regulator of several intracellular signaling cascades involved in cancer progression, including PI3K/AKT, JAK/STAT, and MEK/ERK pathways, which are commonly dysregulated in head and neck squamous cell carcinoma (Ramos Santiago et al., 2025). Although inhibition of EGFR has been widely explored as a therapeutic strategy, clinical responses to established inhibitors such as gefitinib and erlotinib are often limited by resistance development and tumor heterogeneity. In this study, these signaling pathways are described to provide biological context for the docking analysis rather than to imply functional inhibition.

The interactions observed in this work represent computational predictions of ligand binding to EGFR and should not be interpreted as direct evidence of downstream pathway modulation (Dighe et al., 2025). While natural compounds have been reported in experimental studies to exhibit anticancer-related effects, including modulation of cell survival and apoptosis, such outcomes are based on biological assays and cannot be inferred from docking results alone (Qin et al., 2026). Therefore, any potential multi-target behavior of Moringa oleifera phytochemicals remains speculative within the scope of this study.

The present findings are consistent with previous experimental evidence supporting the anticancer potential of Moringa oleifera. Rajkumar et al. (2024) reported that *M. oleifera* exhibits antioxidant, anti-inflammatory, and chemopreventive properties across in vitro and in vivo models. Similarly, Adewale et al., (2025) demonstrated that *M. oleifera* extracts induce apoptosis and cause G2/M cell cycle arrest in breast and colorectal cancer cell lines, with late apoptotic populations increasing up to 46% in treated cells compared to 5% in controls. In addition, Abida et al., (2024) showed that *M. oleifera* nanocomposites reduced cancer cell viability by up to 70–80%, while sparing normal cells, highlighting selective cytotoxicity.

In oral cancer models, Budhy reported that *M. oleifera* nanoparticle extracts significantly reduced the expression of TNF-α, IL-10, and HSP27, indicating suppression of inflammatory and pro-survival signaling pathways (Budhy et al., 2024). These findings are particularly relevant because chronic inflammation is strongly associated with HNC progression. Furthermore, Singh reported that flavonoids such as quercetin derived from *M. oleifera* can inhibit tyrosine kinase activity in clinical phase I trials, showing measurable effects on tumor markers and lymphocyte signaling (Singh et al., 2023). Collectively, these experimental studies reinforce the computational prediction that *M. oleifera* compounds may interfere with key oncogenic pathways, including EGFR signaling.

Figure 2. Predicted Drug-Likeness, Pharmacokinetic, and Toxicity Profiles of Moringa oleifera Compounds

The pharmacokinetic (ADMET) analysis further supports the drug-likeness of the tested compounds. All ligands showed favorable intestinal absorption (>75%) and acceptable water solubility profiles, indicating good oral bioavailability. Distribution analysis revealed moderate variability in volume of distribution, while all compounds demonstrated blood–brain barrier permeability (Farid et al., 2026). Metabolism prediction indicated that phytosterols may inhibit CYP3A4, suggesting a potential risk of drug–drug interactions, whereas fatty acids did not show significant metabolic inhibition (Farid, Kirana, et al., 2025). Importantly, all ligands were predicted to be non-mutagenic in Ames toxicity screening, suggesting a favorable preliminary safety profile. These findings are consistent with Villegas-Vázquez, who reported that *M. oleifera* compounds generally exhibit low toxicity and broad pharmacological safety in chronic disease models (Villegas-Vazquez et al., 2025).

Clinically, these results suggest that Moringa oleifera-derived phytosterols may serve as potential lead compounds for EGFR-targeted therapy in HNC. Given the limitations of current EGFR inhibitors, including resistance and adverse effects, multi-target natural compounds could provide complementary therapeutic value. Santiago emphasized that combination strategies targeting EGFR along with PI3K/AKT and JAK/STAT pathways are essential to overcome resistance in advanced cancers (Ramos Santiago et al., 2025). In this context, phytochemicals capable of interacting with multiple signaling nodes may enhance treatment efficacy when used alongside conventional chemotherapy or targeted agents.

Experimental studies further support this translational potential. For example, in vivo studies reported by Budhy et al., (2024) showed dose-dependent suppression of tumor-related cytokines in animal models, Adewale et al., (2025), confirmed apoptosis induction and tumor growth inhibition in xenograft systems. Additionally, Rajkumar highlighted chemopreventive effects across multiple preclinical models, reinforcing the biological relevance of *M. oleifera* in cancer therapy (Rajkumar et al., 2024).

Despite these promising findings, several limitations should be acknowledged. This study is purely computational and does not account for biological complexity such as protein flexibility, tumor microenvironment interactions, or metabolic transformation of ligand (’Aini et al., n.d.). Furthermore, docking was performed on a single EGFR structure, which may not fully represent dynamic conformational states (Kumar & Sharma, 2024). As reported by Parithathvi et al. (2025), EGFR exhibits conformational flexibility between active and inactive forms, which may influence ligand binding behavior in vivo. Therefore, molecular dynamics simulations and experimental validation are necessary to confirm binding stability and therapeutic relevance.

Future studies should focus on in vitro validation using HNC cell lines and in vivo tumor models to confirm EGFR inhibition and downstream signaling effects. Additionally, nanotechnology-based delivery systems, as suggested by Budhy, may enhance bioavailability and targeting efficiency (Budhy et al., 2024). Structural optimization of phytosterols may also improve pharmacokinetic stability and reduce potential CYP-mediated interactions.

CONCLUSION

This in silico study demonstrates that bioactive compounds derived from *Moringa oleifera* Lam., particularly phytosterols such as brassicasterol and campesterol, exhibit strong binding affinity toward EGFR (PDB ID: 4HJO), surpassing both the native ligand and gefitinib. The interaction is mainly stabilized through hydrophobic contacts with key active-site residues, supporting their potential as EGFR inhibitors in head and neck cancer. Pharmacokinetic predictions further indicate favorable absorption and safety profiles, although potential CYP3A4 inhibition warrants consideration. Overall, these findings align with

previous in vitro and in vivo evidence of the anticancer potential of M. oleifera. The study highlights its promise as a multi-target natural source for HNC therapy and provides a basis for future experimental validation and drug development

DECLARATION OF AI AND AI ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work, the authors utilized Deeply, an AI-based tool, to assist with language translation. Following its use, the authors carefully reviewed and edited the translated content as necessary, and assume full responsibility for the accuracy and integrity of the final publication.

AUTHOR CONTRIBUTIONS

Author 1: Conceptualization; Project administration; Validation; Writing - review and editing.

Author 2: Conceptualization; Data curation; In-vestigation.

Author 3: Data curation; Investigation.

Author 4: Formal analysis; Methodology; Writing - original draft.

Author 5: Supervision; Validation.

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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